



Review and Approval Process for Rapid HIV Tests at FDA



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Purpose of This Presentation

- ◆ To explain the FDA approval process for rapid HIV tests
- ◆ To understand the timeline for the review process
- ◆ To identify measures FDA has taken to facilitate the approval of new rapid HIV tests
- ◆ To inform the Council of progress made toward the approval of new rapid HIV tests

Regulation of Rapid HIV Tests

- ◆ All HIV tests are reviewed in FDA at the Center for Biologics Evaluation and Research's Office of Blood Research and Review
- ◆ Rapid HIV tests are reviewed as Class III devices
 - Premarket review necessary to provide reasonable assurance of safety and efficacy
- ◆ Regulatory scheme discussed here is for a rapid HIV test to be used as an aid in the diagnosis of HIV infection and NOT as a blood donor screening test

Regulation of Rapid HIV Tests, cont.

- ◆ Trials conducted to determine effectiveness of tests require Investigational Device Exemption (IDE) applications (21 CFR 812)
- ◆ Applicants submit Pre-Market Approval (PMA) applications (21 CFR 814)
 - Basis for approval of the device

Investigational Device Exemption (IDE) Application

- ◆ Clinical evaluation of devices that have not been cleared for marketing requires:
 - Approval by an institutional review board (IRB)
 - Informed consent from all study participants
 - Labeling for investigational use only
 - Monitoring of the study
 - Particular records and reports
 - Detailed protocols to conduct the studies
 - Approval of the IDE by FDA for significant risk devices
 - Others, specified in 21 CFR 812

Pre-Market Approval (PMA) Application

- ◆ Summary of safety and effectiveness
- ◆ Device characteristics
 - Detailed device description and manufacturing information
- ◆ Preclinical, non-clinical, and clinical data
 - To demonstrate device performance
 - Sensitivity, specificity, reproducibility
- ◆ Labeling
 - All device labels and the product insert
- ◆ Other requirements
 - Specified in 21 CFR 814

How Long Does the Review Process Take?

◆ IDE review

- Decision to approve or not approve must be made by FDA within 30 calendar days following receipt at FDA
- Approval: clinical studies may proceed following submission of IRB approvals for each clinical trial site
- Not approvable: clinical studies may not proceed, new IDE submission required

Review Timelines, cont.

IDE Approval → Submission of PMA

**TIMELINE DETERMINED
BY THE APPLICANT**



Pre-PMA Meeting(s)

Review Timelines, cont.

◆ PMA review

- Decision to approve or not approve must be made by FDA within 180 calendar days following receipt of complete PMA
 - » FDA review committee consisting of product and clinical experts, statistician, etc.
- Interactive review, with requests by FDA for additional information and submission of that information as PMA amendments before 180 days

PMA Review Outcomes

- ◆ Not approvable

- Review issues remain that stand in the way of approval (specifically identified in letter to applicant)
- Requires submission of PMA amendment by applicant to respond to issues
- Results in additional review cycle

PMA Review Outcomes, cont.

◆ Approvable

- PMA substantially meets the requirements of the applicable part of the regulations
- FDA believes that it can approve the application if specific additional information is submitted or specific conditions are agreed to by the applicant

◆ Approval

- Ultimate goal
- Includes successful inspection of manufacturing facility

Inspection of Manufacturing Facility

- ◆ Provides evidence that domestic or foreign manufacturers have a quality system for the design, manufacture, packaging, labeling, storage, installation, and servicing of finished medical devices intended for commercial distribution in the United States
 - Good Manufacturing Practice (GMP) requirements set forth in the Quality System (QS) regulation (21 CFR 820)
- ◆ Generally occurs after most review issues resolved
 - In compliance or not in compliance with QSR

What Has FDA Done to Facilitate the Approval of Rapid HIV Tests?

- ◆ Setting rational standards for approval
 - Blood Products Advisory Committee (BPAC); Draft Guidance Document
 - 98% sensitivity and 98% specificity (*lower bound of 95% confidence interval*)
 - Based on state-of-the-art clinical performance levels
- ◆ Simplifying clinical trial requirements
 - Based on intended use of rapid HIV tests vs. intended use of blood donor screening tests
 - BPAC; Draft Guidance Document

FDA Actions to Facilitate Rapid HIV Test Approvals, cont.

- ◆ FDA is prioritizing the review of rapid HIV test submissions
- ◆ FDA has met with other agencies (CDC, NIH), consulted with testing personnel, and held public meetings to develop a plan for facilitating approval of rapid HIV tests
- ◆ Ongoing dialogue with sponsors
 - Pre-IDE meetings; Pre-PMA meetings; Conference calls
- ◆ Expanded access to rapid tests while they are still under development

Discussion of Submission Status

- ◆ FDA is prohibited from releasing any information related to submissions, as this is considered proprietary
- ◆ Limited to discussion of public information only, or information authorized for release by the applicant

Public Information Related to Rapid HIV Test Submissions

- ◆ On May 1, 2002, MedMira Incorporated announced, “the completion of a site inspection of the Company's facilities in Halifax by the U.S. Food and Drug Administration in connection with MedMira's application for Pre-Market Approval of its Reveal™ Rapid HIV Test.”
(http://www.medmira.ca/press_releases_f.htm)
- ◆ In addition, MedMira has given FDA permission to disclose that they received an approvable letter for their PMA on May 24, 2002

Public Information Related to Rapid HIV Test Submissions, cont.

- ◆ On May 13, 2002, OraSure Technologies, Inc, announced, "it has received notification from the U.S. Food and Drug Administration ('FDA') that the OraQuick[®] Rapid HIV-1 Antibody Test is approvable... Final approval is subject to the Company submitting product labeling and resolving specific validation and design control issues identified during FDA's recent pre-approval inspection of the Company's manufacturing facilities..."

(http://www.orasure.com/news/default.asp?art_id=185)



Closing Comments

- ◆ FDA is committed to bring safe and effective rapid HIV tests to market as quickly as possible
 - Manufacturer contacts
 - Sought input and solutions regarding perceived barriers to obtaining premarket approval
 - Expedited, interactive review
- ◆ FDA has received PMA application submissions for rapid HIV tests
 - Evidence of progress from information made public by two applicants