HIV Diagnostics Conference
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To Be Covered

• Why are HIV tests regulated as they are?
• Criteria used to evaluate a test
• How to read package inserts
• Consideration for Home Use HIV test
Why are HIV tests regulated as they are?

• Basis for regulatory authority
  – Laws/Acts
  – Regulations
  – Guidance documents

• Risk-based regulatory approach

• Data-driven marketing approvals
  – To provide EVIDENCE that the device is SAFE and EFFECTIVE for its INTENDED USE
Bringing an IVD to Market in the US: Device Classification

Risk-based regulatory approach

– Class I (low risk)
– Class II (moderate risk) [premarket notification, or 510(k)]
– Class III (high risk) (premarket approval application, or PMA)
HIV Diagnostics

• IVDs used for the detection of HIV infection are Class III devices
  – This is similar to other viral diagnostics (HBV, HCV, HPV)

• Require submission of a premarket approval application (PMA). 21 CFR 814
  – Filed by a sponsor to obtain FDA approval to market a device
  – Clinical data to support the claim
Basis for Classification of HIV Tests-I

Individual Risk

- False negative results
  - false assurance of infection status
- False positive results
  - Psychological consequences
  - Unnecessary treatment
Basis for Classification of HIV Tests-II

Public Health Risk

• False negative results
  - Can spread infection
• False Positive results
  - Waste of resources
Criteria Used to Evaluate an HIV Diagnostic Test
Evaluation of HIV Tests: Performance-I

Performance evaluation

• Analytical studies
  - Ability to detect HIV analytes
• Performance in intended use setting
  - Performance in intended population
  - Performance by the user (e.g., lab, untrained users)
• Evaluation of the instructions for use
  (appropriate for the intended users)
  - Clear instructions for use
Evaluation of HIV Tests: Performance-II

• Analytical studies (The capabilities of the device)
  – Seroconversion panels, dilution panels, low titer panels
  – Interfering substances, unrelated medical conditions
  – Non-B subtypes
  – Reproducibility studies
  – Stability studies (shelf-life, shipping)
Evaluation of HIV Tests: Performance-III

• Clinical studies (performance in real-world)
  – Known positives and prospective studies in low and high risk populations primarily in the U.S.
  – Studies for each matrix claimed
  – Multiple geographically distinct sites
  – Multiple independent kit lots

• Size of the clinical trials based on statistical considerations, to provide meaningful performance descriptions
Evaluation of HIV Tests: Manufacturing

Manufacturing
- Review the Quality Management System
- Ensure ability to manufacture consistent product
- Evaluate complaint handling
- Implement Corrective and Preventive Action Plan (CAPA) as needed

Inspection
- Pre-approval and periodic
Package Inserts
• Critical legal role of the package insert
  – The package insert is used to make specific claims about the product.
  – If those claims are not met, then the product is considered to be “misbranded” under the Food, Drug, and Cosmetic Act and cannot be legally marketed

• Test performance established on the basis of following the product insert
  – Not doing so may produce erroneous results (e.g., altering the procedure, using expired reagents, using operating conditions outside of the acceptable range)
Elements of Package Inserts-I

• The proprietary name and established name (common or usual name), if any
• The intended use or uses of the product
• Summary and explanation of the test
• The chemical, physical, physiological, or biological principles of the procedure
• Information on reagents
• Instruments
• A statement of warnings or precautions for users
• Specimen collection and preparation for analysis
Elements of Package Inserts-II

• Procedure: A step-by-step outline of recommended procedures from reception of the specimen to obtaining results
  – A list of all materials provided
  – A list of all materials required but not provided
  – Details of kinds of quality control procedures and materials required

• Results: Explain the procedure for calculating the value of the unknown
Elements of Package Inserts-III

• Limitations of the procedure
• Expected values
• Specific performance characteristics such as accuracy, precision, specificity, and sensitivity
• Bibliography
• Name and place of business of manufacturer, packer, or distributor.
• Date of issuance of the last revision of the labeling identified as such
Home Use HIV Tests
Considerations: Home Use HIV Tests-I

- Can be performed by users with no training
- Test kit obtained over the counter
  - User collects the specimen
  - Performs the test and interpret the results
  - Requires confirmation
  - Counseling by phone is available (optional)
Considerations: Home Use HIV Tests-II

• Proposed studies to validate adequate performance in the hands of intended users
  o Populations to be studied reflecting intended users?
  o Ability of informational materials to provide counseling and other information in a comprehensible manner by intended users
    - Accuracy of testing
    - Correct test interpretation
    - Management of psychological and social issues
    - Medical referral
Studies to Support Approval of Home Use HIV Tests

Phased Approach:

• Identify potential users
  - Qualitative research
• Phase I: Trained users
  - Inherent sensitivity and specificity
• Phase II: Intended users in controlled setting
  Performance in hands of untrained users
  - Evaluate informational material
• Phase III: Intended users/Intended setting
Additional questions?