Why HIV Tests are Regulated as They are and Understanding the Package Insert

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

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
  - Populations to be studied reflecting intended users?
  - 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?