OTC HIV Tests

FDA-Industry IVD Roundtable Meeting

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Goals of Talk

- Describe how FDA addresses critical public health needs for point-of-care IVDs
  - Professional use tests: Rapid HIV tests
  - Home-use HIV test kits (OTC)
- Describe the challenges posed by home-use HIV test kits

Identifying a Critical Public Health Gap

Challenge: How to Get People to Know Their HIV Status

CDC's Advancing HIV Prevention: The Four Strategies

1. Incorporate HIV testing as a routine part of care in traditional medical settings
2. Implement new models for diagnosing HIV infections outside medical settings.
3. Prevent new infections by working with people diagnosed with HIV and their partners.
4. Further decrease mother-to-child HIV transmission.

Rapid HIV Testing: The Key to Stemming the Tide of New Infections?

- Only one visit required to get a test result
- Relatively non-invasive
- Tests can go to where the people are
  - Not lab or clinic-based
  - Opportunity for non-traditional testing sites

Meeting the Need: Part 1

HIV Testing

- Traditional testing for HIV requires two visits to a clinic/healthcare provider
  - Provide sample
  - Receive test result ~1 week later
  - CDC has estimated that each year approximately 8,000 HIV positive individuals do not return to receive their test results
- Point-of-care testing
  - Tests that can provide a test result in a relatively short time so that only a single visit is required

Rapid HIV tests

FDA Actions to Facilitate Rapid HIV Test Approvals

- FDA 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
- Setting rational standards for approval: FDA's current considerations
  - Simplifying clinical trial requirements taking into account intended use
  - Setting performance expectations
    - 98% sensitivity and 98% specificity (lower bound of 95% confidence interval)
- Ongoing dialogue with sponsors

Access to Rapid HIV Tests

- Who is permitted to use rapid HIV tests?
- Device classification
  - Clinical Laboratory Improvement Amendments of 1988 (CLIA)
  - Classifies devices according to complexity
    - High
    - Moderate
    - Waived
  - Classification made by CDRH with guidelines set by Center for Medicare and Medicaid Services (CMS)
- Impact of CLIA waiver
  - Use of rapid tests permits notification of preliminary test results without the need for the subject to be re-contacted
  - Fewer laboratory restrictions permit wider use

The Access Issue: To Waive or Not to Waive

Access to rapid HIV tests is critical in identifying those who are infected. Waive the tests.

Lack of oversight risks no confirmation by additional more specific tests (follow-up testing), or QA. Classify the tests as moderately complex.

Resolution of the Access Issue

- Approve rapid HIV tests as “restricted devices”
  - Sales, distribution restricted to clinical labs with adequate QA system
  - Use restricted to agent of clinical laboratory
  - Must give Subject Information to test subjects and provide information on test results per CDC guidelines
- Customer agreement with each order
- Approve as moderate complexity device
- Company applies for waiver and performs necessary studies. If effective, waive test.

Rapid HIV Tests Waived under CLIA

- Tests that are waived under CLIA
  - OraQuick® for use with whole blood and oral fluid
  - Uni-Gold™ for use with whole blood
  - Clearview® HIV 1/2 Stat-Pak for use with whole blood
  - Clearview® Complete HIV 1/2 with whole blood
- Sales and use restrictions apply to waived rapid HIV tests

Meeting the Need: Part 2

Are there remaining gaps not addressed by CLIA-waived rapid HIV tests?

Home-Use Tests

- Tests that are used at home by untrained persons without the help of a healthcare professional
- Two types
  - Home-use collection kits
  - Home-use test kits

Home-Use HIV Test Kits are Different from Home-Use HIV Collection Kits

- Home-use collection kit
  - Specimen is collected by the test subject
  - Test is performed and interpreted by a trained operator in a certified laboratory
  - Live counseling
- Home-use test kit
  - Specimen is collected by the test subject
  - Test is performed and interpreted by the test subject
    - Lack of a trained operator
    - Lack of live pre-test counseling and post-test counseling at the time the test result is provided
    - Lack of medical referral

Currently Approved Home-Use Collection Kits and Test Kits

- Home-use **collection** kits
  - Hepatitis C virus infection
  - HIV
- Home-use **test** kits
  - Fecal occult blood
  - Glucose
  - Cholesterol
  - Pregnancy
  - Prothrombin time
- **No previously approved home-use test kits for infectious diseases**

Recurring Themes for Home-Use HIV Test Kits

- Benefits
  - Anonymous testing potentially leads to more people knowing their HIV status
  - Earlier diagnosis and therefore earlier intervention
  - Empowerment of consumers in healthcare decisions
  - Potential impact on behavior and public health

Recurring Themes for Home-Use HIV Test Kits, cont.

- Risks
  - Inappropriate use of test or test result
    - Misinterpretation (*e.g.*, relying on test to provide accurate result after a very recent exposure)
  - Potential adverse outcomes after obtaining a test result without live counseling
  - Inability to reach individuals for follow-up and to perform partner notification
  - Coercive testing
  - Testing by minors

Recurring Themes for Home-Use HIV Test Kits, cont.

- Additional issues
  - Obtaining a test result without a supplemental test
    - False positive rate significant in low prevalence populations
  - Availability for those who need the test most
  - Potential conflict with state and/or federal health reporting requirements

Public Discussions

- Blood Products Advisory Committee (BPAC), November 3, 2005
  - FDA sought advice from BPAC regarding the conditions and necessary to support approval of a home-use HIV test kit.
- BPAC, March 10, 2006
  - FDA sought the advice from the Committee on FDA's proposed studies that would be needed to validate a home-use HIV test kit with regard to test accuracy,test interpretation, and medical follow-up based on the provision of informational material in place of a trained test operator and counselor.
- BPAC, November 17, 2009
  - CDC discussion on role for home-use HIV test kits
  - FDA discussion of risk assessment model to deterimine public health impact of tests of varying sensitivity and specificity

FDA's Current Considerations
Studies to Identify Potential Users of the Test

- Potential users of the test should be identified by means of qualitative research
- Clinical trial study populations should reflect the demographics of those users identified in these studies

FDA's Current Considerations
Phase I Studies

- Objectives
  - To establish the inherent sensitivity and specificity of the test and that the test is capable of withstanding operational stress
- Performed by individuals trained in the use of the test
- Studies
  - Analytical and clinical sensitivity and specificity
    - Additional studies not needed for FDA-approved test
  - Operational stress ("Flex") studies

- Evaluate performance
- Identify issues
- Modify test system to address issues
- Validate modifications

FDA's Current Considerations

Phase II: Intended Users/Controlled Setting

- Objectives:
  - Evaluate performance of the test (sensitivity and specificity) in the hands of untrained potential users
    - Lower bound of the two-sided 95% confidence interval at least 95% for both sensitivity and specificity
  - Evaluate reactions of study participants to their test results
  - Validate ability of informational materials to:
    - Communicate the proper use of the test and interpretation of the test result
    - Communicate test limitations
    - Have study participant seek follow-up testing and referral to care
    - Effectively provide a route to counseling
  - Assessment of ability of informational materials to substitute for live counseling without adverse events

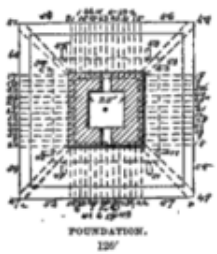
- Evaluate performance
- Identify issues
- Modify test system to address issues
- Validate modifications

FDA's Current Considerations
Phase III: Intended Users/Intended Use Setting

- Objectives:
  - Evaluate performance of the test (sensitivity and specificity) in the hands of untrained potential users
    - Lower bound of the two-sided 95% confidence interval at least 95% for both sensitivity and specificity
  - Evaluate reactions of study participants to their test results
  - Validate ability of informational materials to:
    - Communicate the proper use of the test and interpretation of the test result
    - Communicate test limitations
    - Have study participant seek follow-up testing and referral to care
    - Effectively provide a route to counseling
  - Validate that informational materials mitigate risks associated with receiving HIV test result in intended use setting

Interdependence of Phases of an OTC Trial

A Monumental Analogy



Phase I

Interdependence of Phases of an OTC Trial

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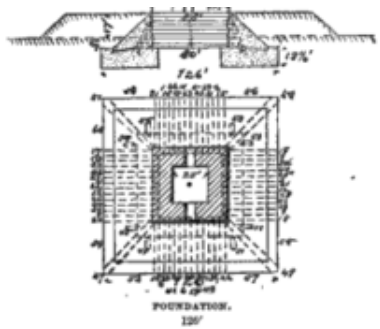

Phase II

Phase I

Interdependence of Phases of an OTC Trial

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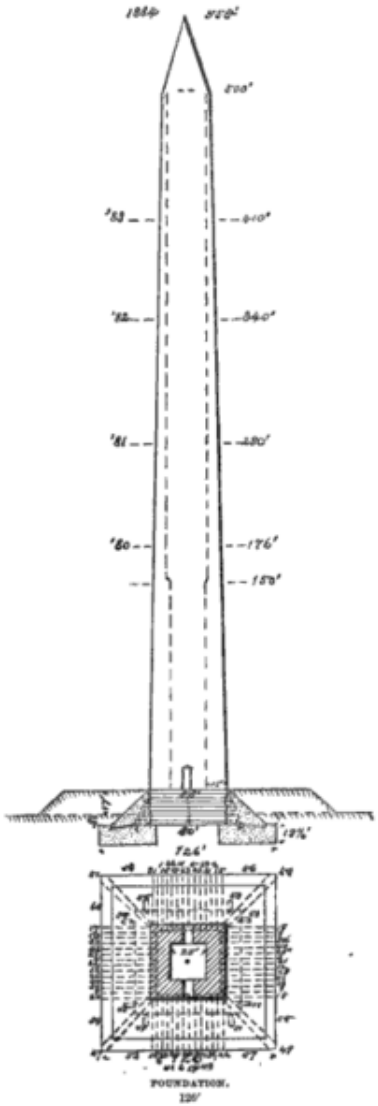


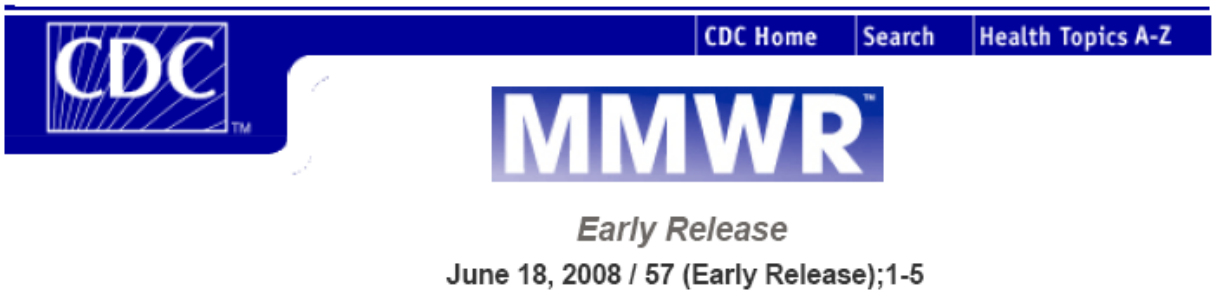
Phase III

Phase II

Phase I

Real World Issues

- Reports of sporadic, localized increased rate of false positive results



- Reports of false negative results
  - Window period testing
  - Documented false negatives with oral fluid specimens from individuals on HAART

In Summary: Meeting Public Health Needs *From Professional Use Tests*

To Home-Use Test Kits