Regulatory Issues for Rapid Tests in the U.S.

2nd International Workshop

Accessible and Quality Assured In Vitro Diagnostic Tests for Public Health Programs

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Disclaimer

This presentation reflects the views of the presenter and should not be construed to represent FDA's views or policies.

Goal of this Talk

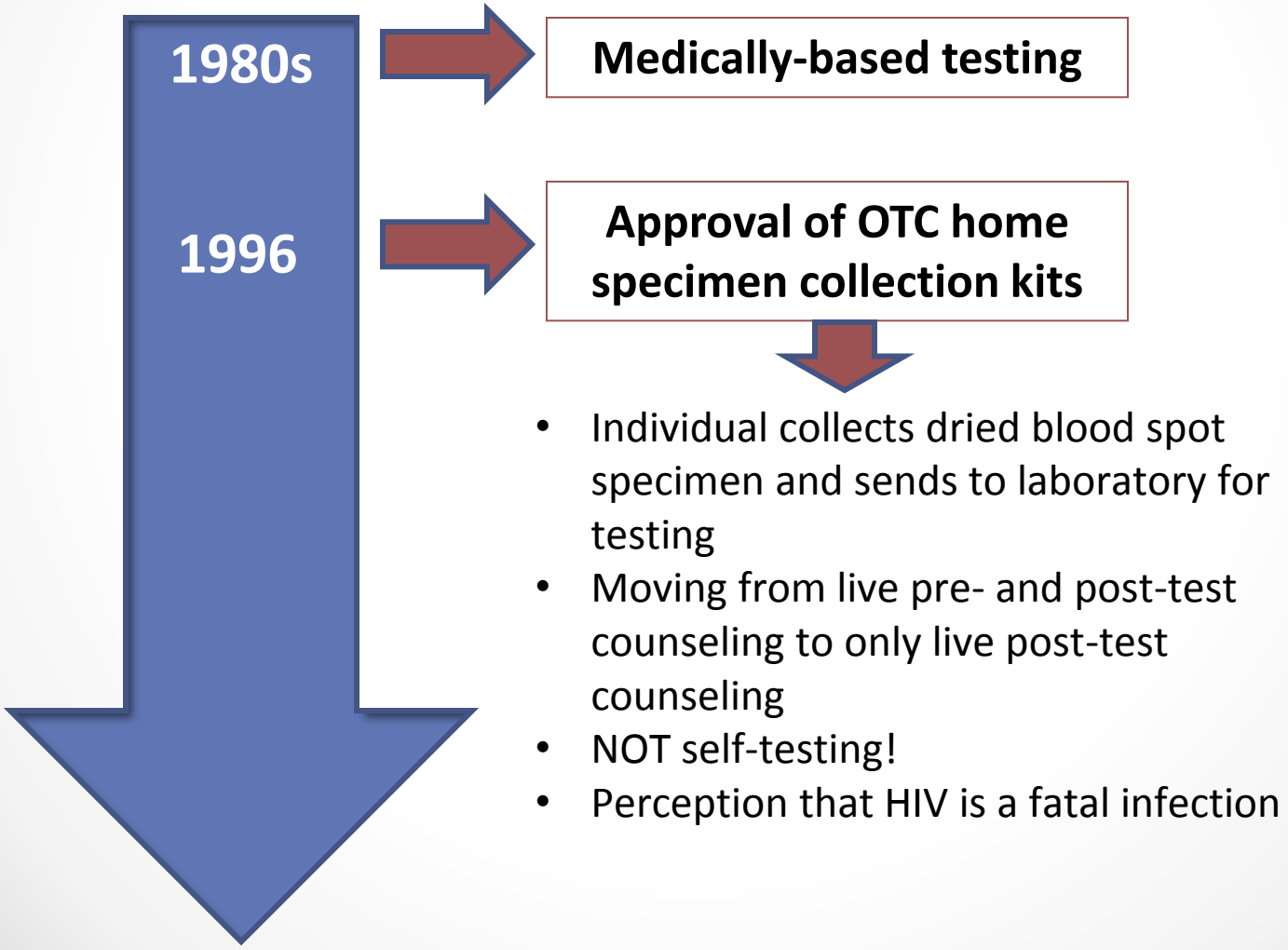
- To show how public health need can drive the regulation of HIV tests
  - Professional rapid HIV tests
  - Over-the-counter home-use HIV tests

Evolution of HIV Testing

Medically-based testing

- Collect specimen
- Send to laboratory for testing
  - Enzyme immunoassays
  - Western blot and immunofluorescence assays
- Technically complex
- Labor and time-intensive
- Complete oversight and interaction with medical system

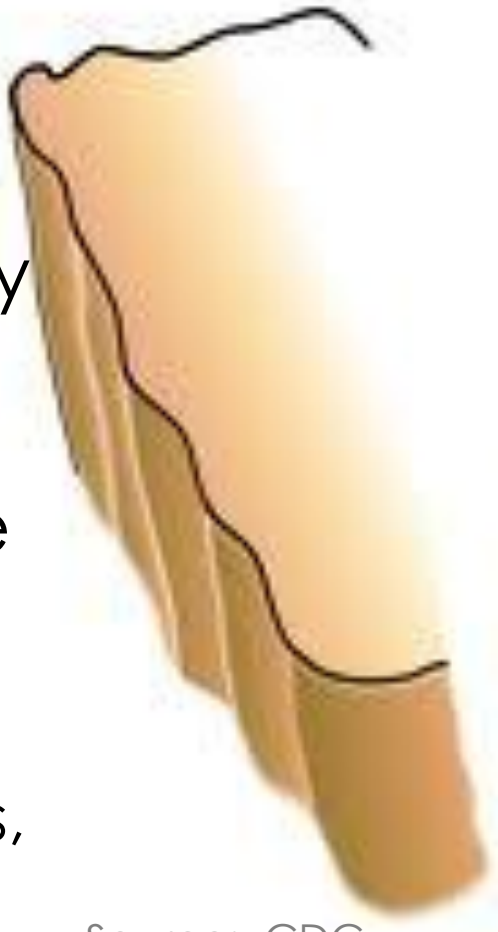
Evolution of HIV Testing



- Individual collects dried blood spot specimen and sends to laboratory for testing
- Moving from live pre- and post-test counseling to only live post-test counseling
- NOT self-testing!
- Perception that HIV is a fatal infection

The Gap: 1990s

- 25% of Americans living with HIV did know they are infected
- 37% first discovered they had HIV ≤1 year before an AIDS diagnosis
- 31% who tested positive at CDC-funded HIV testing sites do not return for results
  - Testing required two visits, with results in 1-2 weeks



Source: CDC

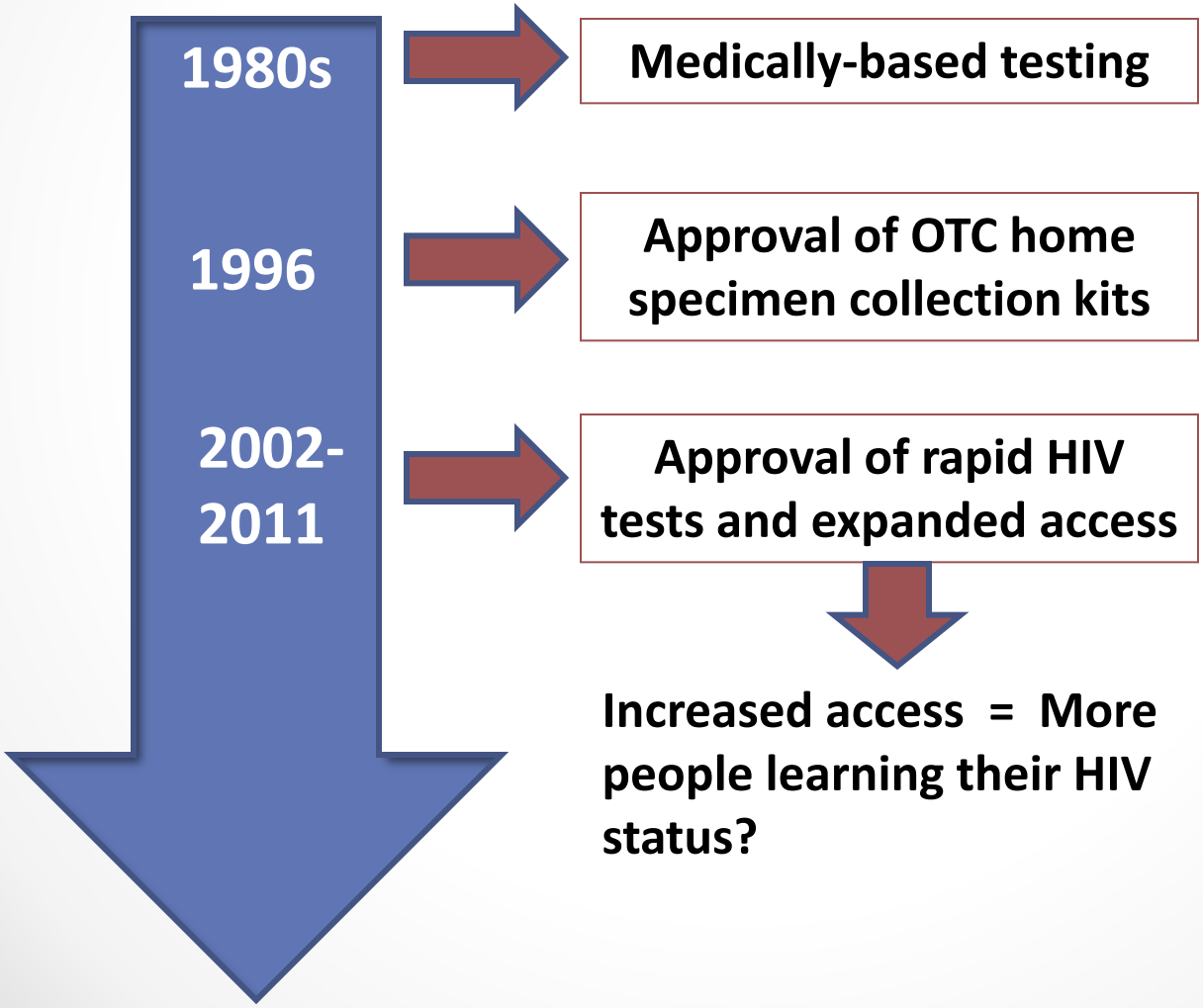
Filling the Gap: Rapid HIV Tests

- 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

Bringing Rapid HIV Tests to Market

- FDA simplified clinical trial requirements
- FDA identified rational performance expectations
  - Sensitivity and specificity ≥98% as the lower bound of the 95% confidence interval

Evolution of HIV Testing



The Gap Persists: HIV in the US (CDC)

Number of Americans newly diagnosed with HIV infection each year

~50,000

Number of HIV-infected people in the US

1.2 MILLION

HIV-infected people in the US who do not know they are infected

1 in 5

Filling the Gap: The Sequel

- Why does the gap exist (barriers to testing)?
  - Stigma
  - Inconvenience
  - Denial
  - Etc.
- Would an over-the-counter rapid HIV test help to bridge the gap?
- Why now?
  - HIV infection perceived as treatable

Over-The-Counter (OTC) Home-Use Test Kits

- An over-the-counter test kit is one that is available for purchase by a consumer for the purpose of self-testing
  - No referral from a medical professional (no prescription needed)
  - Many purchase options
    - Internet purchase
    - Pharmacy/Drug Store/Grocery Store
    - Vending machine

Home-Use Test Kits

- Features
  - Specimen is collected by the test subject
  - Test is performed and interpreted by the test subject
    - No trained operator
    - Results obtained without personal counseling
    - Counseling and medical referral available by phone
    - Screening result needs to be confirmed by an additional professional test

Important Concepts

- Over-the counter tests are COMPLETE test systems that are not only the tests themselves but the entire testing process
  - Design test system for self-testing
  - Validate test performance in the hands of the intended users
- Lower sensitivity and specificity expected in the hands of untrained users compared to professional users.

Expected Performance

- Discussion in public meetings
- FDA Blood Products Advisory Committee recommended sensitivity and specificity ≥95% as the lower bound of the 95% confidence interval (vs. 98% for professional use rapid HIV tests)

OraQuick® In-Home HIV Test System

Professional Test Performance

	Performance of the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test (2-sided 95% CI)	BPAC Minimum Recommended Performance
Specificity	99. 8% (99.6 – 99.9%)	98% (lower bound of the 95% CI)
Sensitivity	99.3% (98.4 - 99.7%)	98% (lower bound of the 95% CI)

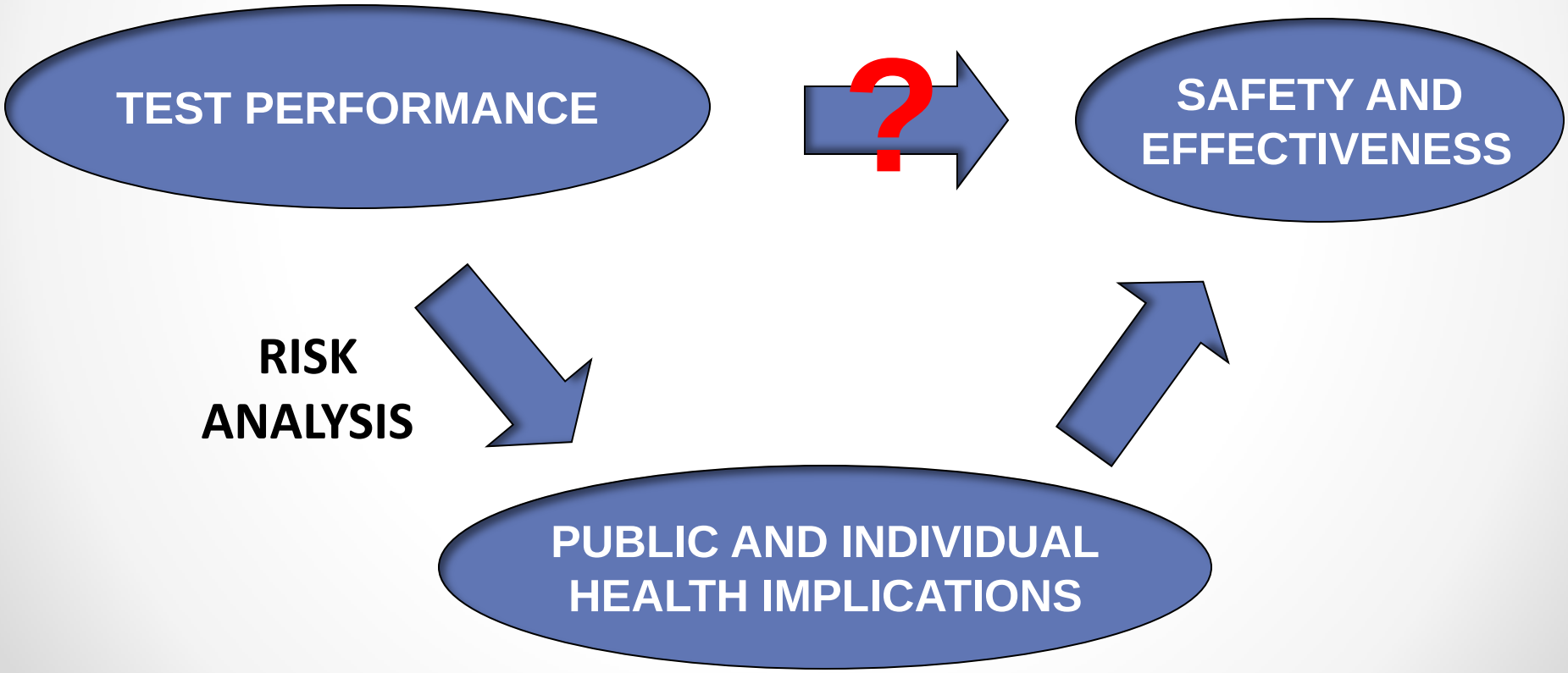
Source: FDA presentation at May 15, 2012 BPAC meeting

Home-Use Test Performance

	Performance of the OraQuick® In-Home HIV Test Kit (2-sided 95% CI)	BPAC Minimum Recommended Performance
Specificity	99.98% (**99.90** – 100%)	**95%** (lower bound of the 95% CI)
Sensitivity	92.98% (**86.64** – 96.92%)	**95%** (lower bound of the 95% CI)

Source: FDA presentation at May 15, 2012 BPAC meeting

Home-Use Test Performance as a Measure of Safety and Effectiveness



Risk Analysis
(FDA)

- Estimated test results for numbers of individuals projected to be tested annually who would not otherwise be tested
  - True positive, false negative
  - True negative, false positive
- Estimated net transmissions averted
- Impact of switching from professional testing to self-testing
- Impact of who will use the test
- Public health implications and individual health implications

Source: FDA presentation at May 15, 2012 BPAC meeting

FDA Projected Outcomes of Testing with the OraQuick® In-Home HIV Test in the 1st Year

(Based on point estimates of sensitivity and specificity)

True Positive	**45,000**
False Negative	**3,800**
True Negative	**2,700,000**
False Positive	**1,100**

13 TP : 1 FN (vs. 128:1)

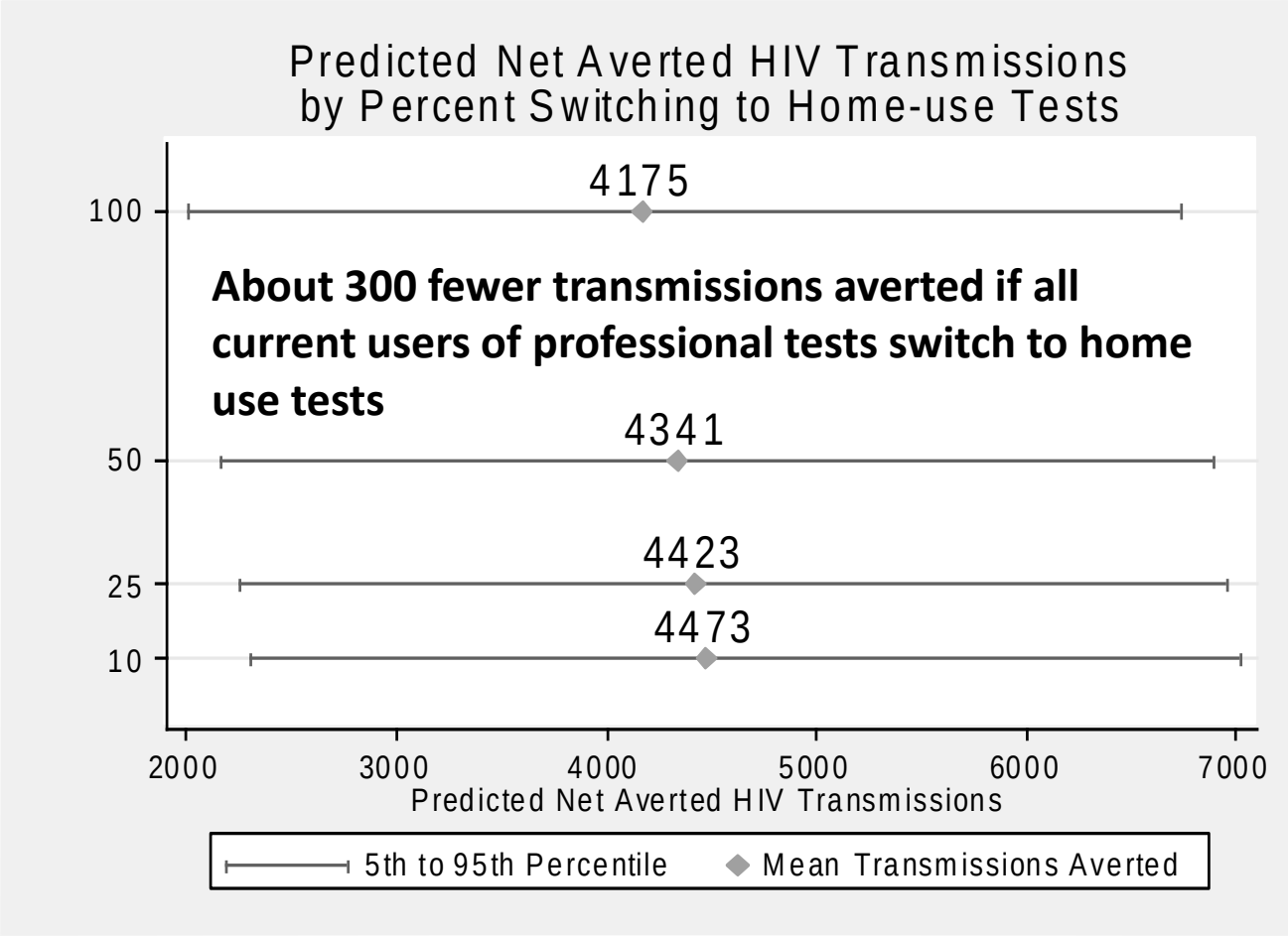
Professional use test

3,750 TN :1 FP (vs. 461:1)

Source: FDA presentation at May 15, 2012 BPAC meeting

Projected Net Transmissions Averted

(Combined Professional and Home Testing)



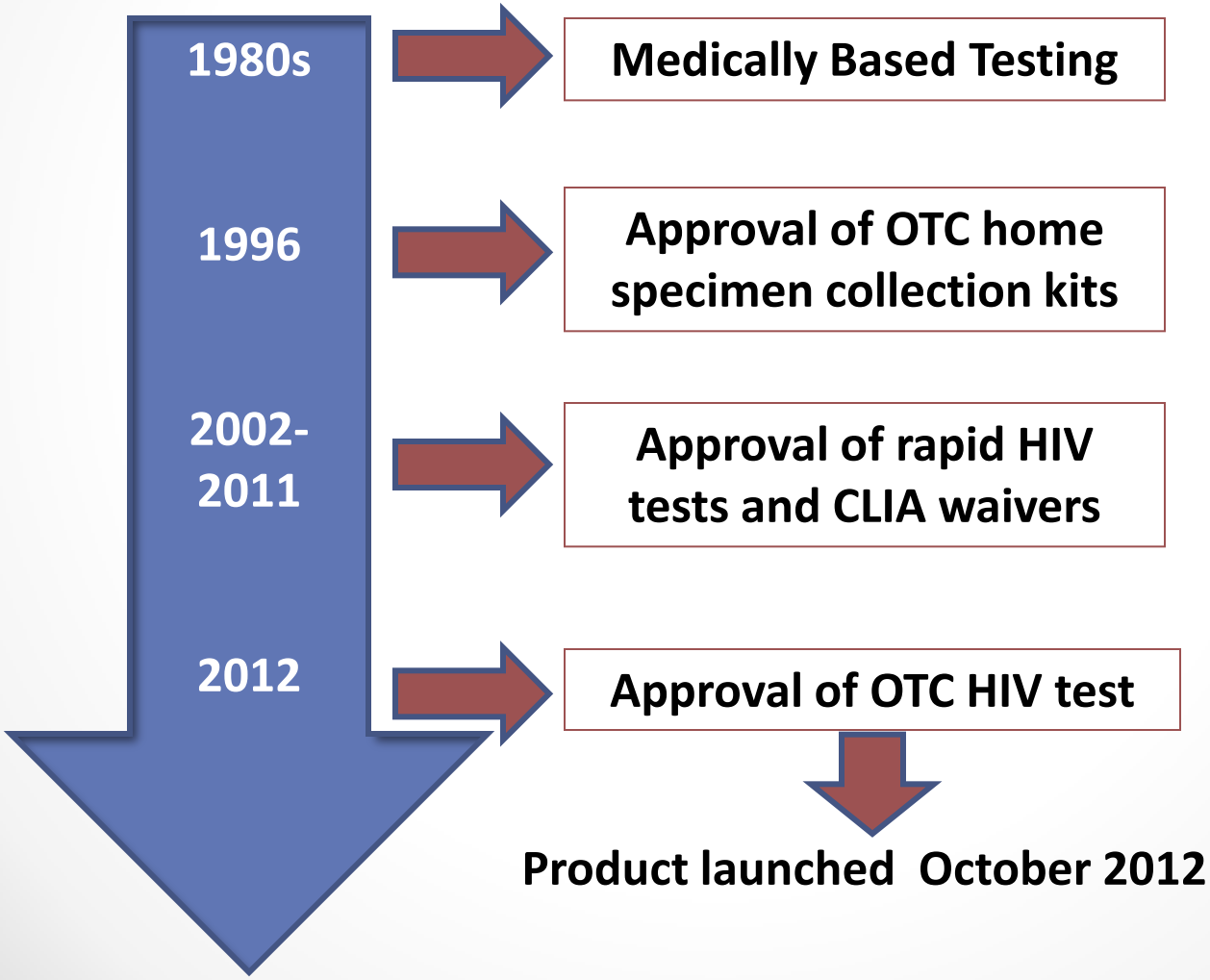
Source: FDA presentation at May 15, 2012 BPAC meeting

Summary of FDA Assessment

- Based on a risk assessment model, FDA projected a net public health benefit to the OraQuick® In-Home HIV Test
  - Net increase in number of HIV infections newly identified in the first year
  - Net transmissions averted
- Individual risk remains in the form of increased numbers of false negative results

Source: FDA presentation at May 15, 2012 BPAC meeting

Evolution of HIV Testing



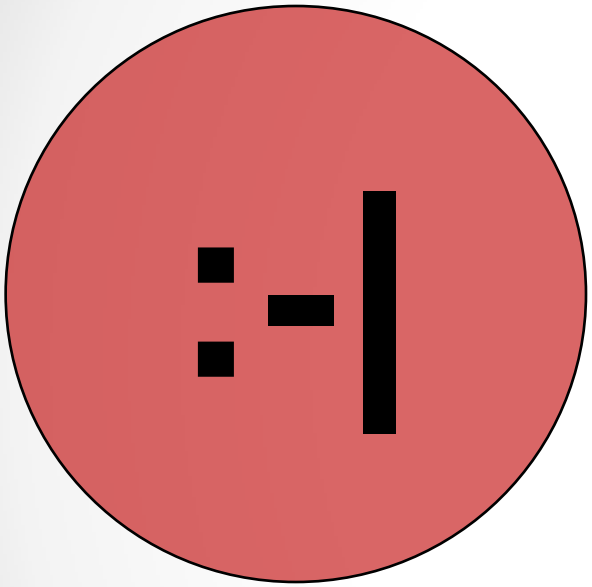
Messages that Came with Approval

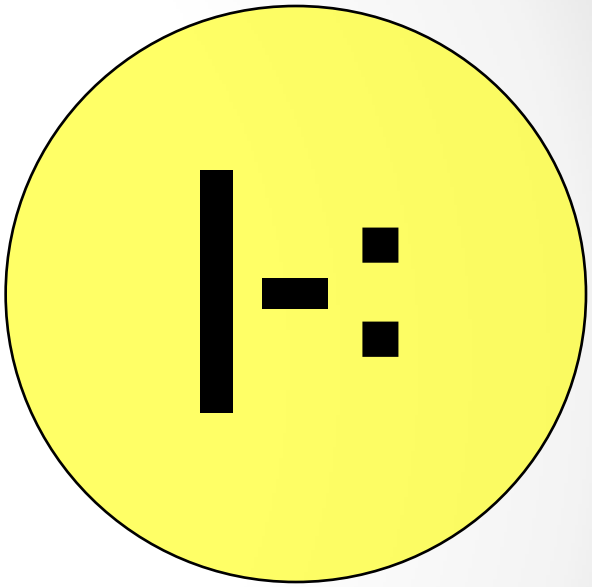
- A positive result with this test does not mean that you are definitely infected with HIV, but rather that additional testing should be done in a medical setting.
- A negative result with this test does not mean that you are definitely not infected with HIV, particularly when exposure may have been within the previous three months.
- Resting is recommended if you test negative and continue to engage in behavior that puts you at risk for HIV infection.
- A negative result does not imply it is safe to engage in risk behavior for HIV infection.

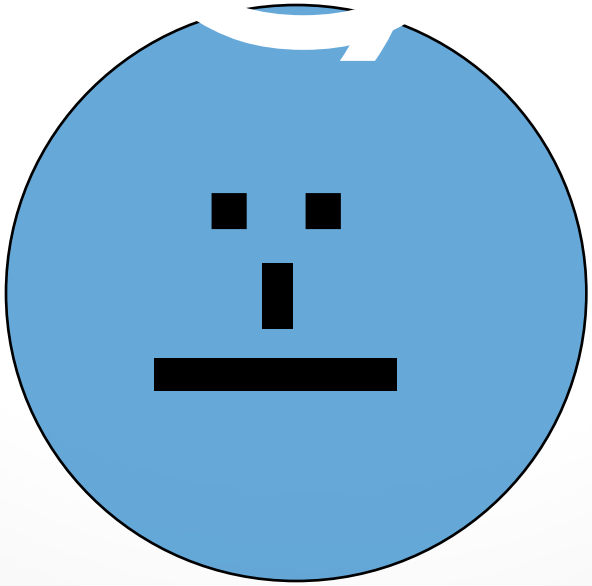
Some Things to Think About

- What is the need?
- What tools are available to meet that need?
- What are the gaps left by existing tools?
- How can those gaps be filled?
- How is the system monitored to determine if the right choices were made?
- Do the benefits outweigh the risks?

The Power of Sharing
(or Emoticommon Sense)







Let the Public Health Need Drive the Process