HIV Self-Testing – How these tests can help to improve the diagnosis of the disease?

The US Experience

IX INTERNATIONAL WORKSHOP

“Quality Assured and Accessible Diagnostics”

“POC and Rapid Tests and their use in the elimination of HIV, Syphilis and Hepatites”

September 3, 2019

Elliot P. Cowan, PhD

Principal, Partners in Diagnostics, LLC

Partners in Diagnostics, LLC

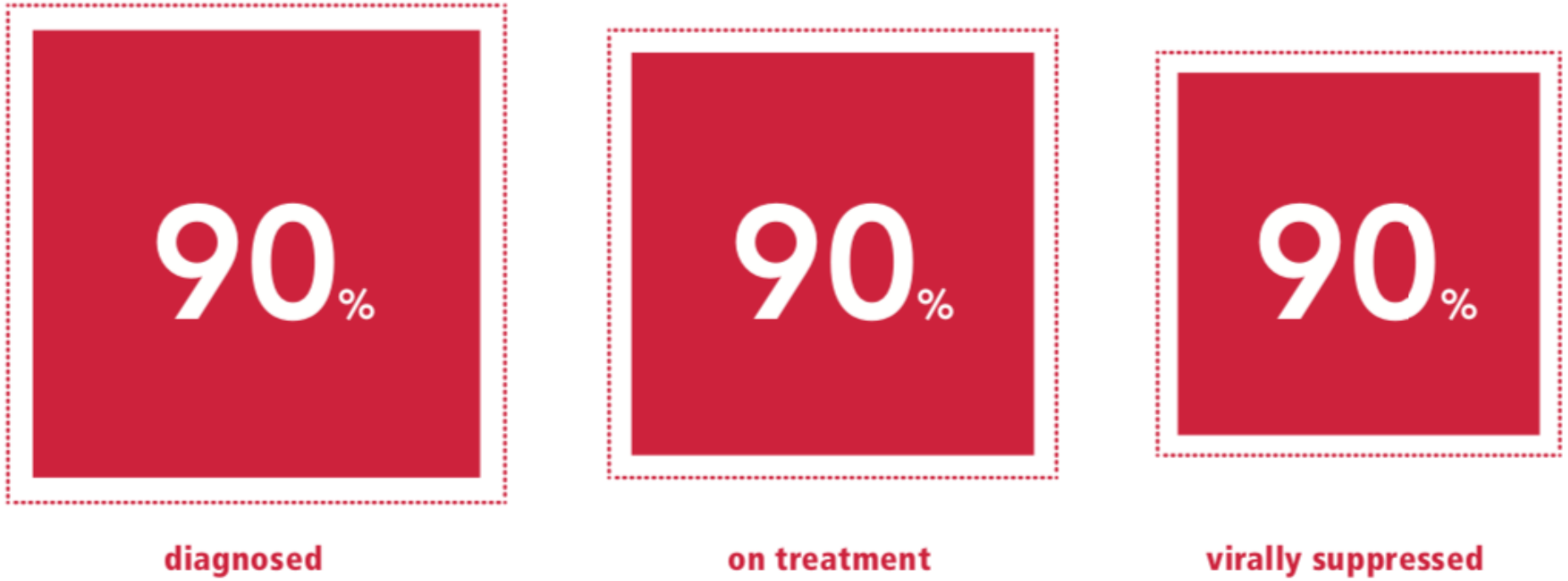
Regulatory Consulting to Advance Global Health

13817 Congress Drive • Rockville, Maryland 20853-2632 USA • Tel: +1 301-233-0897 • Email: elliot.cowan@partnersindiagnostics.com

Agenda

- Describe the approach used by the US FDA to evaluate and approve an HIV self-test.
- Discuss how that approach can be appropriate for others considering HIV self-tests.

Making the case for HIV Self-Testing (HIVST)



Making the case for HIV Self-Testing (HIVST)

diagnosed

Role for HIVST?

Making more of a case for HIVST

- Who isn't being tested and why?
  - Stigma?
  - Lack of access to testing?
- Could HIVST be effective in getting more people to know their status?

Making the case in the US (2006-2012): Responding to a Public Health Need

Number of Americans newly diagnosed with HIV infection each year

~50,000

Number of HIV-infected people in the U.S.

1.2 MILLION

HIV-infected people in the U.S. who do not know they are infected

1 in 5

FDA's thinking on HIVST

- There was a recognized gap in people knowing their HIV status that may be addressed by HIVST.
- Concepts that guided FDA decision-making:

1. Can an HIV self-test be safe and effective for its intended use?
2. Safe = Do the benefits outweigh the risks?

Expected Performance

- Sensitivity and specificity ≥95% as the lower bound of the 95% confidence interval (*vs.* 98% for professional use rapid HIV tests)
- Those numbers should come from testing done by intended users in an intended use setting, compared to a reference testing algorithm.
- Analytical studies should demonstrate that the test can withstand stresses ("flex studies")

Professional Test Performance

(OraQuick ADVANCE® HIV-1/2 Antibody Test with Oral Fluid Specimens: Package Insert)

	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)

Home-Use Test Performance

(OraQuick® In-Home HIV Test for Oral Fluid Specimens: Data shown at Blood Products Advisory Committee, May 2012)

	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)

Risks

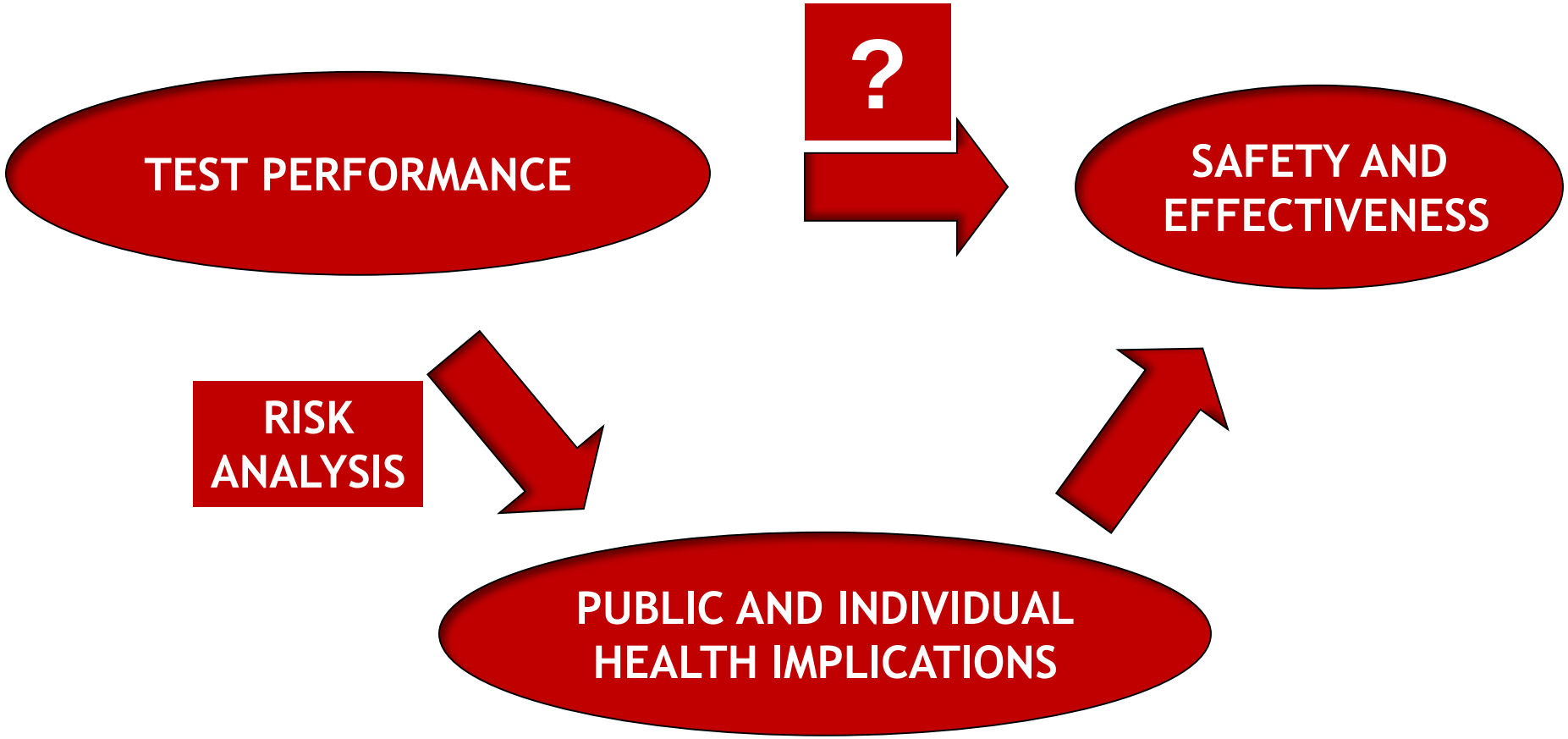
False negative test results

- False sense of security with continued high risk behavior
- HIV transmission

False positive test results

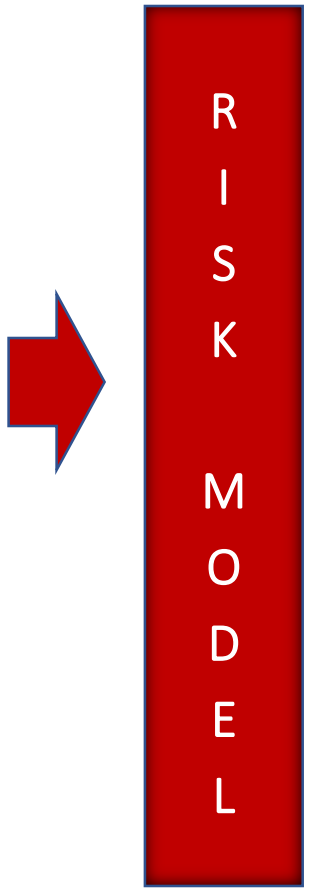
- Unnecessary anxiety (adverse events?)
- Risks associated with treatment when treatment wasn't needed

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



Very High Level View of FDA Risk Analysis

- Estimated test results for numbers of individuals projected to be tested annually who would not otherwise be tested in the 1st year
  - True positive, false negative
  - True negative, false positive



- Estimated net transmissions averted in the 1st year
- Impact of switching from professional testing to self-testing
- Impact of who will use the test
- Public health implications and individual health implications

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

(Based on sensitivity and specificity at the 95% confidence interval lower bound)

True Positive	42,000
False Negative	7,000
True Negative	2,700,000
False Positive	3,600

6 TP : 1 FN (vs. 62:1)

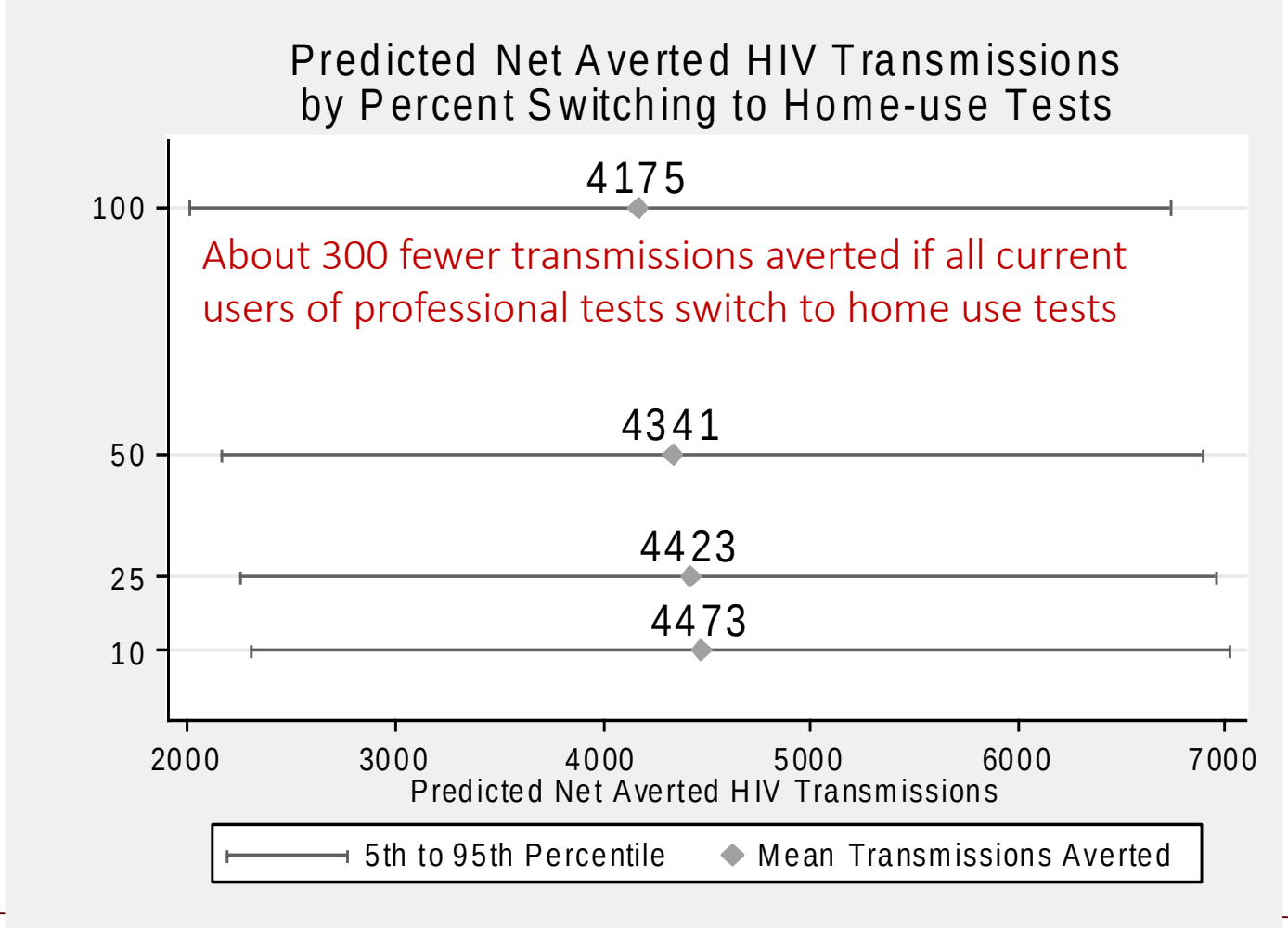
Professional use test

770 TN :1 FP (vs. 249:1)

From FDA presentation at Blood Products Advisory Committee, May 2012

Projected Net Transmissions Averted

(Combined Professional and Home Testing)

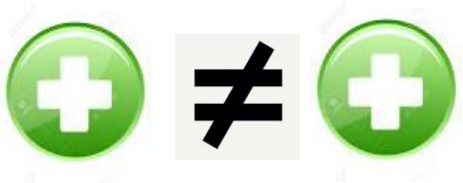


From FDA presentation at Blood Products Advisory Committee, May 2012

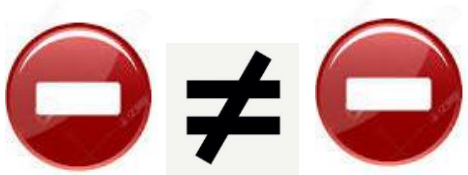
Summary of FDA Assessment

- 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

Messages to Mitigate Risk

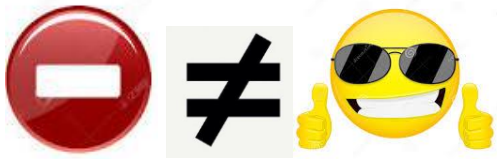


- A positive result with this test does not mean that you are definitely infected with HIV, but rather that additional testing should be done in a medical setting.



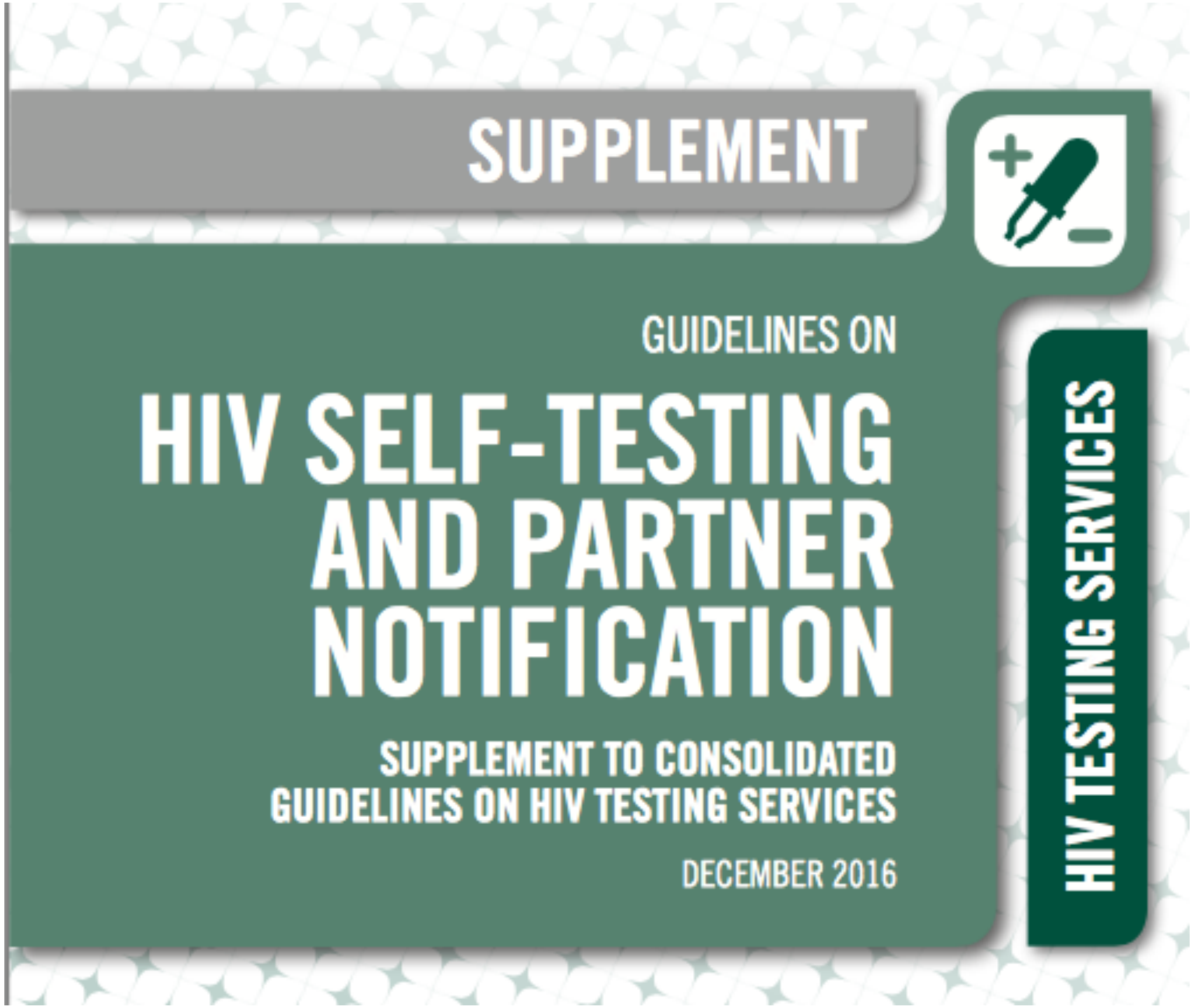
- A negative result with this test does not mean that you are definitely not infected with HIV, particularly when exposure may have been within the previous three months.

- Retesting 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 mean it is safe to engage in risk behavior for HIV infection.

17


SUPPLEMENT
GUIDELINES ON
HIV SELF-TESTING AND PARTNER NOTIFICATION
SUPPLEMENT TO CONSOLIDATED GUIDELINES ON HIV TESTING SERVICES
DECEMBER 2016
HIV TESTING SERVICES

Technical Specifications Series for submission to WHO Prequalification – Diagnostic Assessment

TSS-1

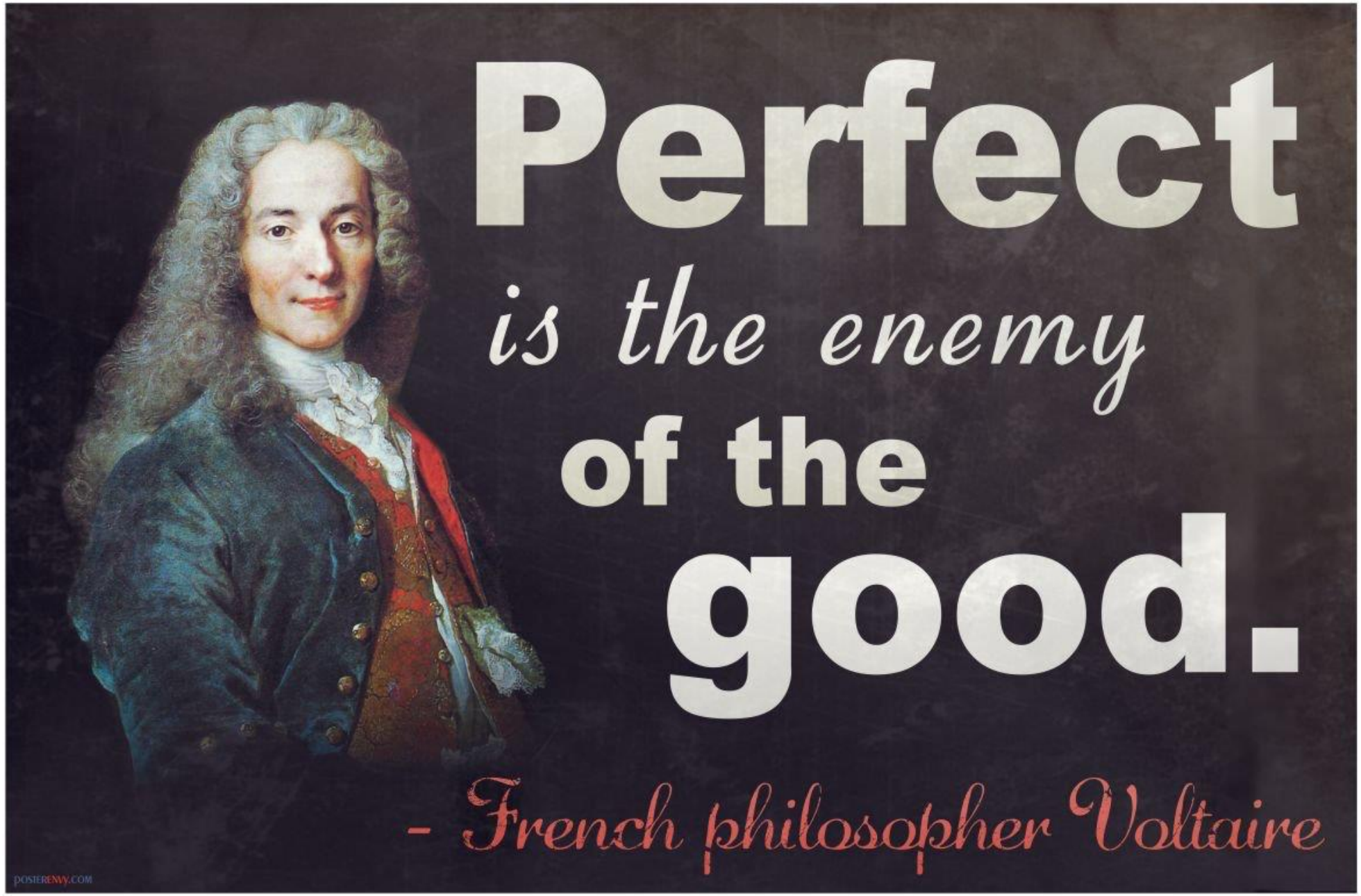
Human Immunodeficiency Virus (HIV) rapid diagnostic tests for professional use and/or self-testing

Challenges for HIVST

- Clinical performance studies
- Post-market surveillance
- Linkage to care and treatment
- Cost
- Tracking incidence and prevalence

Messages/Conclusions

- Understand the risks and benefits.
- Determine if and how risks can be mitigated.
- Assess whether the benefits outweigh the risks.
- Communicate residual risks.
- Use a rational approach to set performance expectations.


Perfect
is the enemy
of the
good.
- French philosopher Voltaire
POSTERENVY.COM


obrigado

Making the case in the US (2006-2012): Responding to a Public Health Need

		2016
Number of Americans newly diagnosed with HIV infection each year	~50,000	37,789
Number of HIV-infected people in the U.S.	1.2 MILLION	1.1 MILLION
HIV-infected people in the U.S. who do not know they are infected	1 in 5	1 in 7