Evolution of HIV Diagnostics and Goals for the 2010 Conference

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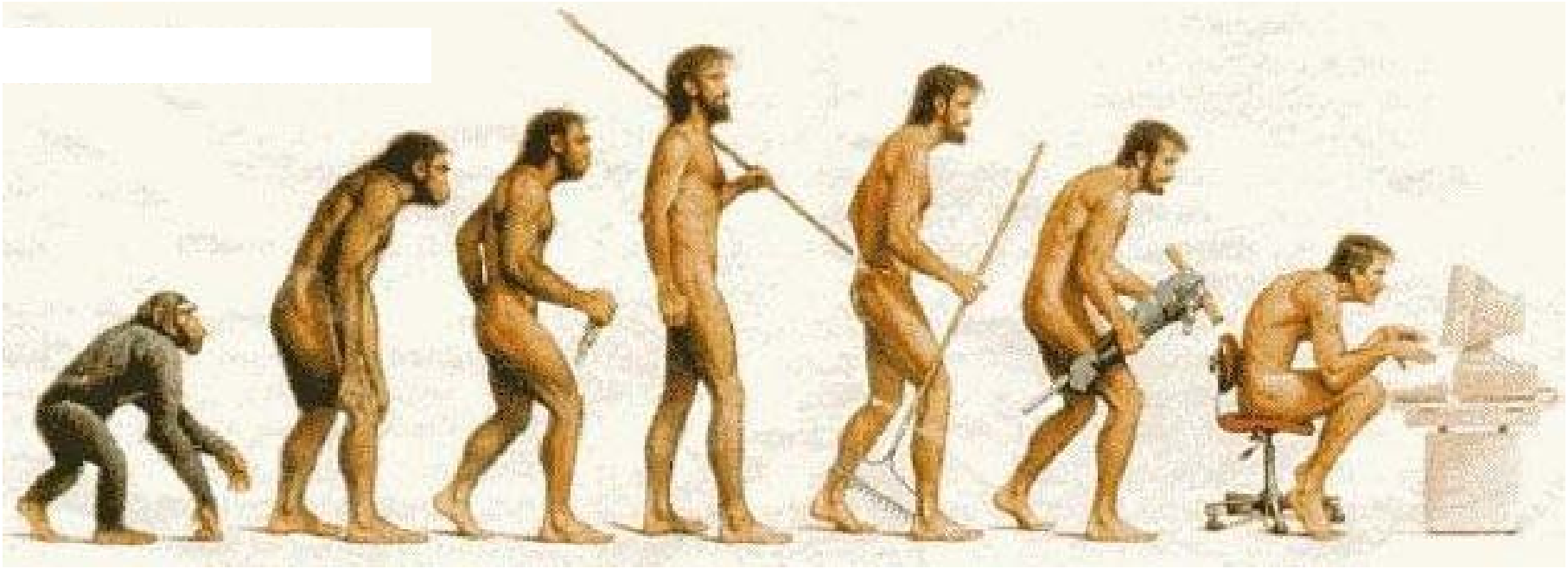
Associate Director for Laboratory Diagnostics

CDC Division of HIV/AIDS Prevention

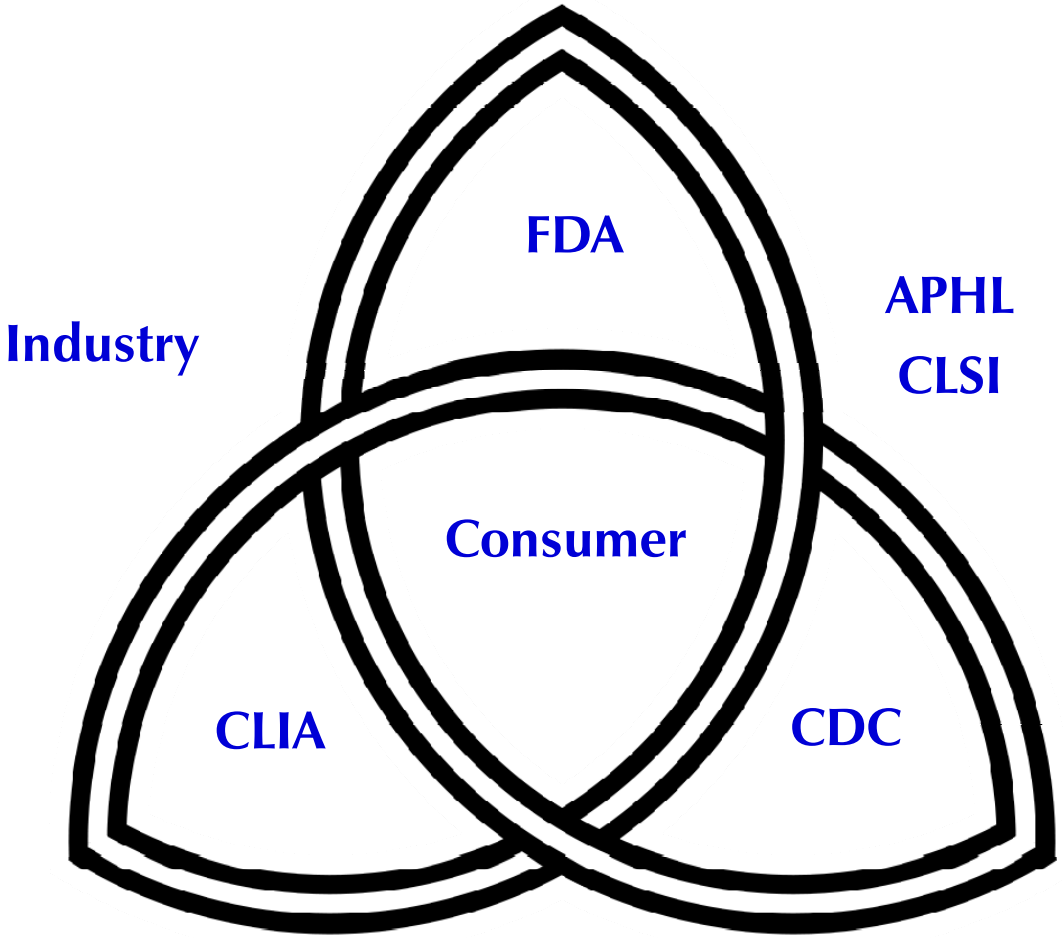
CDC

Centers for Disease Control and Prevention

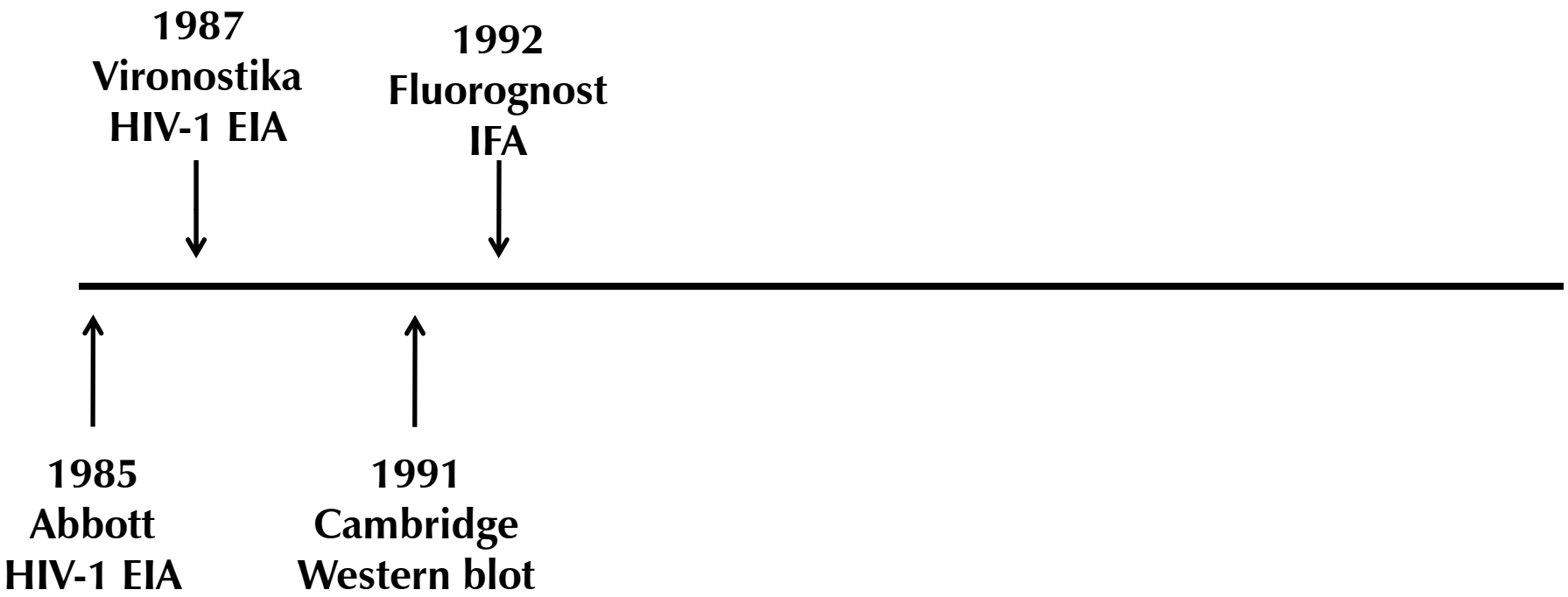
Evolution…

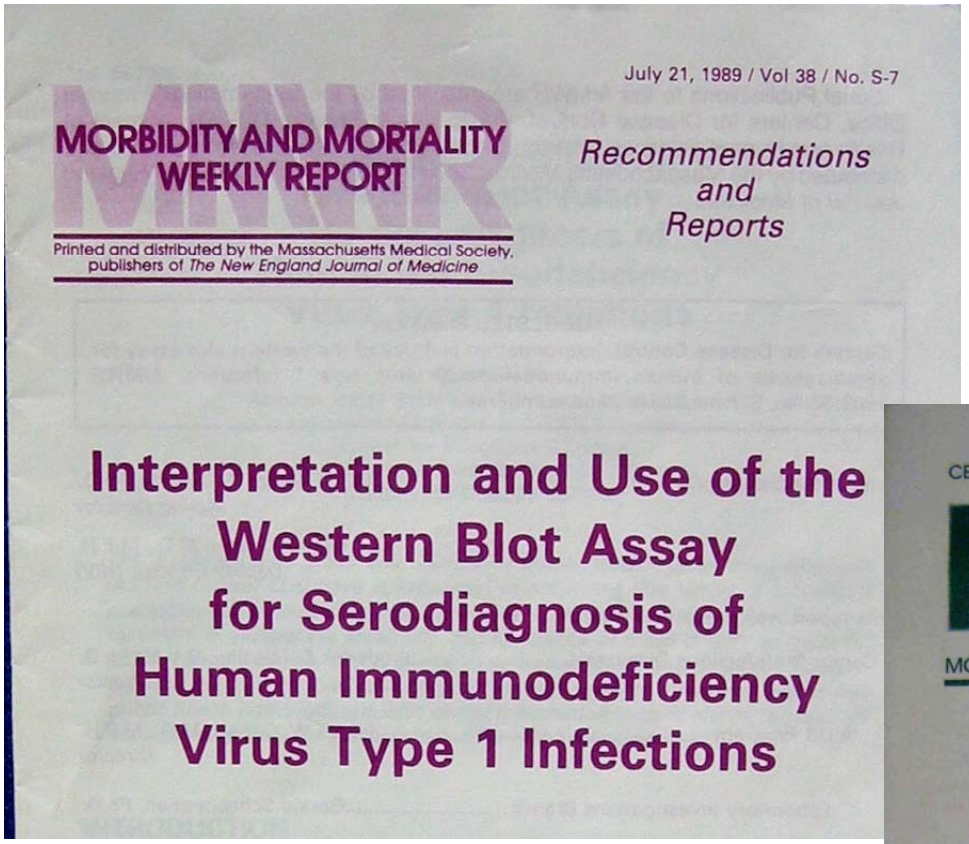


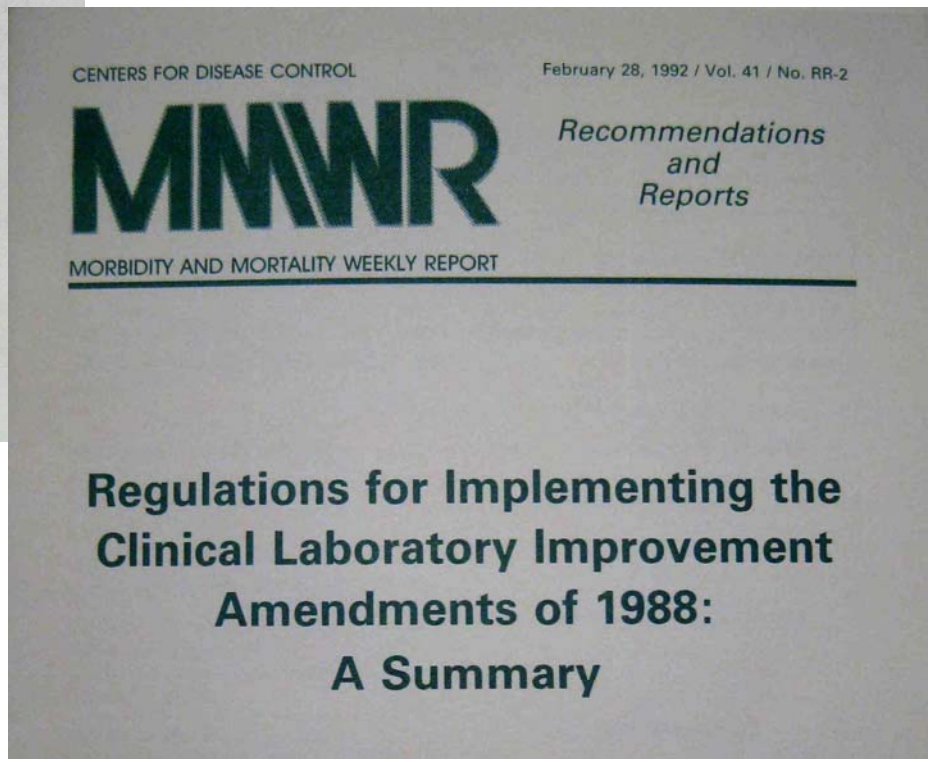
…or other influences – like Creationism?




Intellectual
Property
Rights


1987
Vironostika
HIV-1 EIA
1992
Fluorognost
IFA
1985
Abbott
HIV-1 EIA
1991
Cambridge
Western blot


July 21, 1989 / Vol 38 / No. S-7
MORBIDITY AND MORTALITY WEEKLY REPORT
Recommendations and Reports
Printed and distributed by the Massachusetts Medical Society, publishers of The New England Journal of Medicine
Interpretation and Use of the Western Blot Assay for Serodiagnosis of Human Immunodeficiency Virus Type 1 Infections

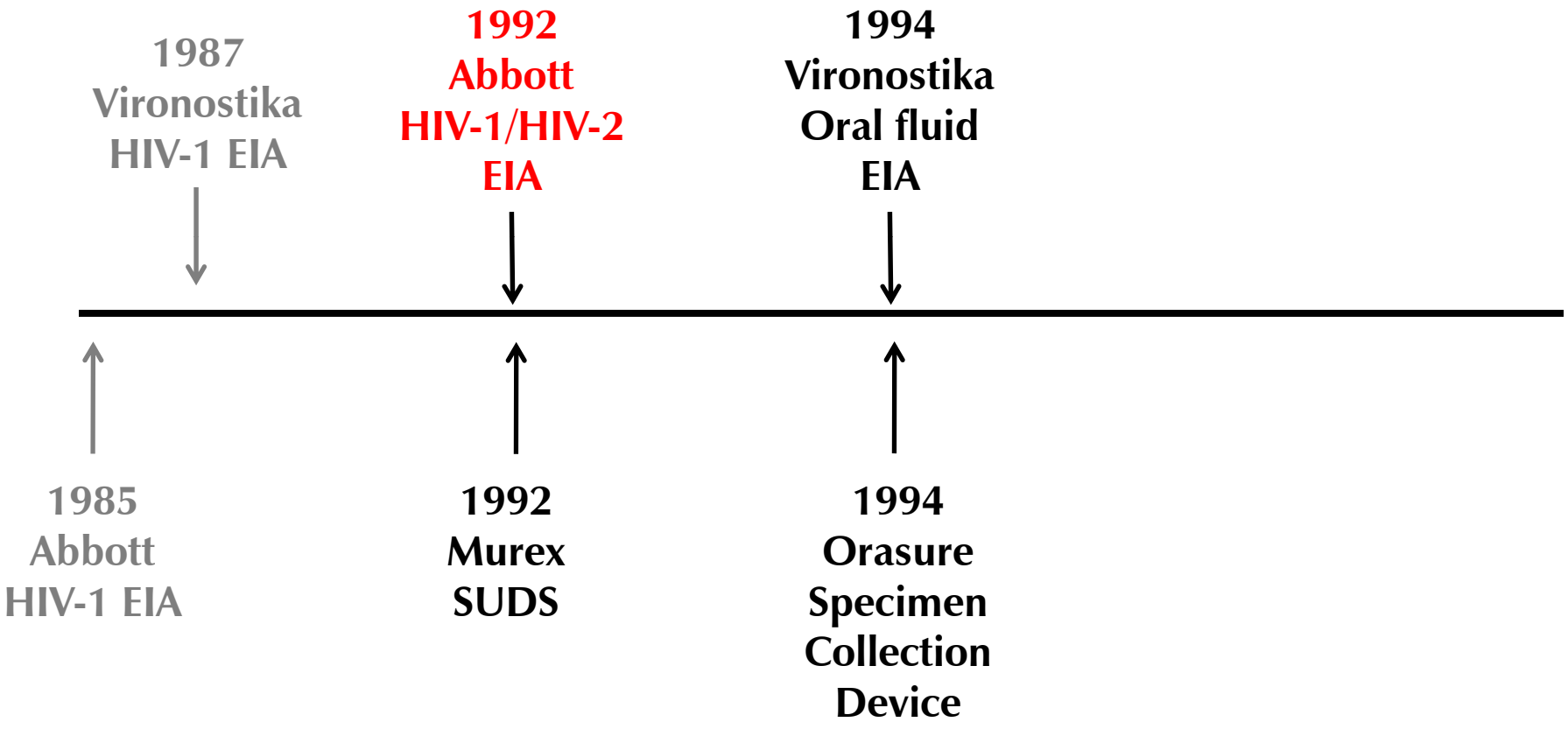

CENTERS FOR DISEASE CONTROL
February 28, 1992 / Vol. 41 / No. RR-2
MMWR
Recommendations and Reports
MORBIDITY AND MORTALITY WEEKLY REPORT
Regulations for Implementing the Clinical Laboratory Improvement Amendments of 1988: A Summary

Diagnostic Algorithm: 1989

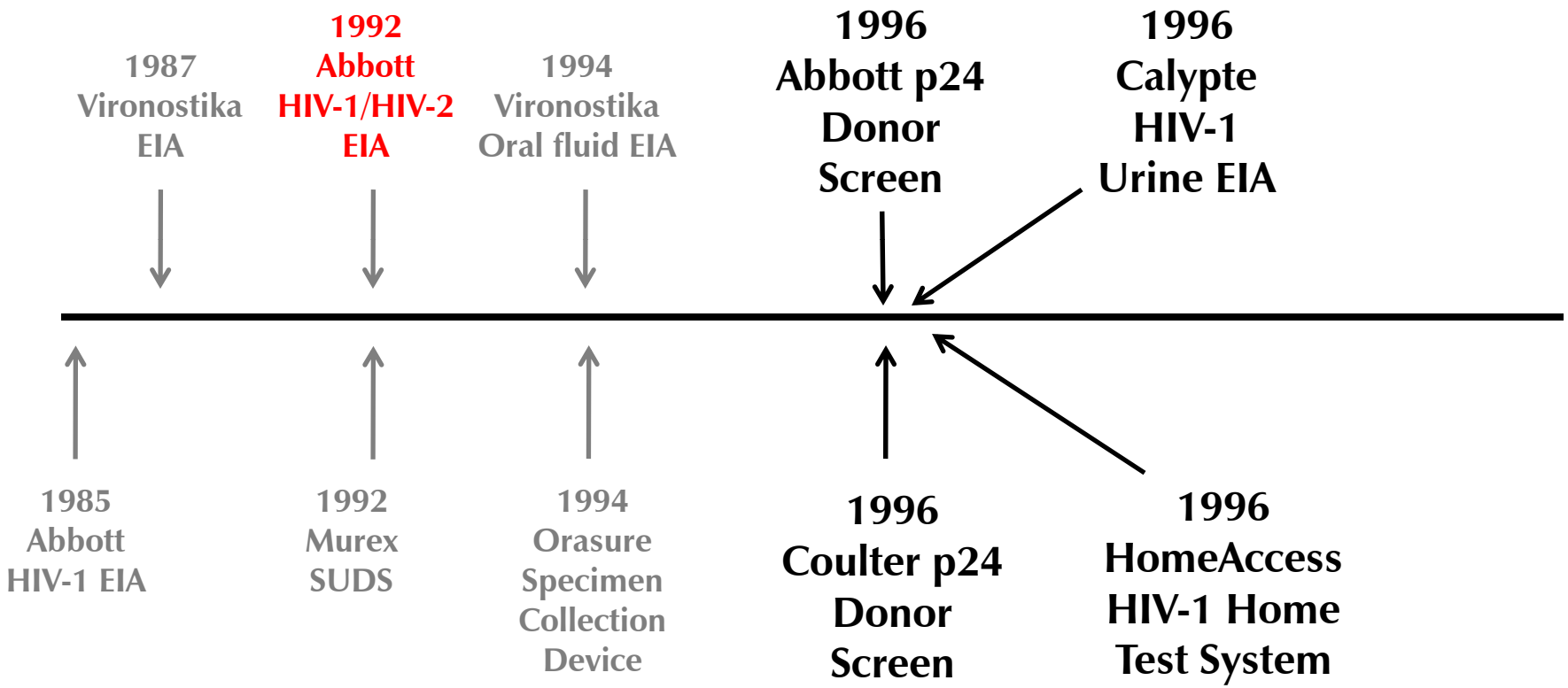
- The Public Health Service recommends that no positive test results be given to clients/patients until a **screening test has been repeatedly reactive** (i.e., greater than or equal to two tests) on the same specimen **and a supplemental, more specific test** such as the Western blot **has been used to validate those resul**ts

1989 Almanac

- Berlin Wall dismantled
- Tiananmen Square
- Exxon Valdez
- U.S. invades Panama


1987
Vironostika
HIV-1 EIA
1992
Abbott
HIV-1/HIV-2
EIA
1994
Vironostika
Oral fluid
EIA
1985
Abbott
HIV-1 EIA
1992
Murex
SUDS
1994
Orasure
Specimen
Collection
Device

1995 Human Retrovirus Testing Conference: Provide results from rapid tests?


1987
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Oral fluid EIA
1996
Abbott p24
Donor
Screen
1996
Calypte
HIV-1
Urine EIA
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Abbott
HIV-1 EIA
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Murex
SUDS
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Orasure
Specimen
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Device
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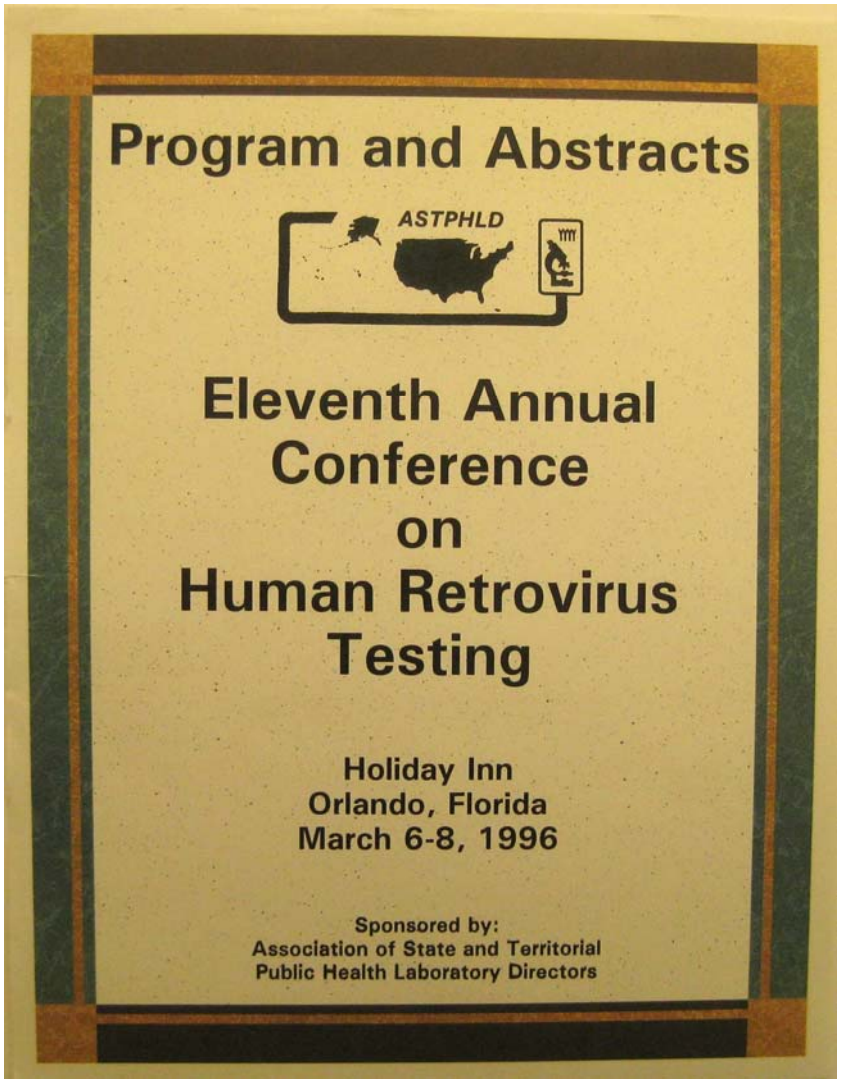
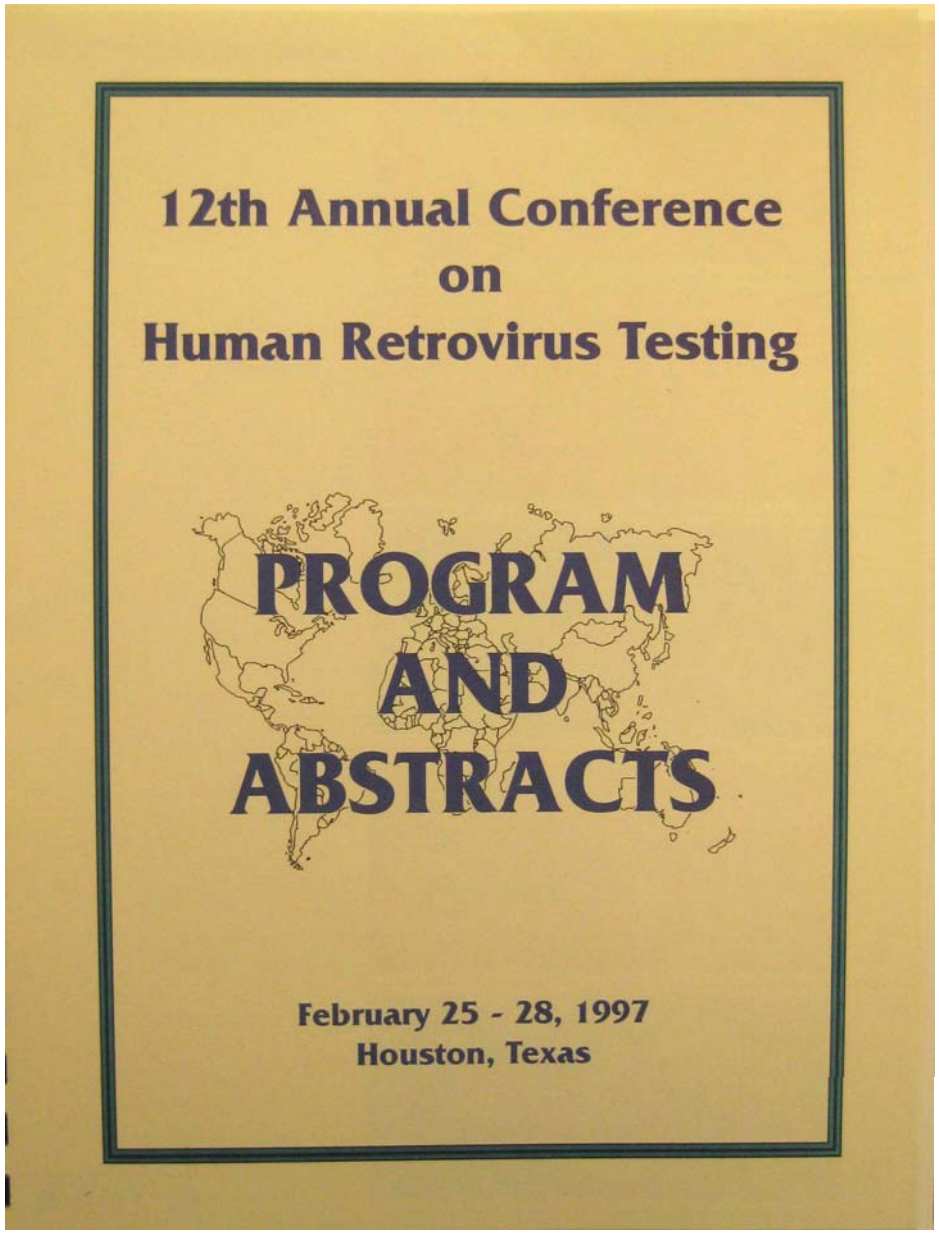
Screen
1996
HomeAccess
HIV-1 Home
Test System



- Alternative specimens
- p24 Antigen testing
- Clinical applications of PCR



- Home collection: impact on public health
- HIV-1 viral load assays
- Mfg demos:
  - RT PCR
  - Urine kit
  - Oral fluid device
  - Home collection

CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

March 27, 1998 / Vol. 47 / No. 11

MMWR™

MORBIDITY AND MORTALITY WEEKLY REPORT

Update: HIV Counseling and Testing Using Rapid Tests — United States, 1995

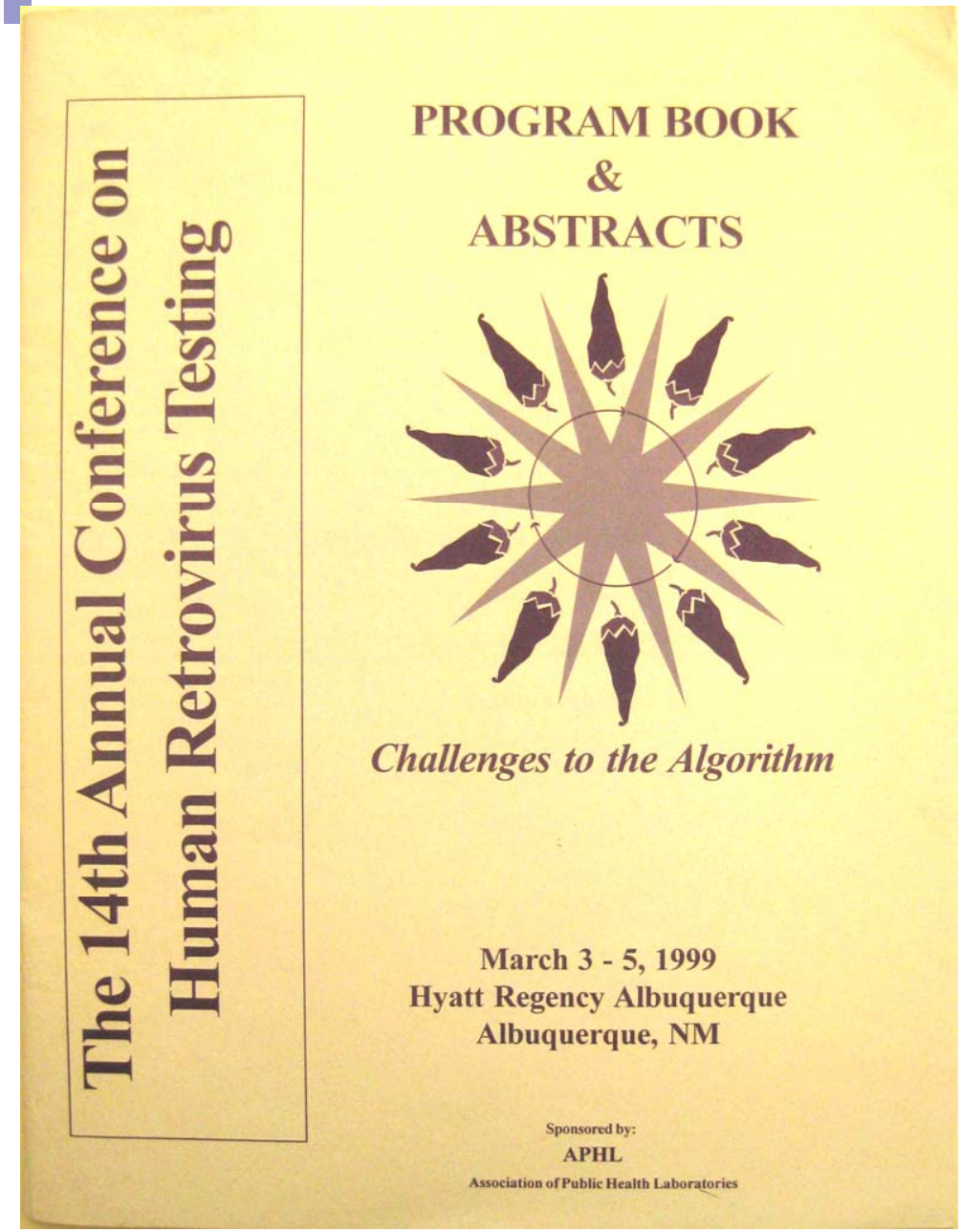
Approximately 25 million persons each year in the United States are tested for antibody to human immunodeficiency virus (HIV). Publicly funded counseling and testing (CT) programs conduct approximately 2.5 million of these tests each year. CT can have important prevention benefits (*1*); however, in 1995, 25% of persons testing HIV-positive and 33% of persons testing HIV-negative at publicly funded clinics did not return for their test results (*2*). Rapid tests to detect HIV antibody can be performed in an average of 10 minutes (*3*), enabling health-care providers to supply definitive

New Recommendation …and a Promise

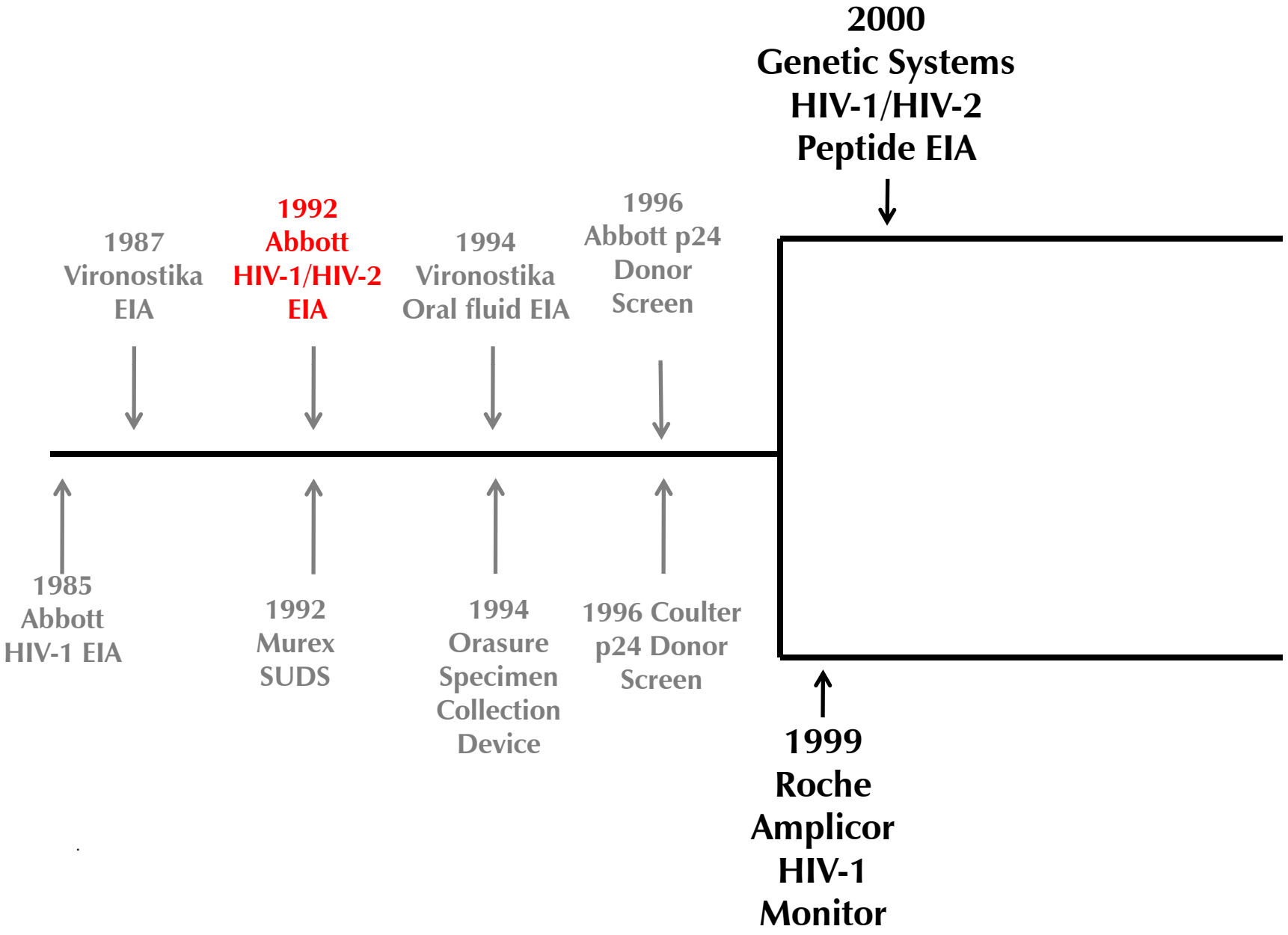
- Health-care providers should **provide preliminary positive test results** before confirmatory results are available in situations where tested persons benefit.

- When additional rapid tests become available for use in the United States, the **PHS will re-evaluate algorithms using specific combinations of two or more rapid tests** for screening and confirming HIV infection.

- Rapid Testing
  - Evaluation
  - Applications
- Challenges to the Testing Algorithm:
  - Repeat sample
  - Oral fluid
  - Nucleic Acid



- Testing Strategies
  - Rapid EIA
  - Double EIA
  - Western blot
- New Testing Strategy: detecting early HIV infection for prevention and for estimating incidence


2000
Genetic Systems
HIV-1/HIV-2
Peptide EIA
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Vironostika
EIA
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HIV-1/HIV-2
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Screen
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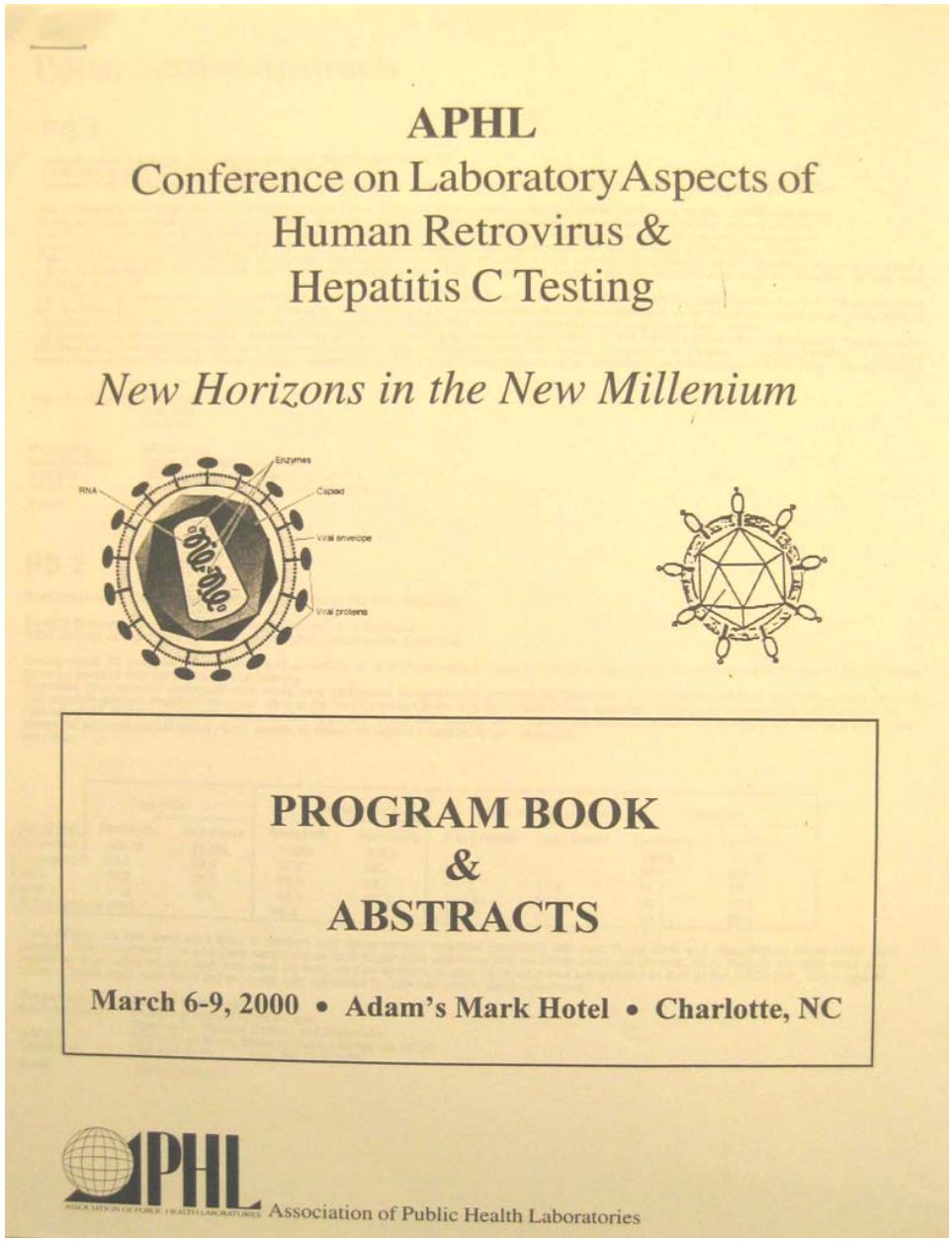
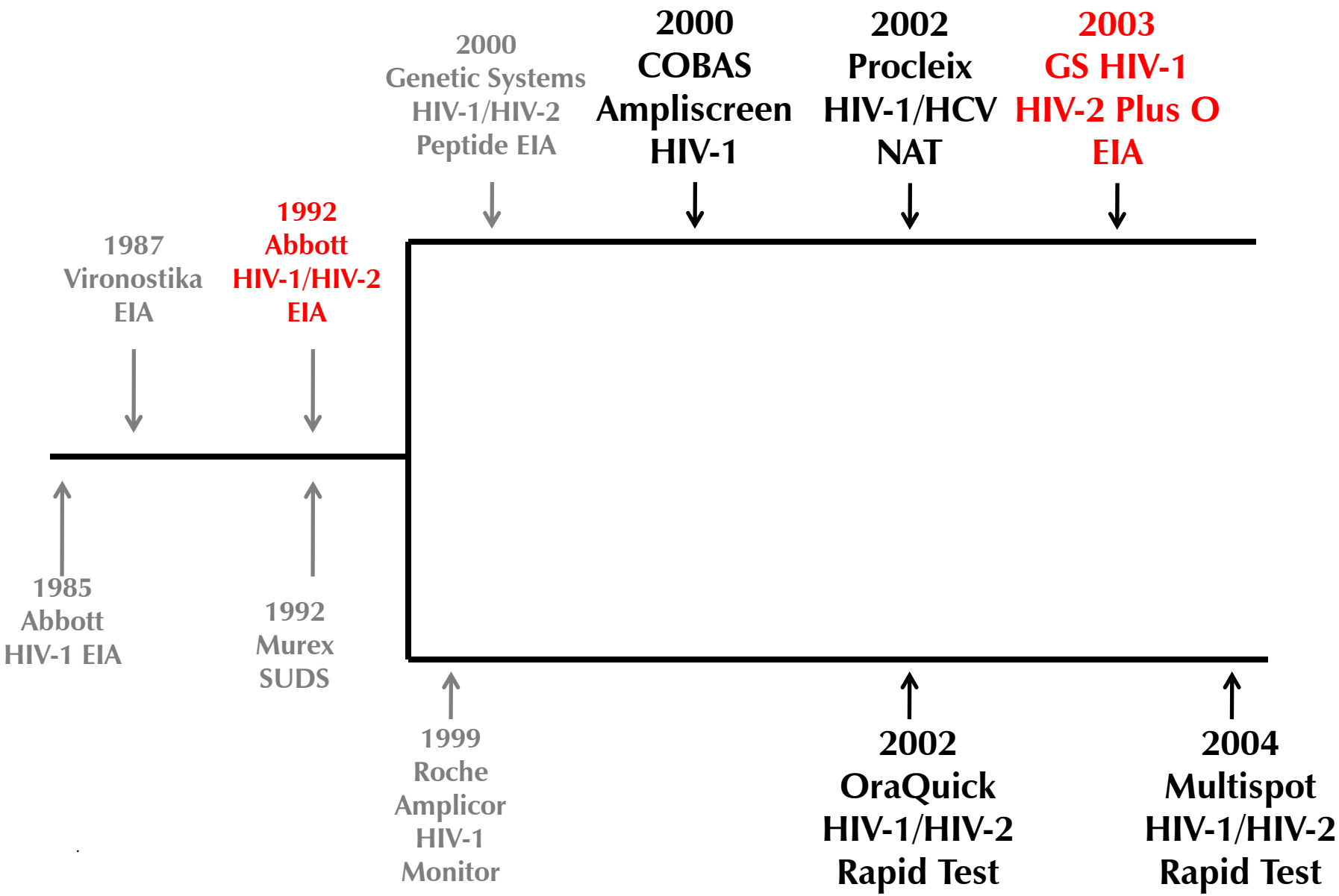
HIV-1 EIA
1992
Murex
SUDS
1994
Orasure
Specimen
Collection
Device
1996 Coulter
p24 Donor
Screen
1999
Roche
Amplicor
HIV-1
Monitor



- Preliminary evaluation of avidity index to distinguish incident vs prevalent infection
- Evaluation of the Inno-LIA in a testing algorithm for elimination of the Western blot


2000
Genetic Systems
HIV-1/HIV-2
Peptide EIA
2000
COBAS
Ampliscreen
HIV-1
2002
Procleix
HIV-1/HCV
NAT
2003
GS HIV-1
HIV-2 Plus O
EIA
1987
Vironostika
EIA
1992
Abbott
HIV-1/HIV-2
EIA
1985
Abbott
HIV-1 EIA
1992
Murex
SUDS
1999
Roche
Amplicor
HIV-1
Monitor
2002
OraQuick
HIV-1/HIV-2
Rapid Test
2004
Multispot
HIV-1/HIV-2
Rapid Test

DEPARTMENT OF HEALTH & HUMAN SERVICES

CMS

Clinical Laboratory Improvement Amendments (CLIA)

Verification of Performance Specifications
Brochure #2

What is it and how do I do it?

The CLIA regulations now include a requirement for verifying the performance specifications of unmodified, moderate complexity tests cleared or approved by the FDA.

Information to assist your laboratory in meeting this CLIA requirement!

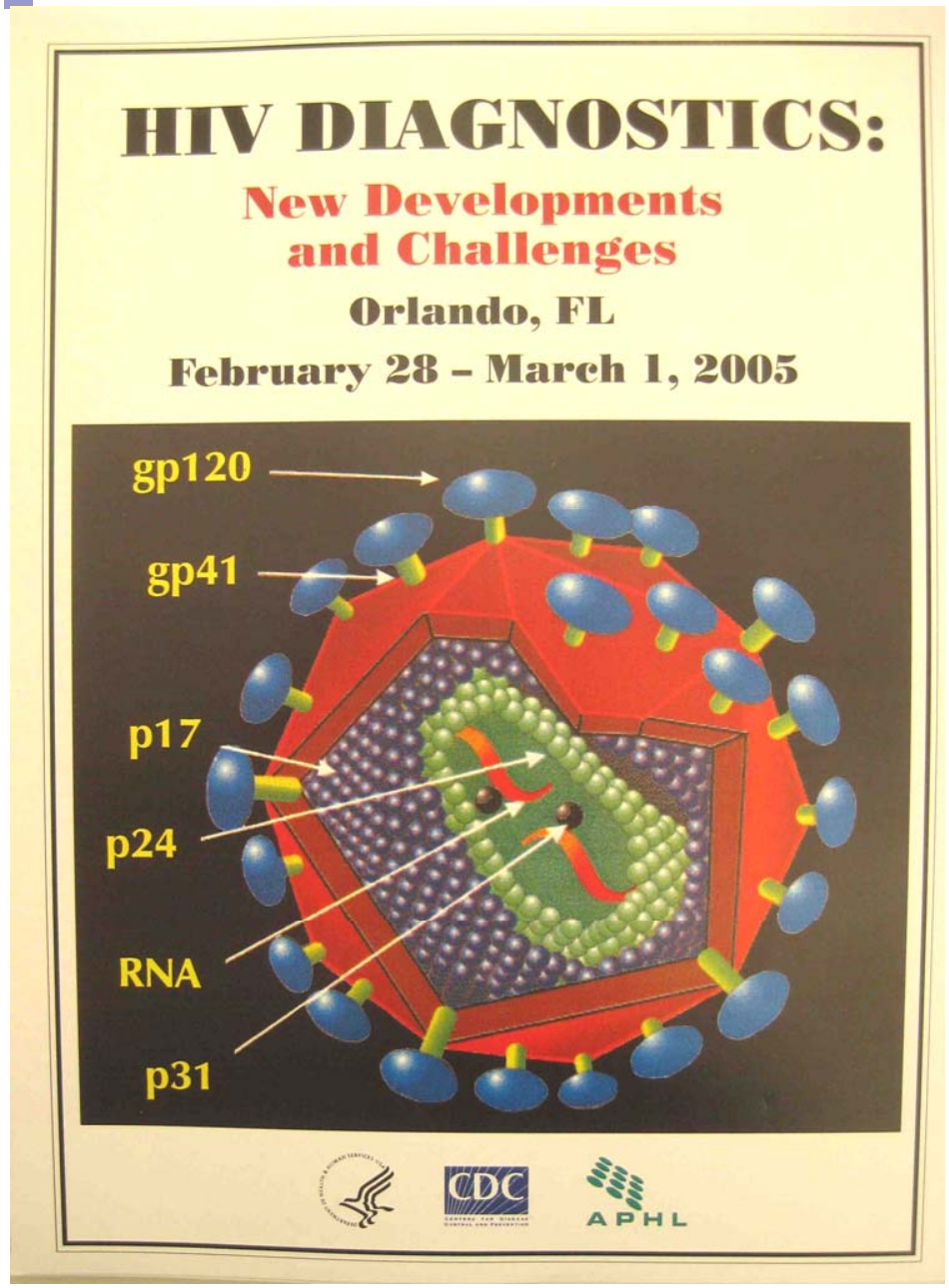
NOTE: On January 24, 2003, the Centers for Disease Control and Prevention (CDC) and the Centers for Medicare & Medicaid Services (CMS) published laboratory regulations (CLIA) that became effective April 24, 2003. A summary of the updated requirements pertaining to performance specification verification are included in this brochure. However, this brochure is not a legal document. The official CLIA program provisions are contained in the relevant law, regulations and rulings. For more complete information, you may access the regulations on the Internet at http://www.phppo.cdc.gov/CLIA/regs/toc.asp.

CDC

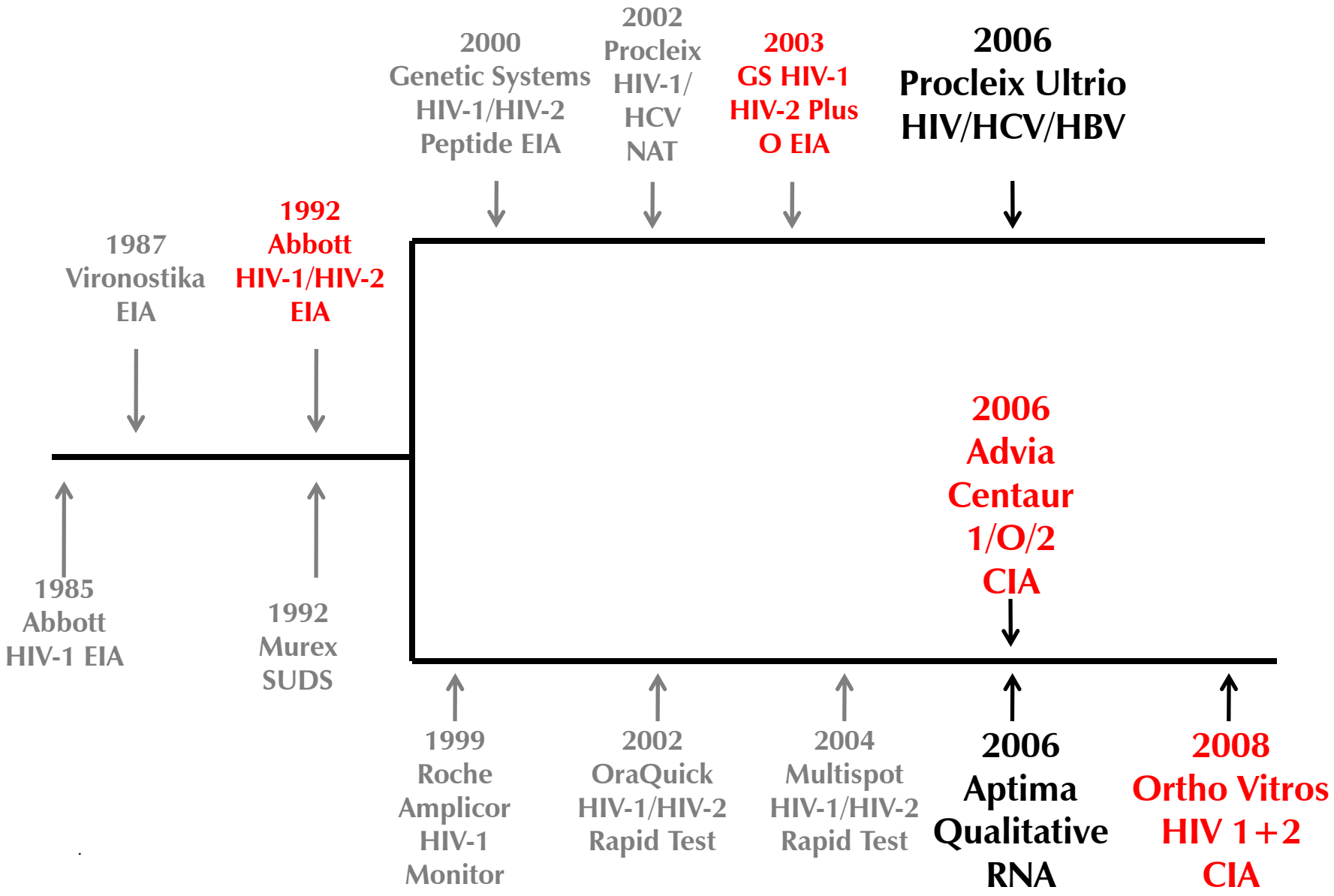
- Approved package insert:
  - Intended Use
  - Biological Principles
  - Restrictions
  - Warnings
  - Directions for Use
  - Interpretation
  - Limitations
  - Performance Characteristics

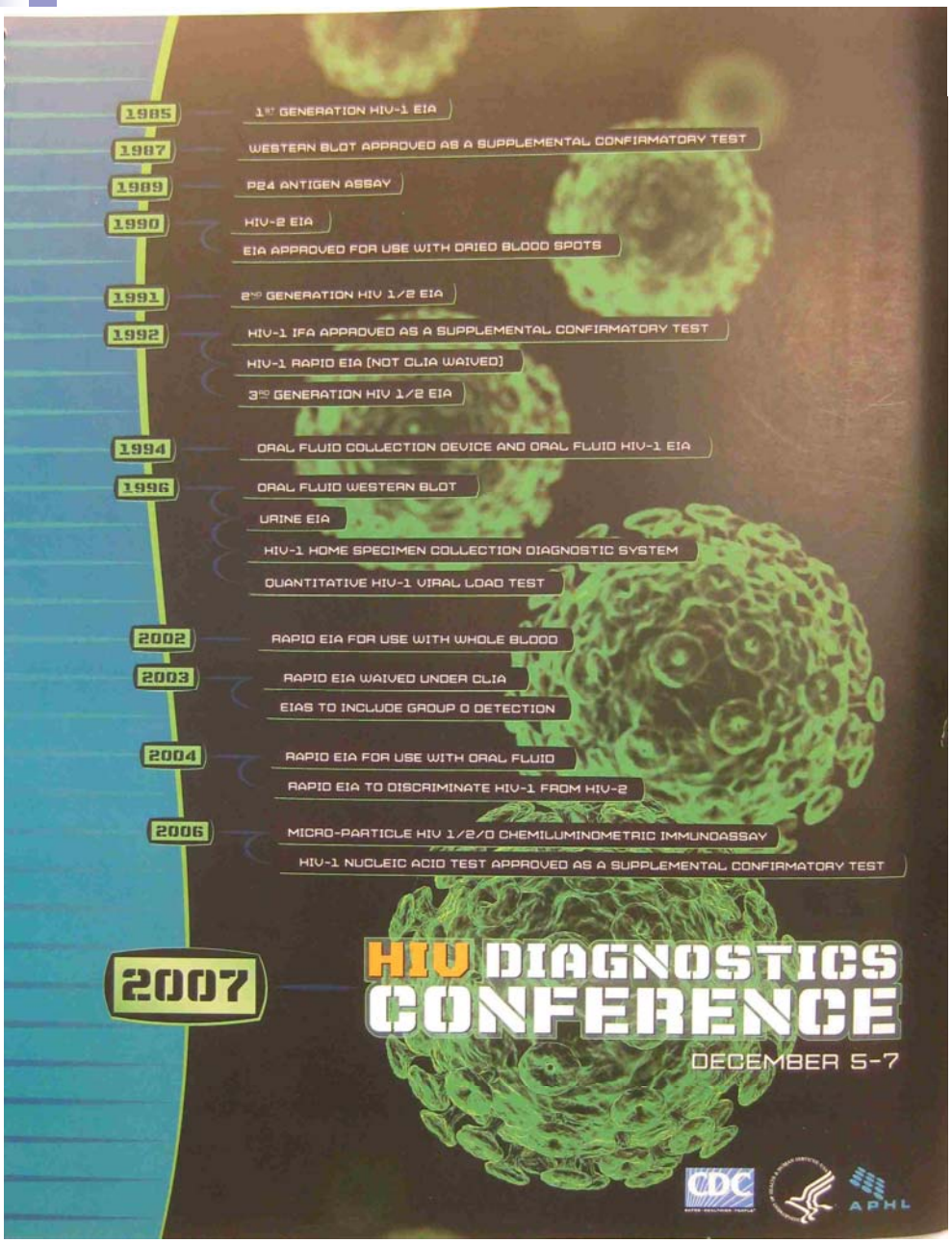
Change in Language

"This test is suitable for use in multi-test algorithms designed for statistical validation of rapid HIV test results. When multiple rapid HIV tests are available, this test should be used in appropriate multi-test algorithms."



- Comparing new EIAs with old stand-bys
- NAAT testing for acute infection
- Roll-out of rapid testing
- Options for confirmatory testing

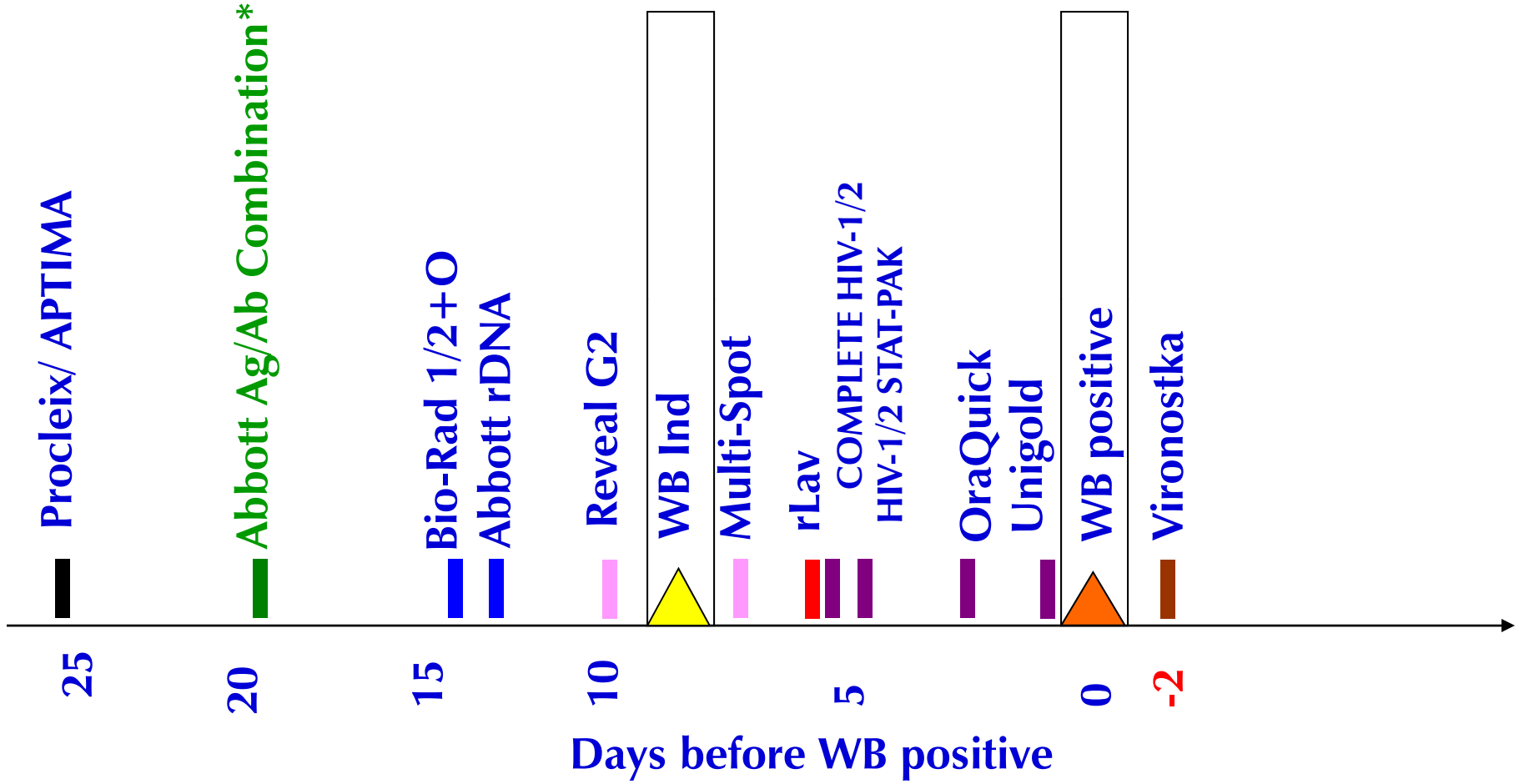

2000
Genetic Systems
HIV-1/HIV-2
Peptide EIA
2002
Procleix
HIV-1/
HCV
NAT
2003
GS HIV-1
HIV-2 Plus
O EIA
2006
Procleix Ultrio
HIV/HCV/HBV
1987
Vironostika
EIA
1992
Abbott
HIV-1/HIV-2
EIA
2006
Advia
Centaur
1/O/2
CIA
1985
Abbott
HIV-1 EIA
1992
Murex
SUDS
1999
Roche
Amplicor
HIV-1
Monitor
2002
OraQuick
HIV-1/HIV-2
Rapid Test
2004
Multispot
HIV-1/HIV-2
Rapid Test
2006
Aptima
Qualitative
RNA
2008
Ortho Vitros
HIV 1+2
CIA



- Random Access EIAs
- Acute HIV screening
- Challenges with the current algorithm
- Alternatives to the current algorithm

Sequence of Test Positivity Relative to WB

50 % Positive Cumulative Frequency



Modified from *Owen et al J Clin Micro 2008*

*** = not currently FDA approved**

Algorithm: Definition

- Overall sensitivity or specificity may be improved by using test combinations under one of two decision rules for resolving discordant results.
  - Assumes that errors in the tests are random and independent, but errors can be systematic, as with false-negative results in early infection.
  - Few testing strategies involve only a single test, but the costs of "confirmation" can be prohibitive.

Limitations of the Current Algorithm

- Antibody tests do not detect infection in ~ 10% of infected persons at highest risk of transmission
- Western blot confirmation is less sensitive during early infection than many widely used screening tests
- Delays inherent with centralized screening reduce the "effective sensitivity" because infected persons do not learn their test results

Limitations of Proposed Algorithms

- Most look like the traditional algorithm
  - Include Western blot
  - Additional (more expensive) tests if WB is negative
- Logistics of multiple POC tests can be daunting
- Cost and space requirements of multiple laboratory platforms is prohibitive
- Tests are usually repeated at care site anyway, with additional tests (e.g., viral load) for clinical staging and management

Problems with Regulatory Constraints

- Not responsive to clinical needs:
  - Preliminary results from rapid tests but not EIAs
  - Use of rapid tests on potentially exposed infants is restricted
  - Not feasible to accumulate sufficient numbers for required validations
- Delays the availability (and improvement) of state-of-the-art technology
- Cost discourages innovation

Goals for 2010 Conference

Goals for 2010 Conference

- Review the available evidence
- Identify the needs of different stakeholders
- Develop a menu for specific applications
- Begin consensus process for updating testing recommendations

Change

The only people who like change…

The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention