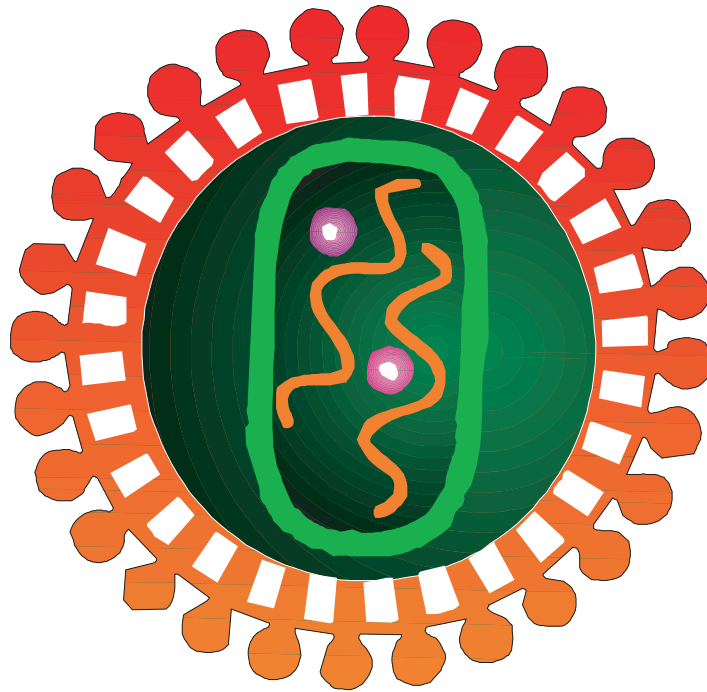


HIV Rapid Testing



Report of Sample Shipment Results, May 2004



DEPARTMENT OF HEALTH & HUMAN SERVICES



HIV-1 Rapid Testing MPEP May 2004 Report of Results

Report of the May 2004 Human Immunodeficiency Virus Type 1 (HIV-1) Rapid Testing (RT) Performance Evaluation Sample Results Provided by Participant Facilities in the Model Performance Evaluation Program (MPEP), Centers for Disease Control and Prevention (CDC).

Coordination of report production

The production of this report was coordinated in CDC by:

Coordinating Center
for Health Information and Services..... James S. Marks, M.D., M.P.H., Acting Director

Office of Public Health Partnerships..... Robert Martin, M.P.H., Dr. P.H., Acting Director

Division of Laboratory Services..... Thomas L. Hearn, Ph.D., Acting Director

Laboratory Practice Evaluation and
Genomics Branch..... Devery Howerton, Ph.D., Chief

Report content

The material in this report was developed and prepared by:

Model Performance Evaluation Program (MPEP)..... Laurina O. Williams, Ph.D., M.P.H.,
Co-Manager

..... G. David Cross, M.S., Co-Manager

MPEP HIV-1 Rapid Testing Performance Evaluation..... Leigh Inge Vaughan, B.A.,
HIV Rapid Testing Project Coordinator

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Contact information

Inquiries should be directed to the Model Performance Evaluation Program managers by calling (770) 488-8130 or (770) 488-8091.

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Donor Report

Table 1 Panel and Vial Designations, CDC Donor Bulk Numbers, CDC HIV Rapid Test Results and Donor HIV Status

Panel Letter	Vial Label	CDC Donor Bulk Number	CDC Test Result ^{1,3}	Donor HIV Status	Laboratory Interpretation ² and/or Results	
					Test Result	Interpretation
A	A1	15	Positive (W)	Infected	_____	_____
	A2	2	Positive (W)	Infected	_____	_____
	A3	7	Positive (S)	Infected	_____	_____
	A4	2	Positive (W)	Infected	_____	_____
	A5	7	Positive (S)	Infected	_____	_____
	A6	3	Negative	Uninfected	_____	_____
B	B1	7	Positive (S)	Infected	_____	_____
	B2	15	Positive (W)	Infected	_____	_____
	B3	3	Negative	Uninfected	_____	_____
	B4	2	Positive (W)	Infected	_____	_____
	B5	2	Positive (W)	Infected	_____	_____
	B6	7	Positive (S)	Infected	_____	_____
C	C1	7	Positive (S)	Infected	_____	_____
	C2	15	Positive (W)	Infected	_____	_____
	C3	2	Positive (W)	Infected	_____	_____
	C4	3	Negative	Uninfected	_____	_____
	C5	7	Positive (S)	Infected	_____	_____
	C6	2	Positive (W)	Infected	_____	_____
D	D1	15	Positive (W)	Infected	_____	_____
	D2	2	Positive (W)	Infected	_____	_____
	D3	3	Negative	Uninfected	_____	_____
	D4	7	Positive (S)	Infected	_____	_____
	D5	2	Positive (W)	Infected	_____	_____
	D6	7	Positive (S)	Infected	_____	_____

¹ The CDC result was obtained after pre-shipment testing for the presence of HIV-1 Antibody with all commercially available HIV Rapid Testing kits licensed by the Food and Drug Administration (FDA), as well as with selected FDA-licensed Enzyme Immunoassay (EIA) and Western Blot (WB) kits. All reactive samples were confirmed positive by WB. The CDC result is consistent with the manufacturers' criteria for interpretation of results.

² Laboratory Interpretation space (to be completed by participant laboratory) provided to facilitate comparison of participant laboratory result with CDC result.

³ Strong (S) and Weak (W) designations are based on qualitative observations of the colorimetric test results for reactive samples.

Report of Results: Overview

Purpose

This report describes the results of the second HIV Rapid Testing Model Performance Evaluation Program (HIV-RT MPEP) shipment. It represents a collection of data on HIV rapid tests done in the field by a variety of testing sites using different test kits on six plasma samples from four donors.

Sample shipment description

The plasma samples for the second challenge shipment of the HIV-RT MPEP were shipped in May 2004.

The six plasma samples from four donors included:

- a strong HIV-antibody positive sample (sent in duplicate),
 - an HIV-antibody negative sample, and
 - three samples derived from two seroconverters (weak positive samples), one sent in duplicate.
-

Response rate

The survey shipment was sent to 431 testing sites within and outside of the United States. Responses were received from 364 of the testing sites (84.5%). Of those who responded:

- 308 (84.6%) were from U.S. testing sites, and
- 56 (15.4%) were from non-U.S. testing sites.

Note: Thirteen testing sites submitted multiple responses, indicating the use of from one to seven different test kits, so that the total number of responses was 388.

Description of challenge samples

All plasma samples were single bleeds drawn from individual donors. The resulting plasma was tested to determine HIV-1 reactivity. The samples were processed as follows:

- All donor samples were clarified prior to dispensing and tested to ensure they were free of bacterial contamination.
 - HIV-1 antibody-positive plasma samples were heat-treated at 56°C for 60 minutes to inactivate infectious agents; HIV antibody-negative samples were not heat treated.
 - The serostatus of both positive and negative samples was confirmed by all FDA-approved rapid HIV antibody tests, as well as selected FDA-approved EIA and Western blot kits.
 - Negative samples were negative for HIV-1 antigen using an FDA-approved monoclonal antibody based p24 antigen test.
-

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Report of Results: Overview, Continued

Description of challenge samples (continued)

- Positive samples were selected using the following criteria:
 - reactive by the Genetic Systems rLAV enzyme immunoassay (EIA) kit at a signal-to-cutoff ratio between 3 and 5 for the seroconverter samples and greater than 5 for the strong positive samples, and
 - positive by the APHL/CDC interpretive criteria for Western blot (WB) patterns.
 - The strong positive sample and one of the seroconverter samples were included in the shipment in duplicate.
-

Summary of findings

The major findings described in this report include the following:

1. Performance results grouped by positive, weak positive, negative and all samples are summarized below:

Sample Type	Overall Accuracy *	Range (by kit)
Positive (strong + weak)	99.3% (1909/1922)	97.1% to 100%
Positive (weak only)	99.4% (1145/1152)	97.1% to 100%
Negative	97.6% (360/369)	95.8% to 100%
All samples	99.0% (2269/2291)	97.1% to 100%

* Accuracy is defined as the percentage of correct results

2. Most (77%, 10/13) of the incorrect results reported on positive challenge samples were reported by two testing sites (see Tables 4 and 5 for complete results):
 - Five out of the seven false negative results were reported by a single testing site using Abbott Determine HIV-1/2.
 - Five out of the six indeterminate interpretations for positive samples were reported by a single testing site using the OraQuick test.
3. The incorrect results on negative challenges were scattered among sites using different kits.
 - Three out of the six false positive results were reported by three different sites using the OraQuick test.
 - The three indeterminate interpretations on negative samples were reported by three different testing sites using the MedMira Reveal test.
4. Other incorrect results were reported by testing sites using the OraQuick test, the MedMira Reveal test, or the Abbott Determine test kits. These were apparently random and could have been a function of the testing environment. This could also be due to the fact that many more observations were reported using these kits since they were the most commonly used.
5. A total of 56.5% (218/386) of respondents reported normally running some type of external quality control (controls not included in the test kit) when performing HIV rapid tests.

Demographics

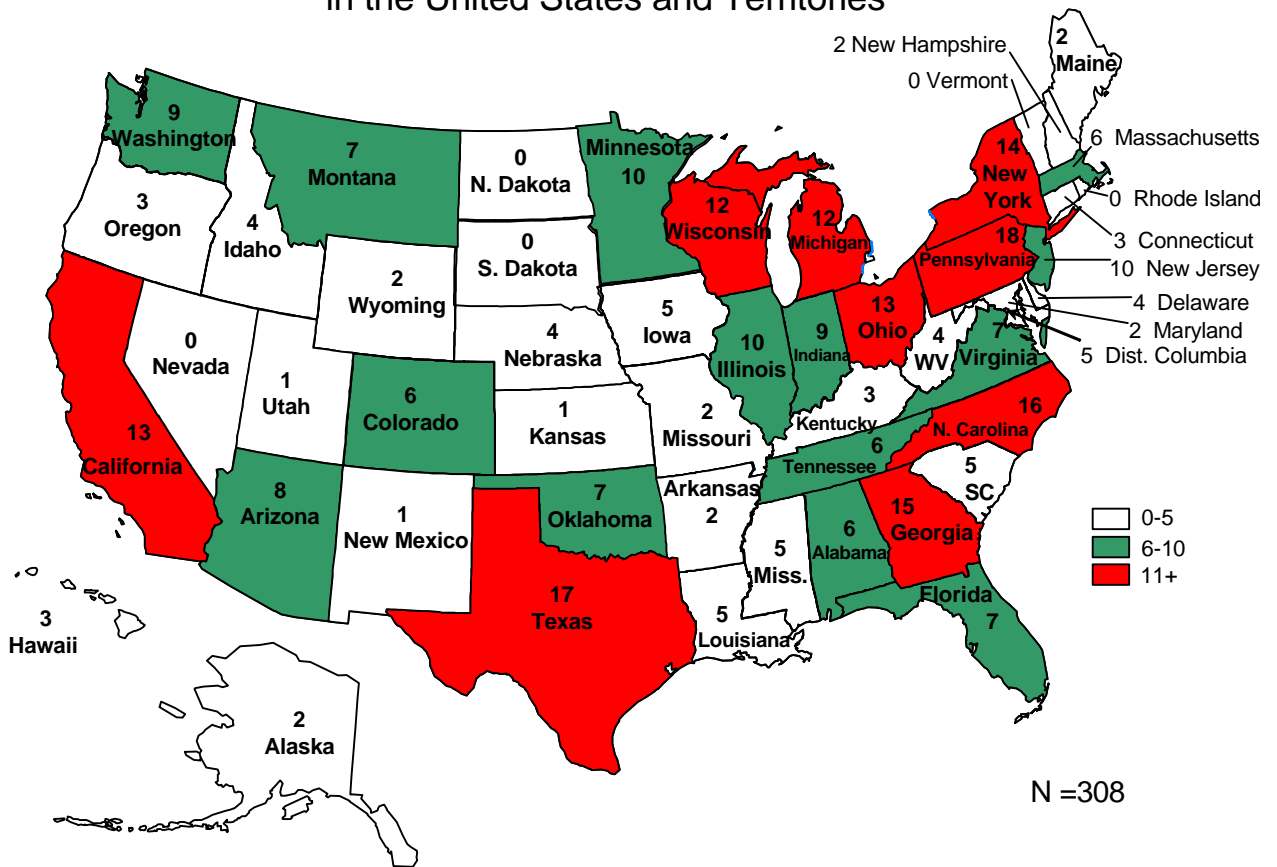
Overview

The total number of different testing sites (foreign and domestic) submitting results was 364. Of these:

- The 308 United States (domestic) testing sites are depicted in **Figure 1**.
- The 56 foreign testing sites are listed in **Table 2**.
- The types of testing site participants responding are depicted in **Figure 2a** and in **Figure 2b**;
 - hospital testing sites predominated.
 - generally, the number of participants in most states increased from the previous shipment.

Figure 1

Number of MPEP HIV Rapid Testing Laboratories Returning Results in the United States and Territories



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Demographics, Continued

The following table shows the breakdown of participants outside the United States, for this MPEP shipment.

Table 2

Country	Number	Country	Number
Australia	2	Hungary	1
Bahamas	1	India	1
Bangladesh	1	Indonesia	1
Belgium	1	Malawi	1
Botswana	3	Malaysia	1
Brazil	1	Myanmar	1
Burkina Faso	1	Niger	1
Burundi	1	Nigeria	2
Cameroon	1	Pakistan	1
Canada	1	Panama	1
Central African Republic	1	Philippines	2
Congo	1	Republic of Singapore	1
Cote d'Ivoire	2	Republic of Yemen	1
Dominican Republic	1	Slovakia	1
Egypt	2	South Korea	1
Eritrea	1	Taiwan	1
Ethiopia	1	Tanzania	5
Ghana	1	Thailand	5
Guyana	1	Uganda	1
Honduras	2	Zambia	1

N = 56

Continued on next page

Demographics, Continued

The types of testing sites for all participants in the current survey are shown in Figure 2a. Figure 2b shows the numbers of each type of testing site, by U.S. and non-U.S. participants.

Figure 2a:

Type of testing sites

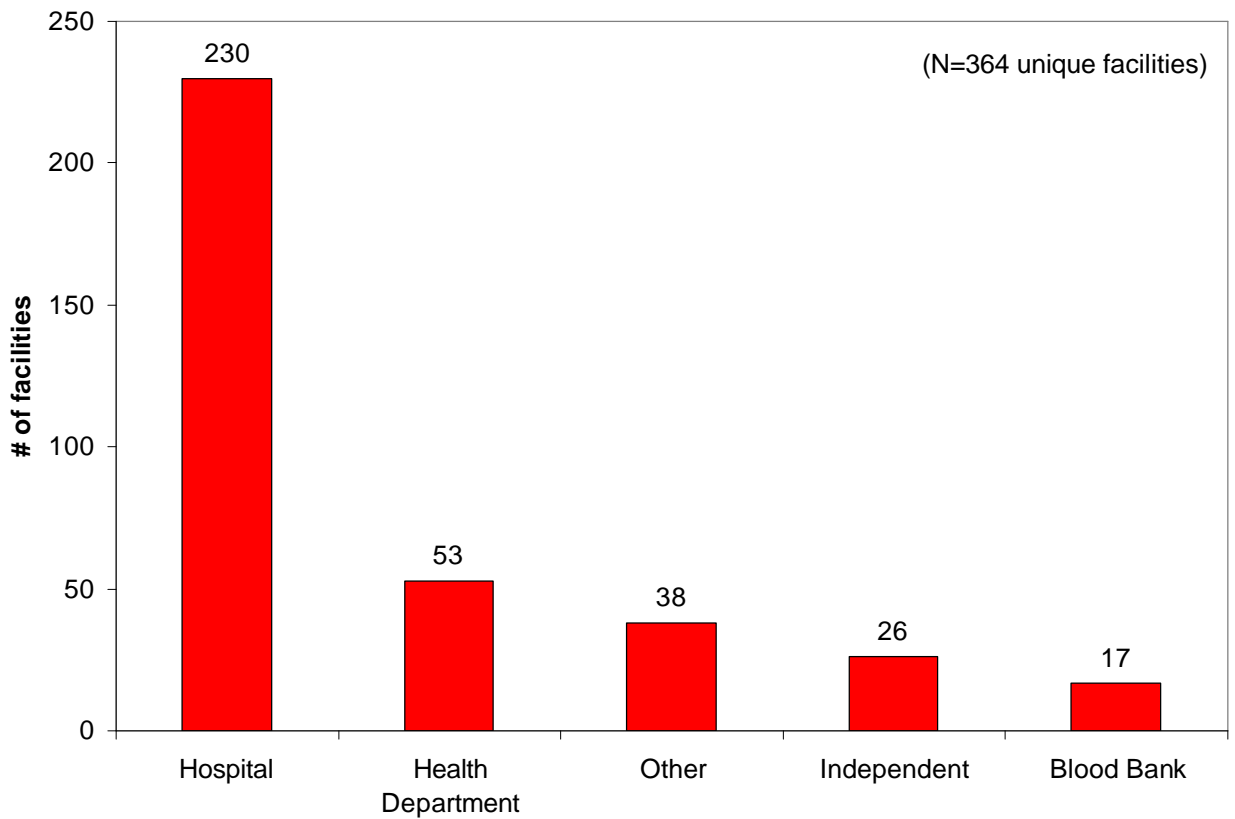
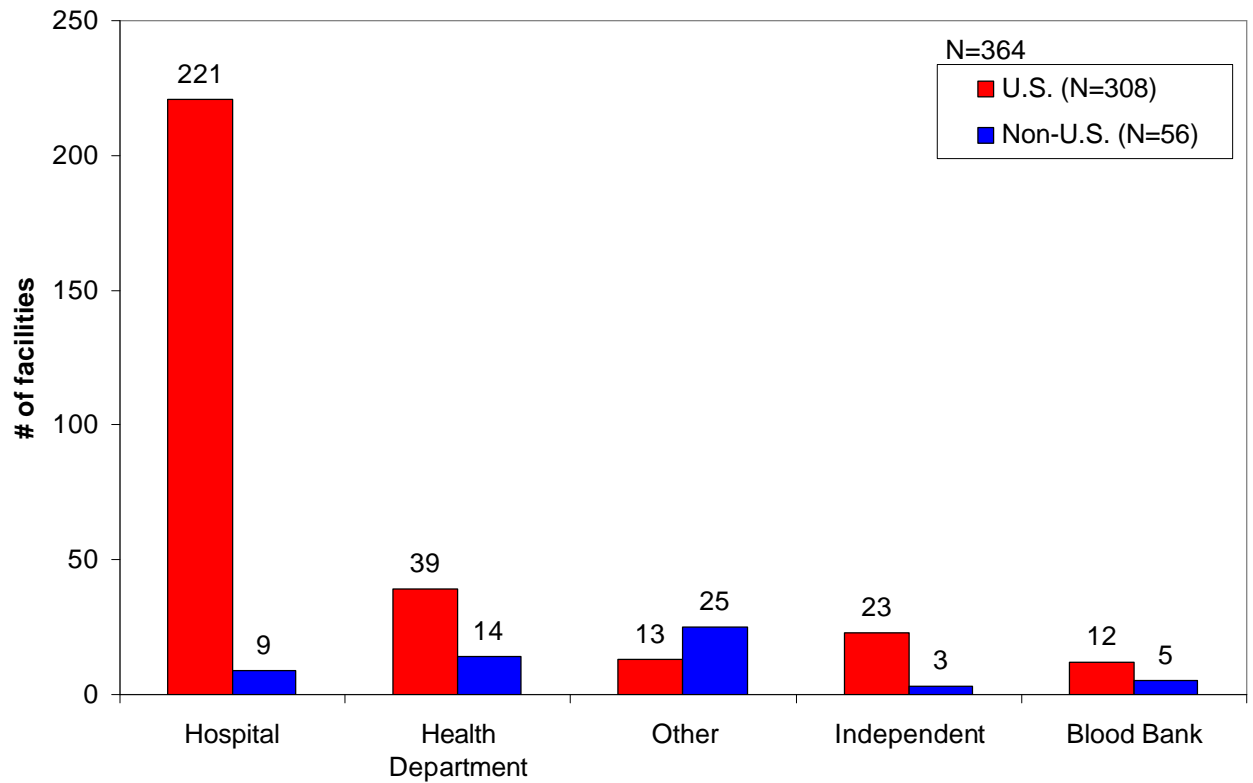


Figure 2b:

Type of testing sites, by U.S. and non-U.S.



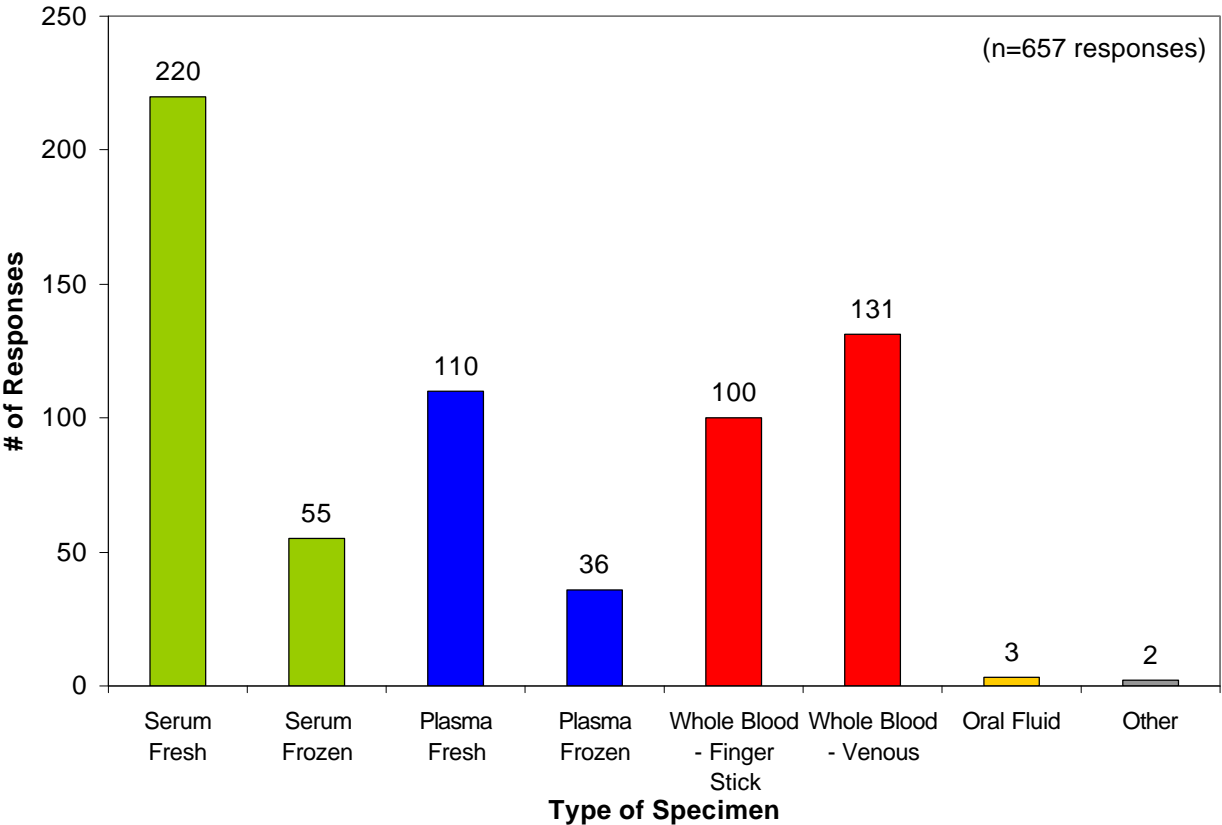
Specimen Types Used by Participants

Participants were asked what type of specimens they normally use for HIV rapid tests.

Overview

- Most specimens typically used for HIV rapid testing were either serum or plasma, as shown in **Figure 3**.
- Testing sites could report using more than one specimen type.
- Testing sites that used the whole-blood finger stick specimens typically used the OraQuick Rapid HIV-1 Antibody Test testing method (90/100).
- Three U.S. labs reported using oral fluid specimens with the OraQuick test.

Figure 3:
specimen
types



Kit Types Used by Participants

Overview

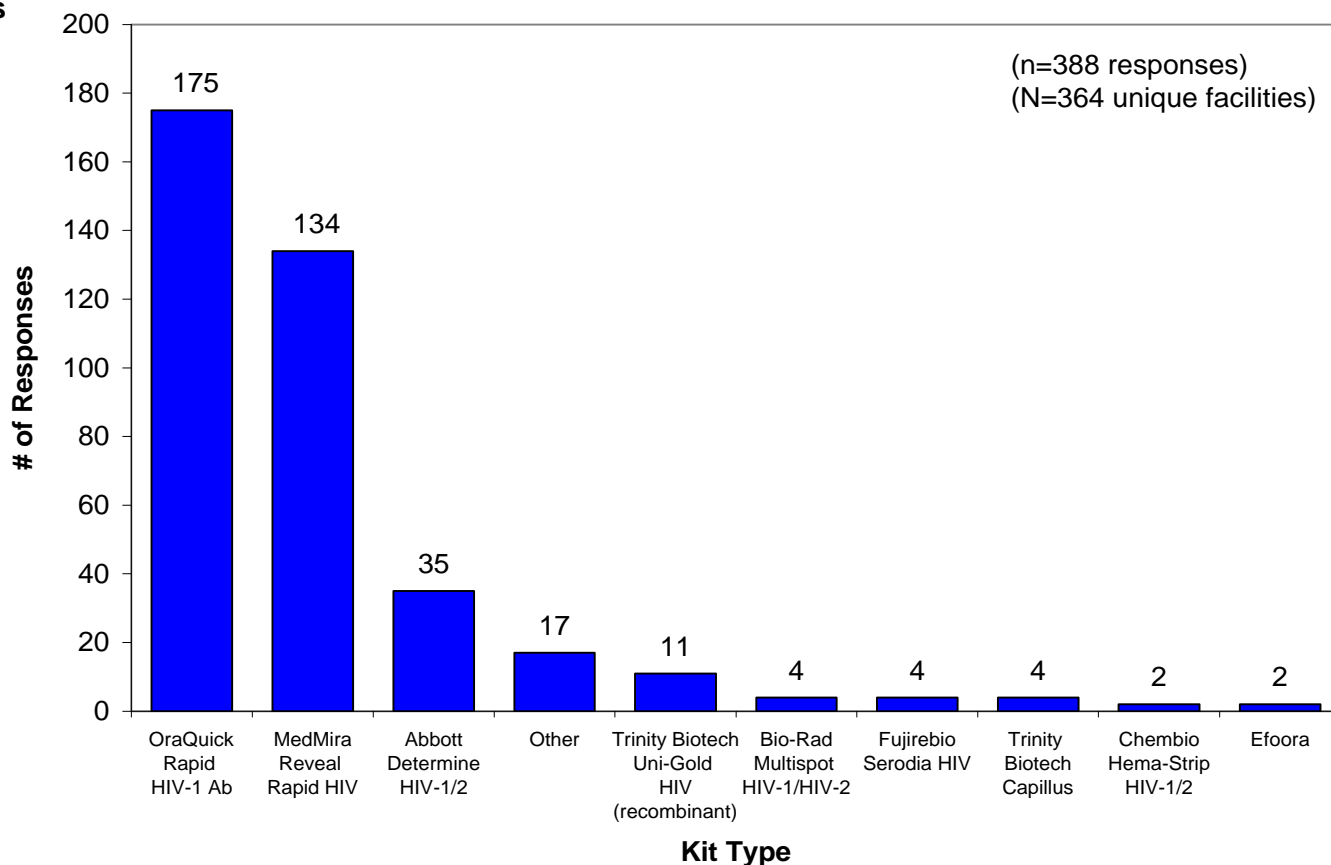
This section describes the kit types used by participants. The predominant kit types used were:

- OraQuick Rapid HIV-1 Ab (45.1%, 175/388),
- MedMira Reveal Rapid HIV (34.5%, 134/388), and
- Abbott Determine HIV-1/2 (9.0%, 35/388) as shown in **Figure 4**.
- Kit usage by lab type is shown in **Figure 5**.
- U.S. laboratories typically used the three FDA-approved kit types (96.9%, 312/322). These kits are:
 - MedMira Reveal Rapid HIV-1 Antibody Test,
 - OraSure OraQuick Rapid HIV-1 Antibody Test, and
 - Trinity Biotech Uni-Gold Recombigen HIV test.

Notes:

1. Test kits for which less than three interpretations were reported were included in the “other” category.
2. The Abbott/Murex SUDS test is no longer on the market.

Figure 4:
kit types



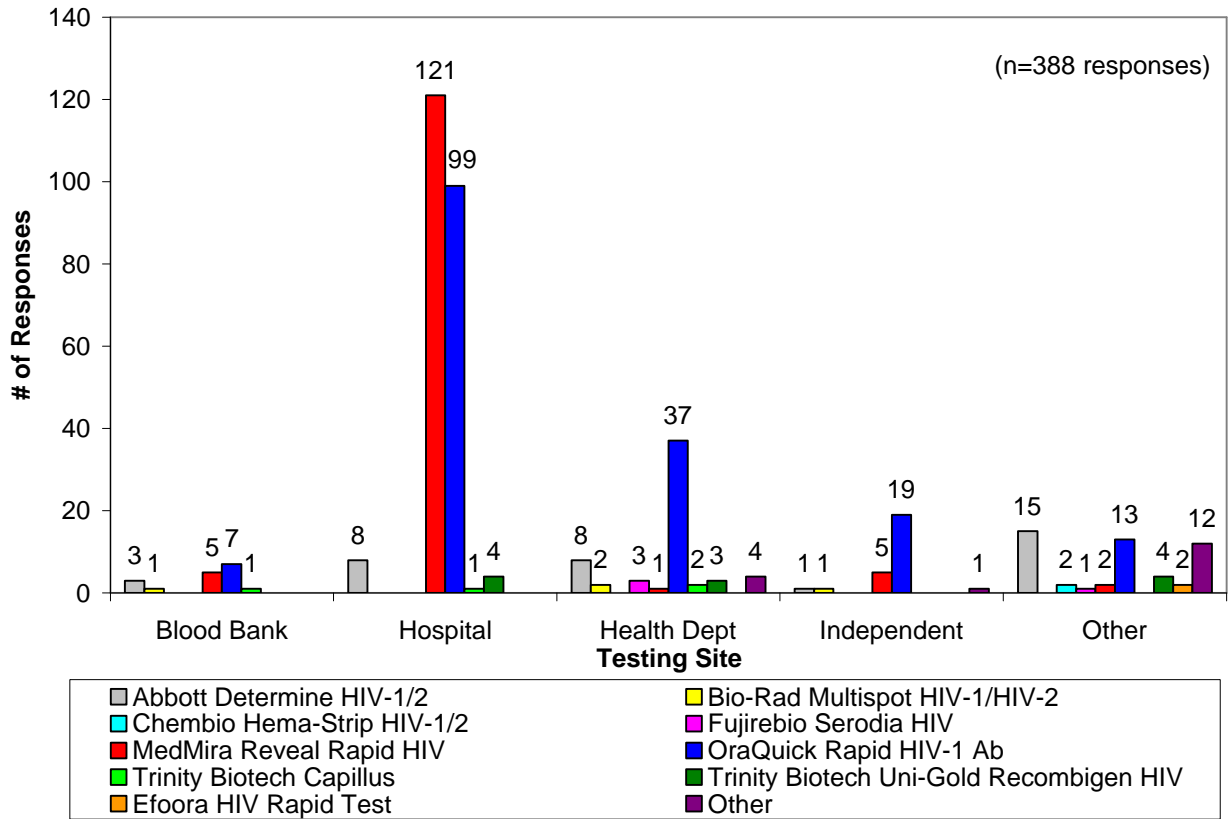
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Kit Types Used by Participants, Continued

The following figure illustrates the usage of the kit types, by type of testing site.

Figure 5:

Testing site by kit type



Performance Results

Overview

The following figures and tables refer to the accuracy (% of correct responses out of the total number of responses) for this HIV-RT shipment.

- The overall accuracy for HIV-antibody positive samples was 99.3% (range 97.1% to 100%).
- The percentages of all reported positive and negative results are shown, by donor, in **Table 3**.
- The results for all participants by kit type are shown in **Table 4**.
- The overall accuracy for the weak positive donors (Donors 2, 2 duplicate, and donor 15) was 99.4% (97.1-100%) as shown in **Table 5**.
- Five out of the seven false negative results were reported by a single testing site using Abbott Determine HIV-1/2.
- Out of six false positive results, four were reported by hospital testing sites and one each by an independent and an “other” testing site using FDA- approved test kits. This observation simply may reflect the demographics of the participants.

The following table gives the percent of positive reported results for donors 2, 7, and 15 (the positive donors) and the percent of negative reported results for donor 3 (the negative donor).

Table 3

Donor Number	Reactive/Positive			Non-Reactive/Negative		
	# of Participants	# of Results	% Positive	# of Participants	# of Results	% Negative
2	361	768	99.5%	n/a	n/a	n/a
3	n/a	n/a	n/a	345	369	97.6%
7	361	770	99.2%	n/a	n/a	n/a
15	361	384	99.2%	n/a	n/a	n/a

Continued on next page

Performance Results, Continued

Table 4: Results for all samples (Donors 2, 3, 7 and 15)

Kit Type	OraQuick Rapid HIV-1 Ab (1034/1044) N=173 Participants	MedMira Reveal Rapid HIV (771/777) N=132 Participants	Abbott Determine HIV-1/2 (204/210) N=34 Participants	Other Kit Type, Specified (100/100) N=15 Participants	Trinity Biotech Uni-Gold Recombigen HIV (64/64) N=10 Participants	Fujirebio Serodia HIV (24/24) N=4 Participants	Bio-Rad Multispot HIV-1/HIV-2 (24/24) N=4 Participants	Trinity Biotech Capillus (24/24) N=4 Participants	Chembio Hema-Strip HIV-1/2 (12/12) N=2 Participants	Efoora HIV Rapid Test (12/12) N=2 Participants	Total (2269/2291)
No. of Determinations	1044	777	210	100	64	24	24	24	12	12	2291
Correct Positive Results	863	658	170	85	53	20	20	20	10	10	1909
False Negative Results	1	1	5								7
Indeterminates [Positive Samples]	6										6
Correct Negative Results	171	113	34	15	11	4	4	4	2	2	360
False Positive Results	3	2	1								6
Indeterminates [Negative Samples]		3									3
Accuracy [% of Correct Results]	99.04%	99.23%	97.14%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	99.04%

Table 5: Results for weak positives (Donors 2 and 15)

Kit Type	OraQuick Rapid HIV-1 Ab (518/522) N=173 Participants	MedMira Reveal Rapid HIV (395/395) N=132 Participants	Abbott Determine HIV-1/2 (102/105) N=34 Participants	Other Kit Type, Specified (51/51) N=15 Participants	Trinity Biotech Uni-Gold Recombigen HIV (31/31) N=10 Participants	Bio-Rad Multispot HIV-1/HIV-2 (12/12) N=4 Participants	Trinity Biotech Capillus (12/12) N=4 Participants	Fujirebio Serodia HIV (12/12) N=4 Participants	Chembio Hema-Strip HIV-1/2 (6/6) N=2 Participants	Efoora HIV Rapid Test (6/6) N=2 Participants	Total (1145/1152)
No. of Determinations	522	395	105	51	31	12	12	12	6	6	1152
Correct Positive Results	518	395	102	51	31	12	12	12	6	6	1145
False Negative Results			3								3
Indeterminates [Positive Samples]	4										4
Accuracy [% of Correct Results]	99.23%	100.00%	97.14%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	100.00%	99.39%

Quality Control

Overview

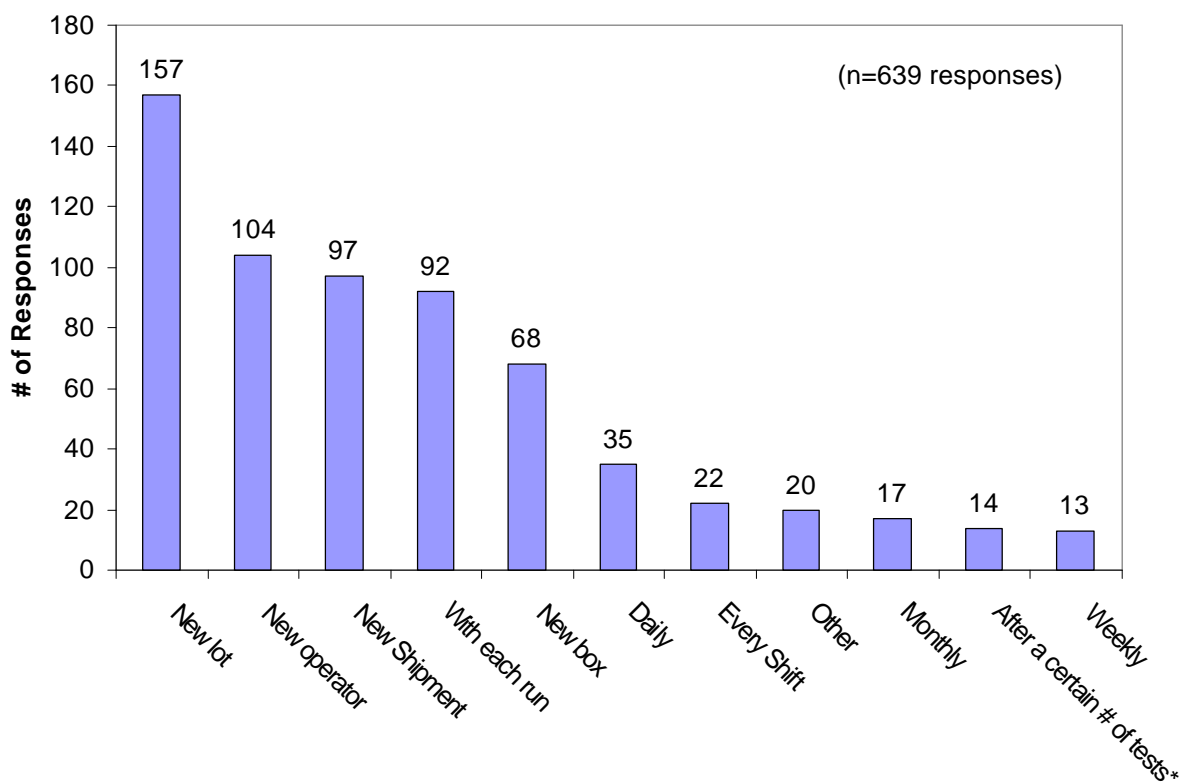
Testing sites were asked if they used external quality control, i.e., controls not included in the test kit, when performing HIV rapid tests.

- Approximately half (56.5%; 218/386) of the responses indicated the use of external quality control. This proportion is similar to that observed in the previous shipment.
- The sources of the external controls tended to be either:
 - controls obtained from the same manufacturer (73.9%; 161/218) or
 - in-house controls (12.8%; 28/218).
- The frequency of use of external quality control materials is shown in **Figure 6**.

Notes:

1. Testing sites could provide more than one answer.
 2. Testing sites reporting the use of multiple kit types answered the question separately for each kit type.
-

Figure 6:
Frequency of use of external controls



* The most frequent response was 25 tests (Range 1-60)

Confirmatory Testing

Overview

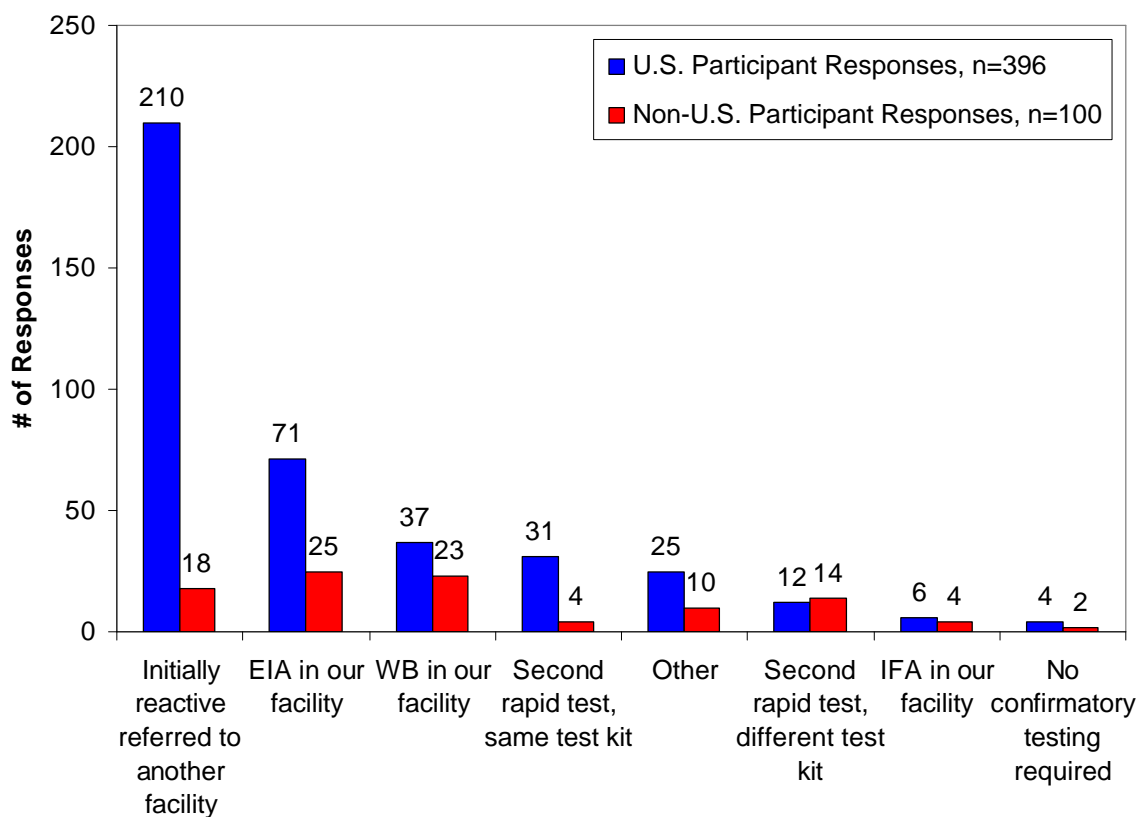
The types of confirmatory testing reported by laboratories varied as shown in **Figure 7**.

Note: Testing sites could answer by indicating more than one confirmatory test.

- Many participants (324/496; 65.3%) reported either
 - sending the reactive (preliminary positive) specimens to another facility (228/496; 46.0%), or
 - performing EIA alone or in combination with other tests (19.4%; 96/496).
- Several participants (61/496; 12.3%) reported using a second rapid test for confirmatory testing.
 - Of these, 25/61 (41.0%) reported using a second rapid test with no other type of confirmatory testing.

Six participants reported that no confirmatory testing was required prior to reporting a positive result. The circumstances surrounding the use of HIV rapid tests without confirmatory testing are unclear.

Figure 7:
Types of confirmatory testing



Conclusions and Discussion

Overall performance

Overall, testing sites performed well in this MPEP shipment.

- Overall accuracy (% of correct results) for all samples, by all sites with all kit types, was 99.04% (2269/2291).
 - Most of the incorrect results were reported by two sites on positive challenges.
 - All incorrect results were reported by testing sites using the three predominant kit types. This could be due to
 - the fact that many more results were reported by sites using these kits than for sites using any other kit types, thus increasing the chances of observing errors with the predominant kits,
 - varying conditions in sites using these kits, or
 - other factors that were not measured in this survey.
-

Confirmatory testing

This survey included a question regarding confirmatory testing.

- The intent was to measure whether or not the testing sites require that confirmatory testing be done on preliminary positive (reactive) samples before reporting a final “positive” result.
- Participants reported a variety of schemes for doing confirmatory testing.
- Some U.S. labs are apparently using algorithms other than the WB or IFA as recommended by CDC.

U.S. participants are reminded that HIV rapid tests are screening tests and reactive results are considered to be “preliminary positives” that must be confirmed by either a Western blot or IFA test (1,3) .

Guidelines

Testing sites should follow appropriate guidelines with respect to performing HIV rapid tests and reporting results (1, 2, 3). Attention to recognized guidelines and good testing practices is crucial to patient safety and to the delivery of accurate test results.

For example, the CDC has published quality assurance guidelines for testing using the OraQuick rapid test. (1) These guidelines:

- stress that a testing site must have an adequate quality assurance (QA) program in place before offering OraQuick testing,
 - provide recommendations for a comprehensive QA program,
 - include recommendations regarding test verification to ensure that the test kits work as expected in a given testing environment,
-

Continued on next page

Conclusions and Discussion, Continued

Guidelines (continued)

- encourage participation in an external quality assessment program, such as the MPEP, and
- address the logistics for providing confirmatory testing for preliminary positive (reactive) results (1, 3).

These guidelines can be applied to other HIV rapid tests performed in U.S. sites.

Discussion references

1. Quality Assurance Guidelines for Testing Using the OraQuick Rapid HIV-1 Antibody Test. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. 2003.
http://www.cdc.gov/hiv/rapid_testing/materials/QA-Guide.htm
 2. CDC. Revised guidelines for HIV counseling, testing, and referral. MMWR 2001; 50(No. RR-19):1-57.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5019a1.htm>
 3. Notice to Readers: Protocols for Confirmation of Reactive Rapid HIV Tests. MMWR 2004; 53(10): 221-222.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5310a7.htm>
 4. Notice to Readers: Approval of a New Rapid Test for HIV Antibody. MMWR 2002; 51(46): 1051-1052.
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5146a5.htm>
-

Topical Issues in HIV Rapid Testing

Introduction

The HIV Rapid Testing Model Performance Evaluation Program (HIV-RT MPEP) strives to be a resource for facilities using HIV rapid testing kits. This section of the HIV-RT MPEP Report of Results, “Topical Issues in HIV Rapid Testing,” is intended to address that part of our mission. We are including:

- **Frequently Asked Questions (FAQs)** by HIV RT MPEP participants to share with all participants our responses to some recent queries,
 - **CDC websites** to provide participants with access to timely relevant material published online by the CDC, and
 - **HIV Rapid Testing Resources** as a link to long-term references.
-

FAQs

This section provides answers to some of our participants’ frequently asked questions (FAQs).

Q: The MPEP letter that came with the HIV rapid testing samples says that your samples are previously frozen plasma, but we use whole blood for our HIV rapid testing. Can we use your samples?

A: Yes. We have verified that our samples perform well with all [FDA](#)³ approved HIV rapid testing kits, including those that use whole blood. If your kit requires special steps for using previously frozen plasma (see your kit’s package insert) then these steps should be taken prior to using our samples.

Q: What protocol should we follow for testing MPEP HIV rapid testing samples?

A: Our samples should be tested according to the methodology described by the manufacturer in your HIV rapid testing kit’s package insert. Specific questions about technique should be addressed to the manufacturer’s technical support area.

Q: We need more control sample material for training purposes. Can you supply us with extra sample material so we can practice with it?

A: No. While we recognize that extra sample volume (i.e. not used to do the test for the survey shipment) in our current panels has been, and will be, used effectively as material for training/practice purposes, we do not have sufficient “left-over” sample material to distribute specifically for those purposes. However, similar material is available from commercial sources.

Continued on next page

Topical Issues in HIV Rapid Testing, Continued

CDC websites *Quick Facts: Rapid Testing April 2003 - April 2004*
http://www.cdc.gov/hiv/rapid_testing/materials/QuickFact_April2004.htm

MMWR:
Notice to Readers: Protocols for Confirmation of Reactive Rapid HIV Tests
<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5310a7.htm>

Quality Assurance Guidelines for Testing Using the OraQuick® Rapid HIV-1 Antibody Test
http://www.cdc.gov/hiv/rapid_testing/materials/QA-Guide.htm

HIV rapid testing resources

1. HIV Rapid Testing MPEP website
<http://www.phppo.cdc.gov/mpep/HIV-1rt.aspx>
 2. Model Performance Evaluation Program (MPEP) Home page
<http://www.phppo.cdc.gov/mpep/>
 3. Food and Drug Administration (FDA) Licensed / Approved HIV, HTLV and Hepatitis Tests
<http://www.fda.gov/cber/products/testkits.htm>
 4. The National Center for HIV, STD, and TB Prevention (NCHSTP) Divisions of HIV/AIDS Prevention (DHAP) website
<http://www.cdc.gov/hiv/dhap.htm>
 5. The National Center for HIV, STD, and TB Prevention (NCHSTP) Home page
<http://www.cdc.gov/nchstp/od/nchstp.html>
 6. The World Health Organization
<http://www.who.int/en/>
-