

SENSITIVITY AND SPECIFICITY OF TEST DATA

DISPLAY OF TEST DATA

	<u>Infection</u>	<u>No Infection</u>	<u>Total</u>
Test Reactive	a	b	a + b
Test Nonreactive	c	d	c + d
Total	a + c	b + d	a+b+c+d=N

a = True positive

b = False positive

c = False negative

d = True negative

DEFINITIONS

SENSITIVITY: Probability that the test will be positive when infection is present, or $a/(a+c)$

SPECIFICITY: Probability that the test will be negative when infection is not present, or $d/(b+d)$

FALSE-POSITIVE RATE: Probability that the test will be positive when infection is not present, or $b/(b+d)$

FALSE-NEGATIVE RATE: Probability that the test will be negative when infection is present, or $c/(a+c)$

PREDICTIVE VALUE OF A POSITIVE TEST: $a/(a+b)$

PREDICTIVE VALUE OF A NEGATIVE TEST: $d/(c+d)$

COMPARISON OF A NEW TEST WITH AN ESTABLISHED ("GOLD STANDARD") TEST

		<u>Results of "Gold Standard" Test</u>		
		<u>Reactive</u>	<u>Nonreactive</u>	<u>Total</u>
<u>New Test:</u>	Reactive	a	b	a + b
	Nonreactive	c	d	c + d
	Total	a + c	b + d	a+b+c+d=N

a = "True" positive

b = "False" positive

c = "False" negative

d = "True" negative

This display of test data can be used to establish the sensitivity and specificity of a new test compared with a "gold standard" test. The correlation between the "gold standard" and the actual condition of the patients must be known, however, to determine the true sensitivity and specificity of the new test.

MODEL OF A SCREENING TEST FOR ASYMPTOMATIC INFECTION
IN DIFFERENT POPULATIONS

ASSUMPTIONS: 100,000 persons being screened.

Test SENSITIVITY is 97.0%.

Test SPECIFICITY is 99.0%.

SITUATION I: Actual PREVALENCE of infection is 30% of population

<u>Test Result</u>	<u>Actual Condition</u>		<u>Totals</u>		<u>Predictive</u>
	<u>Infected</u>	<u>Not Infected</u>	<u>Number</u>	<u>Percent</u>	<u>Value</u>
Reactive	29,100	700	29,800	29.8%	97.7%
Nonreactive	900	69,300	70,200	70.2%	98.7%
Totals	30,000	70,000	100,000	100.0%	

SITUATION II: Actual PREVALENCE of infection is 1% of population

<u>Test Result</u>	<u>Actual Condition</u>		<u>Totals</u>		<u>Predictive</u>
	<u>Infected</u>	<u>Not Infected</u>	<u>Number</u>	<u>Percent</u>	<u>Value</u>
Reactive	970	990	1,960	2.0%	49.5%
Nonreactive	30	98,010	98,040	98.0%	99.97%
Totals	1,000	99,000	100,000	100.0%	

SITUATION III: Actual PREVALENCE of infection is 0.1% of population

<u>Test Result</u>	<u>Actual Condition</u>		<u>Totals</u>		<u>Predictive</u>
	<u>Infected</u>	<u>Not Infected</u>	<u>Number</u>	<u>Percent</u>	<u>Value</u>
Reactive	97	999	1,096	1.1%	8.9%
Nonreactive	3	98,901	98,904	98.9%	99.99%
Totals	100	99,900	100,000	100.0%	

Similar comparisons can be made by varying sensitivity and specificity values (e.g., 90%, 95%, 99%) in relation to each other or by subjecting the population reactive on the screening test to a confirmatory test that has various values for sensitivity and specificity. Assumptions need to be stated clearly, e.g., the independence or linkage between results on the screening test and the confirmatory test.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Fde

Public Health Service

Centers for Disease Control
Atlanta GA 30333

FEB 27 1985

TO: State and Territorial Public Health Laboratory Directors
State and Territorial Epidemiologists

SUBJECT: Availability of Control Reagents for AIDS Serologic Tests and
Reference Tests for HTLV-III Antibody

This memorandum is to inform you of the Center for Infectious Diseases (CID) plans to provide reference reagents and to make available reference tests for HTLV-III antibody to State health department laboratories. Beginning March 15, 1985 the following candidate reference or control sera may be requested from the Biological Products Program, CID by submitting Requisition Form CDC 51.6 Rev 11-83. The distribution policy will be similar to that of other reference or standard material.

Catalog No. VS 2151 - HTLV-III positive antiserum, human
Catalog No. VN 2152 - HTLV-III negative serum, human

Because supplies are limited, the control sera will be available in reference amounts only.

The HTLV-III antigen for use in the Western blot test can be made available by any of the companies that receive approval from FDA for distribution of the ELISA kits. It is anticipated that the HTLV-III antigen will be sold by one or more of these companies for "investigational use only." The positive and negative serum controls listed above may be used for reference purposes with the commercial ELISA kits as well as for checking the reliability of commercially obtained antigen for use in the Western blot antibody assay. If persistent problems with the Western blot antibody assay are encountered or if additional information on HTLV-III reference testing is needed, please contact:

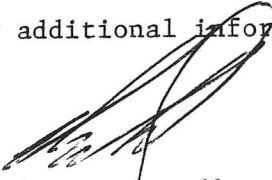
Charles A. Schable
AIDS Serology Laboratory, AIDS Branch
Division of Viral Diseases
Center for Infectious Diseases
Centers for Disease Control
Atlanta, GA 30333
(404) 329-3040

If as a result of consultation inactivated HTLV-III virus is determined to be needed, reference amounts will be provided by the AIDS Branch, Division of Viral Diseases.

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State and Territorial Epidemiologists

Beginning March 15, CID will provide reference service to State laboratories for ELISA and Western blot assay for HTLV-III antibody. These services will be provided primarily to assist State and local laboratories in gaining proficiency with the tests. The anticipated demand for the tests and the commercial availability of kits for the ELISA test, preclude CDC accepting serum specimens for diagnostic purposes. We ask that specimens submitted be accompanied by a completed request form (CDC 50.34 Rev. 8-84). Patient confidentiality can be preserved by placing an identifying number or code where the name is requested.

We will continue to keep you informed of any additional information in this rapidly developing activity.



Walter R. Dowdle, Ph.D.
Director
Center for Infectious Diseases

cc:
Director, Laboratory Program Office
Director, Epidemiology Program Office

**Memorandum**

Date February 28, 1985

From Chief, AIDS Diagnostics Laboratory

Subject Summary of Proficiency Testing Meeting
Concerning anti-HTLV-3/LAV (2nd Memo)

To ✓ Dr. Curran
Dr. LaMotte
Dr. Getchell
Dr. Kalyanaraman
Dr. Feorino
Mr. Parvin
Dr. McDougal
Dr. Dowdle
Dr. Murphy

File

The large volume anti-HTLV-3 serums we have on hand have been titered and all demonstrate high (~1:1600) end-points. This should allow us to make enough material available, through dilutions, to handle the projected needs of reference laboratories for performance evaluation for this year. We will continue to plasmapheresis high-titered local individuals so that sufficient back-up serums are available.

There was a possibility of purchasing serums from a New York Blood Center but since the price was excessive and we now have titered our in-house serums I no longer feel that we need to pursue this option.

The College of American Pathologist (CAP) is actively pursuing construction of their own panel which would be made available to blood banks. This would alleviate CDC having to supply this large community of laboratories. Their first pilot programs are scheduled for June 1985 and they hope to be in full production by January 1986.

Charles A. Schable

Charles A. Schable

File

copy to Charles Schable -
(1) (A) we need to discuss this

CENTER FOR INFECTIOUS DISEASES
ROUTE SLIP

Date: 2/21/85 *today*

TO:

<u> </u> Dr. Dowdle, Director, CID	1-6013
<u> </u> Dr. Bennett, Asst Dir Med Science	1-6106
<u> </u> Dr. Balows, Asst Dir Lab Science	1-6108
<u> </u> Mr. Hicks, Asst Dir Management	1-6013
<u> </u> Dr. Curran, Asst Dir, AIDS Activity	6-292
<u> </u> Arctic Investigations Activity	Alaska
<u> </u> San Juan Laboratories	P.R.
<u> </u> Biological Products Program	1-6042
<u> </u> Hospital Infections Program	1-5065
<u> </u> Scientific Services Program	1-6410
<u> </u> Sexually Trans Dis Lab Program	1-2385
<u> </u> Division of Bacterial Diseases	1-5035
<u> </u> Division of Host Factors	1-1409
<u> </u> Division of Mycotic Diseases	1-6012
<u> </u> Division of Parasitic Diseases	CH-23
<u> </u> Div of Vector-Borne Viral Dis	Ft. Collins
<input checked="" type="checkbox"/> Division of Viral Diseases	7-SB14

Ji
(2) Dr Balows
(3) Dr Murphy -
(4) Dr Jaffe
5/26

ATTN: *ROOM*
Dr. Murphy / Curran

FROM: Albert Balows, Ph.D.
Asst Dir for Lab Sci, CID 6-6108

COMMENTS: Attached is the redrafted version of memo covering distribution of HTLV-III reagents & provision of reference tests. Please review. Return to me by NOON, 2/25/85 as Dr. Dowdle would like to send it out before March 1.



TO: State and Territorial Public Health Laboratory Directors
State and Territorial Epidemiologists

SUBJECT: Availability of Control Reagents for AIDS Serologic Tests and
Reference Tests for HTLV-III Antibody

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the Western blot antibody assay. If problems with commercial HTLV-III antigen persist, reference amounts of inactivated HTLV-III antigen to be used in resolving these problems with the Western blot immunoassay will be available from CID on a prior consultation basis only. This restricted distribution is necessary as our inventory is limited and will be approved *only* for State laboratories with a justifiable need. Shipment must be made in dry ice to maintain stability of the inactivated HTLV-III antigen and will be planned for optimal delivery. Distribution of reference amounts of inactivated HTLV-III virus will be handled by AIDS Branch, Division of Viral Diseases.

Also on March 15, CID will provide State laboratories with ELISA and Western blot assay for HTLV-III antibody as reference tests. We recognize that once the serology test reagents are available commercially, it will be necessary for many laboratories throughout the country to become familiar with the technical aspects of the test and its interpretation. During this period these laboratories will look to their respective State laboratories for assistance and we anticipate that in some instances the States will look to CID for reference tests. CID will provide whatever reference testing is needed to enable State and local laboratories to gain familiarization with the tests. We ask that specimens submitted be accompanied by a completed request form (CDC 50.34 Rev. 8-84). Patient confidentiality can be preserved by placing an identifying number or code where the name is requested. For consultation regarding the need for HTLV-III inactivated antigen or for additional

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State and Territorial Epidemiologists

information on HTLV-III reference testing please contact the following:

Charles A. Schable
AIDS Serology Laboratory
(404) 321-3040

We will continue to keep you informed of any additional information in
this rapidly developing activity.

Walter R. Dowdle, Ph.D.
Director
Center for Infectious Diseases

cc:
Director, Laboratory Program Office
Director, Epidemiology Program Office

bcc:
Regional Offices
Assistant Director for Field Activities, CDC
CDC/W
CID/Asst. Dirs./Dir., Div/Prog/Off

CDC:CID:OD:ABalows:mj 2/21
DOC. 1627L

for Dr. Curran

Reviewed by CPS
for AIDS Hearings
on 2/21/85
WR

(CDC)

Additional Questions and Answers--ELISA TEST/SCREENING SITES/etc

File

1. Does CDC endorse the reporting of seropositive HTLV-III results to the local Health Department? What are the benefits and consequences of reporting these results as viewed by CDC?

Since the initial availability of this test will be through the blood banks, the only reason for the reporting would be to assure that patients were provided appropriate information. This can be achieved by assuring that the blood banks have specific information, and that local areas have a plan for making available the designated personnel for counseling both seropositive and seronegative persons who have questions. When alternate sites are developed and services are expanded for sex partners, States may wish to consider a reporting system to assure that pre-test counseling, post test followup, etc. are provided. A reporting system at this time would only heighten existing concerns about confidentiality without any substantial offsetting public health benefits.

2. Does CDC recommend the establishment of alternate screening sites for the concerned public? If so, what specific types of sites are suggested?

Yes. Sites mentioned for alternate testing have included health department STD clinics, clinics serving high risk populations - such as gay men and methadone clinics, community health centers and private physicians.

Whatever is decided locally, a central site would help coordinate the roles and services offered, and to make the information available to the concerned community. Through alternate sites, persons in high risk groups who might have gone to a blood bank to get tested can instead go to another facility for both accurate information about the test and test results. Confidentiality is a major concern in determining the best alternative sites. Moreover, CDC discourages testing of persons not in recognized risk groups.

3. CDC recommended offering testing to sex partners of high-risk seropositive persons in the MMWR article published on 1/11/85. What is the intent of this recommendation? Which sex partners - how far back in time?

Seropositive persons in high-risk groups should be counseled on the behavioral recommendations associated with having a positive test. One of these guidelines is a change in the sexual lifestyle which will obviously affect the patient's sex partners. Each patient will have personal concerns about the well-being of their sex partners. A sensitive response would be to make the test available to anyone who wants it, so long as the value of the test is made clear to them and alternate testing sites have been established. If alternative sites are not available, seropositive patients should be counseled to discourage sex partners from seeking a test until it is made readily available outside of the blood bank setting. Regarding specific sex partners, those for up to 5 years may be at risk if a seropositive person truly has HTLV-III antibodies. Realistically, however, seropositive people in recognized risk groups should be counseled to inform current sex partners and any others from the last year whom they can readily locate - basically, this should be left to the patient.

4. Who does CDC recommend provide the counseling to seropositive patients?

It is imperative that people be provided information on the test before it is performed and be counseled regarding test results. Persons providing this service should be trained in counseling patients on sensitive issues. Examples of persons who possess these skills and appropriate experiences are STD control personnel, public health nurses and other health professionals. Blood bank personnel, and non-professional personnel at any designated alternative sites, should be trained in pre-test counseling of those who request the test. This training may need to be provided through local programs and will be available in several months through CDC.

5. What type of information does CDC recommend be provided to seropositive patients?

Once privacy is assured and the counselor has confirmed that the individual in the office is the person tested, the counselor should review some basic facts about HTLV-III antibody testing. Among the points to review is that the test is for antibody -- not for the virus. Then the counselor should assess the person's risk factors for AIDS in order to discuss the possible interpretations of the test.

Low risk individuals with an initial positive test should be referred to a physician for repeat testing and further evaluation.

If the person is a member of a recognized risk group, a positive test could mean exposure to HTLV-III, infection with HTLV-III, increased risk for developing the symptoms and diseases associated with AIDS, and the potential to infect others. Thus the person must be referred to a physician for further evaluation. They should also be encouraged to minimize the number of sexual partners, avoid exchanging body fluids (especially semen and blood), and consider informing their partners of the antibody test results. Those who elect to continue engaging in sexual intercourse should be advised to use condoms. It is recommended that they not donate blood, plasma, body organs, or other tissue or sperm; however, they should be encouraged to participate in research studies that require written informed consent and can assure the protection of confidential data.

Seropositive patients should be encouraged to continue social relationships

with family and friends. However, high risk individuals should avoid sharing their razors or toothbrushes and should clean contaminated surfaces and articles. High risk individuals should inform their physicians, dentists, and other health care providers about their serologic status.

6. What information does CDC recommend be provided to high risk seronegative individuals?

A negative antibody test is not an assurance that the person tested has escaped infection with HTLV-III. In this situation, the counselor must be prepared to talk about the false negative antibody test. Some people who are infected with HTLV-III will not test positive, yet they will be capable of transmitting infection. These people will be difficult to identify until better tests are developed. In the meantime, people with risk factors with AIDS should be discouraged from donating blood and should be encouraged to practice "safe" sex.

7. Does CDC recommend that high-risk seropositive persons not work in health care professions?

CDC recommendations regarding precautions for health care workers in serving AIDS patients have been published in the November 5, 1982 MMWR. Basically, blood or serum precautions such as those for Hepatitis B virus should be followed.

8. Does CDC support the "safe sex" recommendations outlined by the various gay organizations? Which ones and why?

Basically, yes. The practices that have been described by organizations that represent the high risk groups seem very rational.

9. Is CDC sacrificing the STD 1990 Objectives by undertaking this HTLV-III testing and counseling program?

No. This is a short term program at this time, and is viewed as an emergency activity. As such, it should only transiently affect the long-term STD program objectives. If additional resources designated for HTLV-III intervention are provided in the immediate future, the ongoing activities related to the 1990 Objectives will be re-evaluated in light of competing priorities and potential resources at the local level.