

USAID Approval of HIV/AIDS Rapid Test Kits

A. Introduction

This document contains information about the process for USAID approval of HIV/AIDS rapid test kits and other technical guidance on rapid test kits. For purposes of USAID approval, an HIV/AIDS rapid test kit is an assay for detection of antibodies to HIV-1, HIV-2, or both, from which test results can be read directly, within 30 minutes of the time specimen is applied to the device, without calibration or calculations.

B. “USAID List of Approved HIV/AIDS Test Kits”

The current “USAID List of Approved HIV/AIDS Test Kits” can be found at http://www.usaid.gov/our_work/global_health/aids/TechAreas/scms/scms.html. **This List replaces the list in AAPD 05-01.** GH/OHA is responsible for maintaining the List.

C. USAID Approval

The Director of the Office of HIV/AIDS, Bureau of Global Health (GH/OHA) has authority to approve rapid HIV/AIDS test kits for use in a clinical setting. A test kit can qualify for USAID approval in one of three ways:

1. FDA-Approved. A test kit approved or licensed by the U.S. Federal Drug Administration (FDA) is considered approved by USAID when approved or licensed by the FDA. No further steps are required for an FDA-approved test kit. We ask that manufacturers contact us when a test kit has received FDA approval to facilitate the test kit being added to the List.

2. SRA-Approved. A test kit can also qualify for USAID approval by being approved by a Stringent Regulatory (SRA) (see section D below for more information on SRAs). For test kits receiving an SRA approval after May 1, 2007, the test kit must also meet the new documentation requirements (section E below).

3. USAID-Evaluated. The third way to qualify for USAID approval is for USAID to evaluate the test kit and determine that it meets the new documentation (section E below) and technical requirements (section F below)

These new documentation and technical requirements replace the old requirements in AAPD 05-01 and apply to test kits submitted for USAID-evaluation after May 1, 2007. USAID-evaluated test kits already approved by USAID under the old requirements continue to be approved, subject to the re-evaluation procedure outlined in Section I.3 below. Test kits submitted for

USAID evaluation prior to May 1, 2007, and not yet approved will be evaluated using the old requirements.

D. Stringent Regulatory Authority (SRA) Approval

1. An SRA is a national drug regulatory authority (NDRA) that closely resembles FDA in its operations. Currently, USAID has designated as SRAs the following NDRAs that participate as members or observers in the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH):

- **Canada** - Health Canada;
- **European Commission - European Union (EU)** - European Medicines Agency (EMA)
- **European Free Trade Association (EFTA)** - Swissmedic, the Swiss Agency for Therapeutic Products Switzerland
- **Japan** - Ministry of Health, Labour and Welfare (MHLW)

2. USAID may designate other NDRAs as an SRA on a case-by-case basis taking into account the extent to which the NDRA resembles FDA in its operations. The World Health Organization (WHO) is not a regulatory authority and inclusion of a product in the WHO pre-qualification program is not considered approval by an SRA.

E. Documentation Requirements

For an SRA-approved or USAID-evaluated test kit, the manufacturer or other entity officially representing the manufacturer the (“applicant”) must submit to USAID the following:

1. Dossier explaining the technical specifications of the product including sensitivity, specificity (including where the studies were performed to generate these values), reproducibility across multiple test kit lots, the test principle, complexity, methodology, types of samples used (e.g., whole blood), and the test procedure, including the time needed to conduct the test, and demonstration of stability throughout the shelf life of the product under recommended storage conditions.

2. Product information, including manufacturer and manufacturer site, any component manufacturers and sites, the items included in the kit, the number of tests in each kit, additional items required to perform the test not included in the kits (e.g. centrifuge, blood collection equipment), shelf life, and recommended storage conditions.

3. Product insert.

4. For an SRA-approved test kit, evidence of SRA approval.

5. For a USAID-evaluated test kit, evidence that the manufacturing and any component manufacturing sites have a certified quality management system, e.g. a Good Manufacturing Practice (GMP) certificate.

F. Technical Requirements

1. The International Laboratory Branch of the Centers for Disease Control of the Department of Health and Human Services (CDC/ILB) assists USAID in evaluating the test kits against the technical requirements. CDC/ILB furnishes a report to USAID which USAID uses in its approval process. USAID will furnish an applicant a copy of its report upon request. CDC/ILB also assists USAID in assessing various additional characteristics of test kits that are not mandatory but have implications for their use in USG-supported programs, such as:

- Reliability of test performance in non-ideal field conditions
- Ease of use
- Training requirements
- Adequacy of packaging and labeling
- Amount of waste generated

2. An applicant must furnish at its expense to CDC/ILB individual test devices, test kits and accessories, in the numbers and lots (at least three lots) as specified by CDC/ILB.

3. A test kit must meet the following technical requirements for USAID-evaluated approval:

a. The test kit must have a sensitivity of at least 99% [false negative rate of <1%] for detection of HIV-1 infection and, if applicable, HIV-2 infection, in each sample matrix for which the test is designed (e.g., whole blood, serum, plasma, oral fluid or urine).

b. The test kit must have a specificity of at least 98% [false positive rate of <2%] in each sample matrix for which the test is designed (e.g., whole blood, serum, plasma, oral fluid or urine).

c. Invalid test results must be less than 2% of the total tested.

d. Inter-lot variability must be less than 5% among the lots evaluated.

e. The test kit must have an internal control or other failure alert mechanism to notify the operator if sufficient sample has been applied and if the assay malfunctions.

f. The test kit must use direct, unprocessed specimens (e.g., unprocessed whole blood or oral fluid) or samples that require minimal processing (e.g., serum, plasma or urine).

g. All reagents including diluents must be included in the test kit, and must not require any technique-dependent reagent manipulation (e.g., no reconstitution)

h. After initial addition of specimen and reagents, the test kit must not require operator intervention or procedural steps during the analysis.

i. The test kit must not require specialized equipment in its operation (e.g., temperature control devices, washers, spectrophotometers, etc).

G. Request for Re-evaluation by the Applicant

1. A manufacturer or other entity requesting a second evaluation of a rapid test kit that did not meet the technical specifications in the initial evaluation must submit to CDC/ILB data from an independent laboratory evaluation that demonstrates that appropriate changes have been made to the test kit. If CDC/ILB determines that the independent laboratory evaluation demonstrates acceptable performance, CDC/ILB will conduct another evaluation. Please note that an independent laboratory evaluation is not a substitute for the CDC/ILB validation using its own diverse specimen panel.

2. A second evaluation is considered a new application and will be considered in turn with other applications on a first-come first-served basis.

3. If the test kit fails the second evaluation, the manufacturer may not apply again for at least six months from the date of the completion of the second evaluation.

H. Notification to USAID by Applicant of Changes in Test Kit or Manufacturing Site.

1. USAID approval is given for the specific test kit and its components that were submitted for USAID approval. An applicant is required to notify USAID of any changes in the test kit or components that is likely to have an impact on the performance of the test kit.

2. USAID approval is given for a specific manufacturing site and specific component manufacturing sites. An applicant is required to notify USAID of any change in manufacturing or component manufacturing sites.

3. USAID will determine whether the change is significant enough to warrant re-evaluation.

I. Miscellaneous Provisions.

1. The requirements for USAID-approval are subject to change at any time.

2. USAID may request additional information as it determines necessary to approve test kits and assure ongoing quality.

3. USAID reserves the right to re-evaluate USAID-evaluated test kits against the new documentation and technical requirements, as well as periodically to assure ongoing quality. USAID expects to begin re-evaluation of currently approved test kits using a more diverse panel of specimens later on in 2007.

K. Points of Contact.

1. USAID.

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2. CDC.

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L. Further Information.

The Rational Pharmaceutical Management Plus (RPM Plus) Program of Management Sciences for Health (MSH) has developed a document entitled "HIV Test Kits Listed in the USAID Source and Origin Waiver: Procurement Information" to assist in procuring the test kits. It can be found at <http://www.msh.org/projects/rpmpplus/3.3.2b.cfm>

USAID List of Approved HIV/AIDS Rapid Test Kits as of December 7, 2006

Product	Manufacturer	FDA or USAID
1. Aware HIV-1/2 BSP	Calypte Biomedical	USAID
2. Bionline	Standard Diagnostics	USAID
3. Bionor	Bionor A/S	USAID
4. Bundi Rapid HIV 1/2	Bundi International Diagnostics Ltd.	USAID
5. Capillus	Trinity Biotech	USAID
6. Care Start HIV 1-2-O	Access Bio, Inc.	USAID
7. Determine	Abbott Laboratories*	USAID
8. Double Check	Orgenics	USAID
9. Double Check Gold HIV1&2 Whole Blood	Orgenics	USAID
10. First Response	Premier Medical Corporation	USAID
11. Genie II	BioRad	FDA
12. HIV 1/2 STAT-PAK	Chembio Diagnostic Systems, Inc.*	FDA
13. HIV 1/2 STAT-PAK Dipstick	Chembio Diagnostic Systems, Inc.*	USAID
14. HIVSav 1&2	Sayvon Diagnostics Ltd.	USAID
15. Immunocomb	Orgenics	USAID
16. InstantCHEK	EY Laboratories	USAID
17. INSTI HIV Antibody	Biolytical Laboratories	USAID
18. OraQuick	OraSure Technologies	FDA
19. Reveal G2	MedMira	FDA
20. Sero-Strip	Saliva Diagnostic Systems, Ltd.*	USAID
21. StatSure HIV 1/2	StatSure Diagnostics*	USAID
22. SURECHECK HIV1/2	Chembio Diagnostic System, Inc.*	FDA
23. Unigold	Trinity Biotech	FDA
24. Parent Company is a United States based firm		