An Approach for a Rapid HIV Antibody Home-Use Oral Fluid Test

OraSure Technologies, Inc.

Meeting of the Blood Products Advisory Committee
03 November, 2005

Agenda

- Intended Use Statement
- Product Demonstration
- OTC Oral Fluid Home-Use Test Kit Configuration
  - Internal Control
  - Interpretation
  - Clinical Performance
- Proposed Studies
- Labeling/Packaging Concept
- Conclusion

Rapid HIV Antibody Home-Use Oral Fluid Test

Intended Use Statement

The Rapid HIV Antibody Home-Use Oral Test is a single-use, qualitative test system to detect antibodies to HIV-1 and HIV-2 in oral fluid. The Rapid HIV Antibody Home-Use Oral Fluid Test is intended to enable testing for individuals.

Product Demonstration
Specimen Collection

- Place the flat pad above the teeth against the outer gum.
  - Gently swab completely around the outer gums, one time around, using the flat pad.
- The product works by collecting antibodies from the gum.

- Insert Flat Pad of device into the bottom of Developer Vial.
- Start timing test.
- Fluid will travel up result window.
- Read results after 20 minutes but *not more* than 40 minutes.

Rapid HIV Antibody Home-Use Oral Fluid Test Kit Configuration

- Pre-test information and risk assessment pamphlet
- Pictorial-based collection, testing, and interpretation sheet
- Important post-test support information
- Single-Use Device (individually packaged)
- Developer vial (individually packaged)
- Test stand (built into package)
- No hazardous components

No significant risk to user from test kit contents

Internal Control

- Indication that a sample has been collected
- Indication conjugate was active
- Indication that the test is working properly

Interpretation

- **Negative**: Single line appears in the C (control) triangle
  - A negative result indicates the absence of HIV antibodies in their sample.
- **Preliminary Positive**: Two lines appear
  - One at the C (control) triangle and the other at the T (test) triangle
  - May indicate the presence of HIV antibodies in their sample.

Clinical Performance

- Clinical performance of our product using oral fluid has been demonstrated in clinical studies conducted to support product approval (PMA BP010047)

- Proven ease of use through CLIA waiver
  - Granted on January 31, 2003
    - HIV-1 – fingerstick whole blood
  - Granted on September 30, 2003
    - HIV-1 – venipuncture whole blood
  - Granted on June 25, 2004
    - HIV-1 and HIV-2 – whole blood (fingerstick/venipuncture) and oral fluid

Rapid HIV Antibody Oral Fluid Test Clinical Populations

Negative Population

- Subjects known to be low risk, negative for HIV

Positive Population

- Subjects included patients at various clinical stages of HIV infection, including AIDS patients

High Risk Population

- Subjects included those with unknown HIV status who were at risk for infection

Rapid HIV Antibody Oral Fluid Test Performance Summary

(PMA BP010047)

Sensitivity **834/840 = 99.3%**
(95% C.I. = 98.4% - 99.7%)

Specificity **3674/3682 = 99.8%**
(95% C.I. = 99.6% - 99.9%)

*All sample collections were done by individuals being tested

Rapid HIV Antibody Oral Fluid Test CLIA Waiver Studies- Demographics of Study Population

Gender and Age Summary						
Site	Male	Female	Age Categories			
			20-30	*31-40*	*41-50*	*51+*
1	16	9	10	9	5	1
2	8	18	15	3	5	3
3	11	14	3	5	7	10
4	14	12	6	7	4	9
Total	**49**	**53**	**34**	**24**	**21**	**23**
% of Total	**48%**	**52%**	**33.3%**	**23.5%**	**20.6%**	**22.5%**

Demographic Summary							
Site	Hispanic	Caucasian	African-American	Asian	American-Indian	Alaska-Pacific Islander	Other
1	8	10	2	2	0	1	2
2	0	24	1	0	0	0	1
3	2	1	22	0	0	0	0
4	0	20	0	0	2	1	3
Total	**10**	**55**	**25**	**2**	**2**	**2**	**6**
% of Total	**9.8%**	**53.9%**	**24.9%**	**1.96%**	**1.96%**	**1.96%**	**5.9%**

Rapid HIV Antibody Oral Fluid Test CLIA Waiver Studies- Demographics of Study Population

Educational Demographic Summary							
Site	Grades 11-12	GED	Some College	2-Year Degree	4-Year Degree	Graduate Degree	Technical School
1	2	1	13	2	5	2	1
2	0	0	6	2	23	8	1
3	3	3	7	2	8	2	1
4	7	0	11	2	3	2	2
Total	**12**	**4**	**37**	**8**	**39**	**14**	**5**
% of Total	**12%**	**4%**	**36%**	**8%**	**38%**	**14%**	**5%**

Note: Some of the subjects checked more than one box; therefore total responses are greater than 102.

Professional Experience Summary										
Site	Medical Lab Diagnostic Testing		Used Rapid Test(s)		Seen OraQuick Device in Use		Used OraQuick Device		Certified HIV Counselor/Tester	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
1	0	25	1	24	1	24	1	24	11	14
2	1	25	4	22	0	26	0	26	4	22
3	0	25	3	22	0	25	0	25	11	14
4	0	26	0	26	0	26	0	26	0	26
Total	**1**	**101**	**8**	**94**	**1**	**101**	**1**	**101**	**26**	**76**
% of Total	**1%**	**99%**	**8%**	**92%**	**1%**	**99%**	**1%**	**99%**	**25%**	**75%**

Rapid HIV Antibody Oral Fluid Test CLIA Waiver Studies – Results

- The Untrained user study validated device safety and efficacy
- The User study validated the accuracy of device interpretation by untrained users

Untrained Users Rate of Correct Test Results			
Negative Sample	**Low Positive Sample**	**High Positive Sample**	**Total**
98.5% (197/200)	**98.0% (196/200)**	**99.5% (199/200)**	**99.5% (592/600)**
95% C.I. (95.7%-99.7%)	**95% C.I. (95.0%-99.5%)**	**95% C.I. (97.3%-99.9%)**	**95% C.I. (97.4%-99.4%)**

Rapid HIV Antibody Oral Fluid Test
CLIA Waiver Interferent Study

CLIA Waiver Interferent Study conducted with both positive and negative population with no effect on device performance

Interferents

- Tooth brushing
- Alcoholic beverages
- Tobacco products
- Mouthwash
- Drugs of abuse

Procedural

- Temperature variation 2-40°C
- Movement of device during operation
  - Shaking
  - Rocking
- Device on uneven surface

All Results Concordant with True Serological Status

Proposed Validation Studies

- Untrained user study to validate device safety and efficacy
- User study to validate the accuracy of interpretation by untrained users
- User study to validate ability of labeling and printed materials to ensure counseling and linkage to care
- Post-market non-clinical study to evaluate counseling and linkage to care

Proposed Untrained User Study to Validate Device Safety and Efficacy

Study Objective

- Validate that the OTC HIV Oral Fluid Home-Use test can be carried out effectively by the expected untrained user population
  - Verify efficacy of sample collection
  - Verify accuracy of result interpretation

User Study to Validate the Efficacy of Sample Collection by Untrained Users

- Study population will reflect demographics of expected users
- Untrained users will collect oral fluid specimens after reading product labeling
- Devices will be interpreted for presence of control line (valid test result)
- Acceptance criteria (proportion of test devices with valid test results) will be developed prior to the study in order to assure verification of efficacy of sample collection in untrained users
- Size of user study population will be sufficient to provide statistical verification of result

User Study to Validate the Accuracy of Interpretation by Untrained Users

- Study population will reflect demographics of expected users
- Untrained users will interpret test results after reading product labeling
- Untrained users will interpret results generated using a panel of positive and negative test specimens
- Each test result will be interpreted by untrained and trained user
- Acceptance criteria (concordance with interpretation by trained user) will be developed prior to the study to assure verification of accuracy of test interpretation in untrained users
- Size of user study population will be sufficient to provide statistical verification of result

Validate Ability of Labeling and Printed Materials to Ensure Counseling and Linkage to Care

- Study population will reflect demographics of expected users
- Size of user study population will be sufficient to provide statistical verification of result
- Study will focus on ability of user to understand:
  - Options available for pre/post counseling and linkages to care
  - Key messaging such as “Window Period” for HIV, Risk Factors and potential for False Positive/Negative Results

OTC HIV Home-Use Oral Fluid Test Interpretation of Results

- Proposed approach to bilingual (Spanish/English) instructions on how to interpret the results

Negative Result	Positive Result
• Explain Risk Factor • Describe Potential for False Negative (Window of Detection) • Recommend Retest in 3 Months Based on Risk Factor Self Assessment	• Use term “preliminary” positive (reflex to “seek counseling”) • Referral to Care by Providing Access to 24X7 Post-test Counseling • Explain Potential for False Positive and the need for confirmatory testing and counseling

Educate with Packaging

- Counseling and linkages to care
  - Pre-testing counseling information in packaging with additional support by phone, web-site with linkage to local public health services and community-based organizations
  - Post-testing counseling through phone, web-site, local public health services and community-based organizations
  - Access to multilingual counselors
- Manufacturer 1-800-number for assistance

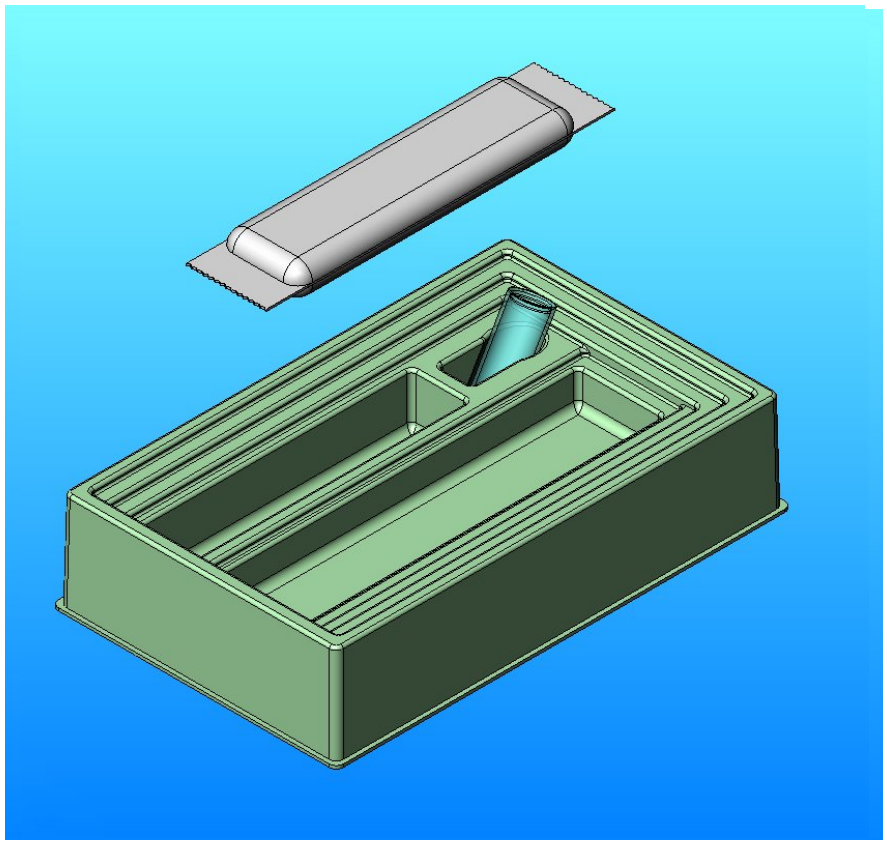
Proposed Post Market Non-Clinical Studies

- Post Marketing Studies
  - Anonymous
  - Collect demographics - age, sex, race, and risk behavior factors
  - Provide counseling options used during their decision and testing process
  - Evaluate effectiveness of counseling and linkage to care
- Website
  - Potential to collect survey data that will capture the same information as above

Conceptual Package Design

- Preliminary packaging criteria
  - Promote methodical step-by-step procedure
  - Enable multiple visual options to communicate
  - Minimize “missed steps” or “race through” procedure sequencing

Conceptual Package Design*



*Patent Pending

Conclusion

- The performance of the **Rapid HIV Antibody Oral Fluid Test** has clinical performance that is appropriate and effective for OTC use
- Product packaging & labeling will direct the user through the correct test sequence
  - Package design will ensure user engages with product labeling prior to accessing the device
  - Correct use, including counseling and linkages to care, will be reinforced by repetitive instructions for use and pictorial/ graphical representations
- Studies will be conducted to demonstrate that lay users are able to understand the instructions for use and use the device effectively
- Pre and post test instructions will direct the user to appropriate counseling and linkages to care
- Post-market surveillance will monitor effectiveness

Thank You