Final Advisory Committee Briefing Materials: Available for Public Release

OraQuick® In-Home HIV Test

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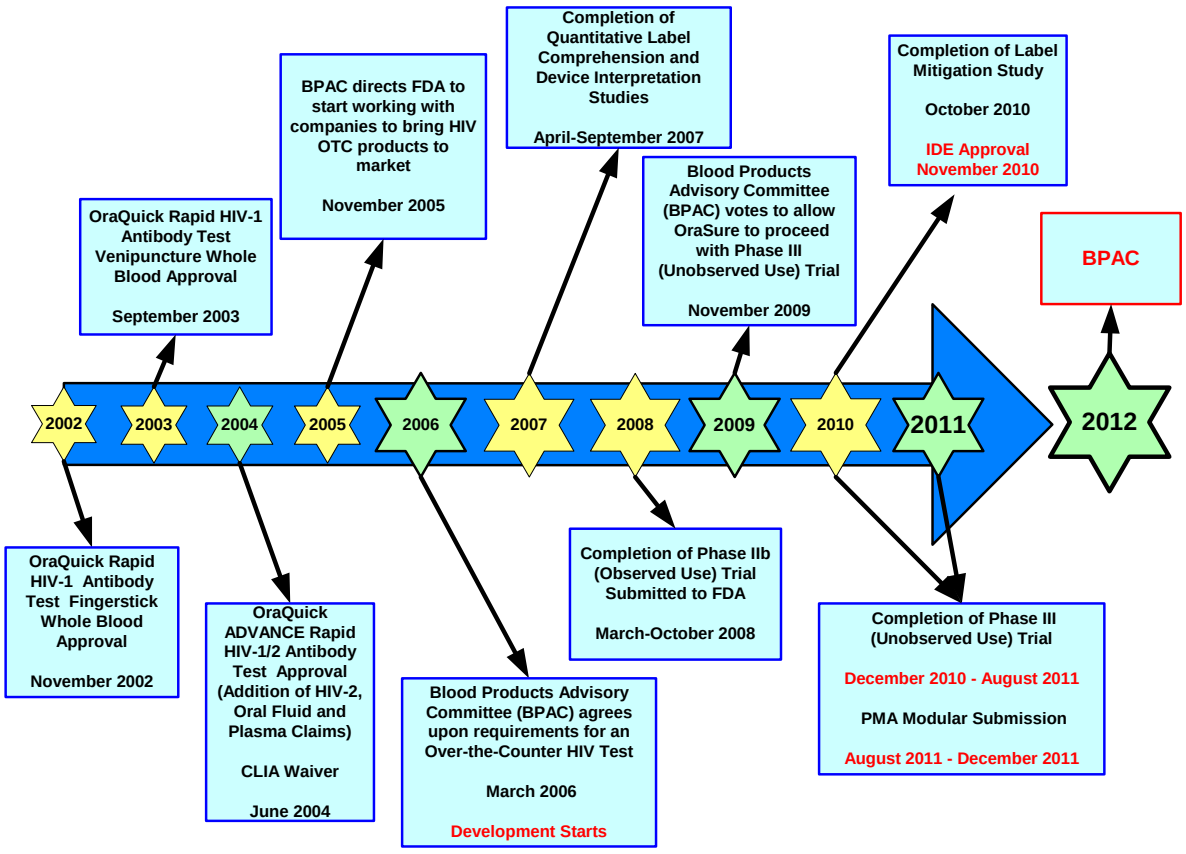
1. Overview of Critical Milestones

Figure 1



2. OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test

The OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test was approved originally on November 2, 2002 as the OraQuick HIV-1 Rapid Antibody Test for use with fingerstick whole blood specimens. In 2003 OraSure submitted a supplement to allow for the additional use of venipuncture whole blood specimens. The supplement was approved on September 5, 2003. On June 24, 2004, OraSure obtained approval for the following additional claims: Oral Fluid, Plasma and HIV-2. At this time the name of the product was changed to OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test. CLIA Waiver was granted for the product on June 25, 2004. Since that time, over 20 million units have been used for HIV testing in the US. Table 2.1 summarizes the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test oral fluid performance as described in the FDA approved labeling.

Table 2.1 OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test Claims

Description	Sensitivity	Specificity
Oral Fluid	99.3% (95%CI; 98.4%, 99.7%)	99.8% (95%CI; 99.6%, 99.9%)

3. Over-the-Counter HIV Test Requirements (As originally recommended by BPAC in 2006)

3.1 Background

In March 2006, FDA presented to the BPAC (Blood Products Advisory Committee) the concepts with respect to over-the-counter (OTC) HIV tests. At the meeting BPAC agreed upon the requirements for an Over-the-Counter HIV test. The first step for any product was to obtain FDA (PMA) approval in the professional market. Another pre-requisite was that the product be CLIA-waived on the basis that it be sufficiently simple to use and demonstrate comparable performance in the hands of untrained users. On this basis, the company could then move forward and create a development plan for approval in the OTC market. The critical components of the approval process recommended by FDA and BPAC were: the completion of a device interpretation study, an observed self-test study and an unobserved self-test study. In addition, there was a requirement for a 24/7 call center for consumers to access if needed. The following are brief descriptions of those studies along with the success criteria as originally conceived at the 2006 BPAC meeting. The design requirements for the unobserved use study were subsequently modified during the clinical development process as a result of review of study results. This is noted in section 3.4.3 below.

3.2 Device Interpretation Study

3.2.1 Study Definition

Results of interpretation of static (pre-made) devices by untrained users (prospective consumers)

3.2.2 BPAC Requirements

Lower bound of 95% CI was 98% correct interpretation for negative, high positive, invalid, and 95% for the low positive

3.3 Observed Use Study

3.3.1 Study Definition

Observed self-testing by untrained users, compared with blinded trained user testing

Two (2) Study Cohorts

- Known HIV Positive
- Healthy, Normal at unknown risk for HIV

3.3.2 BPAC Requirements

- Lower bound of 95% CI was 95% for sensitivity and specificity
- 10 newly identified HIV infections among the unknown risk cohort

3.4 Unobserved Use Study

3.4.1 Study Definition

Unobserved self-testing by untrained users in a setting of their choosing. Performance assessed by comparison with FDA-approved laboratory testing.

3.4.2 BPAC Requirements (from 2006 BPAC)

- Lower bound of 95% CI was 95% for sensitivity and specificity.
- 100 newly identified HIV infections (revised requirement based upon review of Phase IIb observed self-test study). The original requirement as defined by 2006 BPAC was for 10 newly identified HIV

infections. Since the design was modified to remove testing of HIV positive individuals and only test subjects of unknown HIV status after review at the 2009 BPAC, the required number was subsequently increased to 100 to allow for a sensitivity calculation in this population (refer to section 6).

3.4.3 Revised Unobserved Self-Test Study Requirements based on 2009 BPAC Meeting

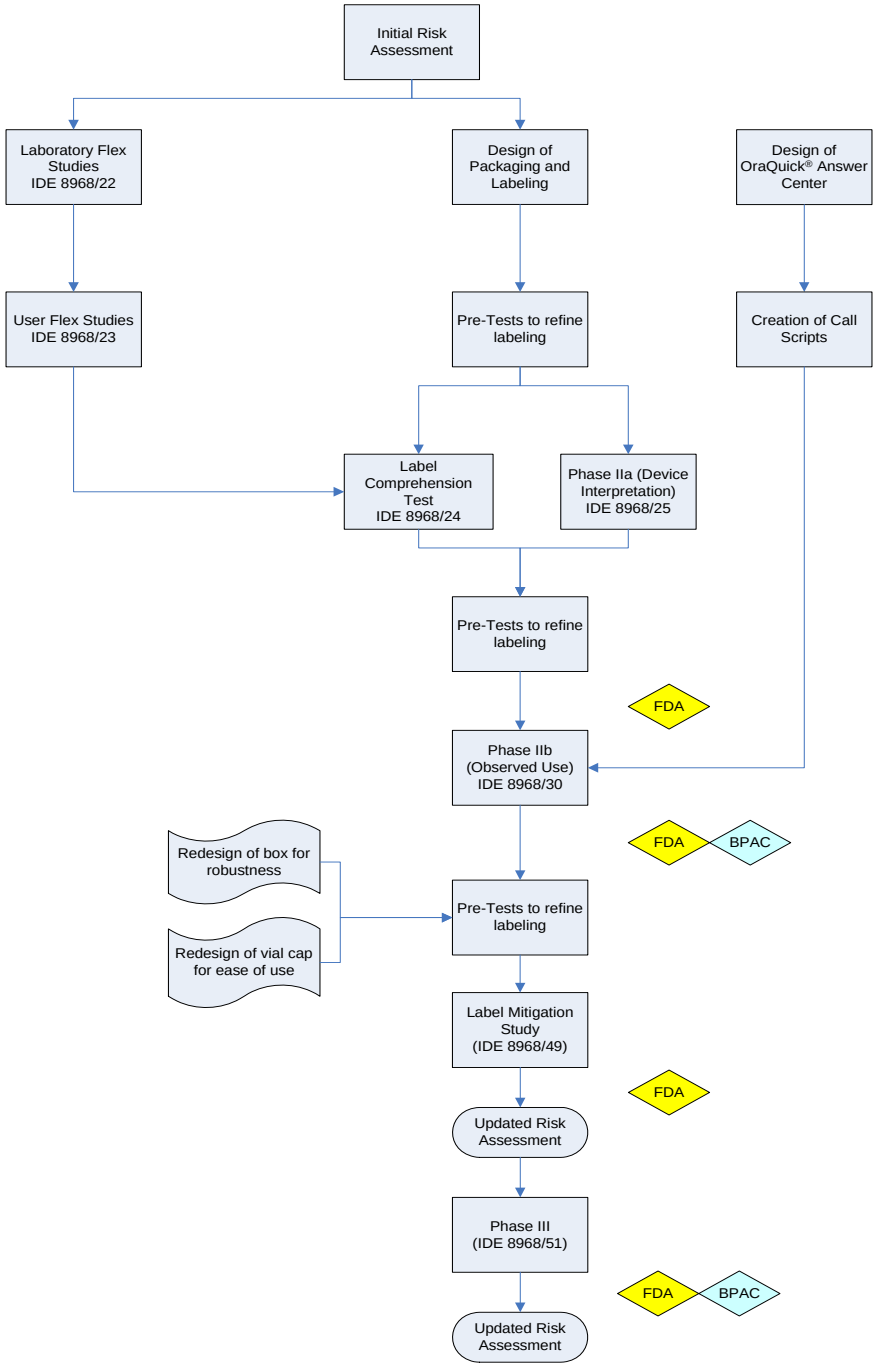
- Comparison based on laboratory blood test.
- Requirement to run known positives was eliminated. Trial population modified to consist only of individuals of unknown status. As a result of this change, the number of newly identified HIV positives was increased to provide some assessment of sensitivity in the unknown population.
- Requirement to study at least 100 newly identified positives
- A new metric was introduced to assess the reliability of the product in the consumers' hands and measure the rate at which a user obtained no result (either positive or negative). This was termed the Test System Failure Rate and its target was set at ≤ 2%.

4. Development of the OraQuick® In-Home HIV Test System

4.1 Background

In May 2006, OraSure met with FDA and presented the initial Clinical Development Plan, which was based on a phased approach to allow an iterative design and development process. FDA agreed and was supportive of this approach. Figure 2 is a flow chart of the high level design steps that have been completed as part of the design and development of the OraQuick® In-Home HIV Test.

FIGURE 2



The initial effort was to complete a risk assessment to identify any new risks associated with the implementation of the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test in the over-the-counter (OTC) market and the use of the device by consumers. This focused on potential risks and failure modes associated with consumer use of the professional product. The risk assessment was used to design flex studies to determine what, if any mitigations needed to be put into place to reduce risk prior to initiation of the larger clinical trials.

In laboratory-based flex studies, the current professional product the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test, was put through various operational stress studies in order to model how it would perform in the hands of the consumer. Additionally several flex studies were completed assessing performance when used by trained and untrained users in order to help OraSure understand the failure modes that would be more specifically focused towards the use of the product in a consumer type setting. The professional product was used for this testing because the over-the-counter (OTC) version of the product was being designed in parallel.

OraSure contracted a design firm [redacted] to design and develop consumer friendly packaging and labeling for an over-the-counter HIV test using the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test. [redacted] used a methodology for designing consumer products, which included human factor testing. The final concept presented by [redacted] was designed to mimic a laptop type box that contained step-by-step instructions, a pre-test informational booklet on HIV and AIDS and a post test informational booklet on result interpretation and follow-up. The laptop design provided for a robust testing platform by building the test stand into the design of the box. In addition, it allowed the user to progress through step-by-step instructions which resided in close proximity to the test device during the test procedure. The laptop design was built into prototypes and tested in an iterative process to ensure that the consumer could comprehend key messages and perform the test accordingly. Throughout this process, revisions were made to the prototype product to maximize ease of use, operational robustness, and label comprehension. In total, there were 32 iterative versions of the product throughout this process, which were tested by over 800 intended users.

In addition to the design and development of the packaging and labeling, OTI contracted [redacted] to design and develop a 24/7/365 call center that would provide support for consumers in the following areas: HIV/AIDS general information, assistance with how to correctly perform and interpret the OraQuick® In-Home HIV test and referral to care. OTI chose [redacted] to design the call center due to their experience running the CDC's HIV INFO Call Center. The call center was designed to allow the caller to remain anonymous. No personal information is stored in the system once the call is completed. The call center can report out on critical parameters to assist OTI in monitoring the performance of the product and the system. The call center was operational (8-8, M-F) during the Observed Use (Phase IIb) trial and (24/7) during the Unobserved Use (Phase III) trial.

In 2007, OTI initiated the Quantitative Label Comprehension Study (OQ-OTC-LC-1) and the Device Interpretation Study (Phase IIa: OQ-OTC-2). These studies were completed in mid 2007 and results were presented to FDA in January 2008 during IDE discussions for the Observed Use Study (Phase IIb: OQ-OTC-4).

Minor revisions were made to the labeling based on the results from the Label Comprehension and Phase IIa studies. The revised labeling was again tested for comprehension along with the ability of untrained users to perform the test by following the step-by-step instructions. The fully optimized product was then used as the investigational test in the Observed Use Trial; where untrained users tested themselves in an observed setting (Phase IIb). The Phase IIb trial was completed in late 2008. The trial design included self-testing by two populations: HIV Positive individuals and individuals of unknown HIV status. All subjects had no previous exposure to the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test. Subjects self-tested and then were professionally tested by a trained technician to determine their HIV status. Subjects who were preliminarily positive in the OraQuick *ADVANCE*® Rapid HIV-1/2 HIV test were confirmed by Western blot. Sensitivity and Specificity of the OraQuick® In-Home HIV Test were calculated based on comparison with results with FDA approved testing algorithms. The results of the Phase IIb trial were submitted to FDA in Oct. 2008 and were presented to BPAC in Nov. 2009. Following the review of the results of the Observed Use Study and the

proposed design of the Unobserved Use Study, BPAC voted to allow OraSure Technologies Inc. (OTI) to move forward into the Unobserved Use trial (Phase III).

In the Phase IIb Observed use trial, a small but measurable frequency (approx 2%) of operational errors by intended users were observed. These errors prevented users from obtaining an HIV test result. Based on the discussions at the BPAC meeting and with FDA, OTI agreed to re-evaluate the product packaging and labeling again to determine if additional revisions could be made to further reduce the possibility of error modes in the hands of intended users. These label evaluations were conducted in three (3) pre-studies where >325 individuals and 7 variants of the prototype labeling were tested. Based on the results of the pre-tests, OTI made small, but significant revisions to the packaging and labeling and then validated it in the OQ-OTC-LM-1 (Label Mitigation) study. The results from the Label Mitigation Study were submitted to FDA in the IDE Amendment along with the proposed Phase III (unobserved self-test) protocol. The IDE was approved on Nov. 15, 2010.

One of the key revisions to the design of the unobserved use study based on discussions at the 2009 BPAC Meeting was to conduct the study exclusively in subjects of unknown HIV status. This was done to better reflect intended users. As a result FDA raised the minimum requirement for identification of previously undiagnosed individuals from 10 to 100 in order to be able to assess sensitivity in the intended use population. Additionally a new success criterion was introduced for "test system failure rate" representing the frequency at which subjects failed to obtain an HIV test result due to an operational error. The Unobserved Use Study (Phase III: OQ-OTC-5) was initiated in December 2010 and completed in August 2011. The results from the Phase III study were submitted to FDA in December 2011.

4.2 OraQuick® In-Home HIV Test System Design

4.2.1 Key Design Aspects

The OraQuick® In-Home HIV Test is based on the current PMA approved and CLIA-waived OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test. No changes were made to either the design or manufacturing process of the test device. All design changes were made to the packaging and labeling of the product. The following table is a summary of the changes that were made to the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test (professional product) to transition it to the OraQuick® In-Home HIV Test.

Table 4.1 Summary of Design Changes

Device Component	Change
Filled Developer Vial	The Developer Vial cap was modified to add thumb indentations to make it easier and more intuitive for the consumer to open the vial without spilling the developer solution. The cap is made of the same material as the cap of the approved professional product. The Developer Vial Label artwork has been revised to reflect consumer labeling. The Developer Vial is called the Test Tube for the over-the-counter product. The solution contained in the Test Tube is the same Developer Solution as in the professional product.
Device Label	The artwork present on the Device Label was modified to reflect the branding for the OraQuick® In-Home HIV Test. Construct of the label is the same as the current device label.

Pouched Device and Developer	The test device and developer vial are pouched in a divided pouch with separate compartments for the device and developer vial. Its artwork has been designed to reflect consumer use in an OTC setting. The artwork was developed to show a pictorial of the device and test tube to allow the consumer to follow the step-by-step instructions. The material used to make the divided pouch is the same as that of the foil laminate pouch of the professional product. The two sides of the divided pouch are separated
Test Stand	The test stand into which the device is placed for the test to run and the result to be interpreted was developed to physically incorporate it into the laptop box design. The angle that the laptop opens to is consistent with the angle of the test stand used with the professional product.
Instructions for Use	The instructions for use are provided to the consumer in easy to follow step-by-step instructions. Graphics are used for emphasis and to assist with understanding. The Instructions for Use make frequent reference to the toll free number of the Consumer Support Center throughout.
Pre-Test Informational Booklet	The OraQuick® In-Home HIV Test provides a pre-test informational booklet called "HIV, Testing, & Me". This booklet is found in the drawer containing all of the components needed for testing. The instructions for use reference the booklet in the introduction page and again at the point in the instructions where the user is waiting for their test results.
Post-Test Informational Booklet	The OraQuick® In-Home HIV Test provides a post-test informational booklet called "What Your Results Mean to You". This booklet is found in the drawer containing all of the components needed for testing. The instructions for use direct the user to read this booklet once they have interpreted their test results.
Packaging	The OraQuick® In-Home HIV Test contains components to perform a single HIV test. All of the contents are contained within the plastic laptop like box that also serves as the test stand into which the developer vial and test device are placed in order for the test to run. The instructions for use are attached to the box and situated so that the pictures that help an individual to conduct the test and interpret their results are immediately adjacent to the consumer's test device. The labeling references the toll free number to the Consumer Support Center throughout.

4.2.2 OraQuick In-Home HIV Test Kit Contents

The following figures depict the final design of the packaging and labeling for the OraQuick® In-Home HIV Test. This is the product that was utilized by subjects that participated in the Unobserved Use Trial (Phase III). This is also the product that will be made available to consumers upon FDA approval and launch.

The Test Kit consists of the following items:

- Outer carton containing plastic molded laptop box
- Instruction Booklet (flipchart design) attached to the plastic molded laptop box
- 1 Test Device
- 1 Developer Vial
- 1 Pre-Test Informational Booklet (HIV, Testing & Me)
- 1 Post Test Informational Booklet (What Your Results Mean to You!)
- 1 Pencil for writing down the read times (not shown)
- 1 Disposal Bag (allows for discrete disposal - not shown)
- Accessibility to the OraQuick® Answer Center

Figure 3


ORAQUICK
Because you should know
Porque debe saber
ORAQUICK
Testing Directions
English
Español
Test Tube
Tubo de Prueba
ORAQUICK
What your results mean to You!
Please Read This Book First
ORAQUICK
HIV, Testing & Me

Figure 4

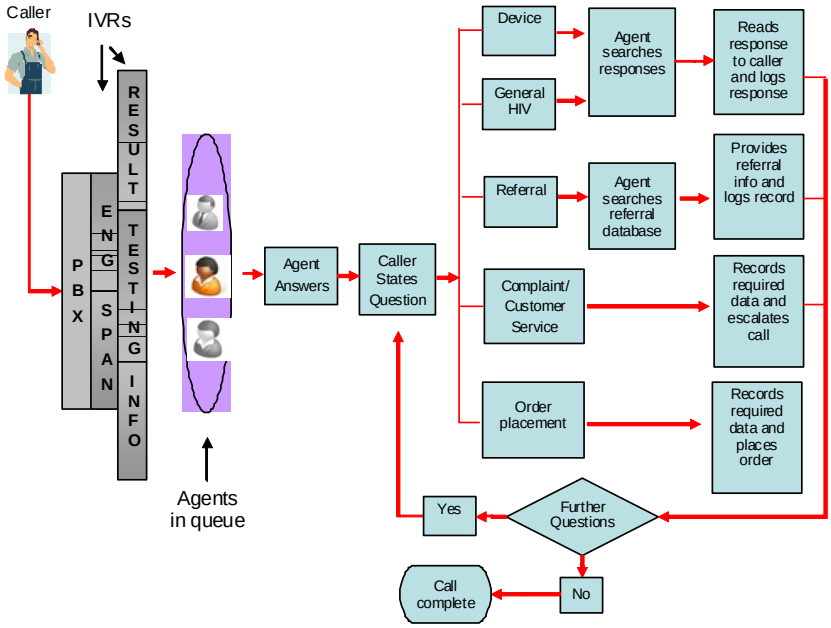
4.3 OraQuick® Consumer Support Center

The OraQuick® Consumer Support Center was designed in conjunction with [redacted] utilizing CMMI (Carnegie Mellon Management Institute) methodology and Constella's Project Management Methodology. The system is designed as a 24/7/365 call center with bilingual capability (English and Spanish). The call center was designed to be able to provide consumers with information regarding basic HIV/AIDS information, assistance in how to correctly perform the test and referrals for follow-up (confirmatory) testing and HIV care. The call center system allows for consumers to remain anonymous. No personal identification information is requested by the call center agent; however, the system does allow for the agent to capture consumer self reported information if provided.

The information relayed to the consumer by the agents is based on call scripts that have been developed through information from the CDC website and product specific information provided by OraSure. The Referral dataset is the same dataset that supports the CDC NPIN referral system. OraSure has received agreement from CDC to utilize this dataset and to receive updates to the dataset at the same frequency as CDC. OraSure will also supplement the list with toll-free numbers from public health departments. The call center is also designed with the capability to complete "warm" transfers if needed. The functionality of the system is depicted in Figure 5.
Upon initiating a call, the caller will be asked to specify their preferred language (English or Spanish). The caller will then be asked if they are calling about their test results, help with performing the test or

for additional HIV/AIDS information. This allows for prioritization of calls and immediate assistance for those who may have a positive result or are in the middle of their testing experience.

Figure 5



The Consumer Support Center was fully functional and available for subjects that participated within the Observed Use (Phase IIb) and the Unobserved Use Study (Phase III).

The following information can be collected through the Consumer Support Center for reporting once the system is commercial.

System Generated:

- Date of Call
- Time call was answered
- Time call ended
- Area Code
- Agent
- Mode of Contact
- Questions asked
- Action Taken
- Language
- Resolution
- Topic

Self-Report

- Zip Code
- Test Results
- Gender
- Age Group
- Repeating Caller (self-report)
- Emotional Status (inferred)

4.4 Flex Studies

Flex studies were completed demonstrating suitable robustness of the product across a broad range of operational and environmental condition consistent with over-the-counter use. Labeling was revised accordingly based on the results of these studies.

4.5 Quantitative Label Comprehension Study (OQ-OTC-LC-1)

The Quantitative Label Comprehension Study executed July through August 2007, tested 427 individuals on their ability to correctly comprehend key messages from the packaging and labeling. These included proper self-selection, understanding of key warnings, proper test procedure and device interpretation. The study included both English and Spanish speaking individuals and teenagers (14-

17). Demographics included low income and low education subjects. The observed comprehension scores were all >80% with the majority being >90%, with the exception of two (2) regarding reading a negative test result (70%) and what to do next if you are negative (77%). Comprehension scores for correct actions following a negative result were generally lower throughout due to the diversity of expressed reactions which did not necessarily conform to the range of acceptable answers. These label comprehension results were presented to FDA in January 2008 prior to the conduct of the Phase IIb observed use trial. Table 4.3 summarizes the results of the comprehension scores obtained in Quantitative Label Comprehension Study key messages. Subsequently, label comprehension was tested as part of the Label Mitigation Study performed after the Observed Use Study, but prior to the Unobserved Use Study. The final results for Label Comprehension can be found in Section 7.

Table 4.2 Comprehension of Key Messages

Question	Comprehension Score
What is this product used for?	99.30%
What to do if nervous and anxious?	95.32%
Can product be used to see if HIV is getting better?	93.21%
Is it okay to use product if pregnant?	91.80%
What to do if tamper-resistant seal is broken?	99.30%
What to do if kit has expired?	98.59%
Is it okay to use if 13 years old?	88.99%
Time between contracting HIV and when tests can detect it	85.01%
How long to wait after eating or drinking?	90.16%
What steps to follow when swiping gums?	95.55%
After swiping, what to do next?	95.55%
When to start timing test?	88.29%
Shortest amount of time before result is ready to be read?	92.04%
After how long is result no longer accurate?	97.19%
What does it mean when there are no lines on the stick?	70.26%
What is the result when lines are next to “C” and “T”?	91.80%
What is the result when there is a line next to “C” and a faint line next to “T”?	95.08%
What is the result when there is a line next to “C” and no line next to “T”?	94.85%
If result is an initial positive, what to do next?	98.13%
If result is negative, what to do next?	77.52%
If test not working, what to do next?	86.42%

4.6 Device Interpretation Study (OQ-OTC-2 (Phase IIa))

The Device Interpretation Study tested 2001 individuals on their ability to interpret pre-determined test results. Devices were fabricated to represent a Negative, High Positive, Weak Positive and Invalid test result. Individuals were given the laptop designed box and instructions containing each device and asked to interpret the results. The study included both English and Spanish speaking individuals and teenagers (14-17). Demographics included low income and low education subjects. The study was executed in August through October 2007. Results were presented to FDA in January 2008.

Table 4.3 **Device Interpretation Results and Analysis**

Test Device	Results Observed during the Device Interpretation Study	Adjusted proportions after elimination of "invalid" and "don't know*" results
Negative	93.80% (95% CI; 92.60%, 94.86%)	95.57%
High Positive	95.00% (95% CI; 93.90%, 95.96%)	96.74%
Weak Positive	81.96% (95% CI; 80.19%, 83.64%)	83.84%
Invalid	92.10% (95% CI; 90.77%, 93.30%)	

* A small proportion of subjects reported "don't know" when attempting to interpret the device

The results of the Device Interpretation Study (Phase IIa) are shown in table 4.4 (above). Proportion of correct interpretation for each type of test result studied are shown before and after (3rd column) adjustment by eliminating incorrect results that were reported as invalid ("test not working") or "don't know". This was done to identify the proportion of time when interpretation resulted in an incorrect result reported (i.e., positive results were reported as negative or negative results were reported as positive). Although rates of correct interpretation for all types of result were high, they did not meet the 95% LCI targets originally specified by BPAC in 2006. However, the data underwent further post-hoc analysis to attempt to predict the expected impact on specificity and sensitivity in actual use. This was based on an expected prevalence of weak positive results in an HIV positive test population based on additional empirical evidence derived from studying the observed range of test line reactivities in a population of HIV positive subjects. Using these data, the expected sensitivity was predicted to be approximately 96% and the expected specificity was predicted to be approximately 96%. Based on the data presented to FDA in January 2008, they agreed to allow OraSure to proceed into the Observed Use Study. The IDE was approved in March 2008. The data and post-hoc analyses from the Phase IIa Device Interpretation study were also presented at the 2009 BPAC.

4.7 Observed Use Study (OQ-OTC-4 (Phase IIb))

4.7.1 Design of Observed Use Study

The Observed Use Study was designed to have subjects self-test while under observation by a trained technician at the clinical site. The subject self-tested and interpreted their results. The observing trained technician did not interact with the subject but documented any errors seen during the performance of the test. Once the subject completed interpreting their test device, the trained technician also interpreted the device. The subject was then tested by another trained technician that was blinded to the results of the first test, utilizing the professional OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test with oral fluid.

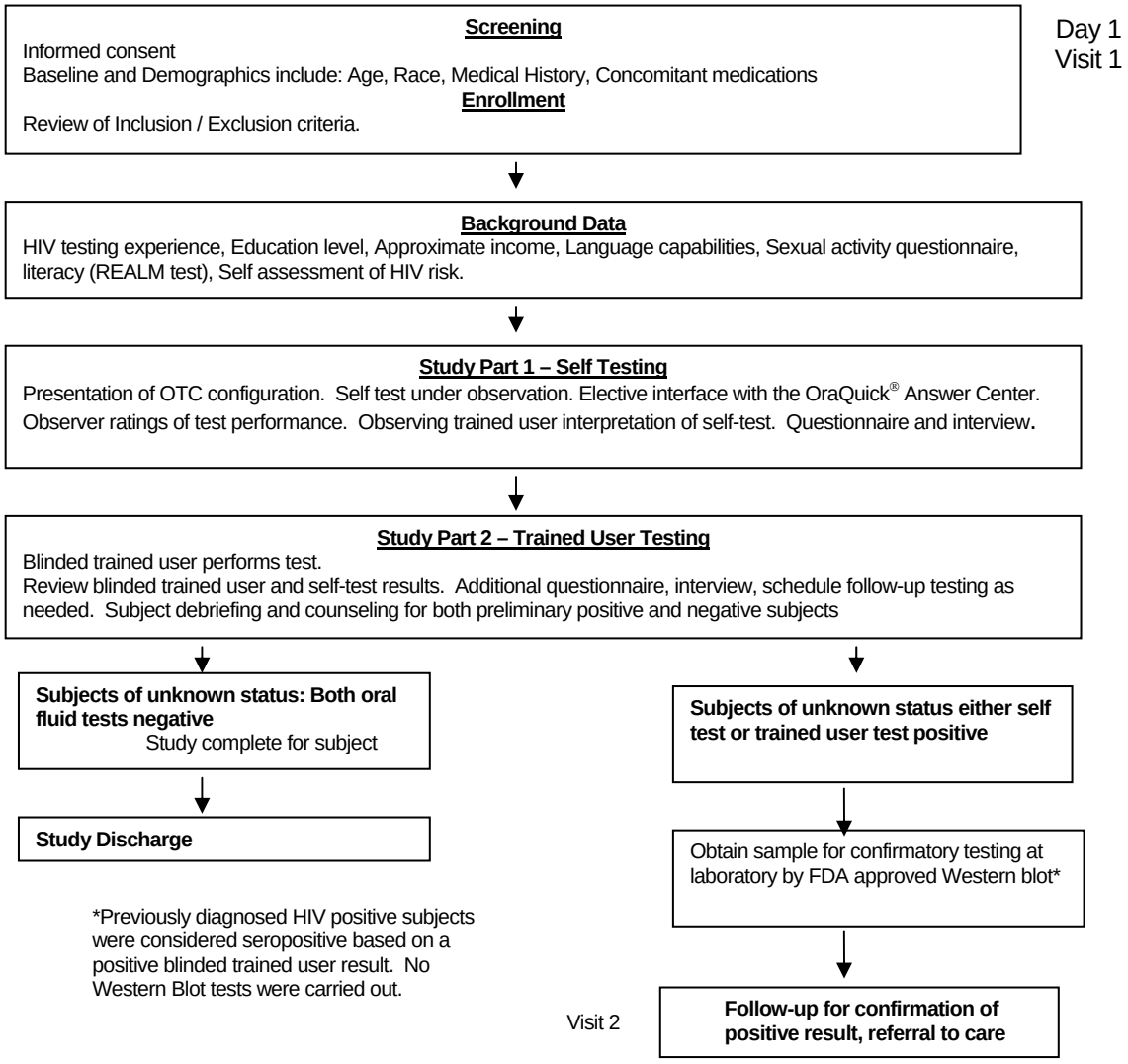
The study was designed to allow testing of up to 2000 subjects of unknown HIV status and 2000 subjects that were HIV Positive. The population of unknown status included general population (adults and teenagers (14-17) enriched for the demographics and risk factors of intended users. The study also included Spanish speaking individuals. There were planned interim analyses at 500 and 1,000 subjects from each arm of the study (HIV positives and HIV unknown status) against the acceptance criteria, to allow for enrollment to be stopped for futility or if the acceptance criteria were met.

Acceptance criteria for sensitivity and specificity for the oral fluid self-test versus trained user were:

- Sensitivity = [TP / (TP + FN)] x 100, where
  - TP (true positive) is positive oral fluid self test in agreement with blinded trained user positive oral fluid test, and
  - FN (false negative) is negative oral fluid self test discordant with blinded trained user positive oral fluid test.
  - Criterion was lower bound of 95% confidence interval of 95%
- Specificity = [TN / (TN + FP)] x100, where
  - TN (true negative) is negative oral fluid self test in agreement with blinded trained user negative oral fluid test, and
  - FP (false positive) is positive oral fluid self test discordant with blinded trained user negative oral fluid test
  - Criterion was lower bound of 95% confidence interval of 95%

Acceptance criteria included the requirement for identification of 10 newly identified HIV infections from subjects of unknown status. Figure 6 is a flow chart that summarizes the study design.

Figure 6



4.7.2 Results of the Observed Use Study

The Observed Use Study was conducted April through June of 2008. Results were presented to the BPAC in November 2009. A total of 1031 subjects were enrolled into the trial (531 Known HIV Positives and 500 of unknown HIV status). Table 4.5 below summarizes the demographics from the Observed Use Study. HIV risk factors information was collected from the subjects with unknown HIV status to ensure that a population with risk factors of the intended use population was being studied. The HIV risk factors were self reported through a questionnaire that was completed by subjects during the trial.

Table 4.4 **Observed Use Study Demographics**

Demographic Characteristics	Demographics by Percent
Male	66.9% (690/1031)
Female	31.9% (329/1031)
African American / Black	46.4% (478/1031)
Hispanic	20.7% (213/1031)
Low Literate (adult English speaking only)	19.0% (197/1031)
High School or Less (adults only)	45.8% (470/1031)
HIV Risk Factors	**HIV Risk Factors by Percent**
Homosexual / Bisexual	13.0% (65/500)
Ever Injected Non-prescription Drugs	11.2% (56/500)
Ever Traded Sex for Drugs or Money	8.4% (42/500)
Ever had a Sexually Transmitted Disease	22.6% (113/500)

FDA asked for specific at risk populations to be included within the populations tested in each of the studies. This was designed to represent the demographics of users who would purchase a HIV Kit over-the-counter, or to whom the kit might be distributed through existing public health testing clinics. FDA affirmed that the demographics of the study population for the Observed Use and Unobserved Use studies were consistent with their expectations.

Subjects who completed the self-test study interpreted their results as one of the following:

- May have HIV/Preliminary Positive
- Don't have HIV/Negative
- Test not working/Invalid
- Not Sure/Don't Know

The disposition of the sensitivity population ended with a total of 504 subjects in the final analysis. These were predominantly known HIV positive subjects along with 12 prospectively identified positives from the population of unknown HIV status. Of those 504 subjects, 24 did not obtain a test result either because they committed an operational error which resulted in an interpretation of Test Not Working or they responded with a result of "Don't know/Not Sure". Of the 480 subjects that obtained a test result, 470 were True Positive (TP) and 10 were False Negative (FN).

Sensitivity was calculated to be **97.9% (95% CI; 95.0%, 99.4%)**

Of the 10 false negatives (2.08%) observed in this study, all were known HIV positive individuals.

There were a total of 12 newly identified HIV positive individuals among the population of unknown status who correctly identified themselves as HIV positive by self-testing. All results were confirmed by Western blot. The observed prevalence rate during this trial was 2.4%. Table 4.6 summarizes the characteristics of the newly identified HIV positive subjects.

Table 4.5 Characteristics of Newly Identified HIV Positive Subjects

Characteristics (self reported)	n=12
African American	67% (8/12)
Female	42% (5/12)
Reported never testing previously	33% (4/12)
Likelihood of testing positive (0 Not at all - 10 Very likely)	Mean 4.1 Range 0 to 9 50% ≤ 4

The disposition of subjects of unknown HIV status for HIV ended with a total of 482 subjects in the final analysis for specificity. Of those 482 subjects, 9 did not obtain a test result either because they performed an operational error which resulted in an interpretation of Test Not Working or they responded with a result of "Don't know/Not Sure". Of the 473 subjects that obtained a test result, 472 were True Negative (TN) and 1 was a False Positive (FP). The following table is a summary of the performance of the test in the unknown HIV population.

Specificity for this population was calculated to be **99.79% (95%CI; 98.1%, 100.0%).**

Table 4.6 Performance of the Test in the Unknown HIV Population

		Blinded Trained User Result		
		POS	NEG	Invalid
Self-Test Result	POS	12	1	0
	NEG	0	472	0
	Invalid*	0	3	0
	Don't Know	0	6	0

Accuracy= 98.0% (484/494)
95% CIs: 96.3- 99.0%

*Reported in self-test as "Test not working"

The error rate observed in the HIV Positive population where individuals failed to obtain either a positive or a negative result was 4.76%. The error rate observed in the population of unknown HIV status was 1.82%. Table 4.8 summarizes the types of operational errors observed during the Observed Use Trial (Phase IIb).

Table 4.7 Operational Errors Observed

Self-Test Result	HIV Known positives n = 504	HIV Negative –unknown status n = 494
Device Interpretation Error	**7**	**4**
Dipping device in developer prior to swabbing gums	**7**	**4**
Spilling the developer	**4**	**0**
Not swabbing the gums	**4**	**1**
Could not find developer vial	**2**	**0**
Total	**24 (4.76%)**	**9 (1.82%)**

During the Observed Use Study, it was noted that a much larger proportion of operational errors were committed by the known HIV positive subjects. An additional analysis of the observational data indicated HIV positive subjects were much less likely to read the instructions for use (Table 4.9). These observations suggested that the HIV positive subjects were less invested in the outcome of the test because they already knew their HIV status.

Table 4.8 Observation of Reading Instructions

Self-Test Steps	HIV known positives	HIV Unknown Status
Read instructions on outside of box	76.1%[1]	90.6%
Read booklets supplied with test	67.5%[2]	85.4%

[1] p<0.001
[2] p<0.001

5. BPAC 2009

The final report for the Observed Use Study (Phase IIb) was submitted to FDA (CBER) in October 2008. In May 2009, FDA informed OraSure that they were going to present the information at the November BPAC Meeting to request a decision on whether or not OraSure should be permitted to move into Phase III (Unobserved Use Study). OraSure submitted the Phase IIb (Observed Use Study) final report with the sensitivity and specificity calculated excluding those subjects that did not obtain a test result. FDA believed that it was necessary to represent additional calculations of sensitivity and specificity including those results. So both sets of calculations were presented to BPAC, in addition to a hybrid model that included some and excluded others.

These results were presented to BPAC in a closed session on November 17, 2009.[1]

5.1 BPAC Outcomes

- Endorsed OraSure to proceed to Phase III (Unobserved Use Trial) after completion of labeling enhancements (to attempt to further reduce operational errors) and a verification of those changes
- Endorsed the conduct of the Phase III study in individuals of unknown HIV status (no known HIV positive subjects)
- Endorsed OraSure's proposed Phase III Trial design
- There was no consensus from the BPAC as to how individuals who fail to obtain a result should be treated in the performance calculations. However, it was generally agreed that obtaining as much definition of the circumstances surrounding a subjects failure to get a result would be critical in trial design in order to allow proper disposition of subjects. Later, FDA provided guidance that the rate of errors leading to a "no result" condition (later termed "Test System Failures") should be no more than ~2%.

Further discussions with FDA post BPAC, resulted in OraSure modifying the packaging and labeling to reduce the occurrence of operational errors observed in the Phase IIb (observed Use Study). Once packaging and labeling enhancements were completed, OraSure conducted a study to verify the changes. Upon completion of the verification of the enhanced labeling OraSure was permitted to move into the Phase III (Unobserved Use Study).

6. Label Mitigation Study

6.1 Packaging and Labeling Changes

OraSure evaluated the errors seen in the Phase IIb (Observed Use Study) to determine what if any changes could be made to the packaging and labeling to further reduce the error rate. These changes consisted of the following:

- **Product**
  - Vial cap was redesigned to include a thumb indentation for ease of use by consumers. This targeted the operational error of spilling the Developer Solution. Previously the cap design intuitively made the consumer twist the cap instead of popping it off, which causes the solution to spill. The motion of popping off the cap is now more intuitive with the new design.
  - The Laptop box was converted from a cardboard stock to a molded plastic box. This allowed for the design to be more robust and stable during use by the consumer.
- **Instructions for Use**
  - The names of the booklets were revised to represent the names that will be used for commercialization. The Pre-Test Informational booklet (HIV/AIDS Information) will now be called "HIV, Testing & Me" and the Post Test-Informational Booklet will now be called "What Your Results Mean to You".
  - The step for removing the cap from the test tube was revised for clarification to target the operational error of spilling the Developer Solution.
  - The step for collecting the Oral Fluid sample was revised to add emphasis that both the top gums and the bottom gums needs to be swabbed to target the operation error of not swabbing the gums.
  - A statement was added to the page that provides the consumer with the directions for interpreting their test results. The statement "If your Test DID NOT WORK or you are NOT SURE what your result is, call the toll free number, 1-866-436-6527." This revision targeted those subjects that did not obtain a test result because they reported "Test Not Working" or "Don't Know/Not Sure".

- Added a detailed list of the types of questions the call center could answer so the consumer understands that there is someone they can call to get clarification.

- **Outer Box**
  - The section explaining the "window period" was revised to include an explanation of a risk event to further help the consumer self-select.

6.2 Label Mitigation Study Design

OraSure entered into discussions with FDA in January 2010 to determine the clinical study design required to verify (packaging and labeling) changes prior to initiating the Unobserved Use Trial. The study design included three (3) cohorts consisting of general population, teenagers (14-17), and Spanish Speaking individuals. The study evaluated the following parts:

- Comprehension of key messages on both the outer box and the instructions for use
- Observed use of the device – Device used for this study were manufactured only to produce a control line. The subjects did not get a self-test result
- Device interpretation – This consisted of 1 - Negative Device, 1 - Invalid Device, 1 - Positive Device and 1- Weak Positive Device.

6.3 Label Mitigation Results

A total of 501 subjects were enrolled in the study. The criteria set for study success was to increase comprehension around what to do if not sure of the test result. The other targeted area was to reduce the operational errors observed in the Observed Use Study. The results of the Label Mitigation Study were included in the IDE Submission for the Unobserved Use Study in October 2010. The IDE was approved November 15, 2010 allowing OraSure to proceed with the Unobserved Use Study.

7. Study Results for Final Labeling

Tables 6.1 through 6.3 summarizes the label comprehension, device interpretation and the test system failure results based on the packaging and labeling of the OraQuick® In-Home HIV Test used in Unobserved Use Study. This shows the robustness of the packaging and labeling to consistently deliver high levels of label comprehension and device interpretation and minimize test system failures.

Table 7.1 Final Label Comprehension

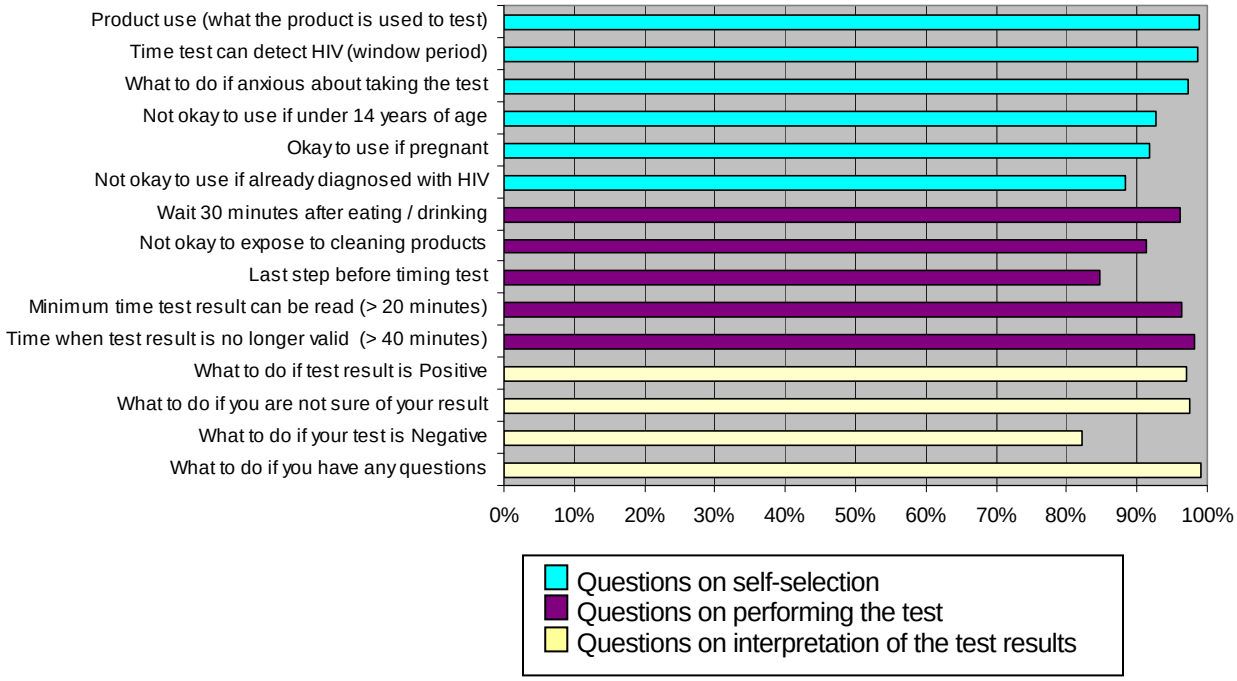


Table 7.2 Final Device Interpretation

Device Category	% Correct		% Correct (excluding invalids and/or "Don't Know/Not Sure")	
	% Correct	95% CI	% Correct	95% CI
Negative	95.2% (477/501)	(93.0, 96.9)	97.1% (477/491)	(95.3,98.4)
High Positive	96.0% (481/501)	(93.9, 97.5)	98.2% (481/490)	(96.5,99.2)
Low Positive	81.6% (409/501)	(78.0, 84.9)	84.2% (409/486)	(80.6,87.3)
Invalid	93.4% (468/501)	(90.9, 95.4)	94.0% (468/498)	(91.5,95.9)

Table 7.3 Final Error Rate

Operational Error	n=496
Did not swab	6 (1.21%)
Pre-Dipped into Developer and spilled Developer	1 (0.20%)
Pre-Dipped	1 (0.20%)
Spilled Developer	1 (0.20%)
Did not place test stick in vial	1 (0.20%)
Total	**10 (2.02%)**

8. Unobserved Use Study

The design of the unobserved use (Phase III) study was based on the results and observations from the previous studies and input from the 2009 BPAC. Specifically, FDA agreed that testing known HIV positive individuals in this study would not be required, since they do not have a vested interest in learning their status through the use of the product and do not represent intended users. The product warns against use by individuals that are HIV Positive. Consequently, FDA informed OraSure that the original requirement of prospective identification of 10 new HIV positive individuals originally recommended by BPAC in 2006 be increased to a minimum of 100 newly identified HIV positive individuals. This modification was made to allow for a sensitivity calculation within the HIV Unknown Status Population. Additionally, FDA requested that in addition to a population of high prevalence for HIV infection, OraSure study a low prevalence cohort representative of the general population. FDA also provided guidance that the rate of "Test System Failures" (instances where users fail to get an HIV result due to error) to be ~2%. Finally, following the discussion of cases of "no result" from the 2009 BPAC, the study algorithm was designed to include a series of questions to determine the subject's knowledge of their HIV status as a result of interacting with the test in those cases where they reported that they did not get a positive or negative result.

The Final IDE including the Unobserved Use Study Clinical Protocol was submitted to the FDA in October 2010. Approval of the IDE was received on November 15, 2010. The first patient was enrolled into the study on December 9, 2010.

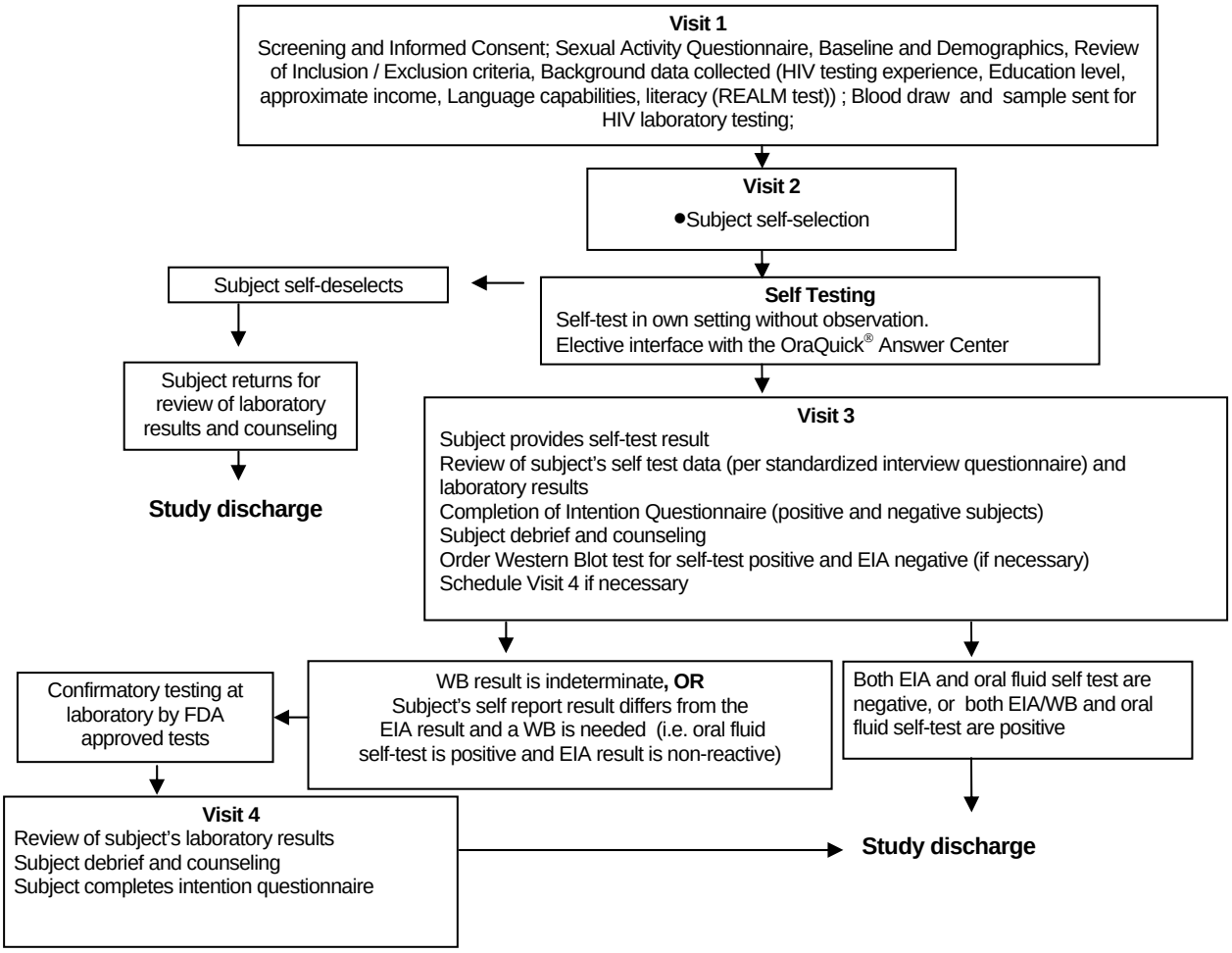
8.1 Unobserved Use Study Design

The Unobserved Use Study was designed to have subjects self-test as if they purchased the product. The study was designed to allow for up to 5000 subjects of unknown HIV status at high prevalence sites and 1000 subjects from a low prevalence cohort representative of the general population. The demographic composition of the high prevalence population reflected the major risk categories for HIV infection as defined by CDC. There were 17 high prevalence sites and 3 low prevalence sites representing broad geographic distribution across the US. The study population included both English and Spanish speakers.

Each subject made multiple visits to the study sites. At Visit 1, enrolled subjects had blood drawn for HIV laboratory testing. Subjects then returned for Visit 2 and were able to review the outer package to allow for them to self-select to self-test for HIV. At Visit 3, subjects retuned to the site and provided their self test result by responding to questions asked by site staff according to a standardized script. At this

visit subjects were provided their laboratory test results and received appropriate counseling. Additional information on the intended next actions of both HIV positive and HIV negative subjects was collected. In the rare event that additional laboratory testing was required in order to definitively determine a subject's HIV status a Visit 4 was a scheduled to communicate the results. In addition to self-testing with the OraQuick® In-Home HIV Test, all subjects were tested for HIV antibodies by an FDA approved serum EIA and Western blot (as needed). The sensitivity and specificity were calculated based on the comparison of the self-test result to the subject's true HIV serostatus determined by FDA approved laboratory testing. The study procedures are further summarized in Figure 10. The OraQuick® Consumer Support Center was available 24/7 for the subjects to access as needed during the conduct of the study.

Figure 10 Unobserved Use Study Outline

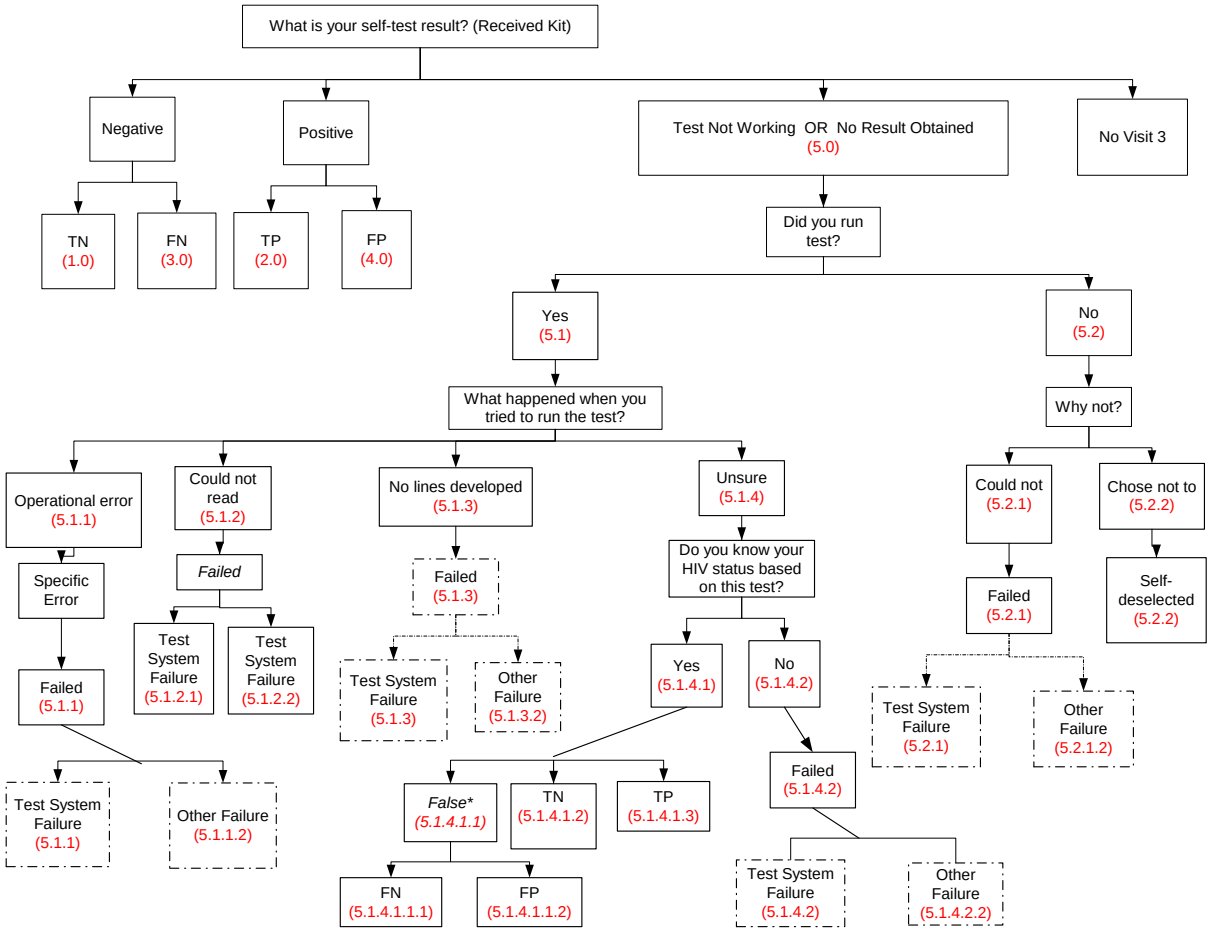


The Unobserved Use Study Analysis was based on the following:

- Sensitivity – Calculated point estimate and lower CI in HIV positive subjects identified from unknown risk and high risk populations.
- Specificity - Calculated point estimate and lower CI in HIV uninfected subjects identified from unknown risk and high risk populations and the general population
- Test Reliability – Percent of occasions when the user did not obtain positive or negative results was assessed. FDA has indicated that this should be no more than ~2%
- Prospective identification of at least 100 previously undiagnosed HIV positive subjects

The flow chart in Figure 11 describes the categorization of self-test results that FDA and OraSure agreed upon for this study. This algorithm design was intended to allow all self-test results to be correctly categorized as included in, or excluded from sensitivity and specificity calculations as well Test Reliability (%) calculations. The numbering scheme was annotated at a later date to facilitate review and discussions in determining the pathways to which each subject was assigned.

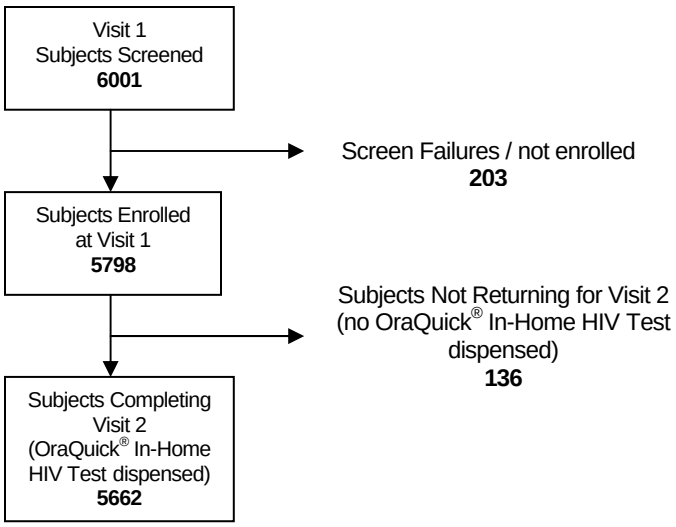
Figure 11: Annotated Final PMA Decision Tree



8.2 Disposition of Subjects

A total of 6001 subjects signed informed consent and were screened at Visit 1. Figure 12 provides a high level flow diagram of the disposition of subjects. A total of 203 subjects failed to meet the inclusion/exclusion criteria and were not enrolled. The remaining 5798 subjects were consented and enrolled. Of the 5798 subjects enrolled, 5662 subjects received the investigation OraQuick In-Home HIV Test.

Figure 12 Disposition of Subjects for Visits 1 & 2



Subjects were enrolled across 20 clinical sites, with 17 sites enrolling subjects from a high prevalence population, and 3 site enrolling subjects from a low prevalence (general) population. Table 5.1 summarizes the distribution of subjects by location and observed prevalence. The higher prevalence areas were further subdivided into east coast, south central, and mountain/west. This summary also includes the newly identified HIV positive subjects.

Table 5.1 Prevalence by Site

Site #	City	State	# Enrolled	# Safety Population (Received Kit)	HIV Infected (according to FDA approved blood test)	Approximate Prevalence*
03	Fort Lauderdale	FL	500	488	36	7.4%
04	NY	NY	103	103	0	0.0%
07	Miami	FL	170	169	0	0.0%
10	Washington	DC	173	170	0	0.0%
13	Philadelphia	PA	69	63	2	3.2%
14	Lexington	KY	272	265	2	0.8%
21	Miami Beach	FL	130	123	3	2.4%
Higher Prevalence areas: EAST			**1,417**	**1,381**	**43**	**3.1%**
06	Houston	TX	469	448	13	2.9%
11	Austin	TX	247	243	2	0.8%
12	Houston	TX	500	500	18	3.6%
19	Metairie	LA	250	246	2	0.8%
23	Mobile	AL	297	290	7	2.4%
Higher prevalence areas: SOUTH CENTRAL			**1,763**	**1,727**	**42**	**2.4%**
05	San Francisco	CA	106	102	2	2.0%
09	Phoenix	AZ	305	290	1	0.3%
15	Palm Desert	CA	497	495	8	1.6%
18	San Francisco	CA	292	285	9	3.2%
20	Beverly Hills	CA	309	282	14	5.0%
Higher Prevalence areas: MT / WEST			**1,509**	**1,454**	**34**	**2.3%**
Higher Prevalence area sites: ALL			**4,689**	**4,562**	**119**	**2.6%**
01	Allentown	PA	327	321	1	0.3%
17	Rochester	NY	389	387	0	0.0%
22	Omaha	NE	393	392	0	0.0%
Lower Prevalence population (general population)			**1,109**	**1,100**	**1**	**0.1%**
Total – ALL SITES			**5,798**	**5,662**	**120**	**2.12%**

8.3 Demographics

Of the 5798 subjects enrolled, 1109 were from a low prevalence population and 4689 were from a high prevalence population. Table 5.2 below summarized select demographics and HIV risk for subjects enrolled in the study. Information regarding HIV risk was self reported by subjects through the use of a questionnaire completed at Visit 1.

Table 5.2 Select Demographics of Enrolled Subjects

Demographic Characteristics	High Prevalence by Percent	Low Prevalence by Percent	Total by Percentage
Male	53.5% 2509/4689	35.7% 396/1109	50.1% 2905/5798
Female	46.0% 2159/4689	64.3% 713/1109	49.5% 2872/5798
African American/Black	53.0% 2483/4689	21.7% 241/1109	47.0% 2724/5798
White	36.4% 1708/4689	71.1% 788/1109	43.0% 2496/5798
Hispanic*	17.9% 839/4689	8.6% 95/1109	16.1% 934/5798
Low Literate (English speaking only)	31.5% 1478/4689	13.2% 146/1109	28.0% 1624/5798
High School or Less	58.0% 2719/4689	35.5% 394/1109	53.7% 3113/5798

* Can be of any Race

8.4 Most-Affected Subpopulations

A total of 4689 subjects were enrolled from a high prevalence population. Table 5.3 below presents the HIV categories and seropositvity data among the 4562 subjects receiving an Investigational Kit. These categories align with select sub-populations identified by CDC.

Table 5.3 Summary of HIV Confirmed Positive Subjects in the High Prevalence Population by Select Sub-Population

Select Sub-Population*	Received Investigational Kit (n)	Confirmed Positive by FDA-approved Serology	Positive Rate within Risk Category
White MSM	191	7	3.7%
Black MSM	189	29	15.3%
Hispanic MSM	71	6	8.5%
Black Heterosexual Male	1033	30	2.9%
Black Heterosexual Female	859	21	2.4%
Hispanic Heterosexual Female	370	2	0.5%
Hispanic Heterosexual Male	307	5	1.6%
White Heterosexual Female	414	2	0.5%
White Heterosexual Male	527	5	0.9%
All others	601	12	2.0%
Black Male IDU	201	4	2.0%
Black Female IDU	88	3	3.4%
Traded Sex** - All Races/Gender	913	33	3.6%
Prior STD - All Races/Gender	1624	52	3.2%

* Subjects may fall into multiple categories, therefore, the preceding numbers do not add up to the total that received an Investigational Kit.

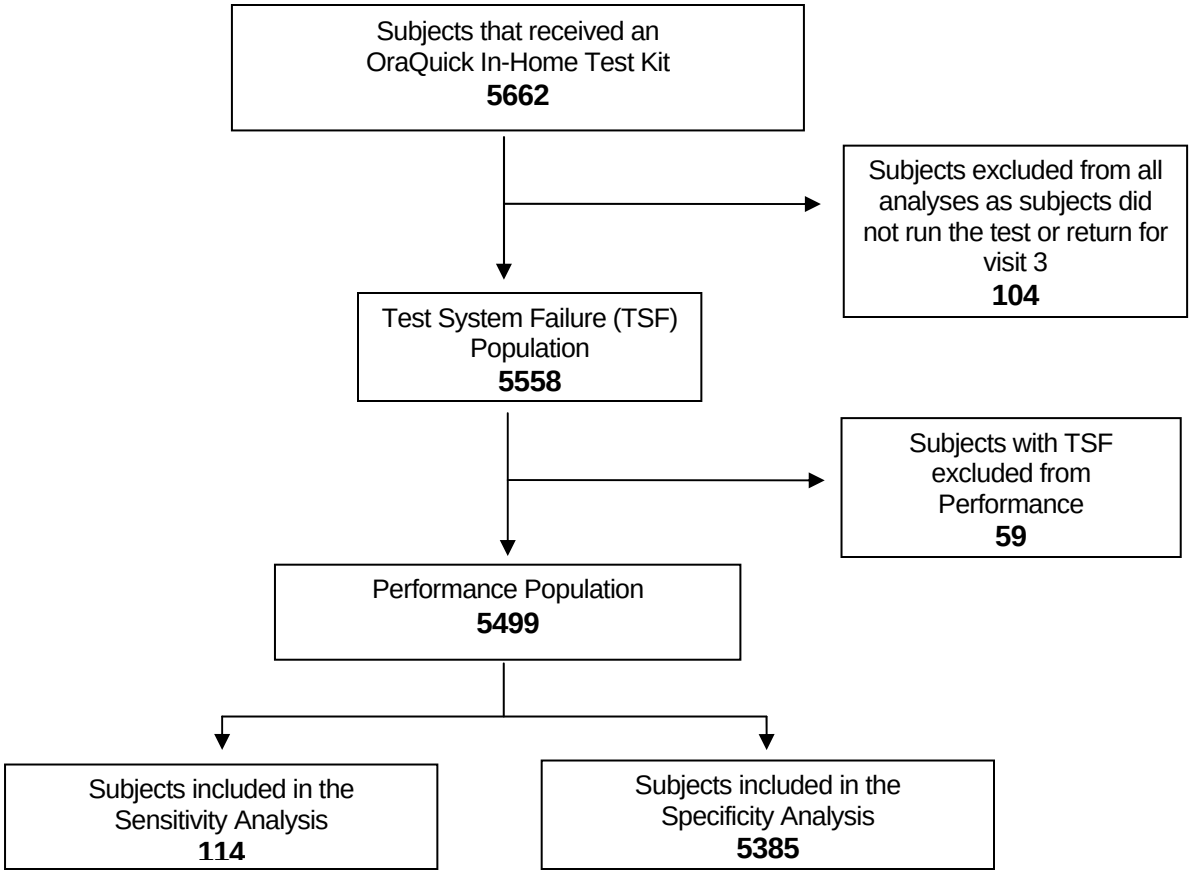
** traded sex for drugs or money

8.5 Analysis Populations

8.5.1 Disposition

Of the 5662 subjects that received an OraQuick® In-Home HIV Test, 5499 were included in analysis of sensitivity and specificity. Figure 15 provides this information in a flow diagram.

Figure 15: Disposition of Subject in Analyses Populations



8.5.2 Subjects Excluded from Performance Analyses

Of the 5662 subjects that received an OraQuick® In-Home HIV Test, 163 subjects were not included in the sensitivity and specificity calculations. Information about the disposition of these subjects by their FDA approved test result is provided in Table 5.4.

Table 5.4 Summary of Subjects in the Safety Population who were Excluded from the Sensitivity and Specificity Analyses

	FDA-Approved Test Results		
Subjects, n	Negative	Positive	Total
Total number of subjects excluded from sensitivity and specificity analysis	157	6	163
Reason for exclusion (flowchart pathway)			
Excluded from the test system failure calculations	102	2	104
Did not return for visit 3 (no pathway)	65	1	66
OraQuick self-test result not recorded in source(no pathway)	7	0	7
Lost kit prior to taking test (5.2.1.2)	18	0	18
Chose not to run test (5.2.2)	8	1	9
Did not run test – no liquid in vial (5.2.1.2)	2	0	2
Tried to run test – operational error (5.1.1.2)	2	0	2
Included in test system failure calculations	55	4	59
Could not run test (5.2.1)	17	0	17
Ran test – operational error (5.1.1)	13	0	13
Ran Test – Could not read (5.1.2.1 and 5.1.2.2)	1	1	2
Ran test – no lines developed (5.1.3)	12	0	12
Ran test – unsure of (did not know) HIV status (5.1.4.2)*	12	3	15

*One subject (14-0116) was included in both the test system failure calculation and specificity calculation as TN per the request of FDA. Comments from subject state: 'I was in a hurry and did not wait the entire 20 mins. I think the test was neg. I didn't look at my directions to see what the results meant. Then I waited the entire time. Pretty sure it was neg."

A total of 104 subjects were excluded from both the Test System Reliability Calculations and the Sensitivity and Specificity Calculations. Most of these subjects (63%) were excluded because they did not return to complete Visit 3. Of those that failed to return, one subject was found to be HIV positive per laboratory based tests; however, because they did not return to the site, they were not informed of their positive status. This subject was determined lost to follow-up after a minimum of three documented attempts to contact the subject. There were also seven (7) subjects that returned to report a self-test result, however, this result was not recorded in the source documents. The remaining 31 subjects returned to complete Visit 3, however, they did not run the test. Eighteen (18) of these 31 subjects did not run the test because they lost it prior to running the test. Nine (9) subjects stated they chose not to run the test for various reasons. Of these nine (9) subjects, one subject was HIV positive. This subject stated he was too scared to reveal his results, so he chose not to interpret his results. He was informed of his positive HIV status at Visit 3. Two (2) subjects that reported an operational error due to missing components were excluded from the Test System Failure Calculations after discussion with CBER. This is in addition to two (2) other subjects who reported missing components, but did not attempt to run the test.

Subjects that returned for Visit 3 and stated they ran the OraQuick® In-Home HIV Test but did not report a Negative or Positive result were asked "What happened when you tried to run the test"? Responses fell into one of four categories: 1) Operational Error 2) Could Not Read 3) No lines Developed 4) Unsure. Subjects who stated they were unsure were subsequently asked "Do you know your HIV status based on this test result?" This question was intended to determine whether the individuals who were unsure of their result believed that they knew their HIV status as a result of the test. Subjects who were unsure of their test

result and stated that they did not know their HIV status based on the test were excluded from the sensitivity and specificity calculations. All subjects that attempted to run the OraQuick® In-Home HIV Test, but did not generate a result, or they could not run the test due to a test system failure were included in the Test System Failure Calculations as per the approved protocol algorithm (see section 7.1).

Among all subjects who used the OraQuick® In-Home HIV Test, there were 5498 successful tests (98.92%; CI = 98.61%–99.18%) and 60 failed tests (1.08%; CI = 0.82%–1.39%). A total of 60 subjects that attempted to run the OraQuick® In-Home HIV Test, but did not generate a result, or they could not run the test due to a test system failure, and were thus include in the test system reliability calculation. A summary of the overall test system failure rate and test reliability rate along with the reasons for failure are presented in Table 5.5 and 5.6, respectively.

Table 5.5: Test Failure Rate and Test Reliability (All Subjects)

	Prevalence Area		
	High	**Low**	**Total**
Number of subjects who tried to run test	4465	1093	5558
Test System Failure	56 (1.25%) (95%CI: 0.95%-1.63%)	4 (0.37%) (95%CI: 0.10%-0.93%)	60 (1.08%) (95%CI: 0.82%-1.39%)
Successful Test	4409	1089	5498

Table 5.6: Summary of Test System Failures (All Subjects)

	Prevalence		
	High	**Low**	**Total**
Test System Failures, n (%)	**56 (1.25%)**	**4 (0.37%)**	**60 (1.08%)**
95% confidence interval, % [a]			**0.82%, 1.39%**
Reason for failure (flowchart pathway)			
Ran test – operational error (5.1.1)	**11**	**2**	**13**
Spilled liquid	3	2	5
Did not understand directions	4	0	4
Pre-dipped prior to swabbing	1	0	1
Stick fell in toilet	1	0	1
Didn't swab gums	1	0	1
Couldn't determine results	1	0	1
Ran Test – Could not read (5.1.2)	**2**	**0**	**2**
Ran test - No lines developed (5.1.3)	**10**	**2**	**12**
Ran test - Unsure of HIV status (5.1.4.2)	**15**	**0**	**15**
Did not understand what lines meant	10	0	10
No additional comments	2	0	2
Thought investigational center staff would read for them	1	0	1
Did not dip swab, so no line	1	0	1
Read results at visit 3 with help of investigator (took 1h prior)	1	0	1
Could not run test (5.2.1)	**17**	**0**	**17**
No additional comments	10	0	10
Spilled liquid	3	0	3
Did not understand or follow directions	3	0	3
Ran out of time – ran test but didn't read it	1	0	1
Ran test - Unsure of results but aware of HIV status (5.1.4.1.2) [b]	**1**	**0**	**1**

[a] 95% confidence interval calculated using SAS PROC FREQ with the exact binomial option.

[b] One subject (14-0116) was included in both the test system failure calculation and specificity calculation as TN per the request of FDA. Note: Flowchart Pathway is included where applicable

There were four (4) subjects with Test System Failures that were identified as HIV positive based on laboratory results. Per the final PMA decision tree, these subjects were included in the test system failure calculations only.

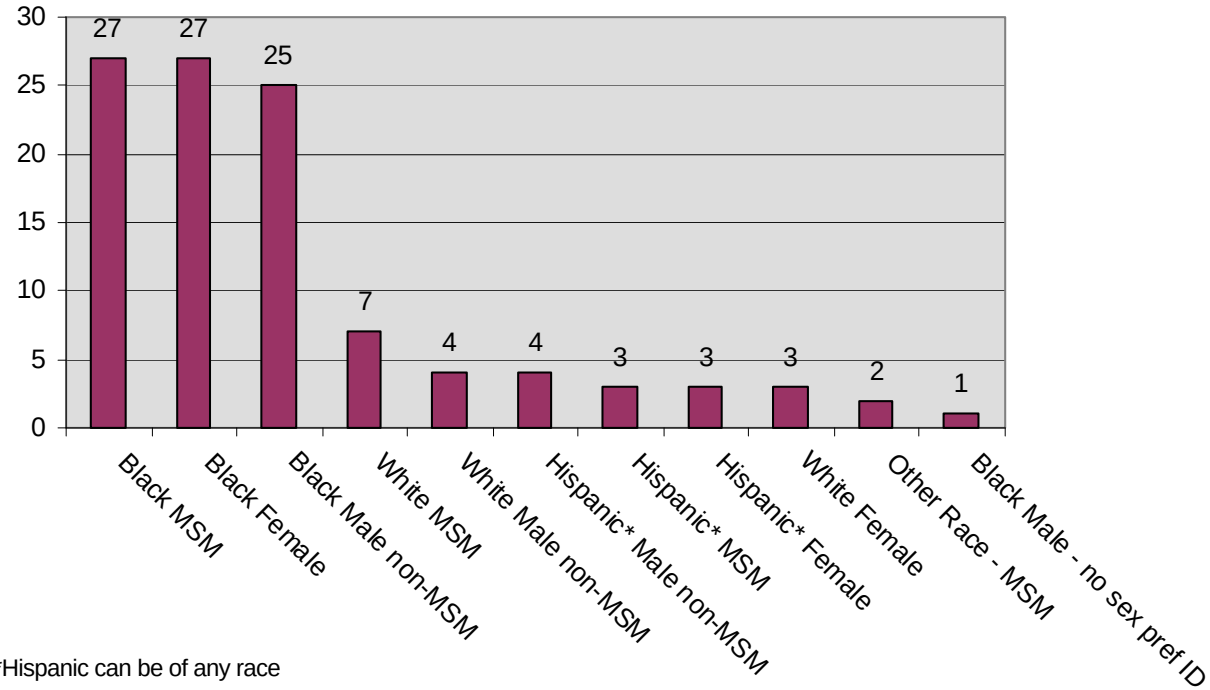
8.5.3 Overall Sensitivity Analysis

A total of 114 subjects were included in the sensitivity analysis. Of these, 106 subjects were true positive, as their self-test results and lab result were both positive. Eight (8) subjects were reported as false negative, with all 8 reporting a negative self-test result and having a positive laboratory result. Sensitivity was calculated as 93.0% (106/114) with a 95% Confidence Interval of 86.6%-96.9%.

8.5.3.1 Most-Affected Subpopulations

Of the 106 HIV positive subjects that reported a positive OraQuick® In-Home Test, most were black MSM (25.5%), black females (25.5%), and black non-MSM males (23.6%), respectively. Figure 16 summarized the risk categories of the 106 subjects who were identified as HIV positive by self-testing.

Figure 16 Distribution of All Subjects Positive with the OraQuick® In-Home HIV Test (n=106)



*Hispanic can be of any race

8.5.3.2 Previous HIV Testing History of Newly Diagnosed HIV Positive Subjects

Of the 114 subjects included in the sensitivity analysis that were newly diagnosed with HIV, a total of 44 (38.6%) had never been tested for HIV before and 70 subjects (61.4 %) had reported they had previously been tested for HIV.

8.5.3.3 False Negative Subjects

Eight (8) of the recorded false negative subjects provided a definitive answer of "negative" when asked to self report their HIV status according to the OraQuick® In-Home HIV Test. Subjects with false negative results were not clustered in any particular site and were not asymmetrically distributed according to race, gender, sexual orientation or measured literacy score. Select demographic and sexual orientation information is provided in Table 5.7.

Table 5.7: Summary Information for Subjects with False Negative Self-Test Results

Subject	Age	Gender	Race	Ethnicity	Language	Sexual Orientation	REALM Score	Wb Result
03-0006	52	female	Black/African American	non-Hispanic	English	heterosexual	65	Pos
03-0125	53	male	Black/African American	non-Hispanic	English	heterosexual	66	Pos
06-0312	47	Male	Black/African American	non-Hispanic	English	heterosexual	62	IND
06-0398	46	female	Black/African American	non-Hispanic	English	heterosexual	49	Pos
13-0056	23	Male	Other: Hispanic	Hispanic	English and Spanish	homosexual	65	Pos
18-0120	20	Male	Black/African America	non-Hispanic	English	homosexual	35	Pos
19-0075	53	Male	Black/African American	non-Hispanic	English	heterosexual	64	Pos
20-0315	26	Male	Black/African American	non-Hispanic	English	heterosexual	65	Pos

Abbreviations: IND = Indeterminate; Pos = Positive, REALM = Rapid Estimate of Adult Literacy in Medicine; Wb = Western Blot

One of the eight (8) false negative subjects was indeterminate in initial confirmatory testing. This subject was Western blot positive in subsequent testing, indicating this subject was in the process of sero-converting at this time of testing. This lack of a fully developed antibody response could have resulted in the false negative result in the investigational test.

The remaining false negative subjects were all Western blot positive at the time of testing. The reasons for these false negative results based on self-reported outcomes of an individual's self-testing are unknown. Review of source documents did not lend any further information as to root cause. As previously noted, previous device interpretation studies (Phase IIa and Label Mitigation with observed use of the Investigational Kit) of a subject's ability to perceive and interpret the range of expected reactivity (strong to low positive results), predicted a sensitivity of >95%[1] compared to the 93.0% calculated from self-reported positive and negative results in the Unobserved Self-Test study.

8.5.4 Overall Specificity Analysis

A total of 5385 subjects were included in the specificity analysis. Of these, 5383 subjects were reported as true negative, as their self-test results and laboratory result were both negative. One subjects self-reported a positive self test result with a negative laboratory result. One subject was also imputed as a true negative (and included in the test system failure calculation) based on the subject's comment that they were unsure of their test result but stated their HIV status was negative based on the test. One (1) subject was reported as false positive.

Specificity was 99.98% (5384/5385) with a 95% Confidence Interval of 99.90%-100.0%.

8.5.5 Overall Positive and Negative Predictive Values and Accuracy

In the calculations below, the values are calculated using data from all subjects who self-reported an Investigational Test result of either "positive" or "negative" and also subjects who were imputed to be either a true or false Investigational Test result by the algorithm employed.

PPV = 99.1% (95% CI: 94.9% - 100.0%) (106/107)

NPV = 99.85% (95% CI: 99.71% - 99.94%) (5384/5392)

The accuracy calculation includes data from all subjects who self-reported an Investigational Test result of either "positive" or "negative" or who were imputed to be either a true or false Investigational Test result by the algorithm employed.

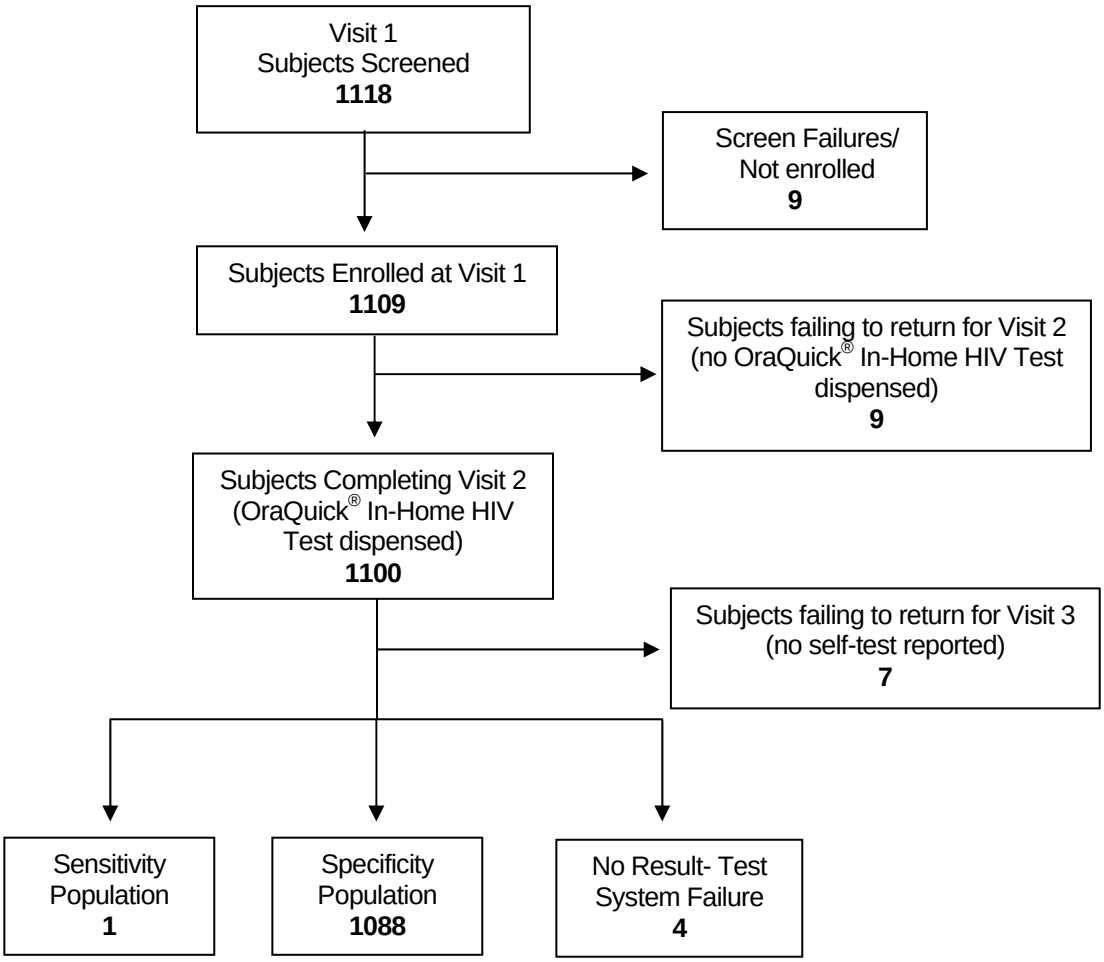
Accuracy = 99.84% (95% CI = 99.69% - 99.93%) (5490/5499)

8.5.6 Individual Population Analysis

8.5.6.1 Low Prevalence Population Analysis

A total of 1118 subjects were initially consented and screened at Visit 1 across three (3) sites that enrolled subjects from a low prevalence population. Nine (9) subjects failed to meet the inclusion/exclusion criteria and were not enrolled. The remaining 1109 subjects were consented and enrolled. Of the 1109 subjects enrolled, nine (9) did not receive an OraQuick® In-Home HIV Test at Visit 2. Of the 1100 subjects that received a kit, seven (7) did not return to the site for Visit 3. The disposition of subjects from these 3 sites is described in Figure 18.

Figure 18 Disposition of Subjects at Low Prevalence Sites



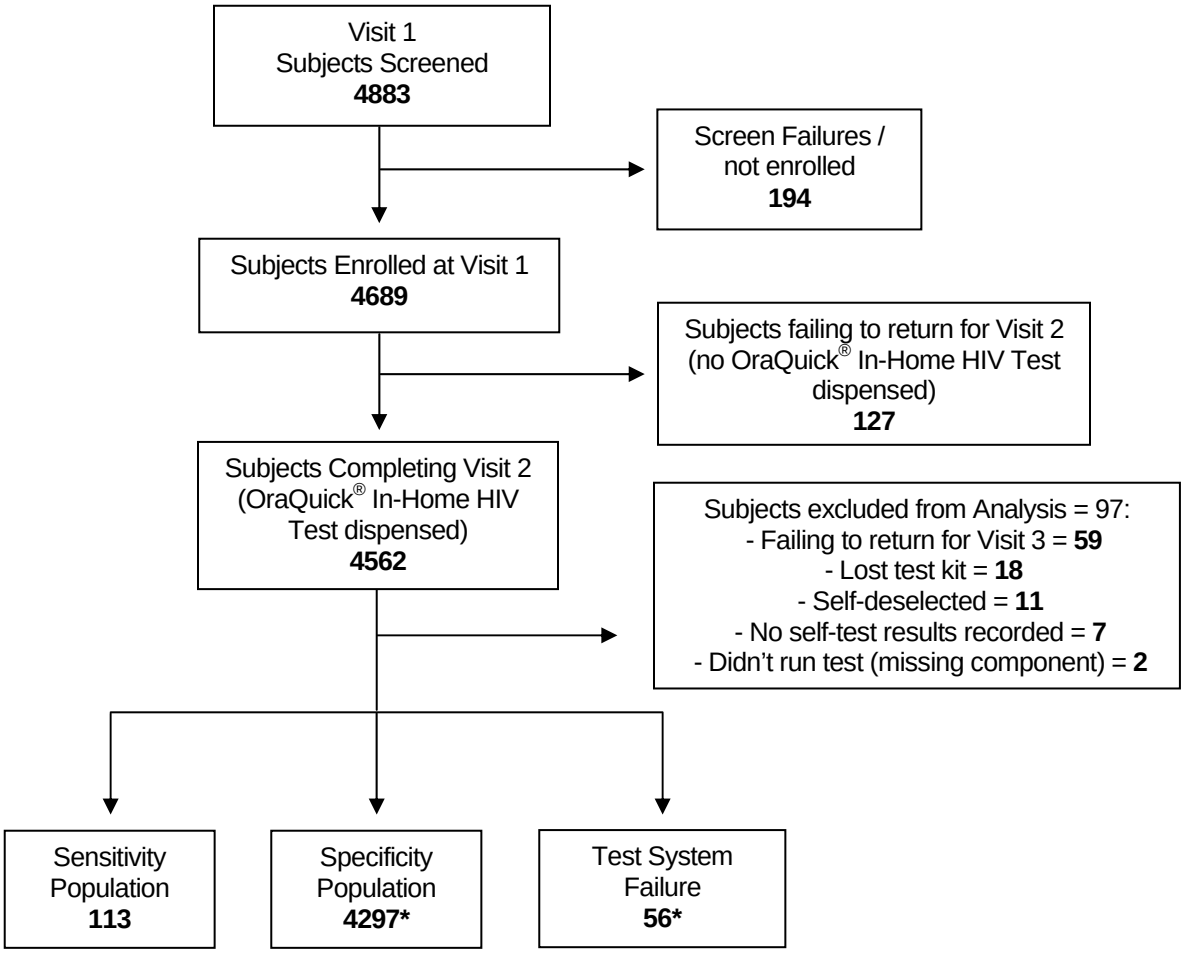
There was 1 subject in the sensitivity analysis set that was positive by both FDA approved test and by self test. The specificity analysis set is comprised of the 1088 subjects who were concordant negatives by the OraQuick® In-Home HIV Test and the FDA approved blood test. Four seronegative subjects self reported they did not obtain a result and constituted Test System Failures. The calculated performance of the OraQuick® In-Home HIV Test for the low prevalence population was:

Sensitivity	**= 100% (95%CI: N/A)** **(1 TP) / (1 TP + 0 FN)**
Specificity	**= 100% (95%CI: 99.66%-100%)** **(1088 TN) / (1088 TN + 0 FP)**
Test System Failure Rate	**= 0.37% (95%CI: 0.10%-0.93%)** **(4 failures) / (1093 failure population)**
PPV	**= 100% (95% CI: 2.5% - 100%)** **(1/1)**
NPV	**= 100% (95% CI: 99.66% - 100%)** **(1088/1088)**
Accuracy	**= 100% (95% CI = 99.66% - 100%)** **(1089/1089)**

8.5.6.2 High Prevalence Population Analysis

A total of 4883 subjects signed consent and were screened across 17 investigational centers recruiting from a high prevalence population. A total of 194 subjects failed to meet the inclusion/exclusion criteria and were not enrolled. The remaining 4689 subjects were consented and enrolled. Of the 4689 subjects enrolled, 127 did not receive an OraQuick® In-Home HIV Test at Visit 2. Of the 4562 subjects that received a kit, 59 did not return to the site for Visit 3. Thirty-eight (38) were excluded for reasons noted in the figure below. The disposition of subjects from these 17 sites is described below in Figure 19.

Figure 19 Disposition of Subjects at High Prevalence Sites



* One subject included in both the Specificity Population and the Test System Failure Population

Of the 4562 subjects who received an OraQuick® In-Home HIV Test, 97 subjects were excluded from the performance analyses, as they did not return for Visit 3, or they did not run the test. There were 113 subjects included in the sensitivity analysis, of which 105 were concordant positives between results self-reported by the OraQuick® In-Home HIV Test and the FDA approved blood test. The specificity analysis set was comprised of 4297 subjects, of whom 4296 had concordant negatives results between the OraQuick® In-Home HIV Test self reported result, and the FDA approved blood test. The calculated performance of the OraQuick® In-Home HIV Test for the high prevalence population was:

Sensitivity **= 92.9% (95%CI: 86.53%-96.89%)**
(105 TP) / (105 TP + 8FN)

Specificity **= 99.98% (95%CI: 99.87%-100.00%)**
(4296 TN) / (4296 TN + 1 FP)

Test System Failure Rate **= 1.25% (95%CI: 0.95%- 1.63%)**
(56 failures) / (4465 population who attempted to run test)

PPV	**= 99.1% (95% CI: 94.86% - 99.98%) (105/106)**
NPV	**= 99.81% (95% CI: 99.63% - 99.92%) (4296/4304)**
Accuracy	**= 99.80% (95% CI = 99.61% - 99.91%) (4401/4410)**

8.6 Ratios

At the 2009 96th meeting of the BPAC, FDA (Dr Richard Forshee) presented the "Risks and Benefits of Home-Use HIV Test Kits". Included in his presentation were three specific ratios he employed in his assessments: TP/FP; TP/FN; and TN/FP. These ratios were calculated to use as surrogates for quantitative estimates of benefit and risk and to provide insight into public health tradeoffs between beneficial and adverse test outcomes.

These ratios were generated corresponding to the minimum (2006) BPAC criteria of 95% sensitivity and specificity as well as those predicted by current FDA-approved tests for professional use. These were also modeled using different levels of seroprevalence. For example, FDA presented ratios corresponding to the 2006 BPAC criteria as 45, 23, and 0.3 for TP/FN, TN/FP and TP/FP ratios respectively.[1] Dr. Forshee also presented TP/FN ratios ranging from 6 (assuming 90% sensitivity) to 20 assuming 99.5% sensitivity.[2] Similarly TN/FP ratios ranging from 13 (97.5% specificity) to 20 (99.5% specificity) were presented.

For the OraQuick® In-Home HIV Test , these ratios have been calculated from the frequency of TP, FP, TN, and FN for the overall unobserved self-test study population. These were

TP/FP = (106 results/1 results) = 106

TP/FN = (106 results/8 results) = 13.3

TN/FP = (5384 results/1 results) = 5384

Each of these ratios is indicative of a net beneficial expected outcome for a product commercialized in the OTC market. In particular, the very high ratios (TP/FP and TN/FP) deriving from the high specificity of the test indicate the appropriateness of this test system as an effective screening tool even in low prevalence populations. The calculated TP/FN ratio predicts a strong benefit to risk from deployment of this test in at-risk populations that would not otherwise test for HIV (see Section 8: Benefit to Risk).

8.7 Subject Intentions After Completion of Testing

Upon completion of testing and counseling for their HIV status (based on laboratory results), subjects were asked a series of Intent Questions. They were asked to provide their response on a scale of 0 to 4 with 0 being "not at all likely" to 4 being "definitely". Subjects were asked the following:

HIV Positive Subjects

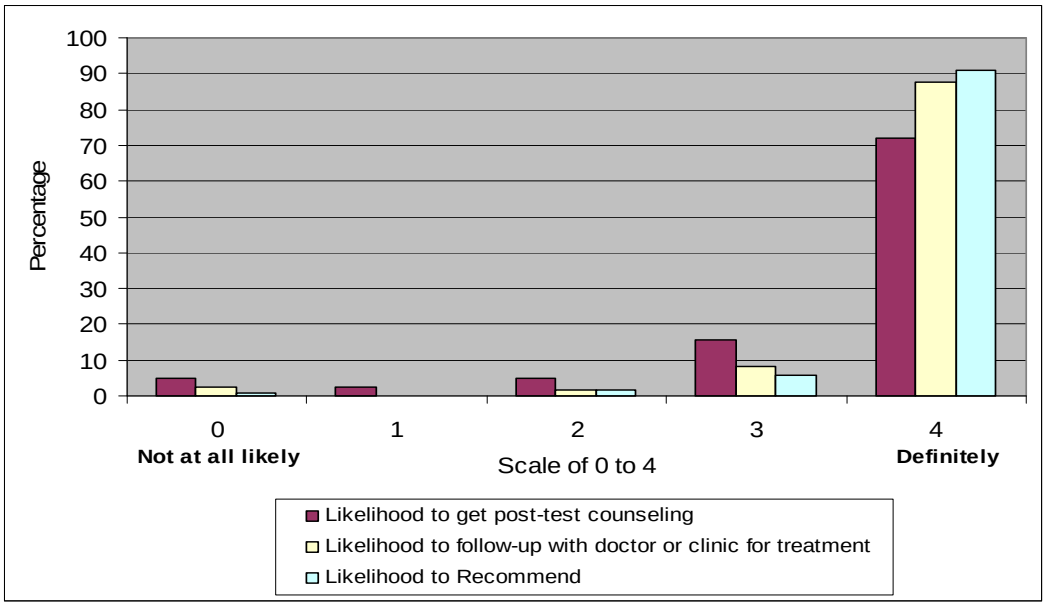
- If you had purchased this kit as an over-the-counter product, how likely would you have been to get post-test counseling?
- If you had purchased this kit as an over-the-counter product, how likely would you have been to follow-up with a doctor or clinic for treatment options?
- When this test becomes available over the counter, how likely are you to recommend this test to someone to help them assess their HIV status?

HIV Negative Subjects

- How likely are you to get tested for HIV again, at a clinic or other center?
- When a rapid HIV home test becomes available over the counter, how likely are you to use it to test yourself?
- When a rapid HIV home test becomes available over the counter, how likely are you to use it to screen sexual partners?
- How likely are you to change your behaviors based on the experience of taking this test?

As depicted in Figure 20, almost all HIV-positive subjects (96%; combined percentage of definitely (88%) and highly likely* (8%)) stated that they would follow-up with a doctor or clinic for treatment options had they obtained the OraQuick® In-Home HIV Test OTC, and 97% (combined percentage of definitely (91%) and highly likely* (6%)) of the HIV-positive subjects reported that, if the OraQuick® In-Home HIV Test is available OTC, they would recommend the test to someone to help them assess their HIV status.

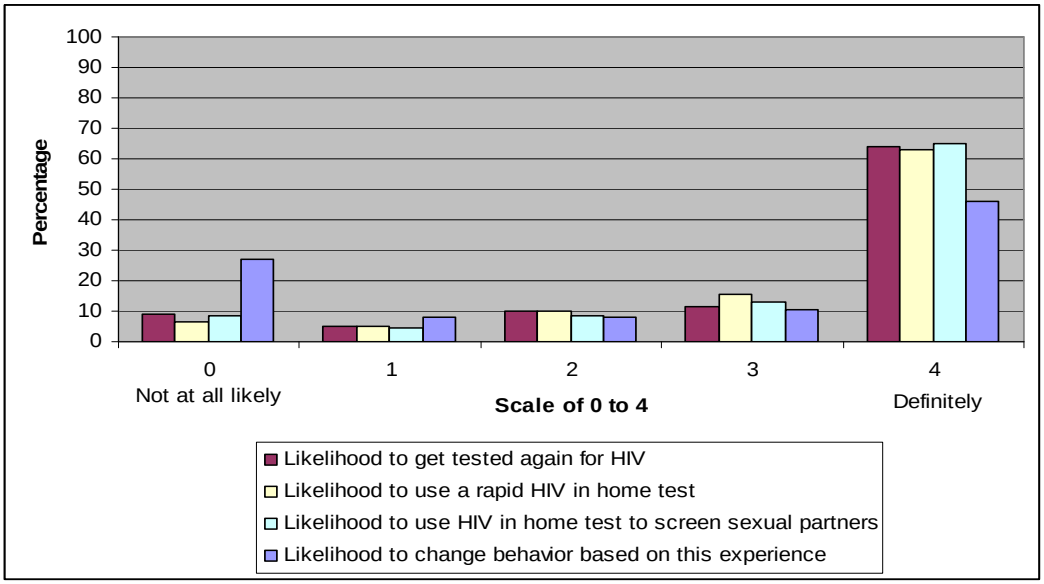
Figure 20 Summary of Intention Questionnaire Responses from all HIV Positive Subjects



Of the HIV negative subjects from the higher prevalence sites that completed the intention questionnaire after counseling, a majority of subjects (75%; combined percentage of definitely (64%) and highly likely* (11%)) stated they would get tested again for HIV. Seventy-nine percent (79%; combined percentage of definitely (63%) and highly likely* (16%)) indicated they would use a rapid in home test if it were available over-the-counter.

* On a scale of 0 to 4, the value of 3 was considered highly likely.

Figure 21 Summary of Intention Questionnaire Responses from HIV Negative Subjects from the higher prevalence sites



8.8 Safety

8.8.1 Adverse Events

There were two device related adverse events reported during the clinical trial – gingival pain [described as "tingling to swab areas of mouth" and paraesthesia oral [described as "stinging gums for 1 minute"]. These two events were considered mild in severity and resolved without treatment.

Of the subjects who received post-test counseling for their HIV positive status, most (68.60%) were calm upon learning of their HIV status, with the remaining subjects (31.4%) verbally communicating some level of anxiety about their status. No intervention from investigational center staff was required for any of the subjects who were informed of their HIV-positive status.

8.9 Adolescents

Among all of the participants in the clinical study, there were 89 subjects between ages 14 – 17 (1.6%). Of the 89, one (1) male did not return to his Visit 2 and did not receive an investigational kit. Two (2) other subjects did not return for their Visit 3. Among the 89 subjects in this category, 43.8% were black/African American, 23.6% were white, and 28% were unspecified. For ethnicity, 38.2% of the subjects described themselves as Hispanic. By gender, 60% of the subjects were female. Regarding sexual preference, 3.4% did not respond, 87.6% classified themselves as heterosexual and 9% as bisexual. A total of 29 adolescent subjects were enrolled from low prevalence sites with the remaining 60 subjects enrolled from the high prevalence sites.

All subjects who self reported a self-test result at Visit 3 were concordant negative with their EIA (100%: 85/85). One (1) additional subject self reported an operational error (pathway 5.1.1) by reason of not understanding where to place the test stick after swabbing. Test System Reliability rate is 1.16% in this collective group.

A total of 86 subjects in this group responded to the questionnaire for negative subjects. Roughly two-thirds of the subjects responded favorably to the two questions on likelihood to test again or likelihood to use an OTC test when retesting. More (76.7%) expressed the likelihood to use a rapid test to screen in the future. Slightly less (60.5%) expressed any likelihood of changing their behavior.

8.10 Consumer Support Center

Of the subjects who returned to the site for visit 3, at total of 151 documented they called the Consumer Support Center (Reference to the Answer Center in the Final Clinical Study Report OQ-OTC-5, Table 14.2.3). The Consumer Support Center logged 217 calls during a span of 37 weeks (the duration from the time the first subject called the center to the time the last subject called the center). A reconciliation of the number of calls reported by subjects and the number of calls logged by the Consumer Support Center was not completed, as not all subjects who called the Consumer Support Center reported their complete subject study identification information. In addition, 9 calls were logged from non-study participants. The average call was 6:30 minutes in length. Most of the calls were conducted in English, rather than Spanish, and the most common questions were associated with the disposal of the OraQuick Test kit or its components (n=120). The reason this question was asked most frequently was due to the fact that subjects were instructed to return the OraQuick Test kit to the investigational center, although the instructions within the OraQuick Test kit described disposal of the kit under the assumption of use in a commercial setting. Other common questions were associated with the use/operation of the OraQuick Test and interpretation of its results (n=74). No calls met the requirements of an SAE for the study or required connection to the suicide prevention hotline.

8.11 Summary and Conclusion

The sensitivity and specificity of the OraQuick Test was high (93.0% and 99.98%, respectively) in untrained users who conducted the self-test in a setting of their own choice. The sensitivity of the OTC test supports a strong benefit to risk for approval and commercialization of the product. The rate of false positive results was extremely low, indicating that the test is highly accurate in low prevalence populations. In addition, the test failure rate was low (1.08%) meaning that of those who attempted to self, test 98.92% successfully obtained an HIV test result. Of the 5499 subjects that returned and reported a result obtained from the OraQuick® In-Home HIV Test Kit, 99.84% reported an accurate result (5490/5499).

Overall, the results of the unobserved clinical study showed that the OraQuick Test, when used by untrained individuals in a location of their own choice, is both safe and effective.

9. Benefit-to-Risk

The expected benefit from commercialization of an OTC self-test kit for HIV is twofold:

- Reduction in morbidity associated with identification of HIV infection earlier in the course of disease in infected subjects
- Reduction in ongoing HIV transmission through self-identification of HIV infection and resultant behavior modification

The results of the Phase III Clinical Study of unobserved self-testing, strongly suggest that both outcomes can be expected from commercial deployment of the OraQuick® In-Home HIV Test Kit.

The study was comprised of two arms: (1) assessing the performance of the device in subjects from lower prevalence areas with presumptively low risk for HIV (3 sites) and (2) assessing the performance of the device in at risk subjects from higher prevalence areas (17 sites). Both of these cohorts have been reported to be the expected users of an OTC self test for HIV.[3] The high prevalence population

represented racial and risk-based demographics that were highly correlated with the major risk factors for HIV established by CDC[4]. The overall prevalence in this population was 2.6%. By contrast, the low prevalence arm of the study had a demonstrated HIV prevalence of 0.1%.

The effective sensitivity of the OTC test device, based on self-reported results compared to serostatus established by FDA approved laboratory testing was 93.0% .Previous studies had indicated 96% sensitivity as an expected threshold for the OTC self-test based on the ability of intended users to correctly interpret device results (Phase IIa study results). While the cause of the incremental self-reported false negatives in the unobserved study is unknown, it is notable that only one of these false negative subjects was in an apparent state of seroconversion based on laboratory serology results. This is significant, since individuals in early seroconversion have been reported to be more likely to transmit HIV due to higher levels of circulating virus.[5,6] It is noteworthy that the rate of correct comprehension of the existence of a 3 month window period during which HIV may not be detected was approximately 99% among intended users of the OTC self-test (See previous study results- Label Comprehension Studies). Crucially, this message is on the outer box and enables appropriate self-selection.

At the observed sensitivity of 93.0%, it is possible to project a strong risk benefit of commercial deployment of the OTC self-test due to the fact that a significant proportion of expected users will not be testing by conventionally available means. In the unobserved use study, 41% of newly identified HIV positive subjects reported never having tested before for HIV. This proportion of the potentially infected population that would otherwise obtain an HIV test is consistent with previously published studies of individuals using Home sample collection tests[7] and with research on at risk individuals who report they would self test.[8,9]

Based on the self-reported HIV testing history, approximately 39% of HIV positive subjects newly identified by the OTC self-test would not have been identified by conventional HIV testing options. As shown in Table 9.1 , this results in 9,087 additional individuals made aware of their infected status, incremental to existing HIV testing practices, if the OTC self-test is used by one million persons with an overall HIV prevalence of 2.1%. Earlier identification of HIV infected subjects has been shown to reduce morbidity and improve quality of life through access to care and treatment.[10,11] Moreover, the direct cost of medical care has been shown to be significantly higher for individuals who present late in disease progression.[12]

The table below presents an analysis of the expected net benefit in terms of HIV transmissions averted arising from deployment of the OraSure OTC self-test compared to the conventional testing options. This model is based on reduced transmission rates associated with persons aware of their HIV infection (2.7 per 100 persons) compared to persons unaware (10.4 per 100 persons) reported by Hall, Holtgrave & Maulsby 2012.[13] This model derives additional inputs from the empirical experience of the OTC self-test in the unobserved clinical study. Therefore we used a 2.1% prevalence and calculated that 61% of the OTC testing population would otherwise test by conventional means. This is based on the actual survey data from the newly identified HIV positives from the clinical trial, of whom 39% reported they have never tested before for HIV. The model uses the observed effective sensitivity of the OTC test (93.0%) and assumes 100% sensitivity by conventional laboratory blood testing (the comparator method in the trial). We further assumed that 99% of users who attempted to run the OTC test obtained their HIV test result (see Phase III study- Test Reliability results) compared to an expected return of laboratory results of approximately 80% based on published studies for laboratory HIV testing in public health.[14] Based on these inputs, it is possible to project an incremental benefit of the use of the OTC test of prevention of 700 onward transmissions annually for every 1,000,000 users of the OTC test. This predicts that use of the OraSure OTC test prevents 68% of the onward annual transmission from the assumed 21,000 infected individuals from the OTC testing population compared to the 36% of transmissions that would have been prevented by conventional testing. In addition to the substantial human benefit in terms of reduced morbidity and quality of life, estimates of the lifetime medical costs of

an individual HIV infection (discounted for the time of infection) have been estimated to be approximately $300,000.[15]

Table 9.1: Benefit of averting HIV transmission arising from deployment of an OTC Self-Test

	Results of OTC testing 1,000,000 subjects of unknown status at 2.1% prevalence (100% of OTC testers)	Results of conventional laboratory testing of sub-population of OTC testers (61% of OTC testing population)
Total HIV positive subjects positive by testing *(Assumes 93.0% sensitivity for OTC and 100% for conventional lab testing)*	19530	12,810
HIV positive subjects made aware of status *(Assumes 99% result delivery for OTC and 80% result delivery for conventional lab testing[14])*	19335	10,248
HIV positive subjects not made aware of status	1665	10,752
Annual transmissions from those unaware of infection *(Assumes 10.4% transmission rate for positives unaware of status)*	173	1,118
Annual transmissions from those aware of infection *(Assumes 2.7% transmission rate for positives aware of status)*	522	277
Transmissions averted by testing intervention *(Assuming 21,000 infected subjects at 10.4% transmission rate= 2184)*	1489	789
Incremental benefit of OTC test in annual transmissions averted	**700**	**N/A**

In surveying the intent of newly identified HIV positive subjects during the unobserved use trial, 88% indicated they would definitely follow up with their doctor or a clinic (see Phase III study results: Intention Responses of HIV Positive Subjects). These findings are consistent with surveys on the intent of HIV positive subjects identified through home sample collection tests[7] and suggest that the vast majority of individuals who identify as positive by self-testing will seek follow-up testing and care. The Call Center is specifically designed to provide local referrals based on a database of testing and treatment centers. The Referral dataset is the same dataset that supports the CDC NPIN referral system. OraSure has received agreement from CDC to utilize this dataset and to receive updates to the dataset at the same frequency as CDC. OraSure will also supplement the list with toll-free numbers from public health departments. OraSure intends to work with state and local agencies to ensure this database is kept current.

Overall specificity of the OTC self-test kit in unobserved use was extremely high at 99.98% (95% CI: 99.90-100.0%). No false positives were observed in the low prevalence population. This is important since the occurrence of false positives has been raised as a potentially important issue with an HIV

self-test, particularly when used by populations at low risk for HIV.[3] The aggregate positive predictive value (PPV) across both arms of the unobserved use study was 99.1%, which is extremely high for a screening test operating in a population with a prevalence of approximately 2%.

The ability of the intended use population to correctly perform the Investigational Test was determined to be suitably high. The aggregate Test System Failure Rate (% of time subjects who attempted to run the test did not obtain an HIV test result) across both arms of the study was 1.08% (60/5558). This rate of system failures resulting in "no results" compares favorably with those obtained in prior safety and efficacy studies of an FDA approved home sample collection test based on dried blood spot.[16] In these studies, the rate at which results could not be provided to individuals who provided a specimen for testing was approximately 8%.

The OTC self-test represents an effective HIV testing tool to augment existing practices aimed at increasing the number of people who are aware of their HIV status. The availability of this test could be of additional utility in rural areas where existing public health infrastructure is more limited. It also represents a convenient testing option for individuals who are motivated to test via an anonymous process.

A further benefit of commercialization of an HIV OTC self-test is the increased awareness of HIV that is expected to result due to local and national advertising. It is expected that this will increase awareness of the need for HIV testing and also obviate stigma associated with existing testing options. The convenience of this option may facilitate a culture of more frequent testing among individuals who perceive themselves to be at risk for HIV. It is noteworthy that in the post-test survey data from the unobserved self-testing study, 75% of HIV negative subjects from the high prevalence population indicated they would test again for HIV and 79% indicated that they would use an OTC test if available.

Overall, the findings from the evaluations of the HIV OTC self-test present a strong risk-benefit argument for approval and commercialization.

10. Consumer Support Resources at Launch

OraQuick recognizes the importance of providing users of the test with education and support regarding HIV testing in general, whether OTC or via the professional markets. As such, considerable resources have been developed and planned that are designed to provide HIV/AIDS education to support taking the test, to understand the results, and to refer for follow-up testing, counseling and care services.

The OraQuick In-Home HIV test system has as a key component a Consumer Support Center operating 24/7/365 and accessed by consumers primarily via a toll-free phone number. The Support Center will be initially operated by 17 full-time dedicated representatives that all have bi-lingual capability (English/Spanish) and have prior experience in providing support through such systems. The number of representatives will be expanded as call volume increases, however this level of coverage is twice the level calculated for need during the first year to provide more than ample coverage and immediate response time. Each representative will go through a rigorous 120 hour training module that was validated during the prior two clinical studies. This training will be supplemented with the AACO's *HIV: An Introduction* on-line course, and a 5 day CDC course called *HIV Counseling, Testing and Referral Services Training* for an additional 40 hours of training. In addition, each support representative will be selected and trained to manage the personal and sensitive nature of calls. All representatives will be required to pass these training requirements to be certified as an active representative, and on-going training and re-certification will occur to ensure the highest standard of support.

The OraQuick® Support Center has been granted the right to use the CDC's NPIN database with over 8,000 HIV/AIDS testing, counseling and care centers throughout the United States. This database will be supplemented with resources from local Public Health departments and other qualified organizations interested in being a part of our vast referral network. The Support Center will be anonymous, so anyone calling the site will not be asked any personal information and referrals will be provided based on a person's zip code.

In addition to the toll-free Support Center, a comprehensive website is being developed for launch. The website will provide a very important supplement or alternative for consumers seeking information. The website will also allow consumers to access the same HIV/AIDS education and referral to professional testing, counseling and care services as the Support Center provides. In addition, the website will have video product demonstrations to facilitate consumer usage. The website will also help direct consumers to retail locations where they can buy the test and also to on-line purchase options for added privacy. Individuals will also be given a choice to click to chat with a support representative.

An additional support network will be health care professionals. OraSure has conducted research with pharmacists and various physician groups with the goal of understanding the best means to educate and promote HIV testing. The launch plan will include extensive pharmacist and physician education tools so that they will be aware of the new OTC HIV test kit offering, how it works and the full array of support services available to their customers. Education will also include actions to take if someone who has tested with OraQuick and received a preliminary positive comes to their pharmacy or office. In addition pharmacy and in-office materials will be made available to educate and promote more widespread HIV testing.

Retail Plans

OraQuick In-Home HIV Test is expected to be broadly distributed to increase access to all those needing to test. Product availability will be both through on-line channels as well as brick and mortar retailers like CVS, Walgreens, Rite Aid, Wal-Mart, Target and other major retailers. Product availability will be national in geographic scope.

The pharmacist's at each retailer will have OraQuick® In-Home HIV Test product knowledge training and will be familiarized with our toll-free Support Center and website to assist product users.

Advertising and Promotion

The OraQuick® In-Home HIV Test will be supported by a substantial investment in advertising and promotional support to drive consumer awareness and testing. The resources OraSure will bring to this launch coupled with strong consumer appeal as seen in our numerous market research studies is certain to expand testing overall as we have seen high levels of purchase intent among non-testers, and greater frequency by current testers.

OraSure has been working closely with a top Advertising Agency on the development of consumer communications and media plans to support the launch. Advertising will be widespread during the first year as we plan to utilize TV, Print, Radio, Digital and out-of-home advertising to reach consumers. Driving widespread awareness with a compelling message to test is likely to have a significant impact on testing habits.

Promotional support will be driven by OraSure and the key retailers selling OraQuick® In-Home HIV Test. This support will re-emphasize the core messaging of the ad campaign while extending and offering incentives to re-test, and to encourage partners and friends to test.

Public Relations

Raising awareness and educating the consumer, especially among the population segments that initially are most likely to choose the option of an OTC HIV test, will be a very important part of the product's launch and availability online and at retail.

OraSure has engaged a leading communications agency a campaign is in development to engage the target audiences through the various media channels most frequented. While the effort will include traditional print media, a large percentage of customers will see benefit in the privacy aspect of the product, and therefore a focus will be on digital and social media channels, as an effective means to reach these audiences.

11. Conclusion

The OraQuick® In-Home HIV Test has now been used to self-test a total of >6500 consumers utilizing only the Instructions for Use (IFU) and the consumer call center in Phase IIb and Phase III clinical trials. In these studies the test demonstrated high level of specificity and sensitivity and extremely high PPV, NPV and overall accuracy when used by untrained users for HIV self-testing. There is a strong benefit to risk case for its approval and commercialization as an additional tool to combat the HIV epidemic. We conclude that the OraQuick® In-Home HIV Test is highly accurate, safe, and effective for commercialization as an OTC HIV self- test system.

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