Poster # 996

False positive rate of rapid oral fluid HIV tests increases as kits near expiration date

Shelley N. Facente, MPH[a]; Teri Dowling, MA, MPH[a]; Eric Vittinghoff, PhD[b]; Deanna L. Sykes, PhD[c]; Grant N. Colfax, MD[a]

[a]HIV Prevention Section, San Francisco Department of Public Health, San Francisco, CA; [b]Division of Biostatistics, University of California, San Francisco, CA; [c]California Department of Public Health, Center for Infectious Diseases, Office of AIDS, Sacramento, CA

Contact:
Shelley N. Facente, MPH
San Francisco Department of Public Health
25 Van Ness Ave, Suite 500
San Francisco, CA 94102
Phone: 415-554-9136
Fax: 415-934-4868
Email: shelley.facente@sfdph.org

Abstract

Background: Since the launch of the OraQuick *Advance* Rapid HIV-1/2 Antibody Test, episodes of excess false positive results with oral fluid specimens have been well documented in several US cities. To date, these false positive clusters have remained unexplained. Because a recent cluster of false positive test results in San Francisco occurred with kits close to their expiration date, we hypothesized that there was a greater probability of false positive results as the test kit approached expiration.

Methods: Results were analyzed for 20,904 tests with either an initial HIV-negative result (n=20,828), assumed to be true negative results, or a preliminary positive result that was then negative on indirect immunofluorescence assay (IFA) or Western blot (n=76), the set of false positives. For each test, we computed time to expiration as the interval from the date the kit was used to the expiration date printed on the test pouch, which were both systematically recorded for each kit. We first computed specificity for kits with time to expiration from $\leq$1 to $\geq$6 months, with exact binomial confidence intervals. Logistic regression was then used to estimate the independent association of time to expiration with false positive results, adjusting for site and technician effects.

Results: For 1,108 kits used in the last month before expiration, specificity was 98.83% (95% exact binomial confidence interval (CI) 98.00%–99.37%); the upper bound is below the specificity of 99.60% claimed by the manufacturer. In a logistic model adjusting for site and technician effects, false positive results were significantly more common for the 1,108 kits with $\leq$1 month remaining to expiration than for 1,251 kits with $\geq$6 months remaining to expiration (odds ratio (OR) 16.7, 95% CI 2.17–129.4, p=0.007); adjusted specificity for those kits was 99.51% (95% CI 99.07–99.75%).

Conclusions: Specificity of the OraQuick *Advance* rapid HIV test used with oral fluid declined significantly with $\leq$1 month remaining to expiration. The specificity of kits used in the last month before expiration appears to leave little margin for error from other sources.

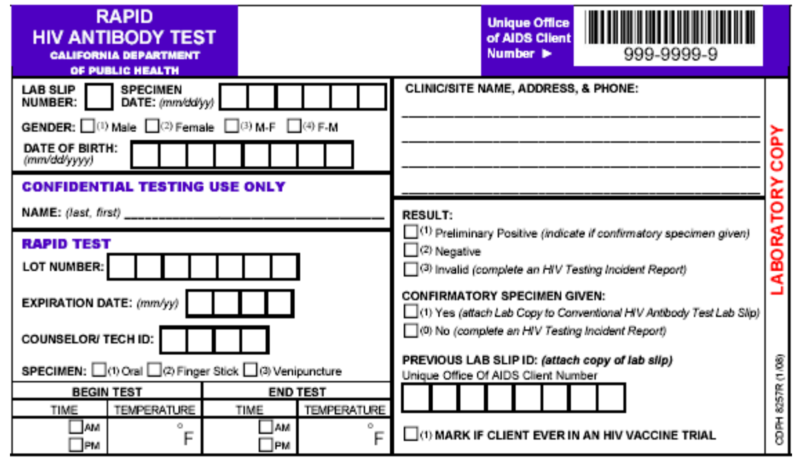
OraQuick Advance Rapid HIV-1/2 Antibody Test

Introduction

- In June of 2004, the OraQuick *ADVANCE*® Rapid HIV-1/2 Antibody Test was approved as a CLIA-waived rapid HIV test for use with oral mucosal transudate (oral fluid) specimens in addition to whole blood.
- According to the manufacturer, the OraQuick *ADVANCE*® has a specificity of 99.8% (95% CI 99.60%–99.89%) when used with oral fluid.
- Episodes of excess false positive results have been well documented and to date have remained unexplained.
- Because a recent cluster of false positive test results in San Francisco occurred with kits close to their expiration date, we hypothesized that there was a greater probability of false positive results as the test kit approached expiration.

Methods

- In San Francisco, all certified test technicians at publicly-funded HIV test sites systematically record expiration date, specimen date, specimen type, and test result on a standardized laboratory requisition slip.



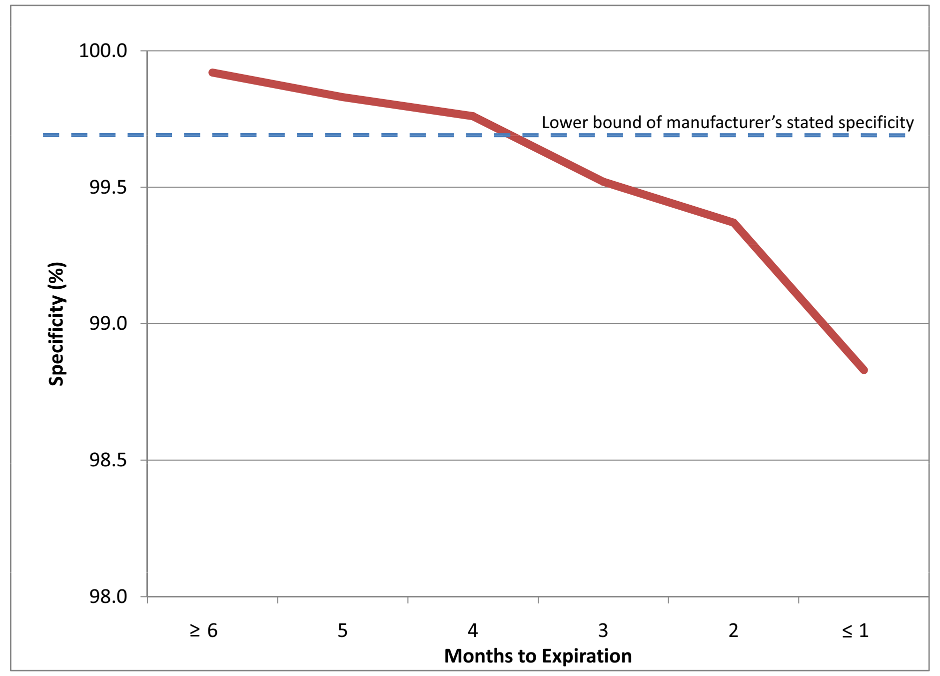
RAPID
HIV ANTIBODY TEST
CALIFORNIA DEPARTMENT OF PUBLIC HEALTH
Unique Office of AIDS Client Number
999-9999-9
LAB SLIP NUMBER:
SPECIMEN DATE: (mm/dd/yy)
CLINIC/SITE NAME, ADDRESS, & PHONE:
GENDER:
DATE OF BIRTH:
CONFIDENTIAL TESTING USE ONLY
NAME: (last, first)
RAPID TEST
LOT NUMBER:
EXPIRATION DATE: (mm/yy)
COUNSELOR/ TECH ID:
SPECIMEN:
BEGIN TEST
END TEST
TIME
TEMPERATURE
RESULT:
CONFIRMATORY SPECIMEN GIVEN:
PREVIOUS LAB SLIP ID: (attach copy of lab slip)
MARK IF CLIENT EVER IN AN HIV VACCINE TRIAL
LABORATORY COPY

- For each test, we computed time to expiration as the interval from the date the kit was used to the last day of the month of the expiration date.
- Specificity was computed for kits for time to expiration by month, from $\leq$1 to $\geq$6 months until expiration, with exact binomial confidence intervals. Logistic regression was then used to estimate the association of time to expiration with a false positive result, first unadjusted, then adjusting for the potential effects of test site and technician. We then calculated adjusted specificity for months to expiration, holding the indicator variables representing the other two factors constant at their sample means.

Results

- Results were analyzed for 20,904 oral fluid tests performed between January 2005 and December 2007 with either an initial HIV-negative result (n=20,828), or a preliminary positive result that proved to be false positive after confirmation by IFA or WB (n=76).
- Of 1,108 test kits used with $\leq$1 month until expiration, 13 (1.17%) were false positive, corresponding to a sample specificity of 98.83% (exact binomial 95% CI 98.00%–99.37%); adjusted specificity was 99.51% (95% CI 99.07–99.75%). As compared to kits with $\geq$6 months until expiration, false positive results were more likely for the test kits used $\leq$1 month before expiration in both unadjusted (OR 14.8, 95% CI 1.94–113.6, p=0.009) and adjusted (OR 16.7, 95% CI 2.17–129.4, p=0.007) analysis.

Observed test specificity by time to expiration



We also found an independent association of test technician in the adjusted analysis (p<0.001). False positive rates were also elevated for 2,206 kits with two (OR 7.98, 95% CI 1.05–60.8, p=0.045) and 4,968 kits with three (OR 6.07, 95% CI 0.82–44.9, p=0.08) months until expiration, although the elevated rate at three months was not statistically significant.

Fitted test specificity by time to expiration, adjusting for site & technician

Time to Expiration (months)	Specificity (%)	95% Confidence Interval
≤1	99.51	99.07-99.75
2	99.77	99.56-99.88
3	99.76	99.60-99.86
4	99.90	99.81-99.94
5	99.93	99.84-99.97
≥6	99.97	99.79-99.99+

Conclusions

- Our results suggest that as test kits age, the overall testing specificity with oral fluid decreases.
- Our data show that tests used within one month of expiration leave little margin for errors from other sources.
- Rapid HIV testing is a critical public health intervention, and false-positive results reduce the confidence of both the public and providers.
- Efforts should be made to minimize false positive results related to the time to expiration. Additional analyses should be conducted with other data sets and, if results are replicated, policy and procedural changes should be considered to discontinue oral fluid testing within one month of kit expiration.
- These data are from a period prior to the manufacturer's announcement of FDA approval to extend shelf life to 12 months. Improvements made to the product which correct the problems outlined here are a major step toward reducing false positives with oral fluid and improving community and provider confidence in rapid testing.

University of California San Francisco
UCSF
AIDS Research Institute