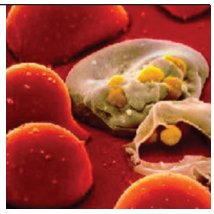

Q: Why do Seroconversion Panels continue to provide the best measure for evaluating HIV screening test sensitivity?

A: Globally, clinical laboratories interested in using the most sensitive HIV screening tests have been moving to HIV antigen/antibody combination (HIV Ag/Ab) assays for several years. Look for this trend to accelerate in the U.S. as well.

Sensitivity for a single analyte is often assessed using a dilution series (a.k.a. linearity panel). IVD manufacturers and regulators recognized soon after Seroconversion Panels were introduced in 1986 that this tactic wouldn't be appropriate for anti-HIV screening tests.[1] Antibodies to at least eight different viral protein epitopes are elicited as viral titer rises; their concentrations change relative to one another, and avidities for their protein targets also change as the antibodies mature. With the addition of HIV p24 antigen (HIVAg) to the analyte mix in screening assays, the situation becomes still more complex.

HIVAg was incorporated into HIV screening assays to allow ten days earlier detection of HIV infection over anti-HIV only tests. Why this push toward ever earlier detection? Experts believe that more than half of new infections could be caused by continued high risk behavior on the part of someone who is recently infected.[2] If infection can be detected sooner in some percentage of these individuals, their potential to infect others may be diminished, and the epidemic slowed.

Seroconversion Panels are developed in the rare circumstance when plasma is collected at frequent intervals from a plasma donor unaware of his or her infection. When a positive result is detected, the donor is permanently excluded from further donation, and all plasma units from that donor are sequestered. Perhaps 200-300 of these donor series have been identified since HIV screening began. Using information from the study of Seroconversion Panels, Fiebig and colleagues were able to establish categories of early infection and their durations, based on the appearance in turn of HIV RNA, HIVAg, and anti-HIV (see Table 1, page 2). They were further able to estimate dates of infection from the consistent patterns and durations observed.[3]

The Fiebig stage classification also allows single samples to be identified as representing early infection, and SeraCare has assembled a number of these into its Low Titer HIV Performance Panel PRB109.

Samples are available from SeraCare as HIV Seroconversion Panels and Low Titer HIV Performance Panels.
See Table 2, page 3.

With the introduction of HIV Ag/Ab assays, the value of Seroconversion Panels has increased. Each panel demonstrates the evolution of infection in a single individual by the HIV strains then circulating, and allows evaluation of each marker in the naturally occurring absence or presence of the others.

SeraCare has identified and developed six new HIV seroconversions, and upgraded the related data sheets with the Feibig stage and a graph illustrating the evolution of an individual infection as tracked by continually improving screening tests.

Seroconversion Panels still provide the single best means to track improvements in HIV assay sensitivity.

Table 1. Laboratory Stages of Primary HIV Infection Based on the Emergence of Viral Markers in 51 Seroconverting Plasma Donors

	Marker					Duration in days (95% CI)[a]	
Stage	RNA	P24 Antigen	Antibody (EIA) NS	Antibody (EIA) S	Western blot	Individual	Cumulative
I	+	–	–	–	–	5.0 (3.1, 8.1)	5.0 (3.1, 8.1)
II	+	+	–	–	–	5.3 (3.7, 7.7)	10.3 (7.1,13.5)
III	+	+	–	+	–	3.2 (2.1, 4.8)	13.5 (10.0, 17.0)
IV	+	+/–	–	+	I	5.6 (3.8, 8.1)	19.1 (15.3, 22.9)
V	+	+/–	+/–	+	+[b]	69.5 (39.7, 121.7)	88.6 (47.4, 129.8)
VI	+	+/–	+	+	+	Open-ended	Open-ended

[a] Calculations are based on a parametric Markov model
[b] Without p31 band
CI = Confidence interval
I = Indeterminate
NS = Not sensitive, refers to second-generation, not IgM-sensitive enzyme immunoassay (EIA)
S = Sensitive, refers to IgM-sensitive, third-generation EIA

References

1. Thorn RM *et al.* Assessment of HIV-1 screening test sensitivities using serially diluted positive sera can give misleading results. Transfusion 1989, 29(1): 78-80
2. Miller WC *et al.* Role of acute and early HIV infection in the sexual transmission of HIV. Curr Opin HIV AIDS 2010, 5(4): 277-82
3. Fiebig EW *et al.* Dynamics of HIV viremia and antibody seroconversion in plasma donors: implications for diagnosis and staging of primary HIV infection. AIDS 2003, 17:1871–1879

About the Author

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Table 2: SeraCare HIV Seroconversion Panel and HIV Performance Panel Products

Product	Members/ Volume	Cat No
HIV Seroconversion Panels		
HIV-1 Panel D	5 x 1.0 mL	PRB904-00-1.0
HIV-1 Panel N	5 x 1.0 mL	PRB914-00-1.0
HIV-1 Panel S	3 x 1.0 mL	PRB919-00-0.25
HIV-1 Panel V	4 x 1.0 mL	PRB922-00-1.0
HIV-1 Panel Y	6 x 0.25 mL 6 x 1.0 mL	PRB925-00-0.25 PRB925-00-1.0
HIV-1 Panel Z	6 x 1.0 mL	PRB926-00-1.0
HIV-1 Panel AE	4 x 1.0 mL	PRB930-00-1.0
HIV-1 Panel AH	3 x 1.0 mL	PRB933-00-1.0
HIV-1 Panel AI	3 x 1.0 mL	PRB934-00-1.0
HIV-1 Panel AP	8 x 1.0 mL	PRB940-00-1.0
HIV-1 Panel AR	4 x 0.25 mL 4 x 1.0 mL	PRB942-00-0.25 PRB942-00-1.0
HIV-1 Panel AS	7 x 1.0 mL	PRB943-00-1.0
HIV-1 Panel AU	6 x 1.0 mL	PRB945-00-1.0
HIV-1 Panel AV	4 x 1.0 mL	PRB946-00-1.0
HIV-1 Panel AW	4 x 1.0 mL	PRB947-00-1.0
HIV-1 Panel AX	4 x 0.25 mL 4 x 1.0 mL	PRB948-00-0.25 PRB948-00-1.0
HIV-1 Panel AY	5 x 1.0 mL	PRB949-00-1.0
HIV-1 Panel AZ	4 x 0.25 mL 4 x 1.0 mL	PRB950-00-0.25 PRB950-00-1.0
HIV-1 Panel BA	6 x 1.0 mL	PRB951-00-1.0
HIV-1 Panel BB	6 x 1.0 mL	PRB952-00-1.0
HIV-1 Panel BC	4 x 1.0 mL	PRB953-00-1.0

[M] = Modified [E] = Extended

Product	Members/ Volume	Cat No
HIV-1 Panel BD	7 x 1.0 mL	PRB954-1.0
HIV-1 Panel BE	5 x 1.0 mL	PRB955-1.0
HIV-1 Panel BF	5 x 1.0 mL	PRB956-1.0
HIV-1 Panel BG	7 x 1.0 mL	PRB957-1.0
HIV-1 Panel BH	6 x 1.0 mL	PRB958-1.0
HIV-1 Panel BI	7 x 1.0 mL	PRB959-1.0
HIV-1 Panel	9 x 1.0 mL	PRB960-1.0
HIV-1 Panel	9 x 1.0 mL	PRB961-1.0
HIV-1 Panel	6 x 1.0 mL	PRB962-1.0
HIV-1 Panel	7 x 1.0 mL	PRB963-1.0
HIV-1 Panel	6 x 1.0 mL	PRB964-1.0
HIV-1 Panel	6 x 1.0 mL	PRB965-1.0
HIV-1 Panel	10 x 1.0 mL	PRB966-1.0
HIV-1 Panel	6 x 1.0 mL	PRB967-1.0
HIV-1 Panel	10 x 1.0 mL	PRB968-1.0
HIV-1 Panel	10 x 1.0 mL	PRB969-1.0
HIV-1 Panel	4 x 1.0 mL	PRB970-1.0
HIV-1 Panel	4 x 1.0 mL	PRB971-1.0
HIV-1 Panel	6 x 1.0 mL	PRB972-1.0
HIV Performance Panels		
Anti-HIV-1 Low Titer	10 x 1.0 mL	PRB109-1.0
Anti-HIV-1 Mixed Titer	25 x 0.25 mL	PRB204-0.25
HIV-1 Incidence/Prevalence	15 x 1.0 mL	PRB601-1.0
HIV-1 Group O	5 x 1.1 mL	PRD301-1.1
HIV RNA Genotype	10 x 1.1 mL	PRD202-1.1

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