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Performance comparison of the 4th generation Bio-Rad Laboratories GS HIV Combo Ag/Ab EIA on the EVOLIS™ automated system versus Abbott ARCHITECT HIV Ag/Ab Combo, Ortho Anti-HIV 1 + 2 EIA on Vitros ECi and Siemens HIV-1/O/2 enhanced on Advia Centaur

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ABSTRACT

Background: A multisite study was conducted to evaluate the performance of the Bio-Rad 4th generation GS HIV Combo Ag/Ab EIA versus Abbott 4th generation ARCHITECT HIV Ag/Ab Combo. The performance of two 3rd generation EIAs, Ortho Diagnostics Anti-HIV 1 + 2 EIA and Siemens HIV 1/O/2 was also evaluated.
Objective: Study objective was comparison of analytical HIV-1 p24 antigen detection, sensitivity in HIV-1 seroconversion panels, specificity in blood donors and two HIV false reactive panels.
Study design: Analytical sensitivity was evaluated with International HIV-1 p24 antigen standards, the AFFSAPS (pg/mL) and WHO 90/636 (IU/mL) standards; sensitivity in acute infection was compared on 55 seroconversion samples, and specificity was evaluated on 1000 negative blood donors and two false reactive panels.
Results: GS HIV Combo Ag/Ab demonstrated better analytical HIV antigen sensitivity compared to ARCHITECT HIV Ag/Ab Combo: 0.41 IU/mL versus 1.2 IU/mL (WHO) and 12.7 pg/mL versus 20.1 pg/mL (AFSSAPS); GS HIV Combo Ag/Ab EIA also demonstrated slightly better specificity compared to ARCHITECT HIV Ag/Ab Combo (100% versus 99.7%). The 4th generation HIV Combo tests detected seroconversion 7–11 days earlier than the 3rd generation HIV antibody only EIAs.
Conclusion: Both 4th generation immunoassays demonstrated excellent performance in sensitivity, with the reduction of the serological window period (7–11 days earlier detection than the 3rd generation HIV tests). However, GS HIV Combo Ag/Ab demonstrated improved HIV antigen analytical sensitivity and slightly better specificity when compared to ARCHITECT HIV Ag/Ab Combo assay, with higher positive predictive values (PPV) for low prevalence populations.

1. Background

Although highly sensitive HIV "antibody only" assays have been developed, including the 3rd generation antigen sandwich assays which can detect very low levels of HIV antibody in blood, these assays have not been able to shorten the window period, defined as the interval between the appearance of HIV RNA in the plasma and the detection of HIV specific antibodies, to less than 3–4 weeks [1–4]. The 4th generation HIV immunoassays, with their added capability of simultaneously detecting HIV antibodies and HIV p24 antigen, have now shortened this serological window to within 2 weeks of the time of initial infection [5,6]. The implementation of these new highly sensitive 4th generation HIV tests has significantly enhanced early detection of HIV infection in the acute phase when the risk of HIV transmission is extremely high due to the high concentrations of HIV and presence of variants that are more capable of causing infection [7–10].

The Bio-Rad Laboratories GS HIV Combo Ag/Ab EIA [11], FDA approved in July 2011 with claims for manual as well as automated systems, is one of two HIV 4th generation enzyme immunoassays approved in the U.S. The GS HIV Combo Ag/Ab EIA incorporates

Abbreviations: Ab, antibody; AFSSAPS, Agence Francaise de sécurité sanitaire des produits de santé; CI, confidence interval; EIA, enzyme immunoassay; FDA, Food and Drug Administration; gp, glycoprotein; IRB, Institutional Review Board; IU, international unit; mL, milliliter; PCR, polymerase chain reaction; pg, picogram; p-NAAT, pooled nucleic acid amplification tests; RNA, ribonucleic acid; S/CO, signal to cut-off; WHO, World Health Organization; PPV, positive predictive value.

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Table 1
Summary of analytical HIV-1 sensitivity.

AFSSAPS HIV-1 p24 antigen standard required: <50 pg/mL		WHO 90/636 HIV-1 p24 antigen standard required: <2 IU/mL	
Bio-Rad LaboratoriesGS HIV Combo Ag/Ab EIA 12.69 pg/mL 95% CI (11.099–14.286)	Abbott ARCHITECT HIV Ag/Ab Combo Test 20.10 pg/mL 95% CI (19.439–20.767)	Bio-Rad LaboratoriesGS HIV Combo Ag/Ab EIA 0.41 IU/mL 95% CI (0.126–0.675)	Abbott ARCHITECT HIV Ag/Ab Combo Test 1.18 IU/mL 95% CI (01.082–1.287)

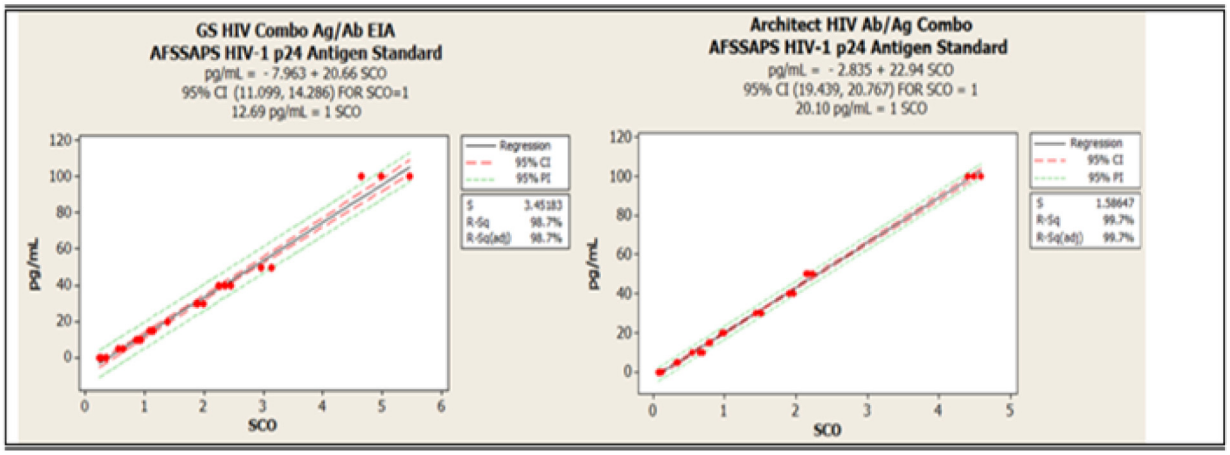

Chart 1. AFSSAPS HIV-1 p24 antigen standard analytical sensitivity required: <50 pg/Ml.

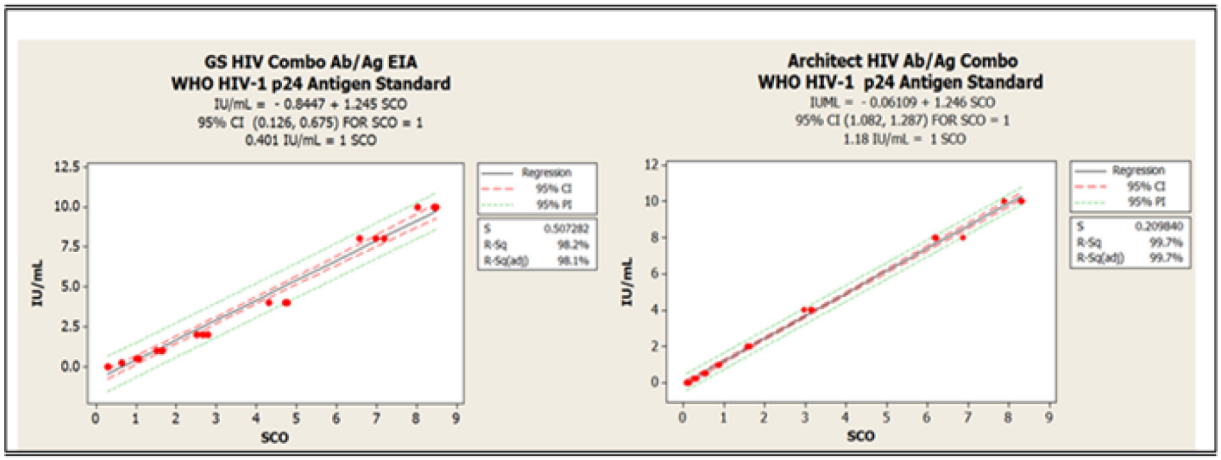

Chart 2. WHO HIV-1 p24 antigen international standard analytical sensitivity required: <2 IU/mL.

highly conserved recombinant and synthetic peptide sequences representing HIV-1 (groups M and O) and HIV-2, as well as monoclonal antibodies specific for HIV-1 p24 antigen, allowing the simultaneous qualitative detection of HIV p24 antigen and antibodies [12–15]. The Abbott 4th generation ARCHITECT HIV Ag/Ab Combo assay (FDA approved in 2010), is a chemiluminescent-based HIV immunoassay which utilizes mouse monoclonal antibodies and HIV antigen coated micro particles for the simultaneous detection of HIV antigen and antibodies within the sample [16]. In recent reports of performance evaluation studies of both the GS HIV Combo Ag/Ab EIA, and the ARCHITECT HIV Ag/Ab Combo assay, these 4th generation HIV immunoassays have demonstrated extremely high sensitivities and specificities, detecting HIV positivity in acute HIV infections only previously detectable by

Table 2
Performance in early RNA positive seroconversion samples.

HIV-1RNA positive samples	Total panel members	HIV-1 RNA positive samples	Bio-Rad GS HIV Combo Ag/Ab EIA EVOLIS	Abbott ARCHITECT HIV Ag/Ab Combo	Siemens HIV 1/2/O Enhanced Advia Centaur	Ortho Anti HIV-1 + 2 EIA VITROS ECi
PRB951	6	4 (66.6%)	4 (66.6%)	4 (66.6%)	1 (16.6%)	1 (16.6%)
HIV9077	24	17 (70.8%)	16 (66.6%)	16 (66.6%)	14 (58.3%)	14 (58.3%)
HIV9079	25	18 (72.0%)	17 (68.0%)	17 (68.0%)	15 (60.0%)	15 (60.0%)
Number	55	39/39 100%	37/39 94.9%	37/39 94.9%	30/39 76.9%	30/39 76.9%