Journal of Clinical Virology Plus 6 (2026) 100249

Contents lists available at ScienceDirect

Journal of Clinical Virology Plus

journal homepage: www.elsevier.com/locate/jcvp

Siemens Healthineers cross-platform verification: Analytical and clinical analysis of HIV Antigen/Antibody Combo assay across ADVIA Centaur and Atellica analyzers

Brenda Ricci [a,e], Michael Anostario [b], Rachel Fonstad [b], Anthony Bonito [b], Brendan Healy [b], Nadia Riverso [b], Neil Birmingham [b], Deidre Kiefer [b], Joe M. El-Khoury [c], Amin A. Mohammad [d,*]

[a] Franey Medical Laboratories, Mashpee, Massachusetts, United States
[b] Siemens Healthcare Diagnostics Inc., 511 Benedict Ave, Tarrytown, New York, United States
[c] Department of Laboratory Medicine, Yale School of Medicine, New Haven, Connecticut, United States
[d] Baylor Scott and White Medical, Temple, Texas, United States
[e] Private Home Care, Buzzards Bay, Massachusetts, United States

ARTICLE INFO

Keywords:
Human Immunodeficiency Virus (HIV)
Serological testing
Clinical performance
Seroconversion
Positive percent agreement (PPA)
Negative Percent Agreement (NPA)
Precision

ABSTRACT

Background & Aims: HIV is a major global public health concern. Accurate serological testing in the clinical laboratory using high-performing, automated analyzers is critical for preventing transmission. This study evaluated the performance of the Atellica CI analyzer, utilizing the Atellica IM HIV Antigen/Antibody Combo (CHIV) assay to determine if this new analyzer's performance was reliable and comparable to existing systems.
Methods: Multicenter reproducibility and cross-platform (Atellica CI, Atellica IM, ADVIA Centaur XP) comparison studies were performed. Clinical concordance analysis comprised 3374 samples which were derived from: native retrospective samples and prospectively collected samples at multiple United States sites representing diverse HIV positive and presumed negative individual categories including subjects at increased risk for HIV exposure. HIV seroconversion sensitivity was assessed using 20 commercially available panels. Regression analyses were performed between analyzers using p24 antigen dilutions.
Result: Maximum reproducibility %CV was less than 8.8 % on the Atellica CI analyzer for all samples at or above 1.00 Index. Cross-platform agreement ranged from 98.0 % to 100 % across all subject samples and seroconversion panels tested. Regression analyses showed strong linear relationships between the analyzers (slope ranging from 0.96 to 1.02, correlation (r) >0.999).
Conclusion: This is the first report on analytical and clinical performance of the Atellica IM CHIV assay on the Atellica CI analyzer. The findings demonstrate its reliability for CHIV serological testing comparable to the Atellica IM analyzer and ADVIA Centaur XP system. It enables interchangeability of Atellica analyzers in hub-and-spoke laboratory operations while supporting transition to the latest Siemens Healthineers analyzers.

1. Introduction

Human immunodeficiency virus (HIV) infection is primarily transmitted through sexual contact. However, it can also be spread from mother to child, through the sharing of needles for intravenous drug use, or by receiving blood products from HIV-positive donors [1]. Despite efficient antiretroviral therapy, HIV infection remains a significant global public health issue. As of 2023, approximately 39.9 million people worldwide are living with HIV, and over 42.3 million people have died from acquired immunodeficiency syndrome (AIDS) since the epidemic began more than 40 years ago [2]. Importantly, it is globally reported that up to 14 % of individuals living with HIV are unaware of their status [2,3]. Reducing the number of new HIV infections is a primary goal for all initiatives aimed at ending the HIV epidemic. HIV testing, which is crucial for early detection and timely linkage to care, is a key component, among others, of this global commitment to

Abbreviations: HIV, Human immunodeficiency virus; NPA, Negative percent agreement; PPA, positive percent agreement.

* Corresponding author at: Baylor Scott and White Medical, 5701 Airport Road, Temple, Texas, United States.
E-mail address: amin.mohammad@bswhealth.org (A.A. Mohammad).

https://doi.org/10.1016/j.jcvp.2026.100249
Received 16 October 2025; Received in revised form 23 January 2026; Accepted 11 March 2026
Available online 12 March 2026

maintaining low HIV incidence [4].

Current World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) guidelines recommend that all adolescents and adults aged 13 to 64 years old, younger adolescents and older adults at increased risk of infection, and women during each pregnancy, undergo testing for HIV [5–7]. Serological assays and more specifically combined HIV antigen/antibody tests, known as "fourth-generation" assays, are recommended for initial testing. These qualitative assays can detect two circulating components: HIV p24 antigen and antibodies to HIV-1 and HIV-2. This includes most genetically diverse types of HIV, such as group M (major) and group O (outlier) for HIV-1, as well as HIV-2 which is predominantly found in West Africa. This combined antigen/antibody testing offers enhanced detection of acute/early infection, which might be missed by antibody-only tests. Upon a positive result from these qualitative tests, a follow-up HIV-1/HIV-2 antibody differentiation test should be conducted [5,6,8,9].

Multiple HIV automated fourth-generation assays are commercialized and routinely used in diagnostic laboratories [8,10–14]. To further support the global need for HIV testing using high-performing, automated HIV serology assays, Siemens Healthineers has recently extended the Atellica IM HIV Antigen/Antibody Combo assay (CHIV) to the Atellica CI analyzer, a recent stand-alone, high-throughput integrated clinical chemistry and immunoassay analyzer [15]. Added advantages of the Atellica CI include its compact 1.9 square meter footprint and support for sustainability efforts with low water consumption ($\leq$ 25L/h). It uses autonomous engines to process up to 1000 chemistry tests and 120 immunoassay tests per hour simultaneously. The system shares reagents, workflows, and user interfaces with the Atellica IM and CH analyzers facilitating cross-training and operational consistency within hub-and-spoke clinical laboratory networks. The CHIV assay, used across the ADVIA Centaur system [16,17], Atellica IM [18,19] and Atellica CI [20,21] analyzers, shares the same formulation for all reagents and the same instrumental operating principles.

While the key clinical performance metrics (sensitivity and specificity) for the U.S. Food & Drug Administration (FDA) and CE-approved CHIV assay has already been established and documented in publicly available package insert studies [16–21], this manuscript focuses specifically on providing additional analyses to support the agreement between the recent Atellica CI analyzer and the Atellica IM analyzer and/or the ADVIA Centaur system when using the CHIV assay. This is intended to aid users adopting or transitioning to the newer Atellica CI analyzer in various clinical settings.

2. Materials and methods

2.1. Reproducibility

Assay precision was evaluated following the five-day protocol described in Clinical and Laboratory Standards Institute (CLSI EP05-A3), with testing performed at Baylor Scott and White Medical (BSWM; Temple, TX), Franey Medical Laboratories (FMLM; Mashpee, MA), and Siemens Healthcare Diagnostics Inc. (STTN; Tarrytown, NY). A nine-member serum specimen panel was prepared by spiking negative human serum pools with individual native serum samples from HIV infected individuals to target levels spanning the analytical measuring interval of Atellica IM CHIV assay and included samples near the cutoff concentration (Index 1.00). The panel samples were aliquoted, stored frozen at $\leq -20^{\circ}$C, thawed and centrifugated on the day of testing. The 9 panel samples (Serum 1-9), negative and positive Atellica IM CHIV quality controls (QC 1-5) were assayed in triplicate in two runs per day, with a minimum of 2 hours between runs, for five days. Concentrations were established using a single two-point calibration. The calibrators and QC materials were handled according to the manufacturer's instructions. Each site used one reagent lot with their respective calibrators and controls using one Atellica CI analyzer per site producing a total of 90 replicates per sample and per analyzer (Table 1).

2.2. Qualitative method comparison

The analytical method comparison performance of the Atellica IM CHIV assay (Siemens Healthcare Diagnostics Inc., Tarrytown, NY) was evaluated at the STTN site on the Atellica CI analyzer, the Atellica IM analyzer as well as the ADVIA Centaur XP system. Known HIV positive and negative serum specimens were purchased from Complex Antibodies, Margate, FL; Boca Biolistics, Pompano Beach, FL (n = 105) and Precision for Medicine, Norton, MA (n = 110), respectively. Samples were stored frozen until tested in singlicate using two reagent lots across multiple platforms (Table 2).

The clinical performance of the Atellica IM CHIV assay (Siemens Healthcare Diagnostics Inc., Tarrytown, NY) was evaluated on the Atellica CI analyzer and the ADVIA Centaur CHIV assay on the ADVIA Centaur XP system which is the parent analyzer designated as the predicate device to support the CHIV assay migration and registration (Table 3).

The clinical method comparison samples consisted of both vendors purchased retrospective, as well as prospectively collected specimens from across multiple U.S. collection sites (Supplemental Table S1).

Table 1
Reproducibility estimates for the Atellica IM CHIV assay on the Atellica CI analyzer.

Sample	N	Mean (Index)	Repeatability		Between-Run		Between-Day		Between-Site		Reproducibility	
			SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
HIV-1 Serum Pool 1[a]	90	0.55	0.034	6.2	0.000	0.0	0.023	4.2	0.044	8.0	0.060	10.9
HIV-1 Serum Pool 2	90	1.02	0.047	4.6	0.017	1.7	0.018	1.8	0.024	2.4	0.059	5.8
HIV-1 Serum Pool 3	90	5.89	0.142	2.4	0.000	0.0	0.059	1.0	0.122	2.1	0.196	3.3
HIV-2 Serum Pool 4	90	1.47	0.053	3.6	0.007	0.5	0.046	3.1	0.064	4.4	0.095	6.5
HIV-2 Serum Pool 5	90	3.79	0.110	2.9	0.044	1.2	0.066	1.7	0.120	3.2	0.181	4.8
Group O Serum Pool 6[b]	90	5.84	0.245	4.2	0.198	3.4	0.000	0.0	0.333	5.7	0.458	7.8
p24 Ag Serum Pool 7	90	3.94	0.120	3.0	0.052	1.3	0.072	1.8	0.155	3.9	0.215	5.5
p24 Ag Serum Pool 8	90	7.13	0.179	2.5	0.096	1.3	0.078	1.1	0.287	4.0	0.360	5.0
Negative Serum Pool 9	89[c]	0.18	0.030	16.7	0.003	1.7	0.028	15.6	0.014	7.8	0.043	23.9
Negative Control 1	85[c]	0.14	0.033	23.6	0.022	15.7	0.010	7.1	0.031	22.1	0.052	37.1
HIV-1 Control 2	90	5.15	0.158	3.1	0.000	0.0	0.055	1.1	0.069	1.3	0.181	3.5
HIV-2 Control 3	90	3.19	0.090	2.8	0.064	2.0	0.046	1.4	0.126	3.9	0.174	5.5
Group O Control 4[b]	90	6.32	0.344	5.4	0.000	0.0	0.000	0.0	0.426	6.7	0.547	8.7
p24 Ag Control 5	90	3.52	0.109	3.1	0.045	1.3	0.050	1.4	0.082	2.3	0.153	4.3

Ag: antigen; CV: coefficient of variation; SD: standard deviation.
[a] HIV-1 antibody high negative sample.
[b] HIV-1 Group O antibody sample.
[c] At least one result was out of the measuring interval.

Table 2
Qualitative agreement of the CHIV assay across all Siemens Healthineers analyzers using internal verification study specimens.

Atellica CI analyzer	ADVIA Centaur XP			Atellica IM analyzer		
	Nonreactive	Reactive	Total	Nonreactive	Reactive	Total
Nonreactive	109	0	109	110	0	110
Reactive	0	104	104	0	105	105
Total	109	104	**213**	110	105	**215**
Negative Percent Agreement (95 % CI)	100 % (109/109) (96.6 – 100)			100 % (110/110) (96.6 – 100)		
Positive Percent Agreement (95 % CI)	100 % (104/104) (96.4 – 100)			100 % (105/105) (96.5 – 100)		

CI, 95 % Wilson confidence interval. Two samples out of the 215 sourced samples could not be evaluated on ADVIA Centaur XP system due to insufficient volume.

Table 3
Qualitative agreement of the CHIV assay on Atellica CI analyzer and ADVIA Centaur XP system using clinical study specimens tested at three independent sites.

Population	Agreement	# of Discordants	Total # Tested	Percent Agreement (%) [95 % CI]
Healthy	729/730	1	730	99.9 [99.2, 99.9]
Healthy pregnant	246/246	0	246	100 [98.5, 100]
Hospitalized	49/50	1	50	98.0 [89.4, 99.9]
Pediatric low risk	74/74	0	74	100 [95.1, 100]
High risk (H, IIDU, MSM, MT, other RD, STD, pregnant, pediatric)	930/932	2	932	99.8 [99.2, 99.9]
High risk HIV-2 endemic area	457/457	0	457	100 [99.2, 100]
HIV positive (pediatric)	45/45	0	45	100 [92.1, 100]
HIV positive (pregnant)	37/37	0	37	100 [90.5, 100]
HIV-1 positive	519/519	0	519	100 [99.3, 100]
HIV-2 positive	193/193	0	193	100 [98.1, 100]
HIV-1 Group O (native, contrived)	39/39	0	39	100 [91.0, 100]
P24 (native, contrived)	52/52	0	52	100 [93.2, 100]
Total	**3370/3374**	**4**	**3374**	**99.9 [99.7, 99.9]**

H: hemophiliacs; IIDU: illicit injection drug users; MSM: men who have sex with men; MT: multiply transfused; RD: renal dialysis; STD: sexually transmitted disease. Specimens were classified under HIV category when HIV type information was not available.

Clinical samples encompassed diverse categories representative of the CHIV assay intended use population listed in Table 3. These serum or plasma samples were stored frozen at $\leq -20^{\circ}C$ until tested. Out of a total of 3505 samples sourced or collected, 49 samples had insufficient volume for testing on both analyzers, resulting with 3456 samples that had initial results on both instruments. Demographics for the 3456 subjects analyzed were as follows: 46.3 % were male (1599/3456), 51.4 % were female (1777/3456), and 2.3 % were unknown (80/3456). The mean subject age was 35.9 years ranging from 1 to 96 years old, including 15.0 % (517/3456) of subjects within pediatric age (<21 years), 82.7 % (2859/3456) within adult age (> 21 years), and 2.3 % (80/3456) unknown.

Sample testing was performed at the three sites (BSWM, FMLM, STTN). Specimens were distributed such that approximately one-third of the total population were tested at each site on both the ADVIA Centaur XP and Atellica CI analyzers. Testing was performed using one reagent lot within a single calibration.

According to the algorithm found in the assay instructions for use, specimens with an Index value <1.00 were considered nonreactive while specimens with initial Index value result ≥ 1.00 were retested in duplicate. If one or both of the duplicates were ≥ 1.00 Index, specimens were considered reactive. Out of a total of 3456 samples initially tested, 82 HIV initial reactive samples had insufficient volume for duplicate testing on both analyzers, resulting with 3374 samples (>97.6 %) that had final results on both instruments.

Each site obtained approval by their local Institutional Review Board (IRB) prior to the start of testing or prior to prospective subject enrollment.

2.3. Seroconversion sensitivity panels testing

Twenty HIV seroconversion panels, ranging from 4 to 19 longitudinal samples per panel, were purchased from Zeptometrix (Buffalo, NY, USA). Five out of 20 panels (panel IDs: 65376, 65389, 65522, 77840, 10434874) were reactive within 7 to 21 days following the initial blood draw date when there was no presence of any of the analytes tested (HIV-1 Ab, HIV-2 Ab, p24 Ag). These five panels classified as early seroconversion HIV specimens as defined by the European Common Specifications (i.e., HIV-1 p24 antigen and/or HIV RNA positive, and not recognized by the antibody first-line assays and indeterminate or negative in confirmatory assays). A total of 169 samples were assayed in singlicate over 4 testing days, using a single calibration event, on the Atellica CI analyzer and the ADVIA Centaur XP system at the STTN site. The testing involved one instrument and one reagent lot combination, using two reagent lots, three Atellica CI and one ADVIA XP. Data were evaluated by comparison of the Atellica CI analyzer results to those of the ADVIA Centaur XP system. The first reactive result from the initial draw date marked the seroconversion point (Table 4).

2.4. p24 antigen analytical method comparison

p24 antigen analytical method comparison was performed by testing a series of dilutions of the HIV-1 p24 antigen World Health Organization (WHO) International Standard (NIBSC code: 90/636). The standard was reconstituted in 1.0 mL distilled water to 1000 IU/mL, then 40-fold diluted using a p24 antigen negative human serum pool followed by serial 2-fold dilutions using the same pool. This resulted in 11 samples with Index values ranging from 0.05 to >12.00. Each sample was tested in four replicates on a single test day. The study was performed with one reagent lot on one Atellica CI analyzer, one Atellica IM analyzer and one ADVIA Centaur XP system. Index values were determined using a single 2-point calibration for each analyzer. Ten dilutions within the assay range (0.05 -12.00 Index) were used to calculate Deming regression equations (Table 5).

2.5. Statistical analysis

All analyses were performed using SAS software (version 9.4, SAS Institute, Cary, NC, USA) or Microsoft Office 365 Excel with Analyse-IT software (version 6.10.1 or higher). Concordance analyses for the evaluation of qualitative test performance were performed following CLSI EP12-A2 guidelines. Positive percent agreement (PPA) and

Table 4
Clinical Ab and Ag sensitivity assessment using HIV seroconversion panels.

Seroconversion Panel Donor ID (Catalog number)	First Reactive Bleed (Days from Initial Draw)	ADVIA Centaur CHIV R/NR (Index)	Atellica IM[a] CHIV	Atellica CI CHIV	Total Number of Bleeds	Percent Positive Agreement (R CI/Total R XP or IM)	Percent Negative Agreement (NR CI/Total NR XP or IM)
62216 (9075)	3 (22)	R (4.25)	R (3.66)	R (4.55)	4	100 (2/2)	100 (2/2)
63215 (9081)	2 (24)	R (2.41)	R (3.05)	R (2.25)	4	100 (3/3)	100 (1/1)
63753 (9076)	7 (66)	R (9.47)	ND	R (10.46)	9	100 (3/3)	100 (6/6)
64578 (9022)	7 (25)	R (2.27)	R (2.50)	R (2.30)	7	100 (1/1)	100 (6/6)
65376 (9089)	4 (16)	R (2.47)	R (3.29)	R (2.48)	5	100 (2/2)	100 (3/3)
65389 (9012)	6 (16)	R (1.21)	R (1.07)	R (1.14)	8	100 (3/3)	100 (5/5)
65522 (9014)	2 (12)	R (1.57)	R (1.33)	R (1.48)	5	100 (4/4)	100 (1/1)
65685 (9019)	3 (38)	R (4.66)	R (5.49)	R (5.28)	3	100 (1/1)	100 (2/2)
66048 (9031)	17 (146)	R (5.39)	ND	R (5.65)	19	100 (3/3)	100 (16/16)
66575 (9018)	8 (28)	R (2.59)	ND	R (2.49)	10	100 (3/3)	100 (7/7)
66632 (9034)	12 (50)	R (6.44)	ND	R (5.45)	13	100 (2/2)	100 (11/11)
68106 (9032)	5 (38)	R (4.99)	R (6.32)	R (5.98)	8	100 (4/4)	100 (4/4)
68205 (9026)	7 (44)	R (4.63)	R (3.89)	R (4.54)	7	100 (1/1)	100 (6/6)
68582 (9030)	14 (47)	R (2.14)	ND	R (2.15)	16	100 (3/3)	100 (13/13)
73695 (12007)	5 (119)	R (1.20)	ND	R (1.08)	9	100 (5/5)	100 (4/4)
73698 (12008)	9 (28)	R (>12.00)	ND	R (>12.00)	13	100 (5/5)	100 (8/8)
75062 (9079)	9 (40)	R (1.70)	ND	R (1.70)	15	100 (7/7)	100 (8/8)
77600 (9084)	4 (49)	R (7.72)	R (6.08)	R (8.36)	4	100 (1/1)	100 (3/3)
77840 (9082)	3 (13)	R (1.22)	R (1.50)	R (1.23)	4	100 (2/2)	100 (2/2)
1043487 (9092)	3 (7)	R (>12.00)	R (>12.00)	R (>12.00)	6	100 (4/4)	100 (2/2)
Overall Agreement					169	100 (59/59)	100 (110/110)

Each seroconversion panel summarizes serial bleeds. As an example, for the first panel Donor 62216, 4 total number of bleeds were tested. The first CHIV-reactive bleed across all three analyzers (ADVIA Centaur XP (XP), Atellica IM (IM), and Atellica CI (CI)) was bleed 3, obtained 22 days after the initial draw (3 (22)), with reactive (R) Index values of 4.25 (XP), 3.66 (IM), and 4.55 (CI). Bleeds 1 and 2 were nonreactive (NR), yielding 2/2 NR and 100 % negative agreement (100 (2 NR CI / total 2 NR XP or IM)). Bleeds 3 and 4 were reactive (R), yielding 2/2 R and 100 % positive agreement (100 (2 R CI / total 2 R XP or IM)).

[a] These are historical results from previous seroconversion testing conducted using the Atellica IM CHIV assay on the Atellica IM analyzer. Not determined (ND) indicates that the panel was not previously tested on this analyzer.

negative percent agreement (NPA) were determined by comparing performance of the Atellica IM CHIV assay using the Atellica CI analyzer at the cutoff of 1.00 Index to the initial and final interpretation results obtained using the ADVIA Centaur CHIV assay on the ADVIA Centaur XP system. For both PPA and NPA, 95 % confidence intervals were calculated using the Clopper-Pearson method.

For the 10 dilution samples, Deming regression was performed between each pair of analyzers with the predecessor analyzer as the reference analyzer in the equation. Regression output included slope and intercept to demonstrate the linear relationship between the analyzers, the correlation to demonstrate the relationship strength, and estimated systematic bias at the cutoff of 1.00.

3. Results

3.1. Reproducibility

Observed reproducibility (total imprecision) results of Atellica CI CHIV across three testing sites ranged from 3.3 % CV to 8.7 % CV across all 11 samples ≥1.00 Index tested (Table 1 and Supplemental Table S1) and were all within the manufacturer's recommendations for reproducibility. For the three samples not containing analyte (HIV-1 serum pool 1, negative serum pool 9 and negative control 1), all results remained nonreactive throughout the study and showed no change in clinical interpretation.

3.2. Qualitative agreement

The analytical method comparison analysis was performed using a total of 215 known positive and negative samples. The data was analyzed using the initial results from a single replicate and showed strong agreement with 100 % NPA and PPA comparing the Atellica CI analyzer to both the Atellica IM analyzer and the ADVIA Centaur XP system (Table 2).

The clinical method comparison analysis using a total of 3374 results obtained across the three sites, showed that the Atellica IM CHIV assay on the Atellica CI analyzer performed similarly on the ADVIA Centaur XP system with percent agreement at or close to 100 % and no noticeable differences between groups (Table 3).

There were four samples where the final agreement between the

Table 5
p24 antigen analytical method comparison.

Analyzer	Deming Regression Analysis				Estimated Systematic Differences			
	Average Concentration (N = 10) Intervals Index ["test" analyzer, Y] [reference analyzer, X] (Min-Max)	(r)	Slope (95 % CI)	Intercept (Index) (95 % CI)	Cutoff Index on X	Mean Difference (Y – X) Index (95 % CI)	Relative difference	p-value
CI vs. **XP**	0.11-7.56 **0.13-7.82**	>0.999	0.97 (0.96, 0.98)	-0.01 (-0.03, 0.00)	1.00	-0.04 (-0.06, -0.03)	-4.0 %	<0.001
IM vs. **XP**	0.14-7.48 **0.13-7.82**	>0.999	0.96 (0.95, 0.96)	0.01 (0.00, 0.03)	1.00	-0.03 (-0.04, -0.02)	-3.0 %	<0.001
CI vs. **IM**	0.11-7.56 **0.14-7.48**	>0.999	1.02 (1.01, 1.03)	-0.03 (-0.04, -0.02)	1.00	-0.01 (-0.02, 0.00)	-1.0 %	0.017

CI: confidence interval; (r), correlation coefficient.

Atellica CI and ADVIA Centaur XP results were discordant (4/3374, 0.12 % discordance rate). Two samples that had initial nonreactive results on the Atellica CI had initial reactive results on the ADVIA Centaur XP. Following the algorithm, these samples were tested on the ADVIA Centaur XP and resulted as repeat reactive. Due to limited volume, they were not repeat tested on the Atellica CI. One sample was initial reactive on both the Atellica CI and ADVIA Centaur XP and was repeat reactive on the Atellica CI. However, due to insufficient volume for this sample, repeat testing in duplicate could not be performed on the ADVIA Centaur XP and as such, is included as discordant. Finally, one discordant sample was nonreactive on ACI (0.87 Index) and reactive on XP (1.05 Index). These results were within the imprecision of the assay.

3.4. Seroconversion panels

The twenty seroconversion panels tested showed highly concordant results for CHIV assay, with all three Siemens Healthineers analyzers (ADVIA Centaur, Atellica IM and Atellica CI) having matching interpretations for all samples tested. The overall calculated PPA and NPA for these samples were 100 % (Table 4).

3.5. p24 antigen analytical method comparison

Deming regression analysis and estimated relative percent differences between the three analyzers for p24 antigen samples around the assay cutoff of 1.00 Index using one reagent are presented in Table 5 and Figure S1. The relative percent differences (-4.0 %, -3.0 % and -1.0 %) have statistically significant differences ($p < 0.05$) when comparing each Atellica analyzer to one another and to the Centaur XP system. The smallest bias was estimated between Atellica analyzers (CI vs. IM), with a relative difference of only -1.0 % at cutoff Index 1.00. All estimated biases fall within the assay's imprecision range and are therefore considered minimal, with negligible clinical significance.

4. Discussion

This study demonstrated the equivalent precision and clinical performance of the Atellica IM CHIV assay on the Atellica CI analyzer when compared to the Atellica IM analyzer and the parent ADVIA Centaur system. Conducted across multiple sites using one reagent lot, the CHIV assay precision study on the newer Atellica CI analyzer was designed to assess external site testing variation to better reflect real-life routine testing and included extended panel members (HIV-1 group “M”, HIV-1 group “O”, HIV-2, and p24 specific panel members close to the assay cutoff and across the assay measuring interval). For samples at or above 1.00 Index, the maximum CV estimates from reproducibility (incorporating between-site variability) was 8.7 %. Additionally, a previous 20-day precision verification study performed at a single internal laboratory showed a within-laboratory CV of less than 5.7 %. The reproducibility CV estimates obtained using the Atellica CI analyzer with the Atellica IM CHIV assay were consistent with the manufacturer’s reported performance (<10 %) [21].

Both internal and external qualitative method comparison studies, along with seroconversion panels testing, proved comparable clinical concordance across all Siemens Healthineers methods sharing the same formulation for the CHIV assay. The method comparison performed at multiple sites in this manuscript was a focused study reflective of the intended use for the assay. Previously, the clinical performance of the Siemens Healthineers CHIV assay was evaluated using the ADVIA Centaur system in a broader cohort of donors. That study, part of manufacturer validation, supported the CE-approved use of this assay in children, adolescents, blood donors for transfusion, and living or cadaveric (non-heart beating) organ donors [16].

Previously published studies indicated that most commercially available fourth-generation assays, including Atellica IM CHIV assay [10], are similar and likely effective for diagnosing routinely tested patients generally within the non-acute phase, once anti-HIV antibody seroconversion has occurred. Differences may exist at a very early stage of infection, a tiny 3 to 5-day window, when only the p24 antigen is present, before seroconversion. Due to the scarcity of these early acute patient samples, we conducted an analytical method comparison using contrived samples. Statistical comparison of linear regressions derived from testing of these samples supported equivalent performance in detecting p24 antigen across the Siemens Healthineers methods. The estimated relative difference of −1.0 % observed between the Atellica CI and IM analyzers for samples at cutoff index 1.00 supports analyzer interchangeability and provides valuable information for networked, hub-and-spoke, laboratories settings. Alternatively, well characterized panels from early acute HIV infected patients were used to further evaluate p24 sensitivity in native patient samples. Lemée et al., recently published seroconversion test results, including two HIV acute infection panels 65389 (9012) and 63215 (9081) using three HIV Ag/Ab combo assays from Beckman (ACCESS Duo), Abbott (ARCHITECT HIV Ag/Ab Combo) and Roche (ELECSYS HIV Duo) manufacturers [11]. Beckman HIV reactivity was observed one bleed earlier than Abbott and Roche for the panel 65389 (9012), while first bleed reactivity was identical for panel 63215 (9081) across the three methods [11]. In our study, these two panels were also assessed using Siemens Healthineers instruments with similar results.

A current limitation is the scarcity of independent research evaluating the CHIV assay on the Atellica CI analyzer. Apart from one manufacturer-associated study involving other assays on this platform [15], published data remains limited. Future independent investigations should include broader comparisons with alternative platforms such as Beckman, Abbott, and Roche using fully characterized (true positive /true negative per reference method) HIV specimens to better establish reliability and consistency for HIV Ag/Ab combo assays across systems.

To conclude, the Atellica CI analyzer was designed as a compact analyzer suitable for various clinical laboratories settings from a stand-alone analyzer operated at single site laboratory to a spoke analyzer that complements the Atellica Solution portfolio in the hub of large, networked environments (hub-and-spoke). This study demonstrated that the Atellica IM CHIV assay had comparable precision and clinical performance when used on either Atellica CI or Atellica IM analyzers. These findings support the interchangeability between the Atellica analyzers and the suitability of the new instrument for routine clinical use of the Atellica IM CHIV assay as an aid in HIV serological diagnosis.

Funding

This study was funded by Siemens Healthcare Diagnostics Inc., Tarrytown, NY, USA.

IRB statement

Each site obtained approval by their local Institutional Review Board (IRB) prior to the start of testing or prior prospective subject enrollment.

Informed consent statement

Informed consent was obtained from all prospective subjects (n = 1214) involved in the study. Additional vendor purchased samples were obtained in accordance with the FDA guidance document “Guidance for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are not Individually Identifiable” (April 25, 2006).

Data availability statement

The data that support the findings of this study are available on reasonable request from the corresponding author.

CRediT authorship contribution statement

Brenda Ricci: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Conceptualization. **Michael Anostario:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Rachel Fonstad:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Anthony Bonito:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Brendan Healy:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Nadia Riverso:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Data curation. **Neil Birmingham:** Writing – review & editing, Validation, Supervision, Resources, Project administration, Methodology, Investigation. **Deidre Kiefer:** Writing – review & editing, Writing – original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Joe M. El-Khoury:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Conceptualization. **Amin A. Mohammad:** Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Investigation, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: M. Anostario, N. Birmingham, A. Bonito, R. Fonstad, B. Healy, D. Kiefer, and N. Riverso are employees of Siemens Healthineers. J. El-Khoury has consulting agreements with Siemens Healthineers. No potential conflicts of interest are reported by A. Mohammad and B. Ricci.

Acknowledgements

The authors would like to thank Geraldine Arrode-Bruses, employee of Siemens Healthineers, for writing support.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jcvp.2026.100249.

References

[1] G. Maartens, C. Celum, S.R. Lewin, HIV infection: Epidemiology, pathogenesis, treatment, and prevention, in English, Lancet Conf. Pap. 384 (9939) (2014) 258–271, https://doi.org/10.1016/S0140-6736(14)60164-1.
[2] "UNAIDS, Global HIV & AIDS statistics - fact sheet " https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf (Accessed on May 15, 2025).
[3] C. f. D. C. a. Prevention. "Estimated HIV Incidence and Prevalence in the United States, 2018–2022. ." https://stacks.cdc.gov/view/cdc/156513 (Accessed on May 15, 2025).
[4] K.S. McGee, Overview of the US National HIV Strategy and Ending the HIV Epidemic Initiative, in English, Nurs. Clin. N. Am. Rev. 59 (2) (2024) 297–308, https://doi.org/10.1016/j.cnur.2023.12.003.
[5] W. H. Organization. "Consolidated guidelines on HIV testing services. ." https://www.who.int/publications/i/item/978-92-4-155058-1 (Accessed on May 15, 2025).
[6] W. H. Organization. "Consolidated guidelines on differentiated HIV testing services." https://www.who.int/publications/i/item/9789240096394 (Accessed on May 15, 2025).
[7] D.K. Owens, et al., Screening for HIV Infection: US Preventive Services Task Force Recommendation Statement, in English, JAMA - J. Am. Med. Assoc. Rev. 321 (23) (2019) 2326–2336, https://doi.org/10.1001/jama.2019.6587.
[8] N.W. Anderson, B.A. Parikh, The Diagnosis of HIV: Right Test, Right Interpretation, Right Away, in English, Clin. Microbiol. Newsl. Artic. 41 (22) (2019) 193–202, https://doi.org/10.1016/j.clinmicnews.2019.11.001.
[9] J.M. Miller, et al., Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2024 Update by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM), in English, Clin. infect. dis.: off. publ. Infect. Dis. Soc. Am. Artic. Press (2024), https://doi.org/10.1093/cid/ciae104.
[10] H. Kutvonen, H. Jarva, M. Lappalainen, S. Kurkela, Comparative evaluation of four commercial analyzers for the serological screening of hepatitis A, B, C and HIV, in English, J. Clin. Virol. Artic. 153 (2022), https://doi.org/10.1016/j.jcv.2022.105219.
[11] V. Lemée, et al., Performance evaluation of the new Access HIV Ag/Ab combo assay on the DxI 9000 Access Immunoassay Analyzer, in English, J. Clin. Virol. Artic. 174 (2024), https://doi.org/10.1016/j.jcv.2024.105712.
[12] X. Liu, et al., Clinical performance evaluation of an HIV Duo assay: From HIV screening to acute and non-acute HIV infection detection, in English, Clin. Chim. Acta Artic. 565 (2025), https://doi.org/10.1016/j.cca.2024.119949.
[13] V. Mackiewicz, L. Larrouy, F. Damond, K. Peoc'h, V. Chicha-Cattoir, D. Descamps, Performance evaluation of the Atellica IM HBsAgII (Qualitative), Atellica IM HIV Ag/Ab Combo (CHIV), and Atellica IM aHCV assays at two hospital sites, in English, Clin. Chem. Conf. Abstr. 64 (2018) S162.
[14] A. Mühlbacher, et al., A multicentre evaluation of the Elecsys® HIV Duo assay, in English, J. Clin. Virol. Artic. 112 (2019) 45–50, https://doi.org/10.1016/j.jcv.2018.11.005.
[15] U. Ruffing, S. Mickeler, M. Kraft, P. Findeisen, Analytical performance evaluation of a new integrated clinical chemistry and immunoassay analyzer, in English, Pract. Lab. Med. Artic. 41 (2024), https://doi.org/10.1016/j.plabm.2024.e00427.
[16] Siemens Healthcare Diagnostics. ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay instructions for use (OUS). 10629832_EN Rev. 18, 2024-02, Tarrytown, NY, 2024.
[17] Siemens Healthcare Diagnostics. ADVIA Centaur HIV Ag/Ab Combo (CHIV) assay instructions for use (US). 10697136_EN Rev. 09, 2024-02, Tarrytown, NY, 2024.
[18] Siemens Healthcare Diagnostics. Atellica IM HIV Ag/Ab Combo (CHIV) assay instructions for use (OUS).10995315_EN Rev. 08, 2024-11 Tarrytown, NY, 2024.
[19] Siemens Healthcare Diagnostics. Atellica IM HIV Ag/Ab Combo (CHIV) assay instructions for use (US). 10996984_EN Rev. 04, 2024-02., Tarrytown, NY, 2024.
[20] Siemens Healthcare Diagnostics. Atellica IM HIV Ag/Ab Combo (CHIV) assay on Atellica CI Analyzer instructions for use (OUS). 11204933_EN Rev. 07, 2024-02, Tarrytown, NY, 2024.
[21] Siemens Healthcare Diagnostics. Atellica IM HIV Ag/Ab Combo (CHIV) assay on Atellica CI Analyzer instructions for use (US). 11204935_EN Rev. 04, 2025-03 Tarrytown, NY, 2025.