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SHORT COMMUNICATION

Multicenter Performance Evaluation of Elecsys Anti-HBc II, Anti-HCV II, HIV combi PT, HBsAg II, and Syphilis Immunoassays

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SUMMARY

Background: **The WHO recommends mandatory serological testing of blood donors for hepatitis B virus, hepatitis C virus (HCV), human immunodeficiency virus (HIV), and syphilis. We evaluated the performance of Elecsys® infectious disease immunoassays against commercially available comparator assays.**
Methods: **Prospective, routine, anonymized patient or donor samples (n = 8,821) were analyzed at three German sites using Elecsys anti-hepatitis B core antigen (Anti-HBc II), Anti-HCV II, HIV combi PT, hepatitis B surface antigen (HBsAg II), and Syphilis immunoassays (cobas e 411 analyzer) versus ARCHITECT comparator assays.**
Results: **The Elecsys immunoassays demonstrated comparable sensitivity (≤ 1.54% difference) and equivalent specificity (≤ 0.63% difference) to the respective ARCHITECT comparator assays. Overall sensitivity for the Elecsys and ARCHITECT infectious disease panels was 99.78% vs. 99.40%, respectively, and overall specificity was 99.74% vs. 99.80%, respectively.**
Conclusions: **The Elecsys infectious disease immunoassays demonstrated high sensitivity and specificity, which were similar to comparator assays, supporting their suitability for routine laboratory practice.**
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KEY WORDS

hepatitis B virus, hepatitis C virus, human immunodeficiency virus, sensitivity, specificity, syphilis

INTRODUCTION

According to a 2016 World Health Organization (WHO) report, Germany had the highest volume of transfused red blood cells/whole blood per 1,000 population globally [1]. Accurate blood screening is essential to diagnose and prevent the spread of infectious diseases, both in routine clinical care settings and amongst

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blood transfusion recipients [2]. The WHO recommends mandatory serological testing for human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), and syphilis [1]. Screening for HIV, HBV, and HCV is also compulsory pursuant to the German Transfusion Act of 1998 [3].

A substantial decrease in risk of infection due to blood transfusion has been observed in recent years, attributed in part to blood donor screening using new generation electrochemiluminescence immunoassays [4]. Several automated immunoassays are licensed to aid diagnosis of infectious diseases [5]. The high sensitivity and specificity of these assays is vital in providing accurate diagnostic information, as well as assisting in standardization of screening procedures between centers [4].

We conducted a multicenter performance evaluation of the Elecsys® anti-hepatitis B core antigen (Anti-HBc II), Elecsys Anti-HCV II, Elecsys HIV combi PT, Elecsys hepatitis B surface antigen (HBsAg II), and Elecsys Syphilis immunoassays against commercially available assays, in routine laboratory settings.

MATERIALS AND METHODS

Study design

This was a performance evaluation of the Elecsys Anti-HBc II, Anti-HCV II, HIV combi PT, HBsAg II, and Syphilis immunoassays (all Roche Diagnostics) versus commercially available comparator assays (ARCHITECT Anti-HBc II, Anti-HCV, HIV Ag/Ab Combo, HBsAg Qualitative II, and Syphilis TP [all Abbott Laboratories]). Prospective, routine, anonymized serum and/or plasma samples were collected from first-time and repeat donors, and patients being routinely tested for infectious disease parameters at three sites in Germany (University Hospital Essen, University Hospital of Düsseldorf, and University Medical Center Regensburg). Sample storage conditions are described in the Supplementary Methods. The target was 500 samples per assay at each site; samples were used across several assays. The sites used different reagent lots and laboratories to mimic routine clinical conditions. All sites followed the same study protocol.

The study was conducted in accordance with the principles of the Declaration of Helsinki and ICH Good Clinical Practice guidelines. The overall study protocol received institutional review board approval. Ethical approval was not deemed necessary.

Assays

Test principles for the Elecsys Anti-HBc II, Anti-HCV II, HIV combi PT, HBsAg II, and Syphilis assays are described in the Supplementary Methods. Comparator assays included the ARCHITECT Anti-HBc II, Anti-HCV, HIV Ag/Ab Combo, HBsAg Qualitative II, and Syphilis TP assays. Test principles of these assays are similar to those of the corresponding Elecsys assays [6-15].

Final results for discrepant and repeatedly positive samples were determined using confirmatory methods, including immunoblot testing, or a majority result using a third commercially available assay (full details for each assay in the Supplementary Methods). Samples were excluded from the analyses if results from the confirmatory methods could not be obtained.

Sensitivity and specificity

All samples were initially measured in single determination: measurements were taken in parallel using Roche Diagnostics Elecsys assays (cobas e 411 analyzer) and Abbott ARCHITECT assays (i1000sr analyzer at the University Medical Center Regensburg, i2000sr analyzer at the MVZ Labor Krone Bad Salzuflen, and the University Hospitals in Essen and Düsseldorf). Time between sample testing was < 24 hours, to minimize bias due to handling or storage discrepancies. All initially reactive or borderline samples underwent repeat testing in single or duplicate determination according to the respective method (Supplementary Methods). Sensitivity and specificity, with 95% confidence intervals, were calculated for the assays overall and for the individual test sites according to the same parameters for all sites. Statistical analyses were conducted by AIT Austrian Institute of Technology GmbH, Austria. Statistical significance of the differences between the assays were not calculated.

RESULTS

A total of 8,821 prospective donor or routine patient samples were analyzed (September 2015 - December 2016). Comparable sensitivity (≤ 1.54% difference) and equivalent specificity (≤ 0.63% difference) were observed between each of the Elecsys and the respective ARCHITECT assays (Table 1).

False negative and false positive results for each assay are reported in Table 1. Negative predictive values ranged from 99.84% to 100.00%. Positive predictive values (PPV) were higher for Elecsys Anti-HCV II (100.00% vs. 91.43%) and HBsAg II (100.00% vs. 97.50%) assays compared with the respective ARCHITECT assays. Fewer false positives were determined using the ARCHITECT HIV Ag/Ab Combo (n = 1) compared with the Elecsys HIV combi PT (n = 4) assay, which resulted in a PPV of 96.88% vs. 88.57%. For both syphilis assays, PPVs were 100.00%.

The Elecsys assays showed similar sensitivity and specificity across all sites (Table 2), but slightly lower sensitivity was seen with the Elecsys Anti-HBc II and ARCHITECT Anti-HBc II assays at Düsseldorf (96.23% for both assays vs. 100.00% at the other two study sites).

Overall sensitivity for the Elecsys and ARCHITECT assays was 99.78% vs. 99.40%, respectively, and overall specificity was 99.74% vs. 99.80%, respectively.

Table 1. Overall sensitivity and specificity for Elecsys Anti-HBc II, Anti-HCV II, HIV combi PT, HBsAg II, and Syphilis assays, and ARCHITECT Anti-HBc II, Anti-HCV, HIV Ag/Ab Combo, HBsAg Qualitative II, and Syphilis TP assays.

Parameter	Assay	Samples analyzed, n	Samples excluded, n	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Interpretation				PPV, %	NPV, %
						TP	FP	FN	TN		
HBc	Elecsys Anti-HBc II	1,543	1	99.28 (97.15 - 99.88)	98.97 (98.20 - 99.43)	277	13	2	1,251	95.52	99.84
	ARCHITECT Anti-HBc II	1,543	1	99.28 (97.15 - 99.88)	99.60 (99.02 - 99.85)	277	5	2	1,259	98.23	99.84
HCV	Elecsys Anti-HCV II	1,580	1	100.00 (93.05 - 100.00)	100.00 (99.68 - 100.00)	65	0	0	1,515	100.00	100.00
	ARCHITECT Anti-HCV	1,580	1	98.46 (90.60 - 99.92)	99.60 (99.09 - 99.84)	64	6	1	1,509	91.43	99.93
HIV	Elecsys HIV combi PT	1,565	1	100.00 (86.27 - 100.00)	99.74 (99.29 - 99.92)	31	4	0	1,530	88.57	100.00
	ARCHITECT HIV Ag/Ab Combo	1,565	1	100.00 (86.27 - 100.00)	99.93 (99.58 - 100.00)	31	1	0	1,533	96.88	100.00
HBsAg	Elecsys HBsAg II	1,551	2	100.00 (94.15 - 100.00)	100.00 (99.68 - 100.00)	78	0	0	1,473	100.00	100.00
	ARCHITECT HBsAg Qualitative II	1,551	2	100.00 (94.15 - 100.00)	99.86 (99.45 - 99.98)	78	2	0	1,471	97.50	100.00
Syphilis	Elecsys Syphilis	2,581	6	99.64 (97.68 - 99.98)	100.00 (99.79 - 100.00)	275	0	1	2,305	100.00	99.96
	ARCHITECT Syphilis TP	2,571	16	99.26 (97.06 - 99.87)	100.00 (99.79 - 100.00)	268	0	2	2,301	100.00	99.91
Overall	Elecsys panel	8,820	11	99.78 (93.66 - 99.86)	99.74 (99.33 - 99.87)	726	17	3	8,074	97.71	99.96
	ARCHITECT panel	8,813	21	99.40 (93.05 - 99.85)	99.80 (99.39 - 99.93)	718	14	4	8,077	98.09	99.95

Abbreviations: Ab - antibody, Ag - antigen, CI - confidence interval, FN - false negative, FP - false positive, HBc - hepatitis B core antigen, HBsAg - hepatitis B surface antigen, HCV - hepatitis C virus, HIV - human immunodeficiency virus, NPV - negative predictive value, PPV - positive predictive value, TN - true negative, TP - true positive.

Table 2. Sensitivity and specificity for Elecsys Anti-HBc II, Anti-HCV II, HIV combi PT, HBsAg II, and Syphilis assays, and ARCHITECT Anti-HBc II, Anti-HCV, HIV Ag/Ab Combo, HBsAg Qualitative II, and Syphilis TP assays by study site.

Study site	Assay	Samples analyzed, n	Samples excluded, n	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Interpretation			
						TP	FP	FN	TN
Essen	Elecsys Anti-HBc II	498	0	100.00 (93.85 - 100.00)	99.29 (97.77 - 99.82)	74	3	0	421
	ARCHITECT Anti-HBc II	498	0	100.00 (93.85 - 100.00)	100.00 (98.88 - 100.00)	74	0	0	424
Düsseldorf	Elecsys Anti-HBc II	543	1	96.23 (85.92 - 99.34)	98.57 (96.95 - 99.37)	51	7	2	483
	ARCHITECT Anti-HBc II	543	1	96.23 (85.92 - 99.34)	99.39 (98.07 - 99.84)	51	3	2	487
Regensburg	Elecsys Anti-HBc II	503	0	100.00 (96.93 - 100.00)	98.86 (96.91 - 99.63)	152	4	0	347
	ARCHITECT Anti-HBc II	503	0	100.00 (96.93 - 100.00)	99.43 (97.73 - 99.90)	152	2	0	349
Essen	Elecsys Anti-HCV II	499	1	100.00 (85.44 - 100.00)	100.00 (98.99 - 100.00)	29	0	0	470
	ARCHITECT Anti-HCV	499	1	96.55 (80.37 - 99.82)	99.36 (97.98 - 99.84)	28	3	1	467
Düsseldorf	Elecsys Anti-HCV II	553	0	100.00 (77.08 - 100.00)	100.00 (99.11 - 100.00)	17	0	0	536
	ARCHITECT Anti-HCV	553	0	100.00 (77.08 - 100.00)	99.81 (98.80 - 99.99)	17	1	0	535
Regensburg	Elecsys Anti-HCV II	528	0	100.00 (79.08 - 100.00)	100.00 (99.07 - 100.00)	19	0	0	509
	ARCHITECT Anti-HCV	528	0	100.00 (79.08 - 100.00)	99.61 (98.43 - 99.93)	19	2	0	507
Essen	Elecsys HIV combi PT	500	0	100.00 (59.77 - 100.00)	100.00 (99.03 - 100.00)	8	0	0	492
	ARCHITECT HIV Ag/Ab	500	0	100.00 (59.77 - 100.00)	100.00 (99.03 - 100.00)	8	0	0	492
Düsseldorf	Elecsys HIV combi PT	558	1	100.00 (77.08 - 100.00)	100.00 (99.12 - 100.00)	17	0	0	541
	ARCHITECT HIV Ag/Ab	558	1	100.00 (77.08 - 100.00)	100.00 (99.12 - 100.00)	17	0	0	541
Regensburg	Elecsys HIV combi PT	507	0	100.00 (51.68 - 100.00)	99.20 (97.82 - 99.74)	6	4	0	497
	ARCHITECT HIV Ag/Ab	507	0	100.00 (51.68 - 100.00)	99.80 (98.71 - 99.99)	6	1	0	500
Essen	Elecsys HBsAg II	499	0	100.00 (80.76 - 100.00)	100.00 (99.01 - 100.00)	21	0	0	478
	ARCHITECT HBsAg	499	0	100.00 (80.76 - 100.00)	99.79 (98.65 - 99.99)	21	1	0	477
Düsseldorf	Elecsys HBsAg II	553	2	100.00 (74.65 - 100.00)	100.00 (99.12 - 100.00)	15	0	0	538
	ARCHITECT HBsAg	553	2	100.00 (74.65 - 100.00)	100.00 (99.12 - 100.00)	15	0	0	538
Regensburg	Elecsys HBsAg II	499	0	100.00 (89.56 - 100.00)	100.00 (98.96 - 100.00)	42	0	0	457
	ARCHITECT HBsAg	499	0	100.00 (89.56 - 100.00)	99.78 (98.59 - 99.99)	42	1	0	456
Bad Salzuflen	Elecsys Syphilis	2,082	4	99.40 (96.20 - 99.97)	99.90 (99.58 - 99.98)	166	2	1	1,913
	ARCHITECT Syphilis TP	2,082	4	99.40 (96.20 - 99.97)	99.90 (99.58 - 99.98)	166	2	1	1,913
Regensburg	Elecsys Syphilis	499	2	100.00 (95.76 - 100.00)	100.00 (98.78 - 100.00)	109	0	0	390
	ARCHITECT Syphilis TP	489	12	98.06 (92.48 - 99.66)	100.00 (98.77 - 100.00)	101	0	2	386

Abbreviations: Ab - antibody, Ag - antigen, CI - confidence interval, FN - false negative, FP - false positive, HBc - hepatitis B core antigen, HBsAg - hepatitis B surface antigen, HCV - hepatitis C virus, HIV - human immunodeficiency virus, NA - not applicable, TN - true negative, TP - true positive.

DISCUSSION

In this multicenter performance evaluation, all Elecsys infectious disease assays demonstrated high sensitivity and specificity, with similar performance to other commercially available assays. Overall sensitivity and specificity for both Elecsys and ARCHITECT infectious disease panels tested were equivalent. The Elecsys assays showed similar sensitivity and specificity across all sites; however, slightly lower sensitivity, due to a small increase in the number of false negatives (n = 2), was reported on both the Elecsys and ARCHITECT Anti-HBc II assays tested at Düsseldorf. These Elecsys sensitivity and specificity findings support the suitability of the Elecsys assays in routine laboratory practice.

Sensitivity and specificity for each of the Elecsys assays and the ARCHITECT assays were in agreement with values reported by the manufacturer for controlled laboratory conditions [6-15].

Sensitivity and specificity of the Elecsys Anti-HCV II (100.00%; 100.00%) and ARCHITECT Anti-HCV (98.46%; 99.60%) assays were comparable with those determined in an Asia-Pacific cohort of 7,726 routine samples (Elecsys: 100.00%; 99.66%, ARCHITECT: 97.30%; 99.76%) [16]. For the Elecsys HIV combi PT assay, sensitivity (100.00%) and specificity (99.74%) were also similar to values from a cohort of 1,460 routine and vendor-sourced samples; sensitivity 100.00%, specificity 99.94%. Measurements for the ARCHITECT HIV Ag/Ab assay were not reported [17]. For the Elecsys HBsAg II and ARCHITECT HBsAg Qualitative II assays, sensitivity (100.00%; 100.00%) was equivalent to that reported in a cohort of 1,553 patients with previously diagnosed HBV infection (99.94%; 99.81%); specificity was not reported [18].

A potential limitation of this analysis was the use of stored samples for syphilis testing at one site. However, at both sites that evaluated the syphilis assays, sensitivity (≥ 98.06%) and specificity (≥ 99.90%) were comparable to those in the Elecsys Syphilis (100.00%; 99.88%) and ARCHITECT Syphilis TP (≥ 99.0%; ≥ 99.5%) assay method sheets [7,12]. Our findings mirror those of a previous study reporting equivalent sensitivity and specificity for the Elecsys Syphilis (100.00%; 99.81%) and ARCHITECT Syphilis TP (98.26%; 99.74%) assays in a Chinese cohort of 13,767 routine serum samples [19]. Comparable sensitivity (99.5%) and specificity (99.2%) for the Elecsys Syphilis assay were also reported in 2,506 routine and hospital patient samples from the USA and Argentina [20].

Strengths of our analysis include assay evaluation across multiple sites using a single protocol. A large number of samples from routine patients were evaluated and analyses were conducted in a 'real-life' laboratory setting, in accordance with the intended use of the assays. Overall, the Elecsys infectious disease assays demonstrated sensitivity and specificity similar to other commercially available assays, supporting their use in routine laboratory practice.

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Data Availability:
Qualified researchers may request access to individual anonymized patient-level data through the clinical study data request platform (https://vivli.org/). Further details on Roche's criteria for eligible studies are available here: https://vivli.org/members/ourmembers/. For further details on Roche's Global Policy on the Sharing of Clinical Information and how to request access to related clinical study documents, see here: https://www.roche.com/research_and_development/who_we_are_how_we_work/clinical_trials/our_commitment_to_data_sharing.htm

Appendix A. Supplementary Data:
Supplementary methods associated with this article can be found in the online version.

Declaration of Interest:
Barbara Hottenträger, Hans-Jochen Hagedorn, Eugen Bäcker, Andre Gessner, Nadine Lübke, Jürgen J. Wenzel, Marek Widera, Barbara Bleekmann, Stephan Pabinger, and Jörg Timm have no conflicts of interest to disclose. Peter Ramge is an employee of Roche Diagnostics and owns stocks/shares in Roche.

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Additional material can be found online at:
http://supplementary.clin-lab-publications.com/210201/