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Analytical performance comparison of five new generation immunoassay analyzers

H.A. HENDRIKS[1*], W. KORTLANDT[2] and W.M. VERWEIJ[1]

We evaluated the analytical performance of the new generation immunoassay analyzers (ACS:Centaur®, Architect ™*i*2000, Elecsys®2010, Immulite®2000 and Vitros ECi) for the following analytes: TSH, FT4, vitamin B12, ferritin, folate, CEA, HCG, PSA, estradiol, LH, FSH, prolactin, and progesterone. The characteristics evaluated were: within-run precision, carry-over and comparison of methods with instruments currently in use; ACS:180, AxSYM and Immulite1. The within-run precision of the test results for most assays was good (CV's of between 2 and 4%), and for some assays on the Vitros ECi (HCG, PSA, FSH and prolactin) and Elecsys 2010 (FT4, FSH and prolactin) even very good precision (< 2%) was measured. Relatively higher CV's for the anemia assays (ferritin, vitamin B12 and folate), as observed in the low concentration range, and for some fertility assays (progesterone on the ACS:Centaur and the Immulite 2000 and estradiol on the Architect), were determined. No sample carry-over was found for any of the analyzers. Most methods showed good correlation (r>0.97). Statistical significant slope differences were measured for the prolactin and FSH assays on the Elecsys 2010 and significant intercept differences were measured for the prolactin assay on the Vitros ECi and the vitamin B12 assay on the Elecsys 2010.
The new generation analyzers do not diminish the efforts that have to be made to harmonize the values of different laboratories using different equipment.

Keywords: immunoassay analyzers; ACS:Centaur®; Architect™i2000; Elecsys®2010; Immulite®2000 and Vitros ECi; within-run precision; carry-over; comparison of methods

Immunoassay testing has progressed over the years. Since the introduction of the first radioimmunoassay, several alternative and less hazardous detecting labels have been developed and the methods of antibody production have been improved. Besides these chemical improvements, automation has enabled a further increase in reproducibility and sensitivity, in combination with relatively short reaction times. This is especially relevant in view of the goal of shortening the patients stay in hospitals and the increasing scale of the laboratories.
The introduction of a number of large scale analyzers prompted us to evaluate them for analytical performance and efficiency and capacity. The evaluation of the efficiency and productivity of the five new generation analyzers tested (ACS:Centaur, Architect, Elecsys 2010, Immulite 2000 and Vitros ECi) has been described elsewhere (1). Here we focus on the analytical performance of the five new generation immunoassay analyzers, which comprised a carry-over study, evaluation of the within-run precision and comparison of the new generation analyzers assays with the in-house ACS:180, Immulite 1 and AxSYM assays in order to study the problems involved in arriving at the use of one universal set of reference values in the Netherlands.

MATERIALS and METHODS

Analyzers

The ACS:Centaur (Software version 1.2, Chiron Diagnostics) is a fully automated random access immunoassay analyzer that uses paramagnetic solid-phase particles and an acridinium ester based direct chemiluminescent tracer, coupled to antibodies in a second reagent. Luminescence is initiated by addition of acid and base reagent. The ACS: Centaur has a reagent capacity of 30 reagent packs (2).
The fully automated random access analyzer Architect *i*2000 (Software version 1.00, Abbott) uses chemiluminescent immunoassay technology incorporating an acridinium derivative tracer. This analyzer uses paramagnetic microparticles as solid phase. After exposure to pre-trigger and trigger reagent, the acridinium undergoes a decomposition reaction and the emitted light is amplified and processed. The Architect has 25 reagent pack positions.
The fully automated analyzer Elecsys 2010 (Software version 3.08, Roche- Boehringer Mannheim) incorporates an electrochemiluminescence (ECL) detection cell. The streptavidine coated paramagnetic beads, are coupled to the ruthenium-labeled antigen-antibody complex. Following the addition of tripropylamine, a voltage is applied and the resulting luminescence is measured (4,5). The Elecsys 2010 encompasses 15 reagent positions and 12 different assays which are available simultaneously.

Stichting Artsen Laboratorium[1] and Diakonessenhuis[2], Utrecht, The Netherlands

Correspondence to: H.A. Hendriks, Stichting Artsen Laboratorium, Noorderstraat 8, 3512 VX Utrecht, The Netherlands.
Received: 13.01.00
E-mail: hhendriks@dutch-net.com

The assays of the fully automated continuous random access analyzer Immulite 2000 (Software version 1.2, Diagnostic Products Corporation) are based on an alkaline phosphatase label and a chemiluminescent substrate and employ a centrifugal wash method. The Immulite 2000 encompasses 24 reagent positions (6-8).

The Vitros ECi (Software version 2.0, Ortho Clinical Diagnostics) is a fully automated random access immunoassay system that utilizes an enhanced chemiluminescence technology. This analyzer uses streptavidin coated plastic wells as solid phase. Horse radish peroxidase is used as label and a luminogenic substrate (a luminol derivative and a peracid salt) as signal detection. The Vitros ECi has a reagent capacity of 20 reagent packs (9).

Descriptions of the in-house analyzers ACS:180, AxSYM and Immulite 1 are given in the respective references (10-12, 13-14, 15-16).

Serum samples

Anonymous patient sera were collected, aliquoted and stored at -20°C. To exclude effects of re-thawing a set of 50 aliquots per assay was made available for each analyzer to perform correlation studies. The samples are distributed over the range that is encountered in routine application. The samples were stored in the same manner for all of the analyzers to avoid storage conditions becoming a variable. The samples were thawed and homogenized immediately before commencing the experiment.

Precision

Within-run precision was determined using commercial control sera (Lypocheck Immunoassay Plus Control Levels 1, 2 and 3 and Lypocheck Anemia Control, Bio-Rad). For each assay, replicate measurements (n=20) were performed in one run for each level. This procedure was processed three times within a period of 4-7 days, using a single reagent lot and a single calibration. The within-run precision data are expressed as coefficients of variation (CV%).

Carry-over

Assay carry-over was tested on the analyzers with HCG assays. Ten aliquots of low concentrate sample (~ 5 mIU/l) were measured to generate a base line concentration. Then one aliquot of high concentration sample (~ 100000 mIU/l) was followed by five aliquots of the low concentration sample. This sequence was repeated twice (17). Carry-over was calculated as follows: (concentration of a low sample after pipetting the high samples minus base line concentration) divided by (concentration of high sample) (13).

Comparison of methods

Comparisons of ACS:Centaur, Architect *i*2000, Elecsys 2010, Immulite 2000 and Vitros ECi assays with the in-house ACS:180, Immulite 1 and AxSYM assays were performed. For the complete matrix of method comparisons the Passing and Bablok regression lines and the coefficients of correlation were calculated (18,19).

RESULTS and DISCUSSION

Precision

Table 1 shows the mean concentrations and within-run precision data expressed as coefficient of variation (CV,%). The within-run CV's of the thyroid hormones were less than 4%, with exception of the low concentration TSH assays on the ACS:Centaur (10% at a concentration of 0.06 mIU/L), Immulite 2000 (10% at a concentration of 0.07 mIU/L) and the Vitros ECi (9% at a concentration of 0.17 mIU/L). Very good precision (CV's <2%) were measured for medium and high concentration TSH assays on the Vitros ECi and Elecsys 2010. The Elecsys 2010 showed very good precision for all levels with the FT4 assay. The FT4 assay on the Immulite 2000 showed CV's of above 4% for all levels. These higher CV's are in accordance with the within-run data as given by the supplier for this assay.

The tumor markers showed CV's of 4% or less on all analyzers except for the low CEA levels on the ACS:Centaur and Elecsys 2010. Very good precision, with CV's under the 2%, was measured for all levels of the PSA assay on the Vitros ECi.

CV's of between 2 and 4% (up to 8% at low levels) were observed with most of the fertility hormones, with exception of the methods as mentioned below. Very good precision, with CV's under or equal to 2%, were measured for a large number of Vitros ECi assays, in particular for all levels of the HCG, FSH and prolactin assays. The Elecsys 2010 also showed very good precision for all levels with the LH, FSH and prolactin assays. With exception of the lowest level, the FSH assay on the ACS:Centaur was very good. Only the progesterone assay on the Immulite 2000 exhibited significant higher within-run CV's from 7 to 11%. For the progesterone assay on the ACS:Centaur and the estradiol assay on the Architect CV's of between 4.5 and 6.7% were measured.

The anemia assay vitamin B12 was only available on the ACS:Centaur, the Architect and the Elecsys 2010 and folate was only available on the ACS:Centaur and the Elecsys 2010. On the Architect moderate CV's of between 5 and 7% were measured for all levels of the vitamin B12 assay, and for the low levels of the vitamin B12 and folate assays on the ACS:Centaur. For the Elecsys 2010 a CV higher than 10% was measured for the medium level of the folate assay. The relatively higher CV's for these anemia assays reflect the present state of art for these methods in general (20). The within-run CV's of the ferritin assays on all of the analyzers can be generally rated as being good, with CV's between 2 and 4%. With exception of the low levels on the ACS:Centaur and Immulite 2000 and the high level on the Vitros ECi were CV's of respectively 7.4, 4.2 and 5.7 were measured.

Carry-over

No carry-over (< 10^{-6}) could be demonstrated, on each of the five analyzers. Though sample or reagent-dependent carry-over possibly caused by pipetting steps is eliminated by the use of disposable tips in the

ACS:Centaur, Elecsys 2010 and Vitros ECi, a potential source of carry-over is present in the Architect and Immulite 2000 , as well as the measuring cell in the Elecsys 2010 system. No carry-over was detected, although on the Elecsys 2010 the results of the low concentration samples measured immediately after the high concentration samples were systematically flagged with potential carry-over by the instrument software. When a signal is lower than a calculated limit in respect to prior measurement the sample will be flagged with potential carry-over by the instrument software. In our experiment this flag appeared to be unnecessary.

Comparison of methods

In the comparison of thyroid methods (FT4 and TSH) between all eight assays, each showed correlation coefficients of more than 0.97 (Table 2). The mean slope for the TSH assay on the Elecsys 2010 was 1.32, resulting in higher results. Comparable higher slopes were found in the studies of Forest et al (4) and Ebert et al (21) for the Elecsys 2010 TSH assay with respect to the AxSYM TSH assay.

Table 3 shows the regression results of the fertility assays. Method comparison of the Vitros ECi LH assay with methods on the other analyzers showed large scattering compared with the regression data of

Table 1. Within-run precision of thyroid and fertility hormones, tumormarkers and anemia assays measured on ACS:Centaur, Architect, Elecsys 2010, Immulite 2000 and Vitros Eci

	ACS:Centaur		Architect		Elecsys 2010		Immulite 2000		Vitros Eci	
	Mean	CV(%)	Mean	CV(%)	Mean	CV(%)	Mean	CV(%)	Mean	CV(%)
TSH	0.06[a]	10	0.009[a]	4.3	0.09[a]	3.3	0.07[a]	10.3	0.17[a]	9.3
mIU/l	10.8	2.7	7.0	1.9	11.3	0.9	7.8	2.7	11.2	1.7
	25.2	2.1	25.8	2.4	31.5	1	25.7	2.7	33.2	1.5
FT4	4.8	3.9	5.3	4.6	6.7	1.6	4.0	15.4	17[a]	2.3
pmol/l	18.4	3.0	29.3	2.4	23.2	1	18.2	5.1	53.7	1.5
	60.5	3.6	-	-	63.6	1.7	44.8	4.4	>90	
CEA	2.4	4.4	3.3	3.5	3.3	5.1	2.9	3.1	-	-
µg/l	16.4	2.7	19.6	2.7	21.1	3	19.8	2.8	-	-
	36.5	2.1	42.1	2.5	45.2	2.5	53.7	2.8	-	-
HCG	5.1	6.9	3.6	4.5	10.2	5.1	5.6	7.8	5.2	1.7
mIU/l	20.5	3.7	19.5	2.9	31.3	2.9	34.7	4.1	22.4	1.2
	183	2.8	148	2.3	240	1.9	239	3.2	176	1.6
PSA	1.2	4.0	0.57	2.6	1.0	4.4	0.84	4.6	0.81[b]	1.3
ng/ml	4.2	2.7	2.8	3.5	3.6	1.6	4.3	3.4	2.4[b]	1.7
	36	3.4	19.9	3.1	26	2.0	25.9	3.1	16.8[b]	1.2
LH	1.5	4.4	0.67	3.3	2.4	2.1	0.6	3.6	1.6	4.2
mIU/l	19.8	3.7	25	2.5	28.4	1.2	23.8	2.8	23.6	2.7
	62.9	3.5	87	2.5	87.9	1.2	79.3	2.8	74.2	2.8
FSH	6.7	3.4	6.8	2.0	18.5	1.5	7.3	2.6	6.1	1.6
mIU/l	16.7	1.9	15.9	2.4	36.4	1.5	16.8	2.1	13.7	1.7
	52.3	1.8	42.2	2.2	97	1.6	45.2	2.4	39.9	1.5
E2	301	7.2	340	6.7	196	5.9	283	7.7	236	5.4
pmol/l	562	3.9	391	5.7	771	4.6	746	4.7	903	3.2
	815	3.8	622	4.5	2151	2.5	1194	2.3	2602	2.8
PRG	3.8	6.5	2.9	2.4	<0.48	-	3.2	11.3	1.4	8.0
nmol/l	24.7	4.5	24	4.6	8.1	5.0	24.7	7.7	27.2	3.2
	52.8	4.8	100	1.9	39.7	1.9	59.9	9.8	87.1	4.0
PRL	182	1.8	201	2.6	255	2.1	206	2.7	198	1.4
mIU/l	532	2.3	455	2.8	752	1.9	420	2.3	521	1.2
	1180	2.2	1209	1.9	1648	1.8	1080	2.3	1182	1.1
FER	6.5[a]	7.4	7.4[a]	3.1	11.5[a]	2.1	11.1[a]	4.2	9.6[a]	2.2
ng/ml	134	1.9	35.9	3.2	181	2.8	46.8	3.7	133	4.0
	317	2.8	142	3.6	457	2.7	155	3.6	394	5.7
VB12	60.1[a]	8.9	122[a]	7.0	<22[a]	-	-	-	-	-
pmol/l	475	3.8	173	6.3	348	4.2	-	-	-	-
	760	3.0	455	5.0	599	3.0	-	-	-	-
FOL	4.7[a]	6.3	-	-	<1.1[a]	-	-	-	-	-
nmol/l	12	3.9	-	-	3.5	16.2	-	-	-	-
	22.3	3.3	-	-	10.2	3.9	-	-	-	-

a: anemia control instead of Immunoassay level 1; b: investigational use only; -: test not available at time of study

Table 2. Method comparisons of the thyroid assays TSH and FT4

Method (y)	*Reference method (x)*	*TSH (0.002-95 mIU/l)* *b (Slope)*	*a (Intercept)*	*r*	*FT4 (6-86 pmol/l)* *b (Slope)*	*a (Intercept)*	*r*
ACS:Centaur	ACS:180	1.05	0.003	0.989	0.98	-0.23	0.994
ACS:Centaur	AxSYM	1.16	-0.111	0.976	1.06	-0.28	0.987
ACS:Centaur	Elecsys	0.83	-0.004	0.985	1.03	-1.80	0.988
ACS:Centaur	Immulite 1	1.12	0.010	0.988	0.79	1.86	0.983
ACS:Centaur	Immulite 2000	1.25	0.015	0.995	0.88	0.48	0.980
ACS:Centaur	VITROS	1.13	-0.017	0.996	0.91	2.51	0.984
Architect	ACS:180	0.7	0.012	0.989	0.8	0.91	0.980
Architect	ACS:Centaur	1.5	-0.017	0.999	1.2	-0.93	0.979
Architect	AxSYM	0.77	-0.002	0.993	0.93	0.27	0.985
Architect	Elecsys	0.55	0.014	0.990	0.87	-0.09	0.966
Architect	Immulite 1	0.76	0.001	0.992	0.71	1.85	0.972
Architect	Immulite 2000	0.84	0.010	0.996	0.75	0.94	0.983
Architect	VITROS	0.76	0.000	0.997	0.76	2.68	0.985
AxSYM	ACS:180	0.90	0.041	0.996	0.87	0.48	0.989
Elecsys	ACS:180	1.26	0.010	0.984	0.93	1.39	0.983
Elecsys	AxSYM	1.37	-0.020	0.975	1.07	0.87	0.984
Elecsys	Immulite 1	1.38	0.010	0.995	0.80	2.49	0.984
Immulite 1	ACS:180	0.91	-0.001	0.989	1.18	-1.88	0.986
Immulite 1	AxSYM	1.01	-0.054	0.980	1.36	-2.60	0.987
Immulite 2000	ACS:180	0.83	-0.008	0.998	1.07	-0.14	0.985
Immulite 2000	AxSYM	0.93	-0.051	0.994	1.25	-1.18	0.988
Immulite 2000	Elecsys	0.64	0.035	0.982	1.17	-2.17	0.966
Immulite 2000	Immulite 1	0.94	-0.015	0.991	0.93	1.60	0.977
Immulite 2000	VITROS	0.92	-0.017	0.997	1.04	2.37	0.986
VITROS	ACS:180	0.90	0.025	0.997	1.08	-2.96	0.990
VITROS	AxSYM	1.00	-0.030	0.998	1.22	-3.51	0.994
VITROS	Elecsys	0.73	-0.004	0.992	1.09	-3.75	0.974
VITROS	Immulite 1	1.00	0.001	0.996	0.91	-1.37	0.982

Table 3. Method comparisons of the hormone assays LH, FSH, progesterone, prolactin, oestradiol and HCG

Method (y)	*Reference method (x)*	*LH (1.1-42 mIU/ml)* *b (Slope)*	*a (Intercept)*	*r*	*FSH (0.5-140 mIU/ml)* *b (Slope)*	*a (Intercept)*	*r*
ACS:Centaur	ACS:180	1.01	-0.19	0.994	0.90	-1.23	0.997
ACS:Centaur	AxSYM	0.74	0.28	0.986	0.89	-0.72	0.992
ACS:Centaur	Elecsys	0.75	-0.61	0.987	0.52	-0.64	0.948
ACS:Centaur	Immulite 1	0.94	0.56	0.963	0.84	-0.22	0.994
ACS:Centaur	Immulite 2000	1.14	-0.13	0.964	0.93	-0.33	0.994
ACS:Centaur	VITROS	0.85	0.19	0.912	1.11	-0.89	0.996
Architect	ACS:180	1.47	-0.07	0.988	1	-0.1	0.992
Architect	ACS:Centaur	0.71	-0.24	0.983	0.91	-0.89	0.995
Architect	AxSYM	1.08	0.46	0.994	1	0.34	0.998
Architect	Elecsys	1.06	-0.13	0.980	0.58	-0.01	0.957
Architect	Immulite 1	1.33	1.36	0.982	0.93	0.9	0.996
Architect	Immulite 2000	1.58	0.43	0.981	1.04	0.78	0.992
Architect	VITROS	1.20	0.64	0.947	1.23	0.22	0.998
AxSYM	ACS:180	1.38	-0.65	0.993	1.01	-0.43	0.989
Elecsys	ACS:180	1.39	0.25	0.987	1.76	-0.44	0.947
Elecsys	AxSYM	1.01	0.86	0.978	1.74	0.02	0.946
Elecsys	Immulite 1	1.26	1.36	0.944	1.65	1.00	0.952
Immulite 1	ACS:180	1.09	-0.68	0.966	1.08	-1.02	0.993
Immulite 1	AxSYM	0.79	-0.29	0.973	1.07	-0.55	0.994
Immulite 2000	ACS:180	0.92	-0.17	0.965	0.96	-0.83	0.991
Immulite 2000	AxSYM	0.67	0.10	0.968	0.96	-0.38	0.990
Immulite 2000	Elecsys	0.68	-0.2	0.954	0.56	-0.34	0.953
Immulite 2000	Immulite 1	0.85	0.48	0.986	0.89	0.18	0.996
Immulite 2000	VITROS	0.76	0.15	0.958	1.19	-0.57	0.993
VITROS	ACS:180	1.25	-0.90	0.906	0.82	-0.14	0.992
VITROS	AxSYM	0.89	0.03	0.913	0.81	0.17	0.995
VITROS	Elecsys	0.90	-0.98	0.903	0.46	0.09	0.956
VITROS	Immulite 1	1.11	0.46	0.914	0.76	0.60	0.995

Table 3. Continue

Method (y)	Reference method (x)	estradiol (26-14955 pmol/l) b (Slope)	a (Intercept)	r	progesterone (0.35-120 nmol/l) b (Slope)	a (Intercept)	r
ACS:Centaur	ACS:180	1.13	-22.59	0.996	0.95	-0.65	0.983
ACS:Centaur	AxSYM	0.84	-30.56	0.963	1.27	0.64	0.981
ACS:Centaur	Elecsys	1.06	13.06	0.934	-	-	-
ACS:Centaur	Immulite 1	1.13	-11.20	0.961	1.12	-2.37	0.986
ACS:Centaur	Immulite 2000	1.1	-59.97	0.970	1.36	-2.26	0.976
ACS:Centaur	VITROS	1.19	0.43	0.928	1.62	-0.89	0.984
Architect	ACS:180	1.29	67.53	0.979	0.66	-0.64	0.974
Architect	ACS:Centaur	0.84	-68.59	0.993	1.4	0.32	0.961
Architect	AxSYM	0.96	77.86	0.991	0.85	0.06	0.971
Architect	Elecsys	1.34	129.42	0.959	-	-	-
Architect	Immulite 1	1.29	114.68	0.975	0.77	-1.87	0.981
Architect	Immulite 2000	1.23	55.85	0.995	0.91	-1.63	0.968
Architect	VITROS	1.4	108.62	0.970	1.02	-0.41	0.979
AxSYM	ACS:180	1.38	-32.05	0.993	0.75	-0.73	0.990
Elecsys	ACS:180	1.06	-41.57	0.959	-	-	-
Elecsys	AxSYM	0.77	-58.39	0.923	-	-	-
Elecsys	Immulite 1	1.04	-20.37	0.963	-	-	-
Immulite 1	ACS:180	1.04	-17.54	0.988	0.86	1.32	0.991
Immulite 1	AxSYM	0.74	-3.96	0.970	1.07	3.43	0.989
Immulite 2000	ACS:180	1.03	10.65	0.991	0.68	0.91	0.984
Immulite 2000	AxSYM	0.78	38.54	0.986	0.93	1.73	0.996
Immulite 2000	Elecsys	1.04	69.99	0.947	-	-	-
Immulite 2000	Immulite 1	1.07	36.66	0.994	0.82	-0.04	0.991
Immulite 2000	VITROS	1.02	69.36	0.985	1.14	1.19	0.966
VITROS	ACS:180	0.95	-25.79	0.962	0.61	-0.01	0.982
VITROS	AxSYM	0.77	-52.57	0.979	0.82	0.52	0.967
VITROS	Elecsys	1.06	-48.69	0.975	-	-	-
VITROS	Immulite 1	1.02	-33.27	0.988	0.74	-1.48	0.985

Method (y)	Reference method (x)	prolactin (110-1256 mIU/l) b (Slope)	a (Intercept)	r	HCG (1.2-4988 mIU/ml) b (Slope)	a (Intercept)	r
ACS:Centaur	ACS:180	0.99	-6.04	0.992	0.82	-2.02	0.992
ACS:Centaur	AxSYM	0.99	2.57	0.930	0.79	1.89	0.991
ACS:Centaur	Elecsys	0.76	-7.59	0.974	0.79	-1.14	0.989
ACS:Centaur	Immulite 1	1.16	2.23	0.988	0.97	0.22	0.992
ACS:Centaur	Immulite 2000	1.24	2.27	0.983	0.9	-0.94	0.980
ACS:Centaur	VITROS	1.12	-78.79	0.975	0.94	-0.61	0.987
Architect	ACS:180	0.88	9.98	0.988	0.89	1.51	0.995
Architect	ACS:Centaur	1.17	-25.29	0.993	0.79	-0.68	0.989
Architect	AxSYM	0.85	22.47	0.947	0.97	2.09	0.998
Architect	Elecsys	0.65	12.29	0.987	1.03	-1.89	0.982
Architect	Immulite 1	1.02	18.36	0.991	1.21	-0.34	0.998
Architect	Immulite 2000	1.09	20.93	0.990	1.13	0.33	0.998
Architect	VITROS	0.97	-45.75	0.967	1.14	-1.12	0.997
AxSYM	ACS:180	1.01	-11.55	0.932	1.03	-5.81	0.993
Elecsys	ACS:180	1.36	-8.79	0.971	1.03	-1.80	0.989
Elecsys	AxSYM	1.32	12.24	0.969	1.02	3.71	0.992
Elecsys	Immulite 1	1.53	15.56	0.987	1.26	0.81	0.979
Immulite 1	ACS:180	0.87	-15.13	0.984	0.85	-3.22	0.993
Immulite 1	AxSYM	0.84	-0.26	0.953	0.81	1.27	0.999
Immulite 2000	ACS:180	0.81	-11.71	0.980	0.91	-3.55	0.991
Immulite 2000	AxSYM	0.79	-4.1	0.959	1	1.03	0.999
Immulite 2000	Elecsys	0.61	-10.61	0.990	0.92	-3.05	0.971
Immulite 2000	Immulite 1	0.92	1.571	0.993	1.1	-1.59	0.994
Immulite 2000	VITROS	0.88	-62.44	0.954	1.05	-1.65	0.997
VITROS	ACS:180	0.91	57.87	0.973	0.82	0.64	0.999
VITROS	AxSYM	0.87	70.60	0.910	0.84	2.55	0.997
VITROS	Elecsys	0.65	68.77	0.950	0.86	-0.99	0.982
VITROS	Immulite 1	1.03	71.83	0.962	1.05	0.86	0.997

Table 4. Method comparisons of the tumor markers PSA and CEA

Method (y)	*Reference method (x)*	*PSA (0.12-85 ng/ml)* b *(Slope)*	a *(Intercept)*	r	*CEA (0.4-512 µg/l)* b *(Slope)*	a *(Intercept)*	r
ACS:Centaur	ACS:180	1.01	-0.024	0.999	1.00	-0.10	1.000
ACS:Centaur	AxSYM	0.92	-0.059	0.996	0.85	0.34	0.987
ACS:Centaur	Elecsys	0.88	-0.163	0.996	0.68	-0.14	0.979
ACS:Centaur	Immulite 1	0.76	0.002	0.996	0.71	0.45	0.996
ACS:Centaur	Immulite 2000	0.81	0.01	0.995	0.73	0.31	0.994
ACS:Centaur	VITROS	0.83	-0.153	0.997	-	-	-
Architect	ACS:180	1.23	0.05	1.000	1.34	-0.29	0.989
Architect	ACS:Centaur	1.24	0.06	0.992	0.78	0.08	0.989
Architect	AxSYM	1.11	0.03	0.999	1.14	0.34	0.998
Architect	Elecsys	1.06	-0.09	0.994	0.97	-0.59	0.993
Architect	Immulite 1	0.93	0.04	0.999	0.96	0.38	0.993
Architect	Immulite 2000	1	0.1	0.996	0.97	0.35	0.998
Architect	VITROS	1.02	-0.1	0.999	-	-	-
AxSYM	ACS:180	1.10	0.028	0.996	1.20	-0.52	0.986
Elecsys	ACS:180	1.18	0.158	0.996	1.52	-0.02	0.980
Elecsys	AxSYM	1.05	0.143	0.999	1.24	0.92	0.989
Elecsys	Immulite 1	0.91	0.124	0.998	0.99	1.02	0.976
Immulite 1	ACS:180	1.32	0.002	0.997	1.44	-0.85	0.994
Immulite 1	AxSYM	1.20	-0.028	0.999	1.19	-0.07	0.994
Immulite 2000	ACS:180	1.21	-0.01	0.997	1.41	-0.72	0.993
Immulite 2000	AxSYM	1.12	-0.07	0.995	1.16	-0.08	0.994
Immulite 2000	Elecsys	1.03	-0.19	0.995	1	-0.82	0.987
Immulite 2000	Immulite 1	0.92	-0.04	0.995	0.98	0.09	0.998
Immulite 2000	VITROS	1.01	-0.19	0.997	-	-	-
VITROS	ACS:180	1.19	0.17	0.999	-	-	-
VITROS	AxSYM	1.10	0.122	0.999	-	-	-
VITROS	Elecsys	1.00	-0.010	0.998	-	-	-
VITROS	Immulite 1	0.92	0.156	1.000	-	-	-

the other instruments. The large scattering observed by the comparison of the Vitros ECi LH assay with the other assays could be a result of the difference in method of measurement. The correlation coefficients of the Vitros ECi LH assays and the other assays were between 0.90 and 0.96. Between the other analyzers the range of correlation coefficients for the LH assay was between 0.95 and 0.99.

The FSH methods had correlation coefficients of 0.99, except for the Elecsys assays where correlation coefficients of 0.95 were determined. The mean slope of the regression lines, observed by comparing the FSH assay of the Elecsys 2010 to the other FSH methods, was 1.58. Resulting in higher results for this assay on the Elecsys 2010 analyzer. Comparable differences were found for the values of the control materials measured in the precision experiment.

The relatively poor precision results of the estradiol methods clearly has demonstrated the difficulty with this analyte (20) and therefore can also explain the large number of correlation coefficients of below 0.97. Whilst comparing the prolactin assays on the AxSYM, correlation coefficients of between 0.91 and 0.97 where observed, whilst generally, correlation coefficients of more than 0.97 were obtained between all other analyzers. Against all methods, a significant average slope value of 1.36 was observed for the Elecsys prolactin assay resulting in systematic higher values. The average intercept value of 65.15 mIU/l for the Vitros Eci resulted in significant higher prolactin values, although all prolactin assays were calibrated to the same standard. With progesterone, good correlation coefficients (>0.97) were obtained in all cases tested. No correlation coefficients were calculated for the Elecsys, because on this instrument 35 of the 50 samples were under detection level (<0.48 nmol/l). Good concordance between all of the analyzers for the HCG assays observed, was found.

In table 4, PSA and CEA method comparison studies showed good correlation.

Results of the method comparison of the anemia assays are represented in table 5. The ferritin methods showed very good correlation with coefficients of > 0.99. Correlation of the Vitamin B12 methods exhibited coefficients between 0.97 and 0.99, except for the Elecsys 2010 Vitamin B12 assay where correlation coefficients of between 0.94 and 0.96 were observed. Additionally, the Elecsys 2010 Vitamin B12 assay showed intercepts of more than 100 pmol/l against other methods. Considerably lower folate results were measured on the Elecsys 2010 compared to all of the analyzers and 32 out of the 50 samples were under detection level (<1.1 nmol/l). The remaining sample size was too small for regression analysis. The other available assays showed correlation coefficients of between 0.95 and 0.98, with about 30% higher values for the Immulite 1 in comparison to assays of the two other suppliers.

Table 5. Method comparisons of the anemia assays ferritin, vitamin B12 and folate.

Method (y)	*Reference method (x)*	*Ferritin (1.7-671 ng/ml)* *b (Slope)*	*a (Intercept)*	*r*	*Vitamin B12 (29-1230 pmol/l)* *b (Slope)*	*a (Intercept)*	*r*
ACS:Centaur	ACS:180	0.92	-0.24	0.998	0.84	-2.97	0.989
ACS:Centaur	AxSYM	1.13	-1.27	0.998	0.77	43.95	0.981
ACS:Centaur	Elecsys	0.70	-0.04	0.993	0.80	118.76	0.953
ACS:Centaur	Immulite 1	0.81	2.58	0.997	0.70	38.50	0.978
ACS:Centaur	Immulite 2000	0.81	1.42	0.995	-	-	-
ACS:Centaur	VITROS	1.07	-0.65	0.996	-	-	-
Architect	ACS:180	0.77	-1.34	0.991	1.17	-65.8	0.972
Architect	ACS:Centaur	1.17	1.17	0.994	0.72	44.59	0.970
Architect	AxSYM	0.98	-2.81	0.990	1.08	-2.08	0.977
Architect	Elecsys	0.61	-1.84	0.992	1.03	113.53	0.935
Architect	Immulite 1	0.69	0.23	0.995	1	-12.32	0.975
Architect	Immulite 2000	0.7	-0.02	0.985	-	-	-
Architect	VITROS	0.9	-1.85	0.994	-	-	-
AxSYM	ACS:180	0.81	1.39	0.999	1.06	-52.58	0.974
Elecsys	ACS:180	1.32	0.08	0.991	1.05	-152.09	0.959
Elecsys	AxSYM	1.63	-2.69	0.991	1.04	-113.25	0.963
Elecsys	Immulite 1	1.15	2.86	0.992	0.94	-117.02	0.949
Immulite 1	ACS:180	1.14	-2.74	0.997	1.16	-45.89	0.985
Immulite 1	AxSYM	1.42	-4.71	0.997	1.08	8.48	0.991
Immulite 2000	ACS:180	1.12	-1.92	0.996	-	-	-
Immulite 2000	AxSYM	1.38	-4.02	0.995	-	-	-
Immulite 2000	Elecsys	0.86	-1.33	0.987	-	-	-
Immulite 2000	Immulite 1	0.98	0.56	0.993	-	-	-
Immulite 2000	VITROS	1.3	-3.47	0.992	-	-	-
VITROS	ACS:180	0.87	0.39	0.997	-	-	-
VITROS	AxSYM	1.08	-1.47	0.996	-	-	-
VITROS	Elecsys	0.65	0.48	0.989	-	-	-
VITROS	Immulite 1	0.76	2.84	0.998	-	-	-

Method (y)	*Reference method (x)*	*Folate (0.93-19.5 nmol/l)* *b (Slope)*	*a (Intercept)*	*r*
ACS:Centaur	ACS:180	0.85	0.77	0.981
ACS:Centaur	AxSYM	0.88	0.18	0.974
ACS:Centaur	Elecsys	-	-	-
ACS:Centaur	Immulite 1	0.67	1.21	0.984
ACS:Centaur	VITROS	-	-	-
AxSYM	ACS:180	0.99	0.66	0.946
Elecsys	ACS:180 -	-	-	-
Elecsys	AxSYM	-	-	-
Elecsys	Immulite 1	-	-	-
Immulite 1	ACS:180	1.27	-0.72	0.964
Immulite 1	AxSYM	1.33	-1.63	0.981
VITROS	ACS:180 -	-	-	-
VITROS	AxSYM	-	-	-
VITROS	Elecsys	-	-	-
VITROS	Immulite 1	-	-	-

Slope and intercept differences in the method comparison data demonstrated that not all methods are interchangeable unless prior reference studies are performed. Deviations in some methods referenced to the same standard, such as the TSH methods that are all referenced to the 2nd IRP WHO 80/558 standard, showed that calibration against the same standard does not automatically guarantee inter-method agreement. Recent publications in the Netherlands (22) do at least suggest that there is one universal set of reference values for laboratory tests. Our results indicate the problems that have to be solved to achieve this standardization.

In conclusion: on each of the five analyzers no carry-over was measured. Most of the test results of the new immunoassay analyzers showed good within-run reproducibility (CV <4%) with a few exceptions in the low concentration range of some assays and with all concentration ranges of some fertility assays. The Vitros ECi and Elecsys 2010 even exhibited very good CV's (CV<2%) for a large number of assays.
For most of the method comparisons, good correlation coefficients were determined (>0.97).
Significant slope and intercept differences were measured, for some fertility hormones and anemia assays, on a few analyzers.

The new generation analyzers do not diminish the amount of effort that has to be applied to harmonize the values of different laboratories using different equipment.

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Summary

Analytical performance comparison of five new generation immunoassay analyzers. Henriks HA, Kortlandt W and Verweij WM. Ned Tijdschr Klin Chem 2000; 25: 170-177.
We evaluated the analytical performance of the new generation immunoassay analyzers (ACS:Centaur®, Architect ™*i*2000, Elecsys®2010, Immulite®2000 and Vitros ECi) for the following analytes: TSH, FT4, vitamin B12, ferritin, folate, CEA, HCG, PSA, estradiol, LH, FSH, prolactin, and progesterone. The characteristics evaluated were: within-run precision, carry-over and comparison of methods with instruments currently in use; ACS:180, AxSYM and Immulite1. The within-run precision of the test results for most assays was good (CV's of between 2 and 4%), and for some assays on the Vitros ECi (HCG, PSA, FSH and prolactin) and Elecsys 2010 (FT4, FSH and prolactin) even very good precision (< 2%) was measured. Relatively higher CV's for the anemia assays (ferritin, vitamin B12 and folate), as observed in the low concentration range, and for some fertility assays (progesterone on the ACS:Centaur and the Immulite 2000 and estradiol on the Architect), were determined. No sample carry-over was found for any of the analyzers. Most methods showed good correlation (r>0.97). Statistical significant slope differences were measured for the prolactin and FSH assays on the Elecsys 2010 and significant intercept differences were measured for the prolactin assay on the Vitros ECi and the vitamin B12 assay on the Elecsys 2010.
The new generation analyzers do not diminish the efforts that have to be made to harmonize the values of different laboratories using different equipment.
Keywords: immunoassay analyzers; ACS:Centaur®; Architect™ i2000; Elecsys®2010; Immulite®2000; Vitros ECi; within-run precision; carry-over; comparison of methods.