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Multicentre performance evaluation of the E170 Module for MODULAR *ANALYTICS*

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Abstract

The E170 module was evaluated at 13 sites in an international multicentre study. The objective of the study was to assess the analytical performance of 49 analytes, and to collect feedback on the system's reliability and practicability. The typical, within-run coefficients of variation (CVs) for most of the quantitative assays ranged between 1 and 2% while a range of 2–4% was achieved with the infectious disease methods. Total precision CVs were found to be within the manufacturer's expected performance ranges, demonstrating good concordance of the system's measuring channels and a high reproducibility during the 2–4-week trial period. The functional sensitivity of 11 selected assays met the clinical requirements (e.g., thyreotroponin (TSH) 0.008 mU/l, troponin T 0.02 μg/l, total prostate-specific antigen (PSA) 0.03 μg/l). The E170 showed no drift during an 8-hour period and no relevant reagent carryover. Accuracy was confirmed by ring trial experiments and method comparisons vs. Elecsys® 2010. The reliability and practicability of the system's hardware and software met with, or even exceeded, the evaluator's requirements. Workflow studies showed that E170 can cover the combined workload of various routine analysers in a variety of laboratory environment. Throughput and sample processing time requirements were achieved while personnel 'hands-on-time' could be reduced.

Keywords: immunoanalyser; performance evaluation; practicability; workflow.

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Introduction

MODULAR *ANALYTICS* was introduced to the market by Roche Diagnostics in 1998. It represents a new, modular-designed system platform consisting of a *core unit* for sample distribution/tracking and different types of *analytical modules*. Initially only modules for the analysis of electrolytes (ISE900/ISE1800) and two photometric modules (D2400, P800) for clinical chemistry testing were available (1, 2). A milestone in immunochemistry automation was achieved with the introduction of the E170 module for MODULAR *ANALYTICS* [in the following text (E170) or (E)] together with an extensive menu of heterogeneous immunoassays based on the widely accepted Elecsys® technology (3, 4).

The multicentre evaluation of E170 extended over a period of 10 months and covered 49 analytes from different indication areas – thyroid, cardiac, fertility, anaemia, tumour marker, bone marker, hormones and infectious disease. A total of 13 sites (ten European, one Japanese and two US) participated in the four different phases of the study. The comprehensive evaluation protocol included an assessment of conventional analytical performance characteristics such as precision, functional sensitivity, analytical range limit, drift, carryover and accuracy. Those experiments largely followed the European Committee for Clinical Laboratory Standards (ECCLS) and National Committee for Clinical Laboratory Standards (NCCLS) guidelines (5, 6). Other experiments simulating routine working conditions were designed to check sample workflow, result availability and the overall functionality of E170 (7).

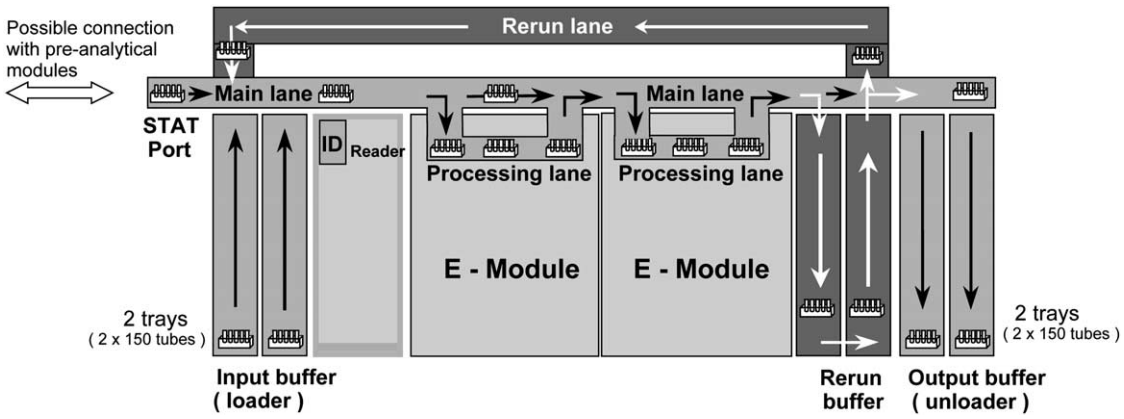

Figure 1 Schematic structure of the MODULAR *ANALYTICS* 〈EE〉 combination installed at the different MCE sites.

Approximately 274,000 individual data were generated and statistically evaluated. Processing and analysis of such large data volumes was made possible using computer aided evaluation (CAEv) software. This facilitated the definition of protocols, sample and test requests for on-line/off-line data capture, and the statistical evaluation of the results (8). Following local validation, all of the data were electronically transmitted to the study control centre.

Materials and methods

Instrument

MODULAR *ANALYTICS* consists of three main parts: a *control unit*, a *core unit*, and analyser *modules* (Figure 1). The number of modules can be adapted to the laboratory's workload and combinations of up to four modules (e.g., E170) are possible.

The *control unit* uses a graphical user interface to control all instrument functions. Its components include a touch screen monitor, keyboard, printer, and a Windows-NT based personal computer (PC).

The *core unit* consists of a bi-directional multi-track transport system, a loader (input buffer), an unloader (output buffer) and a rerun buffer. The rack transport system is a unique feature of MODULAR *ANALYTICS*, consisting of a main lane, one or more processing lanes, and a rerun lane. The five-position sample racks are conveyed to a module by the main lane and then transferred to the processing lane. On completion of the sampling process, the racks are returned to the main lane and then conveyed to the next module or to the rerun buffer. They remain in this rerun buffer until all test results are available. Thereafter, the racks are transported either directly to the unloader or to the rerun lane as appropriate. Efficient sample routing and workload distribution to all modules is co-ordinated by advanced 'intelligent process management' (IPM) queuing software. The *core unit* also includes a STAT port for immediate loading of samples which are given priority processing.

The E170 *module* is an automated, random access, multitest system for heterogeneous immunoassays with a maximum throughput of 170 tests per hour. The temperature-controlled reagent disk accommodates up to 25 different ready-to-use Elecsys® reagent packs. For frequently requested tests several rack packs of the same test can also be loaded with automatic changeover from empty to full rack packs. The two-dimensional matrix barcode on each rack pack facilitates reliable identification and fast data transfer. The E170 *module*, like Elecsys® 2010, uses disposable AssayTips for carryover-free sample pipetting and disposable AssayCups. Trays with consumables for up to 1008 determinations can be loaded before operation. Full or empty trays can be added or removed at any time without compromising the routine operation of the system. This loading/unloading principle also applies to the system reagents. Transportation of tips and cups between the different instrument compartments is performed by a gripper which picks up the AssayCup from the magazine tray and transports it to the 54-position incubator disk. This disk is maintained at a temperature of 37°C to ensure/facilitate reaction between the dispensed sample and reagents in the AssayCups. The standard incubation time for most assays is 18 minutes (2×9). Some assays such as B12, FOL and A-HBs require a pre-treatment step, adding a further 9 minutes to the total assay time. A few assay protocols include a 'pre-wash' step prior to aspiration into the measuring cell and this step is executed in the 'pre-wash' station without any impact on throughput. Otherwise the reaction mixtures from the AssayCups are directly aspirated by two sipper probes into two measuring channels where the electrochemiluminescence detection takes place.

The main specifications of the evaluation instruments shipped to the different laboratories are shown in Table 1.

Reagents

Only commercially available Elecsys® reagent packs were used (see Table 2). E170-specific application and calibration data were coded on a second barcode label affixed to the respective rack packs. The same reagent lots were used at all evaluation sites. For the comparison experiments, the methods and reagent lots from the routine laboratory were used.

Calibration

Test-specific Elecsys® calibrator sets (CalSet) were used for calibration and the calibration frequencies followed the recommendations given in the package inserts.

Control materials

Precision and quality control experiments were performed with control sera from Roche Diagnostics GmbH. Reference

Table 1 System characteristics and specifications.

Type of instrument	Floor-mounted, random access, multi-channel, modular-designed system for fully automated immunoassay testing
System units	Control unit with touch screen monitor, keyboard, printer, Windows-NT based PC; core unit with bi-directional multi-track transport system, loader, rerun buffer and unloader; 1-4 E170 analyser modules
Throughput	Maximum 170 tests/h on one E170 module
Turn-around time	From sample loading to result availability: approx. 30 minutes (minimum of 19 minutes, depending on number of samples loaded per batch, and number of tests requests per sample)
Sampling system	5-position sample racks; loader compartment for up to 300 samples; STAT port for loading of emergency samples; primary or secondary tube sampling; barcode identification of primary tubes; carryover-free sampling with disposable tips; 10–50 µl sample volume, liquid level detection (LLD); clot detection
Reagent area	Temperature-controlled reagent rotor with 25 channels; ready-to-use reagent packs for 100/200 tests; positive reagent identification with 2-dimensional barcode; evaporation protection by automatic cap open/close mechanism; LLD; universal diluent for automatic sample pre-dilution; inventory control; duplicate system reagents (ProCell M, CleanCell M, PreClean M) for automated bottle changeover
Reaction system	54-position incubator (37°C); 18–27 minutes reaction times; non-invasive vortex mixers
Measuring system	Two measuring cells; electrochemiluminescence detection at 28°C; bar coded master calibration, 2-point re-calibration
Consumables and waste	Up to 12 magazines with AssayTips/AssayCups for 1008 determinations can be loaded; 2 waste boxes for used tips/cups and magazine waste; optional 2 containers (20 l) for liquid waste
Water supply	Water quality: deionized, bacteria-free, conductivity <1.5 MΩ (1 µS/cm); reservoir for deionized water with external supply; water consumption during operation: ~30 l/h
Environmental conditions	Temperature: 18–32°C; room humidity: 45–85%
Dimensions	Depth: 1.05 m/height: 1.17 m/length: 1.65 m + (1.20 m × number of E170 modules) Weight: approx. 830 kg (for core + 1 E170)
Electrical rating	AC 400/230 V/50 Hz (Europe/International) or AC 208 V/60 Hz (US)
General system characteristics	Intelligent process management (IPM) for efficient sample routing with automated rerun and support of reflex testing [in conjunction with a corresponding laboratory information system (LIS) feature]; bi-directional host interface capability; automatic calibration notification; automatic sample dilution; automated maintenance functions

materials from the Deutsche Gesellschaft für Klinische Chemie (DGKC) were used for the accuracy experiments (ring trials, see Table 3).

Specimens

Human material pools were used for precision experiments and fresh specimens from single donors were used for the method comparisons and workflow/routine simulation experiments. Most sites only analysed serum samples with only a few using heparinized or EDTA-plasma samples. An additional 50 frozen samples, from acute/chronic HAV/HBV infections, were measured at one site for comparison of the infectious disease methods.

Evaluation protocol

MODULAR *ANALYTICS* combinations with two E170-modules (⟨EE⟩) were evaluated at all but one of the multicentre evaluation (MCE) sites. The exception was the Göttingen site where a MODULAR *ANALYTICS* combination with only one E170-module (⟨E⟩) module was installed. The assays to be evaluated were provided in four phases, 1a, 1b, 2a and 2b (see Table 2). In addition to the assessment of the analytical performance, routine simulation and workflow experiments were done while the overall system practicability was recorded by means of a questionnaire. Figure 2 gives an overview of the protocol and test groups covered by the different sites. All assays were assessed with regard to reproducibility (within-run precision and total precision) and accuracy (recovery in controls and method comparison). Functional sensitivity, drift, carryover, linearity, and high-dose hook-experiments were done for selected tests. The design of the experiments is described as follows.

Within-run precision Two controls and one human serum pool were processed in 21 replicates with each test assayed on all four measuring cells of the ⟨EE⟩ combination.

Total precision according to NCCLS According to a modified NCCLS protocol (EP5-A), two controls and one human serum pool were measured in six replicates on 21 days for test group 1a, and on 10 days for test groups 1b, 2a and 2b. The processing sequence of the aliquots were randomized each day. The precision was determined on the single E-module as well as over both E-modules with random measurements on all four cells.

Method comparison Ten to fifteen fresh human specimens were analysed daily for 10 days on ⟨EE⟩ and on the comparison instrument for non-infectious disease assays at analyte concentrations covering as much of the analytical range as possible. Comparisons of these quantitative methods were done by calculation of the Passing/Bablok regression lines (9). For infectious disease assays, 25 fresh human specimens were analysed each day for 20 days at two evaluation sites. In addition, approx 2000 fresh human samples provided by the Salzburg Blood Bank and the BRK Blutspendedienst (Red Cross blood donor service) were measured in-house by Roche over a 10-day period.

Recovery in controls/reference materials (ring trial) Two controls with concentrations unknown to the evaluators were analysed in triplicate over 5 days. The median, calculated from the respective second determination, was used

Table 2 E170 methods: in all cases the respective Elecsys® assays and the appropriate calibrator materials (CalSet Elecsys®) were used.

Test group	Test code	Analyte	Study unit
1a	TSH	Thyreotropin	mU/l
	T3	Triiodothyronine	nmol/l
	T4	Thyroxine	nmol/l
	FT3	Free triiodothyronine	pmol/l
	FT4	Free thyroxine	pmol/l
	T-UP	Thyroxine binding capacity	TBI
	TN-T	Troponin T	µg/l
	CK-MB	MB isoenzyme of creatine kinase	µg/l
	MYO	Myoglobin	µg/l
	PSA	Total prostate-specific antigen	µg/l
	FPSA	Free prostate-specific antigen	µg/l
	CEA	Carcinoembryonic antigen	µg/l
	AFP	α_1-Fetoprotein	µg/l
1b	B12	Vitamin B_{12}	pmol/l
	FOL	Folate	nmol/l
	FERR	Ferritin	µg/l
	CA15-3	Cancer antigen 15-3	kU/l
	CA19-9	Cancer antigen 19-9	kU/l
	CA125	Cancer antigen 125	kU/l
	CYFRA	Cytokeratin-19 fragments	µg/l
	NSE	Neuron-specific enolase	µg/l
	E2	Estradiol	pmol/l
	TESTO	Testosterone	nmol/l
	PROG	Progesterone	nmol/l
	PRL	Prolactin	mU/l
	LH	Luteinizing hormone	U/l
	FSH	Follicle stimulating hormone	U/l
	HCG+β	Human chorionic gonadotropin+β-subunit	U/l
2a	TG	Thyroglobulin	µg/l
	A-TG	Anti-thyroglobulin	U/ml
	A-TPO	Anti-thyroidea-peroxidase	U/ml
	DIGO	Digoxin	nmol/l
	DIGIT	Digitoxin	nmol/l
	CA72-4	Cancer antigen	kU/l
	DHEA-S	Dehydroepiandrosterone sulfate	µmol/l
	CORT	Cortisol	nmol/l
	β-CROSSL	β-CrossLaps (crosslinked isomerized type 1 collagen fragments)	µg/l
	PTH	Parathyroid hormone	pmol/l
	OSTEOC	Osteocalcin	µg/l
	INSULIN	Insulin	pmol/l
	IGE	Immunoglobulin E	µg/l
2b	HBSAG	Hepatitis B surface antigen	COI
	A-HBS	Antibodies to hepatitis B surface antigen	U/l
	A-HBC	Antibodies to hepatitis B core antigen	COI
	A-HBCIGM	IgM antibodies to hepatitis B core antigen	COI
	HBEAG	Hepatitis B e antigen	COI
	A-HBE	Antibodies to hepatitis B e antigen	COI
	A-HAV	Total antibodies to hepatitis A virus	U/l
	A-HAVIGM	IgM antibodies to hepatitis A virus	COI

for statistical evaluation. The experiment was done for all methods of test groups 1a and 1b (see Table 2), and for TG, CA72-4, β-CROSSL, PTH, OSTEOC. Two levels of DGKC reference material were also measured on one day for the following 31 analytes: TSH, T3, T4, FT3, FT4, PSA, FPSA, CEA, AFP, all methods of test group 1b, A-TG, A-TPO, DIGO, DHEA-S, CORT, INSULIN, and IGE.

Functional sensitivity The functional sensitivity, defined as the smallest concentration corresponding to an inter-assay CV of 20%, was determined for 11 assays. For this purpose, five human serum pools with low analyte concentrations, were measured in duplicate determinations over 10 days. For each pool, two inter-assay CVs were calculated, one using the first value of the duplicate determinations and one using the second value.

Drift Two control materials and a human serum pool were analysed in triplicate at the start of the experiment (t_0) and then in single determination at 1-hour intervals for 8 hours ($t_1 \ldots t_8$). The median value of t_0 was compared with values at other times. Methods tested were: TSH, FT4, TN-T, and PSA.

Carryover (reagent-dependent) Assay A (potentially) influences assay B (carryover caused by reagent probes). The following two test combinations were checked: T4 (test A)

Table 3 Controls and reference materials.

Control names	Short names and levels
PreciControl Universal ELECSYS®	PC U1+2
PreciControl Tumor Marker ELECSYS®	PC TM1+2
PreciControl Cardiac ELECSYS®	PC C1+2
PreciControl Bone ELECSYS®	PC Bone1+2+3
PreciControl Anti-TPO ELECSYS®	PC TPO1+2
PreciControl Anti-TG ELECSYS®	PC ATG1+2
PreciControl Anti-HAV ELECSYS®	PC AHAV1+2
PreciControl Anti-HAV IgM ELECSYS®	PC AHAVIGM1+2
PreciControl Anti-HBc ELECSYS®	PC AHBC1+2
PreciControl Anti-HBc IgM ELECSYS®	PC AHBCIGM1+2
PreciControl Anti-HBe ELECSYS®	PC AHBE1+2
PreciControl Anti-HBs ELECSYS®	PC AHBS1+2
PreciControl HBsAg ELECSYS®	PC HBSAG1+2
PreciControl HBeAg ELECSYS®	PC HBEAG1+2
DG KC reference material HM2/00	HM2/00 A+B
DG KC reference material HM4/00	HM4/00 A+B
DG KC reference material HP1/00	HP1/00 A+B
DG KC reference material HP3/00	HP3/00 A+B
DG KC reference material TM2/00	TM2/00 A+B
DG KC reference material AP1/01	AP1/01 A+B
DG KC reference material IG1/01	IG1/01 A+B
DG KC reference material INS/295	INS/295 11+12

followed by FT4 (test B) and T3 (test A) followed by FT3 (test B). Test B was carried out 21 times while in a second step test A and B are requested 21 times. The carryover was the difference between the medians of both B series. The carryover effects were compared with the precision and the diagnostic relevance of assay B.

Analytical range limits This experiment was used to check the suitability of the recommended dilution material by mixing a high level specimen with the dilution material resulting in an eleven-step dilution series. Triplicate measurements of samples from the 11 concentration steps were performed and the median for each step was calculated (first and last diluted samples in six replicates). The concentration of the undiluted specimen served as a reference (100%); the relative recoveries of the diluted samples were calculated using the dilution formula.

High-dose effect One specimen with an extremely high level was diluted with a low level specimen in 11 steps; at least three of the dilutions showed concentrations within the measuring range. The experiment was done only with the A-HBs and HBsAg assays.

Practicability Practicability was assessed using a standardised questionnaire with 200 questions covering all important attributes of the analytical system (10). The assessment of each attribute is rated on a scale of one to ten. A score of one is defined as unimportant, useless or poor, a score of five is considered acceptable or comparable to the existing laboratory situation while ten is defined as excellent/absolutely necessary.

Routine simulation Three experiments were designed. (1) In the first experiment 300–500 fresh native specimens were processed in two series on ⟨EE⟩ using typical request patterns from the laboratory. The reproducibility of the system was assessed by calculating the percentage deviation of each replicate between the two runs. (2) In a second experiment the first series was run on module E1 and the second series on module E2 thus allowing comparison of the recoveries between both modules. (3) Test results and sampling patterns from the routine laboratory analyser were downloaded from the LIS (Host) and transferred to CAEv. The same run was then repeated on ⟨EE⟩ and the results from both systems were compared using the Passing/Bablok regression analysis (routine simulation download).

Workflow Four of the participating sites performed studies to investigate whether or not MODULAR *ANALYTICS* fulfilled their routine laboratory specific needs. Consequently, the working environment, analyte configuration, and workload were different at each site as shown in Table 4. Two methods were used to monitor and reprocess a full days immunoassay workload: (a) Download of the requests from the LIS to CAEv and the same samples were measured the following day on E170. (b) Test requests were captured directly by CAEv from one or more analysers during routine operation and a corresponding request list was generated for E170 using the same samples. At sites 4 and 7, the samples were actually processed on the E170 using two different scenarios to challenge the flexibility of the system. Site 4 investigated the time to availability of STAT sample results, when introducing these samples via the available STAT port and via the input buffer together with routine samples. Site 7 routinely organised the workload in a test-batch-type sample loading onto multiple analysers. This was compared on the E170 with a typical hospital-type sample workflow (loading upon sample arrival).

The performance criteria listed in the evaluation protocol (see Table 5) were derived from Roche in-house results and from analytical experiences obtained with Elecsys® 2010 systems. Additionally, quality specifications based on biological variation (11) were used for the assessment of data (see Table 6).

Results

Reproducibility

In total 2566 series were performed for the determination of within-run precision of all 49 methods. Of

#	Location	Analytical Performance				Practica-bility	Routine Simulation	Workflow
		Group 1a	Group 1b	Group 2a	Group 2b			
1	Heidelberg	■	■			■	■	■
2	Augsburg	■	■		■	■		
3	Berlin	■				■	■	
4	Zurich	■				■	■	■
5	Vienna	■	■			■	■	
6	Baltimore	■	■			■		
7	Seattle	■				■	■	■
8	Tokyo		1)					
9	Göttingen			2)				■
10	Rostock			■				
11	Florence			■				
12	Brussels			■				
13	Passau				■			

1)only anaemia and fertility 2)only tumour marker

Figure 2 Evaluation programme covered by the different MCE sites.

the coefficients of variation (CVs), 97% were within the expected performance. Typical CVs for most assays ranged between 1 and 2% while CVs of 2–4% were determined for infectious disease methods.

The total precision of a single module was determined from 630 data sets with 93% of the calculated CVs within the expected performance range. Even for total precision over two modules, 96% of the calculated CVs (639 data sets) were within the expected performance range. At 'normal' analyte concentration ranges, CVs of 2–6% were determined for non-infectious disease assays with few exceptions (β-CROSSL 4–8%, HCG+β 4–10%, A-TPO 9–14%). For infectious disease tests at cut-off levels, CVs of 5–10% were determined. Figure 3 shows the CV-distributions for the ten tumour marker assays.

Analytical range limit

For 21 selected assays, 85 dilution series were performed in order to evaluate the dilution claims given in the package inserts. Besides the suitability of the dilution medium itself, the recommended dilution ratio and the requested minimal analyte concentration of the diluted sample were also validated. The MCE results confirmed the respective claims in case of the following 13 tests: PSA, FPSA, CEA, AFP, CA15-3, CA19-9, CA72-4, FERR, DIGO, OSTEOC, IGE, CORT and DHEA-S. For those assays where claims were not confirmed, corrective actions were initiated by the manufacturer (see Table 7).

Functional sensitivity

The samples provided by the laboratories for TG and IGE did not show appropriate low analyte concentrations, so a calculation of the functional sensitivity was not possible. For the other assays, a CV of 20% was yielded at the following approximate concentrations: TSH (0.008 mU/l), TN-T (0.02 μg/l), PSA (0.03 μg/l), FPSA (<0.03 μg/l), CYFRA (<0.4 μg/l), TESTO (0.2 nmol/l), E2 (35 pmol/l), PROG (0.45 nmol/l), HCG+β (0.4 U/l), β-CROSSL (0.04 μg/l), PTH (0.35 pmol/l).

Drift

The analyte recoveries were measured over an 8-hour period for the assays TSH, FT4, TN-T and PSA in seven laboratories. No drift effects were observed and the deviations were within the allowed ±10% recovery range. Indeed, in most cases they were even within the ±5% recovery range.

Carryover

Sample-related carryover is not an issue on the E170 due to the use of disposable tips for sample pipetting. The potential risk for reagent carryover via the rinsed probes was tested in seven labs. Relevant reagent carryover effects were not observed with the test combination T3/FT3 nor with the assay sequence T4/FT4.

Accuracy

In a ring trial experiment performed with 33 assays, the recovery of the assigned values in two controls was calculated from the median of 5 days. In all cases the recoveries were within the manufacturer's claimed ±3 SD-ranges and in most cases even within the ±2 SD-ranges. An overview of the results for the thyroid, cardiac, anaemia and bone marker assays is shown in Figure 4.

In another experiment the recoveries of 31 analytes in DGKC reference materials were determined. When declared by the DGKC, the 'reference method values' and the respective upper and lower limits were used as target values. For all other methods, the 50th percentile values and the 16th to 84th percentile ranges, generated by all participating laboratories using the same method (luminescence/fluorescence methods, including Elecsys®), served as reference. Of 297 median recoveries 78% were found to be within the respective percentile ranges while out-of-range values mainly occurred in case of FOL, CYFRA, and NSE. An overview of the results for the tumour marker and fertility hormone assays is shown in Figure 5.

Table 4 Overview on working environment, analyte configuration and workload at sites performing workflow experiments.

#	Site	Comparison instrumentation	MODULAR combination	No. of analytes	Routine workload
1	Heidelberg	2 * ADVIA Centaur®	⟨EE⟩	8	724 samples with 1108 requests over ~5 hours
4	Zurich	3 * Elecsys® 2010	⟨E⟩	13	210 samples with 326 requests over ~9.5 hours
7	Seattle	1 * ADVIA Centaur® 1 * ACS:180® 1 * AxSYM® 1 * IMMULITE®	⟨EE⟩	18	783 samples with 862 requests over ~5.5 hours
9	Göttingen	1 * ARCHITECT® *i*2000®	⟨E⟩	12	160 samples with 223 requests over ~4 hours

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Method comparisons vs. Elecsys® 2010 were performed for all 49 analytes. For the 41 quantitative, non-infectious disease assays, result assessments were done using the slopes and intercepts of the regression analysis. In case of eight qualitative infectious disease methods, the cut-off indices and their respective classifications as *non-reactive*, (*borderline*), or *reactive* were compared.

Each quantitative assay was processed at two to four different sites on both systems. In Figure 6 all 113 comparisons are shown. The slopes of the regression lines are plotted on the *y*-axis and the intercepts (either as percentage deviation from the decision level, or for a few assays in relation to the functional sensitivity) are plotted on the *x*-axis. Of all results, 77% lie within the central rectangular, expected performance range, boundary and an additional 13% were borderline. Frequent deviations were observed for the assays FT3, B12 and FOL.

Classification of 15,668 samples were determined first on Elecsys® 2010 and then on ⟨EE⟩ for eight infectious disease assays. After re-measurements of some originally discordant test results, the concordance rate was 99.9%. 18 of the remaining 20 discordant results were still within the 'grey zone' (A-HBc-IgM), or within the so-called 'uncertainty bounds' defined by the ±2SD NCCLS precision range at cut-off level. Two results (one A-HBc and one A-HBe) exceeded the expected performance but were still within the ±3SD precision range at cut-off level. Figure 7 shows the overall contingency table of eight infectious disease assays.

Twenty-seven assays were also compared with the routine methods used at the evaluation sites, including Bayer ADVIA Centaur® and ACS:180®, Abbott AxSYM®, DPC IMMULITE® and different radio-immunoassays. In total 73 method comparisons were performed, the regression analysis data are shown in Table 8. In most cases (82%) good correlations with coefficients $r \geq 0.95$ were observed. Slope and intercept data have been more heterogeneous, but still two-thirds of all regression lines showed slopes in a range between 0.8 and 1.2 what deemed to be still acceptable. Higher deviations were seen with FT3, TN-T, MYO, B12, FOL, FERR, CA15-3, NSE, LH, PRL, and E2.

High-dose hook effect

Due to non-availability of suitable sample material, the experiment could only be performed at one site and only for two methods. The sample used for HBsAg with a concentration of approx. 239,000 U/ml revealed a cut-off index (COI) of 30 and thus a correct positive classification. For A-HBs, a specimen with a titre of approx. 220,000 U/l was still found to be above the measuring range. This is higher than the concentration limit of '150,000 U/l' listed in the package insert.

Functionality

Throughout the study the evaluation instruments demonstrated excellent hardware and software reliability. Most of the issues arising were solved during the evaluation period by either hardware re-adjustments or by software upgrades. Additional improvements were made with a post launch software update.

During routine simulation experiments at four sites, native samples were processed in two series. A total of 5052 determinations with 22 analytes were performed revealing no hints of random errors. Of those values, 89% were found to be within an acceptable recovery range of ±10%. Similar recovery rates were achieved when comparing series 1, performed on module E1, with series 2, performed on module E2. In one laboratory method comparisons with the ADVIA Centaur® were performed in the course of routine simulation download experiments. Figures 8 and 9 show the results for the TSH and FERR assays.

Practicability

A questionnaire detailed the following system attribute groups: environment, spatial arrangements, training/operation, start-up/shut-down, sample processing, reagent handling, workflow, timing, monitoring, calibration, quality control, data processing, versatility and maintenance/trouble-shooting.

Using the 0–10 rating scale, 51% of all ratings ranged from 4 to 7 while 44% indicated that the requirements of the laboratories were met or exceeded. When comparing the median grading per attribute

Table 5 Performance criteria.

Quality characteristic	Expected performance			
Precision (at 'normal' concentration ranges, respectively, at the medical decision level)		Within-run CVs	Total precision NCCLS CVs on a single E-module	Total precision NCCLS CVs over two E-modules
	Thyroid (A-TG, A-TPO)	≤3–5% (≤8–10%)	≤4–6% (≤10–15%)	≤5–7% (≤3–18%)
	Cardiology	≤3–5%	≤5–7%	≤6–7%
	Tumour marker	≤2–5%	≤5–9%	≤5–10%
	Fertility/hormones	≤4–6%	≤5–8%	≤6–9%
	Anaemia	≤4–5%	≤7%	≤5–8%
	Bone marker	≤5–10%	≤7–10%	≤8–15%
	Infectious disease	≤5–8%	≤8–20%	≤9–21%
Functional sensitivity	TSH: ≤0.01 mU/l; TN-T: ≤0.05 μg/l; PSA: ≤0.1 μg/l; FPSA: ≤0.1 μg/l;CYFRA: ≤0.5 μg/l; TESTO: ≤0.52 nmol/l; E2: ≤55 pmol/l;PROG: ≤0.64 nmol/l; HCG+β: ≤1.2 U/l; TG: ≤2 μg/l; β-CROSSL: ≤0.5 μg/l; PTH: ≤0.64 pmol/l; IgE: ≤0.5 kU/l			
Analytical range limits (suitability of recommended dilution material)	Manufacturer claims must be fulfilled. Differences between the measured and target values from the dilution series in the upper concentration range for most assays ≤10%, for CA15-3, E2, FOL, A-HBs ≤15%, for A-HAV ≤20%. In the low concentration range the absolute differences are judged with respect to the diagnostic relevance.			
Drift	Systematic deviation from the initial value <10%			
Carryover	<2 SD of within-run precision or <5% of the diagnostic decision level			
High-dose hook	A-HBs: test results above 1000 for samples up to 150 000 U/l; HBsAg: test results positive for samples up to 1 500 000 U/ml			
Recovery of assigned value in control materials	Deviation from the assigned value: within ±3 SD range declared by the manufacturer			
Method comparison	Slope: deviation from identity line ≤10%; Intercept: deviation from diagnostic decision level ≤10%; Qualitative assays: identical assessment of samples (as 'reactive' or 'non-reactive') in both methods, respectively, cut-off indices within the 'uncertainty bounds' defined by the ±2 SD ranges of the NCCLS precision at cut-off level.			
Two series in a simulated routine run	The percentage deviations of the measurements between both series should be <10%. Higher deviations can be accepted in case of low concentrated samples and low sensitive tests.			

group calculated for E170 with that calculated for the currently used routine analysers, it emerged that E170 was graded better in ten cases, equal in two cases and inferior for the attribute groups 'Start-up/Shut-down', and 'Reagent Handling', respectively (see Figure 10).

During the workflow experiments three sites focussed on consolidation of routine instrumentation on a single MODULAR platform. The results proved that the respective MODULAR combination used could easily process the workload of the two to four routine analysers at the respective sites, with identical or better result availability and faster sample turnaround times. At site 1 the anaemia and thyroid analytes processed on two routine dedicated analysers were consolidated on a ⟨EE⟩ combination. The flexibility of module/cell-test assignment on the ⟨EE⟩ was used to optimise the sample flow. The calculated throughput rate was approx. 250 tests/hour. At site 7 a throughput of 280 results/hour was achieved when processing the workload of four routine analysers as samples arrived in the laboratory (see Figure 11). The ⟨EE⟩ combination used at this site could have easily covered the workload using the test-batch-type loading as practised in the current laboratory organisation. The average processing time of approx. 30 minutes at site 4 for routine samples on ⟨E⟩ was lower than on the three Elecsys® 2010 analysers. The results of STAT samples were available in approx. 18 minutes on the STAT dedicated Elecsys® 2010 compared to approx. 33 minutes on ⟨E⟩, processing both routine and STAT samples. This difference was mainly due to the use of the nine-minutes-STAT-applications on Elecsys® 2010. Due to the generally low workload in this study, the STAT result availability was almost identical when samples were introduced via the STAT port or via the input buffer.

Consolidation of two or more routine analysers on a single E170 platform led to a reduction of hands-on time and a corresponding increase in walk-away time at all sites. The operator time required for daily maintenance and handling of reagents, calibrators, quality controls, consumables/waste and samples was documented in detail for all monitored analysers. It can

Table 6 Comparison of quality specifications for imprecision according to Ricós et al. (11) with values determined during MCE.

Analyte	Desirable imprecision CV (%)	Median CVs determined for CS1 (%)	Median CVs determined for CS2 (%)
TSH	9.9	3.4	3.9
T3	4.4	3.7	4.0
T4	3.0	**3.7**	**3.7**
FT3	4.0	**6.5**	**4.3**
FT4	3.8	3.7	3.9
TG	6.5	3.1	3.0
CK-MB	9.2	2.9	3.0
MYO	7.0	5.6	6.4
CA15-3	2.9	2.9	2.6
CA19-9	12.3	3.7	3.5
CA125	6.8	2.5	2.2
CEA	4.7	4.1	4.2
PSA	7.0	2.6	2.7
E2	11.3	5.0	3.4
FSH	5.1	3.6	3.1
LH	7.3	2.6	2.7
TESTO	4.4	2.9	3.7
CORT	10.5	2.6	2.7
INSULIN	10.6	5.9	2.6
FERR	7.5	4.6	4.3

CS1/2: Roche controls (low/high) used for total imprecision; values in bold: exceeding limits.

be expected that these figures will vary daily and that monitoring over a longer period would reveal more stable data. The results yielded, within the scope of this study, showed a reduction of hands-on time by approx. 25% at site 1, approx. 50% at site 4 and by approx. 65% at site 7. The total operator attendance was approx. 40 minutes at site 1, approx. 25 minutes at site 4 and approx. 60 minutes at site 7.

Processing 160 samples with 223 requests according to chronological availability in the laboratory over approx. 4 hours did not challenge the productivity of the E170 nor that of the routine analyser at site 9. At this site the sample processing time was the main focus of interest where they found that results were available approx. 8 minutes earlier on the E170 than on ARCHITECT® *i*2000® (see Figure 12).

Discussion

Reproducibility

The E170 delivered excellent within-run precision values and the total precision results were remarkable. It has to be noted, that the experimental set up (simulating daily routine with randomised distribution of samples) is surely more ambitious and challenging than the 'classical' between-day procedure. The fact that such low CVs were found on a single E- as well as on a double E-combination clearly demonstrate the good agreement of all measuring cells and modules. Only two tests, FT3 (at low analyte concentrations) and HCG + β, have not always shown satisfactory precision. In the interim the manufacturer offers improved '2nd generation tests' for both analytes.

A similar assessment was achieved when comparing the E170 total precision results with proposed quality specifications based on biological variation (11) (Table 6). For nearly all analytes the required specifications were met, borderline but still acceptable values were obtained for T4 and FT4. Only for FT3 (see comments above) the given limits were exceeded.

Functional sensitivity

All 11 assays selected for this experiment showed functional sensitivities within the expected perform-

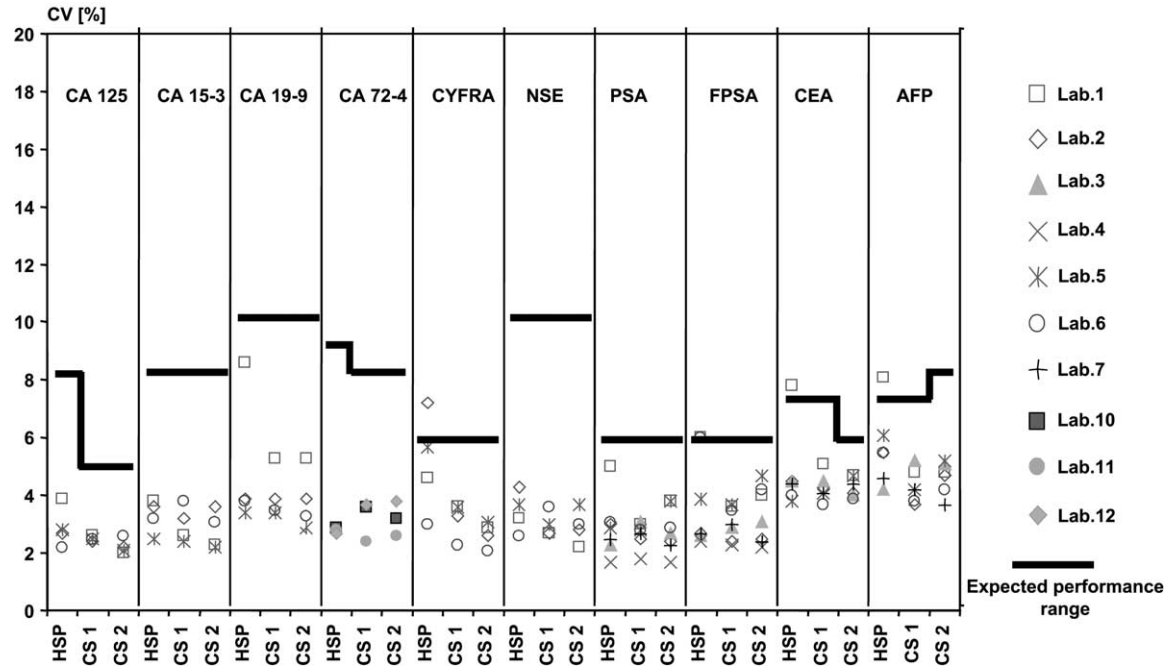

Figure 3 Total precision according to NCCLS over two modules – CVs of tumour marker assays (HSP, human serum pool; CS1/CS2, control sera with different analyte concentration levels).

Table 7 Dilution characteristics.

Assay	Medium	Claims ratio	Concentration of diluted sample	Confirmed by MCE	Changes
TSH	Dil. Uni.[1]	1:10	>10 mU/l	No	1:2 using calibrator (Cal1) from the Elecsys® CalSet; dilution is rather unlikely due to the broad measuring range
PSA	Dil. Uni.[1]	1:50	>2 μg/l	Yes	
FPSA	Dil. Uni.[1]	1:20	>2.5 μg/l	Yes	
CEA	Dil. Uni.[1]	1:50	>20 μg/l	Yes	
AFP	Low sample[2]	1:50	>24 μg/l	Yes	Dilution also possible with Dil. Uni.[1]
CA125	Dil. Uni.[1]	1:10	>200 kU/l	No	1:5 >1000 kU/l
CA15-3	Dil. Uni.[1]	1:10	>30 kU/l	Yes	
CA19-9	Dil. Uni.[1]	1:10	>50 kU/l	Yes	
CA72-4	Dil. Uni.[1]	1:2	>150 kU/l	Yes	
CYFRA	Dil. Uni.[1]	1:10	>50 μg/l	No	1:2 >250 μg/l
NSE	Dil. NSE.[3]	1:5	>50 μg/l	No	1:2
HCG+β	Dil. Uni.[1]	1:20	>100 U/l	No	Improved assay available now
FERR	Dil. Uni.[1]	1:50	>40 μg/l	Yes	
DIGO	Dil. Uni.[1]	1:2	>2.5 μg/l	Yes	
OSTEOC	Dil. Uni.[1]	1:5	>60 μg/l	Yes	
IGE	Dil. Uni.[1]	1:20	>144 μg/l	Yes	
TG	Dil. Uni.[1]	1:10	>50 μg/l	No	1:5
CORT	Dil. Uni.[1]	1:10	>50 nmol/l	Yes	
DHEA-S	Low sample[2]	1:5	>1.5 μmol/l	Yes	
A-HBs	Dil. Uni.[1]	1:100	>10 U/l	No	Note: sample antibodies are heterogeneous; in some cases this may lead to non-linear dilution behaviour
A-HAV	Dil. Hep.[4]	–	>20 kU/l	No	

[1]Diluent Universal Elecsys®; [2]Human sample with low analyte concentration; [3]Diluent NSE Elecsys®; [4]Diluent Hepatitis A Elecsys®.

ance ranges and in some cases were better. As an example, the TN-T assay can be mentioned here with a 20% CV at approx. 0.02 μg/l and a 10% CV at approx. 0.03 μg/l. Recently published guidelines state that TN-T concentrations at 10% CV should be used for clinical discrimination (12). In the case of FPSA

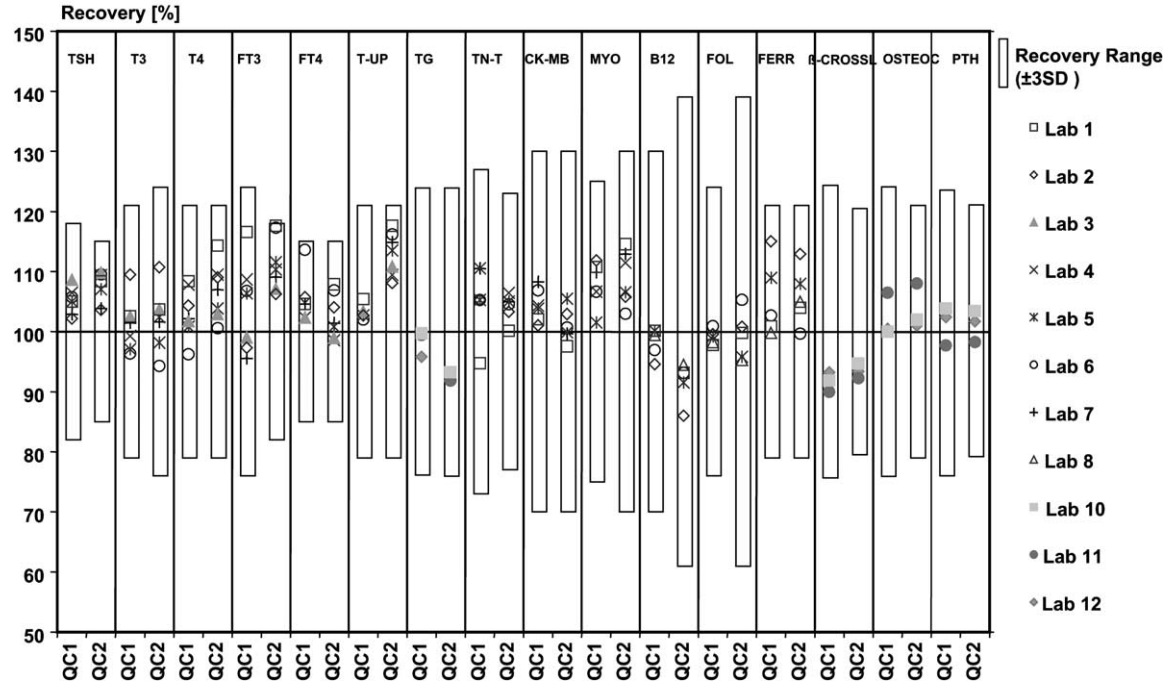

Figure 4 Recovery in controls for thyroid, cardiac, anaemia and bone marker assays. (QC1/QC2, Roche control sera with different analyte concentration levels).

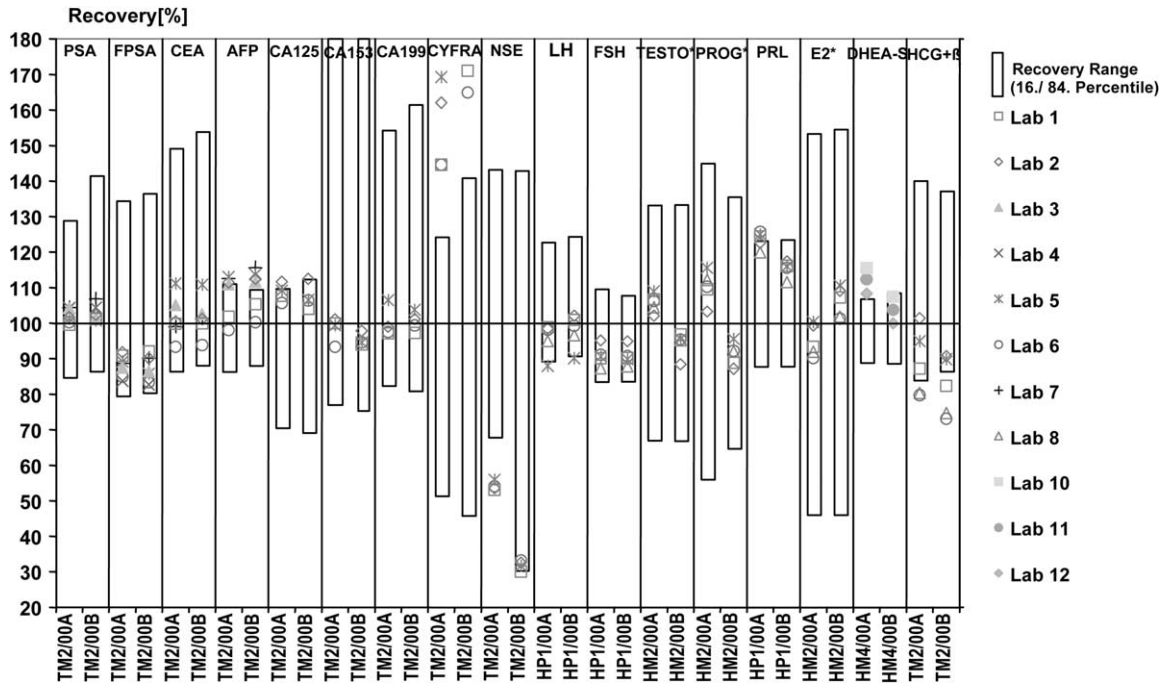

Figure 5 Recovery in DGKC materials for tumour marker and fertility hormone assays. (A/B = DGKC materials with different analyte concentration levels; *in case of TESTO, PROG, and E2 the 'reference method target value' = 100%).

(< 0.03 μg/l) and CYFRA (< 0.4 μg/l) only approximate upper limits could be determined as human serum pools with lower analyte concentrations have not been available at the evaluation sites.

Analytical range limit

The MCE experiments were not designed to show the general assay linearity over the measuring range. The objective was actually to verify the suitability of the recommended dilution media and the specified dilution ratios. The MCE data supported the manufacturer's claims for 13 assays. Discrepancies observed for eight tests led the manufacturer to change package inserts accordingly, or even to revise the test (see Table 7). In the case of TSH, the recommended dilution material was changed although the necessity of dilution is rather unlikely due to the broad measuring range. With regard to CA125, CYFRA, NSE and TG, the recommended dilution ratios were reduced or the minimum sample concentrations increased. The A-HBs and A-HAV inserts were supplemented with a note explaining that in some cases a non-linear dilution behaviour may occur due to the fact that the sample antibodies to be analysed are polyclonal and heterogeneous (with different affinities and directed to different epitopes of the test-immanent antigens). Due to the observed dilution limitations (and some other restrictions) the HCG + β assay was reworked by the manufacturer. In the interim, an assay with improved dilution and precision behaviour is available.

Accuracy

The ring trial experiments using reference materials have in general demonstrated good agreements with the percentile ranges given by the DGKC. The exception was FOL, CYFRA and NSE. The deviations for FOL were reasonable considering that new assay applications were used on E170. In the interim a re-standardisation of CYFRA has been completed by the manufacturer. The low recoveries in case of NSE should not be overestimated considering the dependency of tumour marker assays on the specificity of the used antibodies and the used standardisation method (Elecsys® NSE has been calibrated against the established Roche Enzymun-Test® NSE).

The method comparisons of E170 vs. Elecsys® 2010 revealed acceptable agreement in approx. 90% of all cases. Clear deviations as seen with FT3, B12 and FOL has led the manufacturer to improve the standardisation procedure itself and to re-standardise affected lots accordingly.

Most comparisons with other routine methods yielded good correlations and acceptable regression lines (Table 8). FT3, B12 and FOL showed high deviations which should be reduced by the manufacturer's countermeasures as described above. In case of MYO there is, up to now, no official reference material available, so the observed deviations in comparison to Dade Behring's BN™ II assay can just be stated. There is good reason to suppose that the deviations found for the assays FERR, CA15-3, LH, and E2 can be ascribed to different standardisations. On the other hand, all these Elecsys® methods showed good median recoveries in the ring trial experiment using the DGKC reference materials A/B (103/109%, 100/95%, 98/99%, 93/107%). The NSE comparison vs. LIAISON® revealed a high scatter (r = 0.909) indicating that the test specificities are different. In case of PRL one can

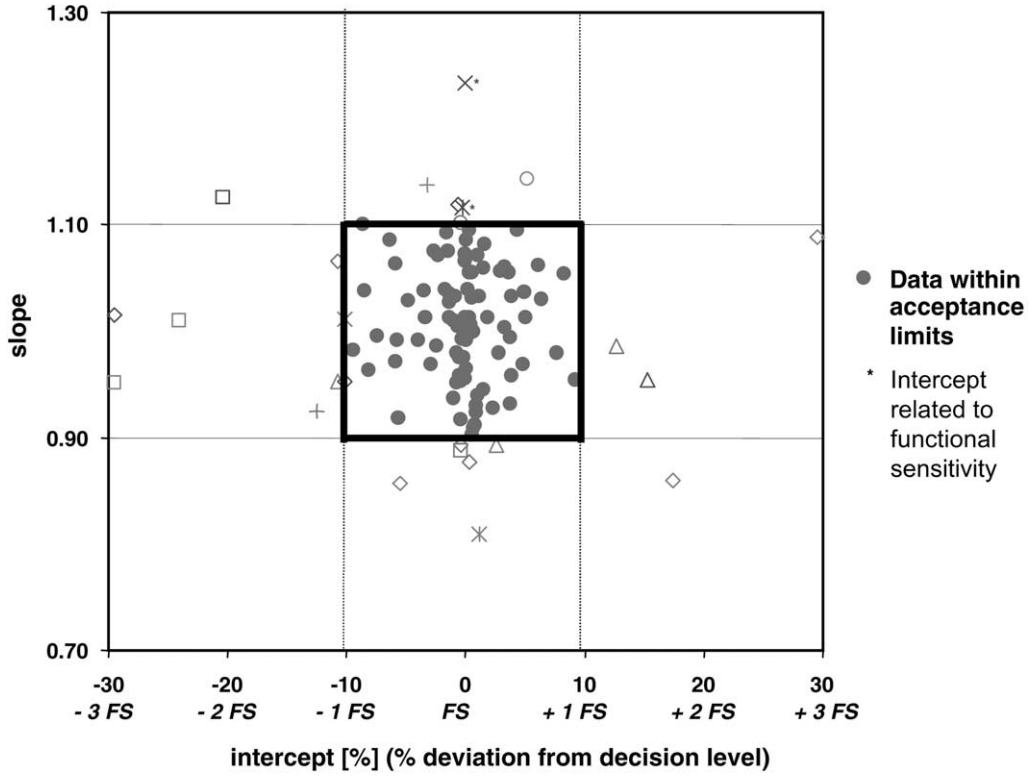

Figure 6 Diagram showing slopes and intercepts of 113 method comparisons (41 analytes). For most analytes the intercept is plotted as percentage ratio from the appropriate diagnostic decision level. In case of TN-T, CK-MB and FPSA the intercept is shown as a multiple of the respective functional sensitivity concentration.

assume that the assays detect different degrees of the serum macroprolactins.

Functionality

The instrument software proved to be reliable and the few malfunctions were rectified by the manufacturer during the course of the study. The instrument hardware was also shown to be very reliable with only one 'phenomenon' observed. This involved simultaneous assay cup pick up errors at different sites due to static electrical interference. As a result the manufacturer has since incorporated hardware- and software-based improvements for all commercial instruments. Another very important outcome of the study was that the MODULAR proven sample/rack transport mechanism worked very reliable with no interruptions or jams.

Practicability

The results show that the E170 met or even exceeded the requirements for 95% of all addressed issues. Special reference was made to the low heat production, low noise level and good accessibility of the instrument components. Most evaluators appreciated the easy-to-use software and the system's general user-friendliness which required less training efforts which in turn supports job rotation within the routine. In general the *Start up/Shut down* attribute group received low ratings. Most criticism related to the fast transition from 'Sampling Stop' to 'Stand-by' mode and the fact that the subsequent start-up procedure took too long. As a consequence the manufacturer improved the user-software by offering a new 'Rack Reception Mode' feature during which the instrument remains in 'Sampling Stop' status for 60 minutes. In addition the restart time from 'Stand-by' to 'Operation' was reduced to approx. 9 minutes. The *Sample Processing/Workflow/Timing* attribute group received relatively high ratings. Here most operators emphasised the benefits of the continuous sample loading/

Concordant results (n=15,648) 99.9%	E170 positive	E170 grey[1]	E170 negative
Elecsys 2010 positive (n=1583)	**1573**	-	10
Elecsys 2010 grey[1] (n=2)	1	**1**	-
Elecsys 2010 negative (n=14,083)	6	2	**14,075**

[1] only relevant for A-HBc IgM (grey zone with COI of 0.9–1.1)

Figure 7 Contingency table summarising the classifications of eight infectious disease assays. The discordant results were either within the 'grey zone' or still within the 'uncertainty bounds' of the assays.

Table 8 Method comparisons of E170 (y) with routine methods (x).

Analyte, unit	Instrument/method	n	Max. conc. of x	Slope	Intercept	md_{95}	r
TSH, mU/l	ADVIA Centaur®	147	81	1.08	0.012	1.776	0.991
	ADVIA Centaur®	130	90	1.11	0.026	3.645	0.988
	ADVIA Centaur®	132	32	1.15	−0.002	1.485	0.994
	ADVIA Centaur®	146	83	1.14	0.016	1.653	0.992
T3, nmol/l	ADVIA Centaur®	149	7.9	0.96	−0.070	0.281	0.951
	ADVIA Centaur®	149	8.1	1.04	−0.015	0.512	0.966
	ADVIA Centaur®	149	8.2	0.95	−0.058	0.568	0.915
	ACS:180®	148	4.8	1.10	−0.135	0.265	0.938
T4, nmol/l	ADVIA Centaur®	149	281	0.97	9.043	12.430	0.974
	ADVIA Centaur®	141	286	1.16	11.718	16.134	0.958
	ADVIA Centaur®	148	229	1.10	7.722	25.283	0.888
FT3, pmol/l	ADVIA Centaur®	150	24	1.23	−0.805	1.332	0.968
	ADVIA Centaur®	150	28	1.23	−0.730	3.052	0.971
	ADVIA Centaur®	150	21	1.59	−2.010	1.091	0.973
	IMMULITE®	144	21	0.85	0.562	1.147	0.859
FT4, pmol/l	ADVIA Centaur®	148	66	1.15	0.342	2.375	0.986
	ADVIA Centaur®	148	67	1.16	−0.055	3.094	0.984
	ADVIA Centaur®	150	51	1.19	−0.444	2.874	0.974
	ADVIA Centaur®	150	88	1.07	−0.616	2.009	0.983
T-UP, TBI	ADVIA Centaur®	149	1.7	0.94	−0.200	0.186	0.766
CK-MB, µg/l	AxSYM®	145	52	0.99	0.235	0.450	0.988
MYO, µg/l	BN™ II	103	288	1.38	5.244	5.890	0.993
	Roche/Hitachi 912	99	2730	1.15	13.196	145.089	0.993
FPSA, µg/l	ACS:180®	139	21	0.91	0.038	0.740	0.969
	AxSYM®	136	10	0.90	0.064	0.406	0.981
	IMMULITE®	148	18	1.06	0.025	0.242	0.988
PSA, µg/l	ADVIA Centaur®	149	87	1.11	−0.029	1.643	0.995
	ACS:180®	139	38	1.21	−0.014	1.748	0.988
	AxSYM®	146	47	1.13	0.081	0.932	0.997
	IMx®	138	21	1.13	0.020	0.333	0.998
	IMMULITE®	150	63	0.95	0.075	0.648	0.992
CEA, µg/l	ADVIA Centaur®	147	159	1.16	1.229	7.162	0.960
	ADVIA Centaur®	124	94	1.36	0.834	11.517	0.961
	AxSYM®	129	121	1.23	0.902	13.427	0.955
AFP, µg/l	ADVIA Centaur®	148	231	0.99	0.634	5.848	0.988
	ACS:180®	150	202	1.03	−0.278	3.665	0.996
	AxSYM®	133	164	1.06	−0.080	2.587	0.997
B12, pmol/l	ADVIA Centaur®	150	692	1.34	−61.980	60.861	0.870
	ADVIA Centaur®	100	1328	1.21	−43.152	104.429	0.982
	ACS:180®	146	832	1.43	−98.100	62.644	0.965
	RIA (SimulTRAC-SNB, DEMEDITEC Diagn.)	139	1427	0.99	21.151	98.954	0.975
FOL, nmol/l	ADVIA Centaur®	148	44	0.94	−0.092	4.461	0.906
	ADVIA Centaur®	98	43	0.41	1.171	4.900	0.832
	ACS:180®	147	45	0.68	1.542	3.404	0.914
	RIA (SimulTRAC-SNB, DEMEDITEC Diagn.)	133	44	0.76	2.695	3.544	0.961
FERR, µg/l	ADVIA Centaur®	150	530	1.24	3.366	25.344	0.983
	ACS:180®	149	1496	1.28	−0.494	52.896	0.985
	LS-2000 (Eiken Chemical Co.)	92	827	1.60	−0.687	45.698	0.982
CA125, kU/l	ADVIA Centaur®	150	593	1.17	5.228	32.205	0.973

(Table 8 continued)

Analyte, unit	Instrument/method	n	Max. conc. of x	Slope	Intercept	md_{95}	r
CA15-3, kU/l	ADVIA Centaur®	149	263	0.70	1.429	11.162	0.942
CA19-9, kU/l	ADVIA Centaur®	149	575	1.12	−0.735	21.967	0.944
CYFRA, µg/l	RIA (Fujirebio Diagnostics)	146	35	1.10	0.505	0.649	0.992
NSE, µg/l	AutoDELFIA™	68	44	1.65	−1.228	2.365	0.967
	LIAISON®	148	29	0.76	−1.365	1.817	0.909
LH, U/l	ADVIA Centaur®	149	198	0.95	0.345	4.760	0.994
	ADVIA Centaur®	150	51	0.96	0.439	2.608	0.991
	RIA (Daiichi RI Laboratories)	97	70	1.32	0.404	5.008	0.979
FSH, U/l	ADVIA Centaur®	149	118	1.21	0.636	6.317	0.991
	ADVIA Centaur®	147	116	1.09	0.727	7.554	0.990
	RIA (Daiichi RI Laboratories)	99	136	0.91	0.012	6.466	0.992
TESTO, nmol/l	ADVIA Centaur®	148	29	0.99	−0.151	1.623	0.986
	ADVIA Centaur®	149	41	0.86	−0.626	3.735	0.970
PRL, mU/l	ADVIA Centaur®	150	1425	1.36	2.484	94.778	0.909
	ADVIA Centaur®	149	7320	1.28	6.468	179.867	0.986
	RIA (Daiichi RI Laboratories)	99	3053	2.23	26.969	303.741	0.982
E2, pmol/l	ADVIA Centaur®	142	2785	0.78	−6.762	172.769	0.979
	ADVIA Centaur®	142	4011	0.87	−141.803	122.490	0.980
	RIA (Diagnostic Products Corporation)	99	5395	1.67	−61.118	417.772	0.978
PROG, nmol/l	ADVIA Centaur®	149	101	0.81	−0.049	2.134	0.987
	ADVIA Centaur®	148	104	0.85	−0.121	2.893	0.995
	RIA (Diagnostic Products Corporation)	95	118	1.12	−1.258	9.894	0.981
HCG + β, U/l	ACS:180®	72	3363	0.90	−0.859	62.098	0.996
	EIA (SRL)	72	30	1.27	−0.611	2.689	0.954

The slope and intercept are derived from Passing/Bablok regression analysis. ADVIA Centaur and ACS:180 are trademarks of Bayer Corporation; AxSYM and IMx are trademarks of Abbott Laboratories; IMMULITE is a trademark of Diagnostic Products Corporation; BN is a trademark of Dade Behring; AutoDELFIA is a trademark of PerkinElmer Life Sciences; LIAISON is a trademark of DiaSorin. md_{95}, median distance from the 95th percentile; r, correlation coefficient.

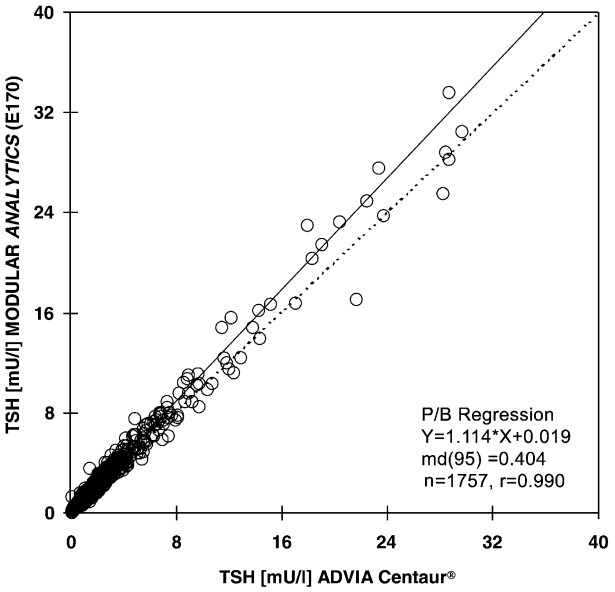

Figure 8 Method comparison. TSH with n = 1757 samples from the daily routine at site 1.

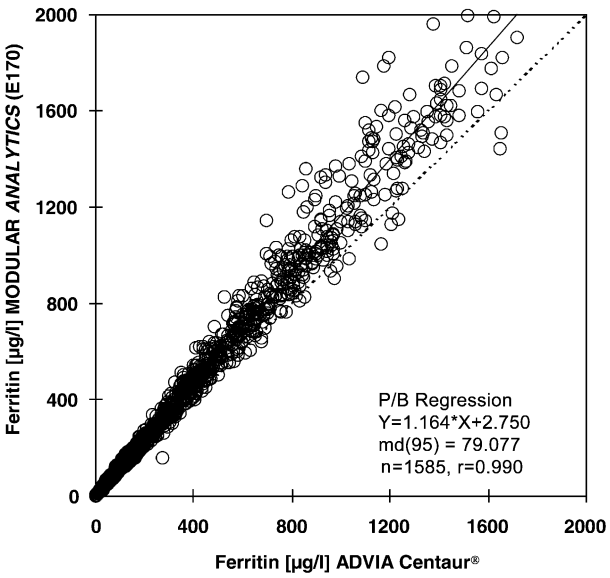

Figure 9 Method comparison. Ferritin with n = 1585 samples from the daily routine at site 1.

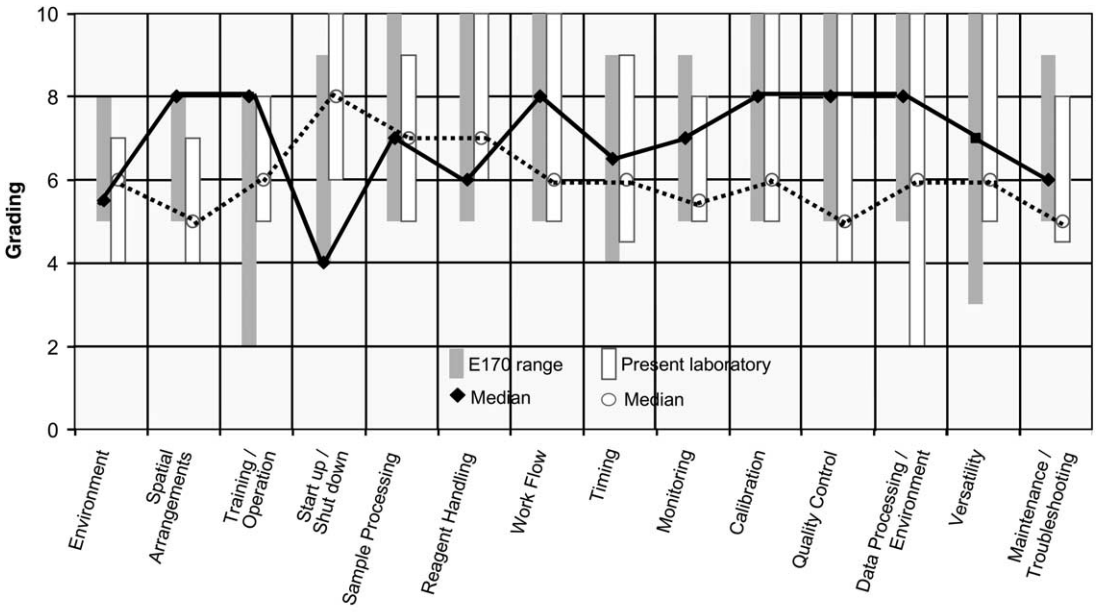

Figure 10 Practicability questionnaire: range and median of grading per attribute group over seven laboratories.

unloading capacity, carryover-free pipetting, optimised sample-/rack-distribution to different modules/channels and in particular the automatic rerun-functionality. *Reagent Handling* issues were rated differently. On the one hand, the easy handling of the ready-to-use reagents (rack packs) was praised. However, others were critical of the need to warm the reagent to room temperature before loading onto the instrument, and especially as there is no reagent reloading capability during operation. Regarding the latter issue, the manufacturer now offers a more convenient reloading procedure as part of a software upgrade. In general, high ratings were given for the *Calibration and Quality Control* features on E170 when compared with the currently used routine instrumentation. The system handles calibrators and controls just like sample material and automatically performs all module-/test-/channel-specific calibrations and quality controls (QCs) when necessary. Frequently requested suggestions for improvement included the availability of multi-analyte calibrators as well as a change from the currently recommended

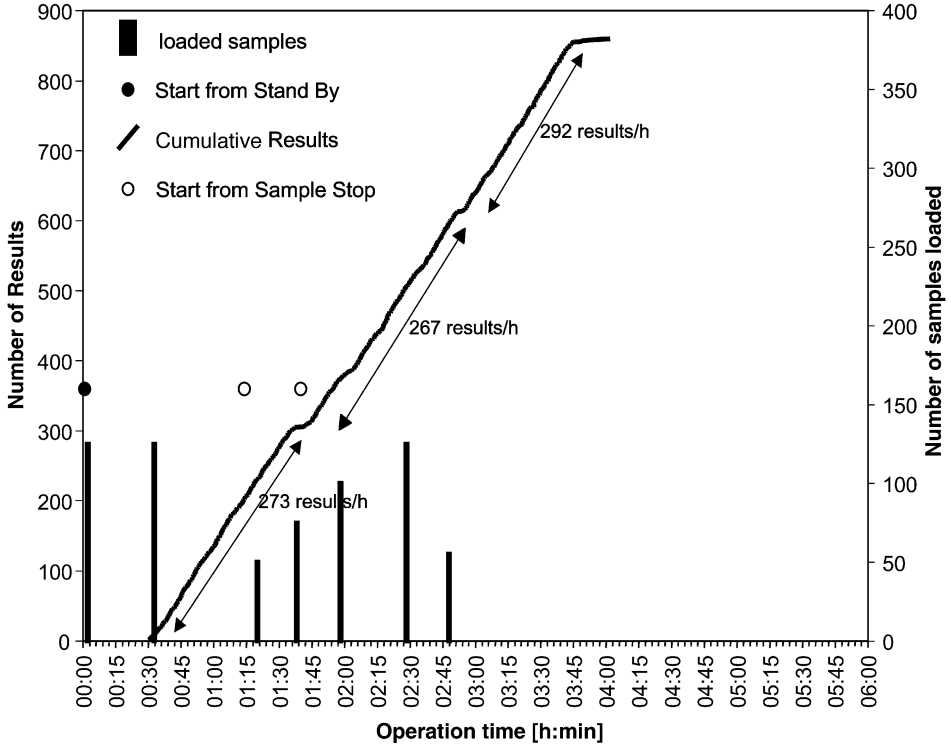

Figure 11 Cumulative result throughput and sample loading pattern on MODULAR *ANALYTICS* ⟨EE⟩ at site 7. A typical hospital-type sample workflow (loading upon sample arrival) was simulated.

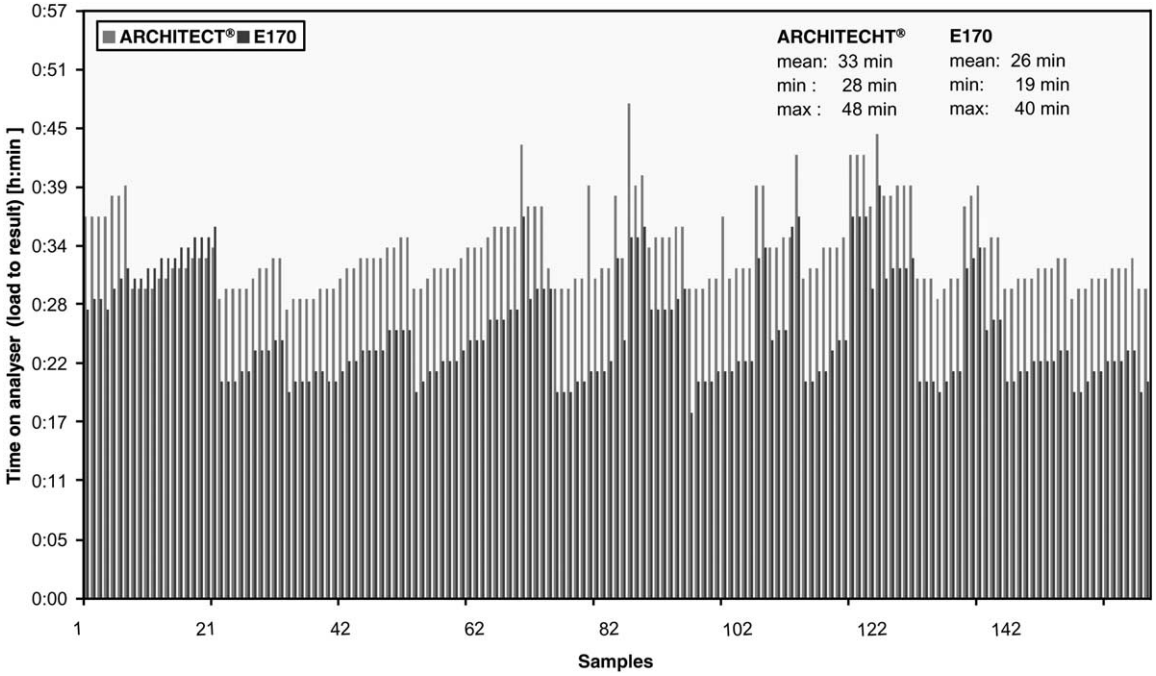

Figure 12 Sample turn-around times determined on MODULAR *ANALYTICS* ⟨E⟩, respectively on ARCHITECT® *i*2000® at site 9.

'time-out'-calibration to a 'QC-triggered' calibration. The manufacturer has since announced this latter feature as part of a forthcoming software update. The *Maintenance/Monitoring/Troubleshooting* procedures generally got good ratings. Due to its modular, customer-designed concept the *Versatility* was graded 'seven' on average. The capability to consolidate a great variety of immunoassays on one system and the resulting simplification of the laboratory organisation was especially appreciated.

The workflow studies at sites 1, 4 and 7 showed that a single platform MODULAR system can cover the workload of various routine analysers in diverse laboratory environments. The evaluators' throughput and sample processing time requirements were met, while personnel 'hands-on time' was substantially reduced. The foreseeable benefit in the elimination of pre-sorting and splitting of sample material was not part of this study.

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