Analytical performance of the selective multianalyser Olympus AU 5200

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The analytical performance of a selective, automatic multianalyser – the Olympus AU 5200 – was tested and assessed for practicability, following ECCLS guidelines. Twenty-two analytes were tested and compared with the Olympus AU 5000 analyser. A Hitachi 747 analyser was also included in this survey in order to obtain correlation data for ISE measurements.

The imprecision data, expressed as median CV values, were found to be below 2% in series for 21 parameters, and below 3% for 19 parameters from day to day. Creatinine measured with the kinetic Jaffe method obtained a median CV value of 4% in series, creatine phosphokinase showed the worst imprecision from day to day with a CV of 9%. Slightly better precision values for the majority of all tests were found on the Olympus AU 5200 than on the AU 5000 analyser.

The recovery of the assigned values in 32 commercial control sera was between 95% and 105% for 14 tests. Five of the remaining tests yielded recoveries with deviations between 5% and 10%, deviations above 10% showed albumine, alanine aminotransferase, aspartate aminotransferase and creatine phosphokinase. The accuracy of most test parameters was slightly better on the AU 5200 analyser than on the comparison instrument.

The range of linearity of the tested methods covered the range stated by the manufacturers; and no sample carry-over was detected. Most parameters tested yielded close correlation to those on the comparison instrument. Amylase measurements on both analysers correlate well but are not comparable without data correction due to different test methods. In addition, no drift effects were observed over a period of 9 hours.

The ion-selective-electrode unit performed well in terms of throughput, precision and stability over time. The whole system showed good practicability with respect to patient sample and reagent handling, a short training period of technicians, ease of system software, maintenance, a robust barcode reader and a flexible host communication procedure.

Introduction

The Olympus AU 5200 series of selective multianalysers is well suited for medium and large laboratories processing several thousand samples per day. This paper reports on the performance characteristics of the AU 5200 analyser comparing it with the AU 5000 analyser. The evaluation procedure followed ECCLS guidelines [1]. Although only a multicentre evaluation allows a truly representative assessment for an analyser, the evaluation data presented here give a first impression of the quality and performance of the instrument.

The AU 5200

The AU 5200 is constructed following a modular concept that originated from the AU 5000 instrument series. Any analyser consists of up to four basic identical units equipped with eight or 16 reagent lines. The stated sample throughput of 330 samples (300 samples with ISE unit), which is twice as much as that of an AU 5000 analyser, is achieved by two cuvette rings per unit with 240 cuvettes each. In an analyser equipped with eight reagent lines per module, 60 cuvettes are assigned to each chemistry channel (this compares with 24 cuvettes in a similar model of the series AU5000). A list of the main specifications of the AU 5200 analyser is given in table 1, along with a survey of possible configurations. Evaluation data on the comparison instrument AU 5000 has been published by Luley *et al.* [2].

The analyser configuration which was evaluated for this paper consisted of three units with eight reagent lines per unit for chemistry tests, and an additional ISE unit for electrolyte measurements.

Materials

Quality-control materials

The commercially available control materials used in the evaluation are specified in table 2.

Calibrators and standards

Multianalyte calibrators obtained from Olympus Optical Co. and Merck Company were used to calibrate the respective substrate methods of both reagent suppliers. Aqueous electrolyte standards obtained from Olympus Optical Co. and Boehringer Mannheim GmbH were used to calibrate flame photometry and ISE measurement on the Olympus AU 5000, AU 5200 and Hitachi 747 analysers respectively. To measure linearity of chemistry procedures analyte-spiked serum materials were obtained from Sigma Chemical Company (Multi-Analyte Lintrol, Multi-Enzyme Lintrol, CK-Lintrol, Lipid-Lintrol) or produced by adding pure analyte to a serum pool (iron and bilirubin standard solutions from Sigma Chemicals).

Chemistry reagents

The reagent kits were supplied by Olympus Optical Co. in Hamburg and Merck Company in Darmstadt, Germany. A list of reagents, reagent manufacturers and methods of chemistry testing is given in table 3.

Table 1. Instrument specification for the AU 5200

<i>General characteristics</i>				
Type of instrument	Fully selective discrete access multianalyser			
Analytical methods	End-point			
	End-point with serum blanking			
	Kinetic serum start			
	Kinetic trigger start			
	ISE or flame photometry			
Nature of specimen	Serum, plasma, urine			
Operation of the system	With and without host computer support, batch and realtime operation			
Specimen identification	Barcode labelled primary tubes, barcode format includes codabar, 2 of 5 and code 39			
Specimen carrier	Straight racks with 10 positions for patient's specimen (white), control sera (green), calibrators (yellow), water and reagent blanks (blue), emergency samples (red) and rerun samples (orange)			
Sample throughput	330 samples per hour maximally (as for 8 reagent lines per unit without ISE)			
Sample tray capacity	300 specimens (30 racks)			
Sampling system	Pipettors in ISE unit (single) and each module (double) with liquid level sensor driven by stepping motors			
Sampling volumes	3–15 µl (1 µl increment)			
Sampling dispensing	Four tests			
Reagent type	Liquid			
Reagent storage	Refrigerated storage (4–12°C)			
Reagent dispenser	Two independent pipettors per method			
Reagent volumes	250–500 µl total (R1 + R2) volume in 1 µl increments			
Reagent bottle capacity	125 ml–2000 ml			
Reaction rotor	Turntable with two rings of 240 cuvettes each			
Reaction cuvettes	480 quartz glass cuvettes per unit, 6 mm path length			
Reaction temperature	37°C			
Reaction incubation	Dry bath with incubation liquid system			
Reaction time	9 min 24 s			
Calibrators	Up to 5 calibrants per test parameter, linear and nonlinear calibration			
<i>Optical characteristics</i>				
Light source	Tungsten-Halogen lamp			
Photometry system	Multiwavelength diffraction grating			
Wavelength	Fixed array of 10 diodes: 340 nm, 380 nm, 410 nm, 480 nm, 520 nm, 540 nm, 600 nm, 660 nm, 800 nm			
Light path	6.0 mm			
Photo detector	Silicon photo cell			
Photometric range	0.00 to 2.00 absorbance units			
Sensitivity	0.0001 absorbance units			
<i>ISE characteristics</i>				
Analytical system	Vertical block flowcell with ion selective electrodes			
Analytical items	Chloride, potassium, sodium			
Sample throughput	300 samples per hour			
Sample type	Serum, urine			
Sample volume	28 µl			
Diluent volume	665 µl			
<i>Data processor</i>				
Main cpu	Intel i8086 with i8087 coprocessor			
Storage devices	40 Mb hard disk, 31/2 in floppy disk			
On line interface	RS232 C serial interface, bidirectional data transfer			
Operating system	CP/M 86			
Operator oriented software	Quality control; correlation correction; linear transformation (Y = AX + B); test result editing; abnormal upper/lower value judgement; user defined calculated tests; user defined inter-item data check; reaction curve monitor; automatic instrument start up capability; repeat run assessment			
<i>Environment</i>				
Power consumption	8.0 kVA (as for AU 5231 with 3 units) (60 A max. by 210V single phase AC)			
Heat output	6880 Kcal			
Water consumption	30 l/hour per unit deionized water			
Waste drainage	Separately expelled: chemical and non-hazardous waste			
<i>Analyser configurations</i>				
	Model	Analyser composition (units × reagent lines)	Assay items (with ISE)	Sample throughput/h (with ISE)
	AU 5211	1 × 16	16 (19)	165 (150)
	AU 5221	2 × 8	16 (19)	330 (300)
	AU 5223	2 × 16	32 (35)	165 (150)
	AU 5231	3 × 8	24 (27)	330 (300)
	AU 5241	4 × 8	32 (35)	330 (300)

Methods

Chemistry methods

Both analysers were operated at 37°C, enzyme activities were converted to corresponding activities at 25°C. All methods employ bichromatic measurements. The chemical basis for each method on both the AU 5200 and the AU 5000 is summarized in table 2.

Electrolyte measurements

Sodium and potassium concentrations were measured by flame photometry on the AU 5000 analyser and indirect potentiometry on the AU 5200 analyser and Hitachi 747 analyser (Boehringer Mannheim, Germany). Chloride was determined by reaction with mercuric nitrate and thiocyanate (chloride reagent obtained from Greiner

BioChemica in Flacht, Germany) on the AU 5000 analyser and by indirect potentiometry on the AU 5200 and Hitachi 747 analyser.

Precision study

To determine the within-run imprecision, seven different control materials and two serum pools were analysed in a series of 20 assays. The series were repeated three times and the medians of the three CV values were taken as the final results.

The imprecision between-days was determined on 15 different days using the seven control materials mentioned above.

Assessment of accuracy

Thirty-two commercial control materials (listed in table 2) were analysed in double assays on three days in both the AU 5200 and AU 5000. The medians of the measured values were compared with the assigned values of the different control materials (if available for the methodology used).

Linearity study

The linearity of each chemistry method was assessed using serum material with high analyte concentrations and 25 equidistant levels of dilution with physiological saline solution or bovine serum albumin (for cholesterol, triglyceride and bilirubin dilutions). The dilutions were prepared using a robotic dilutor system (Tecan RSP 505, Zinsser Analytik). The measured concentrations were plotted against dilution levels and the resulting graphs were inspected visually for linearity.

Carry-over experiments

Due to the construction principle that each cuvette and each mixer blade is used for one kind of test only and that the reagent lines are totally separated from one another, carry-over is restricted to sample carry-over caused by insufficient washing of subsequent cuvettes, the probe needle or the mixer blade.

Sample carry-over, due to insufficient cuvette washing, was tested by determining the activity of creatine phosphokinase during two complete cuvette wheel cycles (120 samples). All samples were taken from a serum pool with a low CPK activity of 27 U/I (25°C), except sample numbers 31 to 45 which contained a high activity of 1500 U/I. Thus, during the second cuvette wheel cycle (sample numbers 61 to 120) samples containing the low CPK activity were measured in cuvettes which had been used for the determination of the high CPK activity in the previous cuvette wheel cycle. If the cuvettes were inadequately washed, elevated CPK activity should be measured in cuvette numbers 91 to 105.

In order to detect sample carry-over caused by the probe needle or mixer blade, groups of five samples with low CPK activity and high CPK activity were alternated

Table 2. Control sera used for the AU 5200 evaluation

Control serum	Lot No.	Manufacturer
Decision 1	1101	Beckman Instruments GmbH, Germany
Decision 2	1102	
Decision 3	1103	
Duotrol	5036	Biomed, Germany
NobiCon I	210 099	
NobiCon II	220 077	Nobis GmbH, Germany
Lytrol N	482870	
Lytrol P	323760	BioMerieux GmbH, Germany
Monotrol	629430 A	
Clinitrol	632780 A	
Zymotrol	715540 A	
Qualitrol L	326	Merck Darmstadt GmbH, Germany
Qualitrol N	390	
Qualitrol H	325	
Precinorm U	166 760	
Precipath U	168 593	Boehringer Mannheim GmbH, Germany
Moni-Trol I	LTD-218	
Moni-Trol II	PTD-119	Baxter Deutschland GmbH, Germany
Lypocheck 1	48901	
Lypocheck 2	48902	BioRad Laboratories GmbH, Germany
Kontrollogen L	62 3131	
Kontrollogen LP	62 3218	Behring Werke AG, Germany
Control Serum N	O 2933	
Control Serum P	3133	Hoffman-La Roche AG, Germany
Testpoint 1	V05623	
Testpoint 2	V05602	Technicon/Bayer AG, Germany
Validate N	743	
Validate A	586	Organon Teknika GmbH, Germany
Biotrol 33 Plus	574	
Biotrol 33 Plus path.	713	Biotrol Paris, France
Accutrol Normal	6165	
Accutrol Abnormal	6166	Sigma Chemie GmbH, Germany

Table 3. Test procedures and reagents used during evaluation

Analyte	Method*	Reagent manufacturer	Analyser
<i>1. Enzymes</i>			
Alanine aminotransferase	IFCC	Olympus	AU 5200
	IFCC	Merck	AU 5000
Aspartate aminotransferase	IFCC	Olympus	AU 5200
	IFCC	Merck	AU 5000
Alkaline phosphatase	DGKC	Olympus	AU 5200
	DGKC	Olympus	AU 5000
Amylase	bl. PNP-G7	Olympus	AU 5200
	Cl-PNP-G7	Merck	AU 5000
Creatine phosphokinase	CK-NAC, DGKC	Olympus	AU 5200
	CK-NAC, DGKC	Merck	AU 5000
g-glutamyl transferase	GCNA 'Szasz'	Olympus	AU 5200
	GCNa 'Szasz'	Merck	AU 5000
Lactate dehydrogenase	SCE	Olympus	AU 5200
	SCE	Merck	AU 5000
<i>2. Substrates</i>			
Albumin	Bromcresol green	Olympus	AU 5200
	Bromcresol green	Merck	AU 5000
Bilirubin	DCA	Olympus	AU 5200
	DPD	Merck	AU 5000
Calcium	o-Cresolphthaleine	Olympus	AU 5200
	o-Cresolphthaleine	Olympus	AU 5000
Cholesterol	CHOD-PAP	Olympus	AU 5200
	CHOD-PAP	Olympus	AU 5000
Creatinine	kinetic Jaffe	Olympus	AU 5200
	enzymatic PAP	Merck	AU 5200
	enzymatic PAP	Merck	AU 5000
Glucose	Hexokinase	Olympus	AU 5200
	Glucose dehydrogenase	Merck	AU 5000
Phosphate	Ammoniumheptamolybdate	Olympus	AU 5200
	Ammoniumheptamolybdate	Merck	AU 5000
Iron	Nitroso-PSAP	Olympus	AU 5200
	Ferrozine	Merck	AU 5000
Total protein	Biuret	Olympus	AU 5200
	Biuret	Olympus	AU 5000
Triglycerides	GPO-PAP	Olympus	AU 5200
	GPO-PAP	Olympus	AU 5000
Urea	GLDH	Olympus	AU 5200
	GLDH	Merck	AU 5000
Uric acid	Uricase/PAP	Olympus	AU 5200
	Uricase/PAP	Merck	AU 5000
<i>3. Electrolytes</i>			
Sodium	ISE indirect		AU 5200
	Flame photometry		AU 5000
	ISE indirect		Hitachi 747
Potassium	ISE indirect		AU 5200
	Flame photometry		AU 5000
	ISE indirect		Hitachi 747
Chloride	ISE indirect		AU 5200
	Hg-Thiocyanate	Greiner	AU 5000
	ISE indirect		Hitachi 747

* IFCC = International Federation of Clinical Chemistry; DGKC = Deutsche Gesellschaft für Klinische Chemie; PNP-G7 = p-Nitrophenyl maltoheptaoside; CK-NAC = Creatine kinase, N-acetylcysteine activated; GCNA 'Szasz' = L-Glutamyl-3-carboxy-4-nitroanilide: G. Szasz u. M. Klin. Chem. u. Klin. Biochem. 12,228 (1974); SCE = Scandinavian Committee on Enzymes; DCA = 2,4-Dichloraniline-diazonium salt; DPD = 2,5-Dichlorophenyl-diazonium salt; Nitroso-PSAP = 2-Nitroso-5-(N-propyl-N-sulfopropyl-amino)-phenol; ISE = ion selective electrode.

Table 4. Imprecision of the Olympus AU 5200 Analyser. Within-run coefficients of variation are median values of three series.

Analyte	Control material	Assigned value	Between days (N = 15 days)		Within-run (N = 20)	
			Found value	Recovery range	CV %	CV %
<i>Enzymes</i>						
Alkaline phosphatase (U/l)	Monitrol 1	70	76	71–84	4.3	0.6
	Monitrol 2	293	317	304–332	2.7	0.5
	Precinorm U	271	282	267–293	2.1	0.9
	Precipath U	316	344	331–357	2.3	1.0
	Qualitrol L	168	142	135–155	3.3	0.6
	Qualitrol N	273	253	245–267	2.2	0.8
	Qualitrol H	397	348	335–370	2.4	0.5
Alanine aminotransferase (U/l)	Monitrol 1	25	24	23–25	2.4	1.6
	Monitrol 2	83	73	70–74	1.5	0.5
	Precinorm U	30	25	24–25	2.1	1.8
	Precipath U	63	53	52–55	1.5	0.4
	Qualitrol L	23	17	16–17	2.5	0.1
	Qualitrol N	31	22	21–23	3.1	2.2
	Qualitrol H	104	82	80–83	1.3	0.8
Amylase (U/l)	Monitrol 1		41	36–48	10.2	2.0
	Monitrol 2		149	133–156	3.1	0.7
	Precinorm U		63	62–65	1.3	1.2
	Precipath U		120	116–124	1.5	0.8
	Qualitrol L		41	38–44	2.0	1.4
	Qualitrol N		59	58–61	3.8	0.8
	Qualitrol H		221	215–227	1.4	0.5
Aspartate aminotransferase (U/l)	Monitrol 1	32	32	28–34	4.6	1.6
	Monitrol 2	76	73	67–74	2.4	0.6
	Precinorm U	26	22	21–23	2.3	1.0
	Precipath U	60	52	49–53	2.2	0.8
	Qualitrol L	22	18	17–21	4.0	2.6
	Qualitrol N	45	38	37–39	1.4	1.8
	Qualitrol H	99	85	81–87	1.9	0.6
Creatine phosphokinase (U/l)	Monitrol 1	56	56	44–62	10.2	1.5
	Monitrol 2	147	150	121–179	9.5	0.8
	Precinorm U	114	95	80–113	7.9	0.7
	Precipath U	207	169	144–185	7.3	1.1
	Qualitrol L	44	37	23–48	15.7	2.2
	Qualitrol N	90	81	71–93	6.1	0.6
	Qualitrol H	200	145	88–189	14.2	0.7
g-Glutamyltransferase (U/l)	Monitrol 1	20	19	19–20	2.6	1.6
	Monitrol 2	46	43	43–45	1.5	0.7
	Precinorm U	38	36	35–38	2.2	1.6
	Precipath U	107	107	103–109	1.3	0.7
	Qualitrol L	15	14	14–15	3.0	3.3
	Qualitrol N	19	19	18–20	2.3	2.3
	Qualitrol H	82	77	75–79	1.4	0.7
Lactate dehydrogenase (U/l)	Monitrol 1	196	193	178–204	3.1	1.0
	Monitrol 2	319	308	294–324	2.5	0.5
	Precinorm U	175	148	135–156	3.2	1.3
	Precipath U	266	229	217–242	2.7	0.9
	Qualitrol L	129	110	104–121	3.0	1.5
	Qualitrol N	306	251	239–259	2.5	0.6
	Qualitrol H	548	447	426–461	2.2	0.4
<i>Substrates</i>						
Albumin (g/dl)	Monitrol 1	4.3	3.5	3.4–3.6	1.7	1.4
	Monitrol 2	3.3	2.5	2.4–2.6	1.7	1.7
	Precinorm U	3.5	2.6	2.5–2.8	2.3	1.7
	Precipath U	3.3	2.5	2.3–2.6	2.6	1.2
	Qualitrol L	2.1	1.8	1.7–1.9	2.5	2.2
	Qualitrol N	4.7	4.2	4.1–4.3	1.4	1.4
	Qualitrol H	4.1	3.9	3.8–4.1	1.9	1.1

Table 4 (continued).

Analyte	Control material	Assigned value	Between days (<i>N</i> = 15 days)		Within-run (<i>N</i> = 20)	
			Found value	Recovery range	CV %	CV %
Total bilirubin (mg/dl)	Monitrol 1	1.3	1.3	1.1–1.3	4.6	1.7
	Monitrol 2	4.6	4.6	4.5–5.0	2.7	1.5
	Precinorm U	2.1	2.0	1.7–2.1	5.5	2.3
	Precipath U	4.4	4.5	4.0–4.8	4.1	1.5
	Qualitrol L	1.5	1.6	1.5–1.6	2.5	1.4
	Qualitrol N	1.2	1.3	1.1–1.4	5.2	2.9
	Qualitrol H	4.5	5.0	4.9–5.2	1.7	1.8
Calcium (mmol/l)	Monitrol 1	2.3	2.3	2.3–2.3	1.0	0.7
	Monitrol 2	3.2	3.2	3.1–3.2	1.2	0.7
	Precinorm U	2.6	2.7	2.6–2.7	1.3	1.0
	Precipath U	3.5	3.5	3.4–3.6	1.4	0.5
	Qualitrol L	1.3	1.4	1.3–1.4	1.5	0.9
	Qualitrol N	2.8	2.7	2.7–2.9	2.3	0.7
	Qualitrol H	3.1	3.1	3.1–3.2	1.2	0.8
Cholesterol (mg/dl)	Monitrol 1	184	176	172–184	1.7	0.6
	Monitrol 2	124	114	112–118	1.3	0.6
	Percinorm U	106	95	92–98	1.4	0.7
	Precipath U	125	115	113–120	1.6	0.7
	Qualitrol L	117	107	102–112	1.8	0.5
	Qualitrol N	114	107	104–110	1.4	0.7
	Qualitrol H	233	218	213–224	1.3	0.5
Creatinine Jaffe (mg/dl)	Monitrol 1	1.2	1.1	1.0–1.2	4.1	3.1
	Monitrol 2	5.0	5.1	4.9–5.3	1.6	1.5
	Precinorm U	1.7	1.9	1.8–2.3	6.2	3.2
	Precipath U	3.3	3.5	3.2–3.7	2.7	1.9
	Qualitrol L	1.2	1.1	1.0–1.2	5.1	4.7
	Qualitrol N	1.0	0.9	0.8–1.0	6.1	4.0
	Qualitrol H	7.1	6.6	6.4–6.7	1.3	1.4
Creatinine enz. (mg/dl)	Monitrol 1	1.1	1.1	1.1–1.2	1.1	1.5
	Monitrol 2	5.7	6.2	5.6–6.4	2.6	1.0
	Precinorm U	1.9	1.9	1.4–2.0	6.9	1.5
	Precipath U	3.9	4.1	3.7–4.2	3.2	0.8
	Qualitrol L	1.2	1.3	0.9–1.4	8.9	1.5
	Qualitrol N	0.8	0.8	0.8–0.9	1.8	1.7
	Qualitrol H	7.2	8.1	7.7–8.4	2.0	0.5
Glucose (mg/dl)	Monitrol 1	75	88	84–91	2.8	0.6
	Monitrol 2	245	254	239–269	4.0	0.7
	Precinorm U	114	120	114–123	1.6	1.0
	Precipath U	236	249	242–257	1.6	0.6
	Qualitrol L	41	45	40–44	5.3	1.4
	Qualitrol N	95	102	98–109	2.4	0.7
	Qualitrol H	206	207	200–213	1.7	0.6
Inorganic phosphate (mg/dl)	Monitrol 1	3.4	3.6	3.5–3.7	1.3	1.8
	Monitrol 2	6.9	7.2	6.9–7.4	2.0	0.5
	Precinorm U	5.2	5.5	5.2–5.6	2.1	1.0
	Precipath U	6.0	6.3	6.0–6.5	2.0	0.8
	Qualitrol L	4.0	4.1	3.9–4.3	2.1	1.8
	Qualitrol N	2.6	2.3	2.1–2.3	2.9	1.5
	Qualitrol H	8.1	8.8	8.5–9.1	2.1	0.6
Iron (ug/dl)	Monitrol 1	108	101	97–109	2.7	2.5
	Monitrol 2	190	214	205–239	4.1	0.7
	Precinorm U	120	115	112–120	1.8	1.2
	Precipath U	136	129	126–132	1.5	1.0
	Qualitrol L	84	84	75–95	6.4	2.3
	Qualitrol N	211	190	184–207	3.1	0.6
	Qualitrol H	181	175	169–185	2.3	1.1

Table 4 (continued).

Analyte	Control material	Assigned value	Between days (<i>N</i> = 15 days)		Within-run (<i>N</i> = 20)	
			Found value	Recovery range	CV %	CV %
Total protein (g/dl)	Monitrol 1	6.8	7.0	6.8–7.2	1.4	0.6
	Monitrol 2	5.1	5.1	5.0–5.3	1.4	0.9
	Precinorm U	5.0	5.0	4.9–5.1	1.2	1.0
	Precipath U	4.9	4.9	4.8–5.0	1.2	0.8
	Qualitrol L	4.7	4.7	4.5–4.8	1.9	1.0
	Qualitrol N	8.7	8.7	7.8–8.1	1.2	0.5
	Qualitrol H	8.9	8.9	8.9–9.3	1.0	0.5
Triglycerides (mg/dl)	Monitrol 1	88	80	77–82	1.6	0.9
	Monitrol 2	184	167	160–173	1.6	0.9
	Precinorm U	105	90	86–93	1.8	0.9
	Precipath U	136	114	103–118	2.6	0.9
	Qualitrol L	93	79	76–81	1.6	1.2
	Qualitrol N	128	107	102–109	1.7	0.5
	Qualitrol H	251	209	202–215	1.7	0.4
Urea (mg/dl)	Monitrol 1	32	31	30–33	2.5	1.9
	Monitrol 2	108	109	106–114	1.9	2.4
	Precinorm U	57	56	55–59	2.1	1.8
	Precipath U	151	157	152–161	1.9	2.2
	Qualitrol L	16	15	14–16	3.5	3.3
	Qualitrol N	38	37	35–39	2.8	1.4
	Qualitrol H	168	174	169–179	1.6	1.1
Uric acid (mg/dl)	Monitrol 1	5.3	5.2	5.0–5.4	2.0	1.2
	Monitrol 2	8.3	8.2	7.6–8.6	2.4	0.7
	Precinorm U	5.9	4.9	4.8–5.2	2.1	1.2
	Precipath U	10.2	10.4	10.1–10.7	1.7	1.1
	Qualitrol L	3.6	3.3	3.1–3.4	1.9	1.7
	Qualitrol N	6.9	7.0	6.7–7.2	1.8	1.0
	Qualitrol H	10.2	10.0	9.5–10.3	2.0	1.6
<i>Electrolytes</i>						
Sodium (mmol/l)	Monitrol 1	139	140	136–145	2.5	0.3
	Monitrol 2	111	112	108–117	2.3	0.9
	Precinorm U	123	124	118–129	2.2	0.7
	Precipath U	137	141	137–147	2.6	0.4
	Qualitrol L	116	120	114–122	2.3	0.4
	Qualitrol N	154	155	150–159	2.4	0.3
	Qualitrol H	161	164	159–167	2.3	0.3
Potassium (mmol/l)	Monitrol 1	4.40	4.41	4.30–4.60	1.8	0.6
	Monitrol 2	6.65	6.81	6.60–7.10	2.3	1.5
	Precinorm U	4.64	4.73	4.70–4.90	1.5	0.8
	Precipath U	6.91	7.06	6.90–7.30	1.7	0.5
	Qualitrol L	2.28	2.32	2.20–2.40	1.7	1.2
	Qualitrol N	5.25	5.45	5.20–5.60	1.9	0.5
	Qualitrol H	6.50	6.69	6.40–6.80	2.0	0.4
Chloride (mmol/l)	Monitrol 1	109	110	107–115	1.9	0.4
	Monitrol 2	90	90	89–93	1.7	0.5
	Precinorm U	77	81	78–84	1.6	0.5
	Precipath U	119	124	121–130	1.9	0.4
	Qualitrol L	84	86	82–90	1.5	0.5
	Qualitrol N	94	95	93–100	1.7	0.4
	Qualitrol H	120	118	114–119	1.6	0.4

several times. If carry-over had occurred, samples immediately following the groups with high activity should have shown elevated activities.

Correlation study

Approximately 250 fresh human sera from daily routine samples were analysed simultaneously in the AU 5200 and in the AU 5000. In addition, sodium, potassium and

chloride concentrations in the same samples were measured in a Hitachi 747 analyser equipped with a ISE unit. Care was taken to include pathological analyte levels.

Assessment of drift effects

Drift effects were studied using seven commercial control sera. The sera were dissolved before starting the drift

experiment and kept at 4°C until use. For determination of alkaline phosphatase, creatine phosphokinase and bilirubin the sera were freshly reconstituted every hour. Five measurements of each control serum were carried out every 60 min for 9 h. Prior to starting a series of

measurements the reagent lines were flushed with fresh reagent.

In order to detect short-term variations or sudden changes, a second experiment was conducted. Chemistry

Figure 1 (a). Imprecision within-run on both the AU 5200 and the comparison instrument. The bars plotted in this figure represent median CV values of the data in table 4.

Figure 1 (b). Imprecision between-run on both the AU 5200 and the comparison instrument. The bars plotted in this figure represent median CV values of the data in table 4.

Table 5. Recovery of assigned values in quality-control materials. The minimum and maximum of the assigned values are shown for all tested parameters. The median, 10th, 25th, 75th and 90th percentiles of the found values are expressed as percentages of the assigned values.

Analyte	N	Assigned		Found (%)				
		Minimum	Maximum	Median	10th P.	25th P.	75th P.	90th P.
<i>Enzymes</i>								
Alkaline phosphatase	22	47	423	103	85	88	107	112
Alanine aminotransferase	22	16	104	85	78	83	88	94
Amylase	11	20	173	95	91	92	100	111
Aspartate aminotransferase	22	10	99	87	82	84	94	104
Creatine phosphokinase	22	22	229	85	74	82	96	100
g-Glutamyl-transferase	22	10	110	101	94	98	106	110
Lactate dehydrogenase	22	123	548	92	86	87	99	102
<i>Substrates</i>								
Albumin	25	2.1	4.7	83	76	78	88	94
Total bilirubin	27	0.7	7.3	108	98	102	114	118
Calcium	29	1.3	3.5	101	97	100	102	104
Cholesterol	27	86	241	94	91	93	96	98
Creatinine Jaffe	23	0.4	6.9	105	97	100	102	108
Creatinine enz.	19	0.7	7.1	108	98	101	112	113
Glucose	23	41	305	105	99	103	107	108
Inorganic phosphate	27	2.0	8.4	105	93	99	109	110
Iron	27	68	268	97	86	93	100	102
Total protein	29	4.1	8.9	103	99	101	106	107
Triglyzerides	27	50	251	90	83	87	96	99
Urea	29	14	169	99	94	96	102	105
Uric acid	27	2.6	10.8	101	95	100	105	107
<i>Electrolytes</i>								
Sodium	25	111	163	99	98	99	100	101
Potassium	25	2.3	7.3	100	98	100	101	103
Chloride	19	84	124	101	96	97	103	104

Figure 2. Recovery of assigned values in 32 commercial control materials on both the AU 5200 and the comparison instrument. The boxes represent the 25th, 75th percentiles and medians, the bars the 10th and 90th percentiles of the recovery ratios in percentages.

and ISE tests were performed continuously over a period of 6 h. Therefore a serum pool was prepared, filtered and stirred on a magnetic stirrer at 4°C. Approximately 1800 aliquots of this serum pool were taken and analysed in the AU 5200 immediately. Blank readings and calibration of the instrument were performed only once at the start of the experiments.

Results

Imprecision

Data on within-run and between-day imprecision are summarized in table 4. The values are medians from

three independent measurement series for seven control sera. Figures 1(a) and 1(b) show coefficients of variation for all tests on both the AU 5200 and AU 5000 analysers. The CV values in these figures are again medians taken across the CV values in table 4 and corresponding values obtained from measurements on the AU 5000 analyser.

As indicated in figure 1(a), 21 of 23 evaluated tests on the AU 5200 analyser yielded a median within-run imprecision well below 2.0%; urea showed a median imprecision of 2.1%. Creatinine, measured with the kinetic Jaffe reaction method on the AU 5200, yielded rather high CV values from 1.5% to 4.7% (not shown in figures 1(a) and 1(b)).

The electrolyte measurements on the AU 5200 analyser showed a remarkably good precision. Slightly lower median CV values for the imprecision in series were found for 18 of 22 tests on the AU 5200, compared with the AU 5000 analyser.

The median between-day CV values were below 3.0% for 19 out of 23 tests on the AU 5200 analyser and were well below 5.0% for all tests, with the exception of the CPK activity measurement which showed CV values from 6.1% to 15.7%.

The majority of all tests gave lower imprecision from day to day on the AU 5200 analyser compared to those on the AU 5000.

The overall precision in series and from day to day on both analysers could be rated as very good, with the AU 5200 performing slightly better than the AU 5000 analyser.

Table 6. Limits of the analytical range.

Analyte	Unit	Measured up to	Upper limit of linearity	
			Found	Declared
<i>Enzymes</i>				
Alkaline phosphatase	U/l	3300 ³	3300	1600
Alanine aminotransferase	U/l	700	600	400
Amylase	U/l	1000 ³	1000	1350
Aspartate aminotransferase	U/l	500	500	450
Creatine phosphokinase	U/l	1200	1200	1100
g-Glutamyl-transferase	U/l	900	900	500
Lactate dehydrogenase	U/l	2500	1750	500
<i>Substrates</i>				
Albumin	g/dl	7.0	7.0	7.0
Total bilirubin	mg/dl	25.0	25.0	30.0
Calcium	mmol/l	7.0	6.0	5.0
Cholesterol	mg/dl	1200	1000	750
Creatinine enz. ¹	mg/dl	30	30	20
Glucose ²	mg/dl	1000	1000	700
Inorganic phosphate	mg/dl	22.5	22.5	20
Iron	ug/dl	1000	1000	1000
Total protein	g/dl	12.0	12.0	12.0
Triglycerides	mg/dl	1200	1000	1000
Urea	mg/dl	400	375	300
Uric Acid	mg/dl	33.0	33.0	20.0

¹ Creatinine PAP (Merck); ² Hexokinase method; ³ Extinction beyond DOD range.

Figure 3 (a). Drift during 9 h for three representative analytes measured in seven control sera. The medians, 10th, 25th, 75th and 90th percentiles of the recovery ratios in relation to the initial measurements are shown as box-plots.

Assessment of accuracy

The recovered values of all analytes in 32 commercial control sera were expressed as percentages of the assigned values. The medians, the 10th, 25th, 75th and 90th percentiles of the respective values are shown in table 5 and in figure 2. Fourteen of 23 tests yielded median recoveries within the 5% range; five tests were in the range between 5% and 10% (lactate dehydrogenase, bilirubin, cholesterol, triglycerides and creatinine measured enzymatically); and three tests were in the range between 10% and 15% (alanine aminotransferase, creatine phosphokinase).

The low recoveries of some enzyme activity tests may be due to the conversion of the values measured to corresponding values at 25°C. These conversion factors are based upon human serum, whereas most commercial control materials are essentially non-human or spiked with non-human analytes. The low recoveries of albumin (83%), cholesterol and triglycerides were caused by calibration errors. As a consequence of this evaluation the calibrator values for these tests were reassigned by the manufacturer.

Linearity

Both the linearities found, and the linearity ranges given by the manufacturers, are shown in table 6. The

Figure 3 (b). Drift during 6 h of continuous operation. Approximately 1800 measurements of all analytes were performed.

linearities found were better than the manufacturers' for all tests, with the exception of amylase. The transaminases showed limited linearities with an upper range of approximately 500 U/l, whereas cholesterol and triglyceride measurement is possible up to 1000 mg/dl.

Carry-over

A potential carry-over of sample residue resulting from an insufficient washing of the cuvettes was investigated by measuring creatine phosphokinase activity (27 U/l in a serum pool) in cuvettes which had been used for the determination of the same analyte with a very high activity (approximately 1500 U/l). The results were compared with measurements of low activity in cuvettes which had also been used for measurements of low activity. Figure 4(a) shows that there was no detectable difference. Sample carry-over due to incomplete washing of the probe needle and the mixer blades was investigated by alternating two serum pools with high and low creatine phosphokinase activity; the samples which immediately followed the groups with high activity did not show elevated activities (figure 4(b)). In conclusion, no specimen-related carry-over could be detected.

Method comparison with patient samples

The Olympus AU 5200 series analyser was compared with an Olympus AU 5000 analyser and a Hitachi 747 analyser (ISE measurements only). The statistical evaluation was performed according to the method of Passing and Bablock [3]. The numerical results are given in

Figure 4 (a). Specimen related carry-over due to incomplete cuvette washing: creatine phosphokinase measurements of 120 samples of two serum pools with a low and a high activity in two complete cuvette wheel cycles. During the first cycle samples with a high activity (approximately 1500 U/I) were measured in cuvettes 31 to 45. In the same cuvettes samples with a low activity were measured during the second cycle (indicated by filled squares).

Figure 4 (b). Specimen related carry-over due to incomplete washing of the probe needles and mixer blades. Groups of five samples with low and high activity of creatine phosphokinase were alternated several times. The arrow bars mark the first samples with low activity immediately following a sequence of samples with high activity.

table 7, and scatterplots are shown in figure 5. The correlations were close for all enzyme and substrate tests. Good agreement was found between flame photometry (AU 5000) and ISE measurement (Hitachi 747) for potassium. Sodium (flame photometry and ISE) and chloride measurement (mercury thiocyanate) showed lower coefficients of correlation.

Alkaline phosphatase, creatine phosphokinase, g-glutamyltransferase, aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, calcium, creatinine (measured enzymatically), inorganic phosphate, total bilirubin, triglycerides, urea, uric acid, potassium (flame photometry and ISE), sodium (flame photometry)

and chloride (mercury thiocyanate method and ISE) did not show a significant deviation from the factor 1 for the slope or from the constant 0 for the intercept. Albumin, cholesterol, glucose (hexokinase method), iron, total protein and sodium (ISE) measurements showed small, but significant, deviation of slope or intercept. Amylase measurements on both analysers correlated well, but are not comparable without data transformation due to different test methods with different amylase substrates.

Possible reason for the discrepancies in the albumin and cholesterol assays could be incorrect calibrator values (see above), or, in the case of iron, to different test methodologies (see table 2).

Drift

The results of the drift experiments are displayed in figures 3(a) (measurements every hour for 9 h) and 3(b) (continuous measurements for 6 h). A continuous trend either increasing or decreasing could not be detected for any of the parameters tested. Median deviations from the initial values did not exceed 5% over 9 h for any test. The electrolyte measurements showed exceptionally low deviations from the starting value, indicating a very stable ISE system. The second drift experiment revealed short-term fluctuations in the measurement of creatinine (Jaffe method). Statistical spectral analysis yielded a fourier frequency of about 0.05, which is equivalent to an oscillation period of 20 samples. The remaining tests did not show any periodic variations or sudden fluctuations.

Assessment of practicability

An instruction period of four days was necessary to acquire the knowledge to operate the Olympus AU 5200 analyser, users of the older AU 5000 analyser can operate the new system instantly. Despite the size and capacity of the analyser, the Olympus AU 5200 is easy to run and can easily be integrated into the organization of a large laboratory. The sample feeding mechanism operates in a linear fashion, allowing continuous supply of subsequent samples. One sample which is nowadays not an aliquot, but delivered in a primary tube, passes through the instrument in 5 min and even tubes on a fully loaded sample tray are accessible after 70 min. The sample belt is in front of the instrument, which is a major advantage over the older AU 5000 series analyser where it is in the rear. The analyser can be reached from all sites and all mechanical movements can be watched.

The system-processing software for routine operation is clearly arranged; the main jobs, for example activating the analyser out of a standby status, starting measurements, washing the cuvettes and flushing the reagent lines, are presented in one menu and are initiated by one keystroke. The software contains an extensive diagnostic program, which allows a specific detection of mechanical or electronic problems.

The preanalytical preparation of the analyser consists of four steps requiring the time periods given in parenthesis: warming up to 37°C (60 min), washing of cuvettes and

Table 7. Method comparison studies in human sera with Olympus AU 5200 (*y*) and comparison instrument (*x*). Regression analyses ($y = a + bx$) were performed according to Passing and Bablock.

Analyte	<i>N</i>	<i>r</i>	<i>b</i> ¹	<i>a</i> ²	median <i>x</i>	median <i>y</i>
<i>Enzymes</i>						
Alkaline phosphatase	223	1.000	1.03	0.69	124.0	129.0
Alanine aminotransferase	242	0.993	0.96	−0.85	15.5	14.0
Amylase	227	0.995	*0.33	*0.27	94.0	32.0
Aspartate aminotransferase	242	0.999	1.00	−1.00	12.0	11.0
Creatine phosphokinase	219	0.993	0.89	1.00	25.0	23.0
γ-Glutamyltransferase	237	0.999	1.09	0.00	26.0	28.0
Lactate dehydrogenase	234	0.997	0.93	1.60	185.5	177.0
<i>Substrates</i>						
Albumin	239	0.977	0.93	*−0.19	3.89	3.43
Total bilirubin	231	0.999	1.11	−0.06	0.70	0.70
Calcium	239	0.963	1.00	0.03	2.34	2.37
Cholesterol	234	0.997	0.95	*−1.54	186.5	174.5
Creatinine enz.	243	0.997	1.00	0.00	1.10	1.10
Glucose	243	0.997	0.99	*1.06	114.0	115.0
Inorganic phosphate	233	0.991	0.98	0.08	3.70	3.80
Iron	216	0.991	*1.02	−5.86	87.5	80.5
Total protein	231	0.971	*1.04	*−0.14	6.90	6.90
Triglycerides	235	0.999	0.93	1.69	143.0	133.0
Urea	238	0.998	1.04	−1.74	42.0	41.0
Uric acid	235	0.992	1.00	−0.20	5.70	5.60
<i>Electrolytes</i>						
Sodium	291	0.834	1.00	−3.00	149.0	147.0
AU 5200 ISE (<i>y</i>)						
AU 5000 Flame (<i>x</i>)						
Sodium	299	0.879	*0.90	*11.10	151.0	147.0
AU 5200 ISE (<i>y</i>)						
Hit 747 ISE (<i>x</i>)						
Potassium	287	0.956	1.00	−0.10	4.70	4.50
AU 5200 ISE (<i>y</i>)						
AU 5000 Flame (<i>x</i>)						
Potassium	298	0.989	1.00	−0.10	4.65	4.50
AU 5200 ISE (<i>y</i>)						
Hit 747 ISE (<i>x</i>)						
Chloride	299	0.864	0.85	14.00	109.0	108.0
AU 5200 ISE (<i>y</i>)						
AU 5000 Hg (<i>x</i>)						
Chloride	297	0.949	0.84	16.48	110.0	108.2
AU 5200 ISE (<i>y</i>)						
Hit 747 ISE (<i>x</i>)						

*, ¹ Significant deviation of slope *b* from 1.0; ² significant deviation of intercept *a* from 0.

filling reagent lines (23 min), reagent blanking, calibration and running controls (20 min). Using the automatic power-on facility reduces the preanalytic phase by the time period for warming up the instrument. Thus, after 45 min, including the time needed for checking the results of calibration and control materials, the analyser is ready for routine operation.

During the evaluation period and the subsequent routine work no total shut down of the analyser occurred. The most frequent problems were rack jams on the transport belt and needle crashes. In such situations the analyser does not stop completely, but stops only the feeding mechanism. Results of tests pipetted so far can still be obtained. The most severe faults were worn out gears of the cuvette wheel motor causing a small displacement of

the cuvette wheel hindering the action of the washer unit; and, a leakage in the vacuum system of the washer unit causing an incomplete draining of the cuvettes. Both problems could be attributed to some kind of material fatigue. The manufacturer has now replaced the materials for these machine parts. Another point of criticism is the badly arranged report format in which the results are printed out – there is no way of achieving patient-oriented reports.

Conclusion

With respect to imprecision, accuracy, linearity and carry-over data, the Olympus AU 5200 analyser compared

Figure 5 (a). Graphical plots of instrument comparison.

Figure 5 (b). Graphical plots of instrument comparison.

Figure 5 (c). Graphical plots of instrument comparison.

Figure 5 (d). Graphical plots of instrument comparison.

Figure 5 (e). Graphical plots of instrument comparison.

favourably with and showed slightly better results than the AU 5000 analyser. The Olympus AU 5200 analyser reaches a sustained peak performance of 300 samples/h including ISE measurements, operates reliably from day to day and is thus well suited for medium and large sized laboratories.

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