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Multicentre evaluation of the Boehringer Mannheim/Hitachi 917 analysis system

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The new selective access analysis system BM/Hitachi 917 was evaluated in an international multicentre study, mainly according to the ECCLS protocol for the evaluation of analysers in clinical chemistry. Forty-three different analytes, covering 56 different methods—enzymes, substrates, electrolytes, specific proteins, drugs and urine applications—were tested in seven European clinical chemistry laboratories. Additionally, the practicability of the BM/Hitachi 917 was tested according to a standardized questionnaire. Within-run CVs (median of 3 days) for enzymes, substrates and electrolytes were <2% except for creatine-kinase MB isoform and lipase at low concentration. For proteins, drugs and urine analytes the within-run CVs were <4% except for digoxin and albumin in urine. Between-day median CVs were generally <3% for enzymes, substrates and electrolytes, and <6% for proteins, drugs and urine analytes, except for lipase, creatine kinase and MB isoform, D-dimer, glycosylated haemoglobin, rheumatoid factors, digoxin, digitoxin, theophylline and albumin in urine in some materials. Linearity was found according to the test specifications or better and there were no relevant effects seen in drift and carry-over testing. The interference results clearly show that also for the BM/Hitachi 917 interference exists sometimes, as could be expected because of the chemistries applied. It is a situation that can be found in equivalent analysers as well. The accuracy is acceptable regarding a 95–105% recovery in standard reference material, with the exception of the creatinine Jaffé method. Most of the 160 method comparisons showed acceptable agreement according to our criteria: enzymes, substrates, urine analytes deviation of slope ±5%, electrolytes ±3%, and proteins and drugs ±10%. The assessment of practicability for 14 groups of attributes resulted in a grading of one–three scores better for the BM/Hitachi 917 than the present laboratory situation. In conclusion, the results of the study showed good analytical performance and confirmed the usefulness of the system as a consolidated workstation in medium-sized to large clinical chemistry laboratories.

Introduction

The Boehringer Mannheim/Hitachi 917 analysis system (BM/Hitachi 917) is the most recent medium to large-sized analysis system which was introduced to the market by Boehringer Mannheim GmbH in December 1994. The functionality under simulated routine conditions was already tested during an international field study in 11 European countries [1].

In contrast to previous analysis systems of comparable size, e.g. BM/Hitachi 717 or 737, the new 917 system offers features making it attractive to different purposes and different sections of clinical laboratories, e.g. a high number of reagent channels, convenient reagent handling, convenient calibration, flexible application settings, short-term applications and automatic predilution. BM/Hitachi 917 can either be used as a kind of 'workhorse' for the most often requested analytes or as a consolidated workstation for the determination of at least 48 different analytes on board covering, besides the classical routine assays, specific protein methods, drug methods in serum and urine, and urine applications for enzymes, substrates, electrolytes and proteins. The analyser is designed as a closed system with a special reagent line and fixed applications; however, five user-defined methods can be set by the operator. A software upgrade was introduced in April 1996; a draft version was tested at the end of the multicentre study. This software version offers more convenience for the operator and an enhanced data management system, and has built-in features related to accreditation aspects.

The versatility of the new instrument required a comprehensive evaluation protocol as already described for the multicentre evaluation of BM/Hitachi 911 [2]. Seven European laboratories participated in the multicentre study in order to assess the analytical performance and practicability aspects of BM/Hitachi 917. Altogether, 43 different analytes covering 56 different methods—enzymes, substrates, electrolytes, specific proteins, drugs and urine applications—were tested in a core programme mainly following the ECCLS guidelines [3]. In addition, a specific satellite programme was carried out for specific tests with less extensive evaluation experiments in order to maintain an acceptable cost/benefit ratio. In total, more than 120 000 individual data were generated and statistically evaluated within a period of 7 months. Processing and analysis of the large data volumes were managed with the programme package CAEv (computer-aided evaluation). CAEv [4] allows the definition of protocols, the sample and test requests for on-line data capture, and statistical evaluation of results. Data were validated by the laboratories and sent via telecommunication to the central study administration.

Description of the instrument

BM/Hitachi 917 is a selective access analyser with a capacity of at least 48 different tests onboard out of 86 stored applications including three ISE methods. The

number of onboard tests can be increased by monoreagents which are distributed on any of the two reagent disks. The theoretical test throughput is 1200 tests per hour. Certain instrument conditions, e.g. predilution, high sample volume pipetting, mixing of short-long-term applications, STAT requests or additional wash steps for the pipettors or the cuvettes needed to eliminate reagent carry-over in certain cases lead to a reduction of the throughput. The pipetting cycle for photometric tests is 4.5 s and for the three ISE assays 18 s. The software has integrated an algorithm for throughput optimization. It recognizes pipetting conflicts—e.g. R2/R3 pipetting—and reschedules the steps so that the additional time needed for the conflict situation is a minimum. The bar-coded system reagents consisting of one–three vials per test are set in any free position of the reagent disk. For frequently requested tests, several bottles of one reagent can be loaded into the reagent disk. An automatic bottle changeover occurs after the first bottle is registered as empty. Application settings are loaded from application floppy disk or from application bar code sheet, both are delivered by Roche Diagnostics GmbH. Five applications are user definable. At present, over 200 applications are available.

Specimens are processed either from primary tubes (5–10 ml), secondary cups (2 ml) or microcups (0.5 ml) positioned on a sample disk with 110 positions. Primary tubes can be identified by four different types of bar codes with the possibility of mixing. A standardized RS232 interface allows a bidirectional communication to a host computer.

One hundred and sixty semi-disposable plastic cuvettes are arranged on a rotor positioned in a waterbath of 37 °C. The cuvettes pass through the beam of the photometer every 18 s; 12 fixed wavelengths between 340 and 800 nm in mono- or bichromatic mode can be selected.

Two pipettors transfer the reagent into a cuvette. The average reagent consumption is ~200 µl per determination. Most of the photometric STAT results are available 10–12 min after test request. Various measurement and calibration procedures can be applied. The main specifications of BM/Hitachi 917 are summarized in table 1.

Materials and methods

Instruments and reagents

The methods and instruments used in this study are listed in table 2. The same reagents were used in all evaluation centres for each method on BM/Hitachi 917. The reagents were available in special system packs designed for BM/Hitachi 917. For the comparison experiments the methods and reagent lots from the routine were used.

Calibration

During the familiarization period, a fixed factor was determined for the enzyme assays in three independent calibration runs per day on three consecutive days. The same lot of the calibrator for automated systems (Roche Diagnostics GmbH) was used for this purpose. The fixed factor is the median from the median factor of the three calibration runs per day, provided that the coefficient of variation (CV) calculated from the nine results is less than 3%.

The substrate, specific protein and drug assays were performed with the autocalibration which is triggered by an analyte-dependent calibration interval. For this reason, the respective calibrator material was placed in the cooled sample disk S2 of the instrument. The type of calibration and the autocalibration data for all analytes were predefined by Roche Diagnostics GmbH in the chemistry parameter settings, stored on the application floppy disk.

The immunoglobulins A,G,M, transferrin and C-reactive protein assays were calibrated according to CRM† standardization. The ISE methods were calibrated daily with the ISE standards and compensator. Detailed information about the calibrator materials employed is shown in table 9 .

Control materials

Imprecision and quality control experiments were performed with lyophilized or liquid control sera from Roche Diagnostics GmbH and control urines from Roche Diagnostics GmbH and BioRad Laboratories; details are shown in table 9.

For accuracy testing standard reference materials, e.g. CRM‡ material for four IFCC enzyme methods and material from NIST§ for several substrate and electrolyte methods were used (table 9, details available on request).

A uniform procedure was applied to the treatment of lyophilized calibrator and control material in order to minimize matrix effects and stability problems. The materials were reconstituted within 30 min and then stored in the dark for a further 30 min before starting the calibration runs of the experiments.

Evaluation protocol

The protocol for the analytical performance of the BM/Hitachi 917 analysis system comprised the testing of the quality characteristics within-run and between-day imprecision, analytical range limits, drift over 8 h, carry-over, interferences and accuracy based on recovery in control materials and method comparison. Forty-three different analytes covering 56 different methods—enzymes, substrates, electrolytes, specific proteins, drugs and urine applications—were tested (table 2).

The total versatility of the new analysis system was covered by a common core programme and by laboratory-specific satellite programmes. The core programme comprised 17 analytes from the classical field of clinical chemistry and was divided into two groups consisting of five laboratories each of which processed the same set of

† CRM 470 [5], BCR information, Community Bureau of Reference, Brussels.
‡ BCR information, Community Bureau of Reference, Brussels.
§ National Institute of Standards & Technology, Office of Standard Reference Materials, Gaithersburg, USA.

Table 1. Instrument specifications.

(1) Type of instrument	Discrete selective multianalyser.
(2) Test channels	Forty-five, with ISE module 48, to be increased with monoreagents.
(3) Test procedures	Endpoint, endpoint with sample blank, kinetic with serum or substrate start with or without sample blank, fixed-time kinetic, combination of two endpoint tests, endpoint and kinetic tests, two kinetic tests performing two tests in one cuvette, two prozone check procedures, measurement with ISE, linear calibration and five non-linear modes of calibration, autocalibration, one- and two-point recalibration, isoenzyme calibration, serum indices indicating haemolytic, icteric and lipaemic specimens.
(4) Throughput	Maximum 800 photometric tests/h, with ISE-module 1200 tests/h.
(5) Sampling system	Sample disk 1 with 110 positions arranged in two concentric rings for routine and STAT samples in bar code identification mode. Up to 55 positions in the inner ring are user definable for STAT samples in non-bar code mode. Sample disk 2 with 57 cooled positions for calibrators and controls, and three fixed positions for wash solutions. Primary tubes from 13 to 16 mm diameter and 75 to 100 mm length, secondary sample cups with 2.0 ml and microcups with 0.5 ml maximum volume. Bar code identification of primary tubes using codabar NW 7, code 39, two out of five interleaved and code 128. Different codes and tube sizes are allowed within one sample disk.
(6) Sample pipettor	Two–thirty-five microlitres (in steps of 0.1 µl), imprecision <1%; for ISE 15 µl for the three determinations of Na, K, Cl.
(7) Reagent cooling	Cold water circuit, refrigerator temperature 5–12 °C.
(8) Reagent bottles	Seven, 20 and 70 ml sizes, two reagent disks with 45 bottle positions. Disk 1 for reagent 1, disk 2 for reagent 1 (monoreagents), 2 and 3.
(9) Reagent dispenser	Two reagent pipettors for dispensing reagents 1–3, 20–270 µl steps in 1 µl steps.
(10) Mixing procedure	Two stirrers mix the reaction solution independently after addition of each reagent with additional mixing programmable.
(11) Reaction rotor	Turntable with 160 cuvettes; quarter rotation (37 cuvettes +4) in 4.5 s = one working cycle.
(12) Reaction cuvettes	Special plastic cuvettes, semidisposable. Volume required: minimum 180 µl, maximum 380 µl. Optical path length: 5 mm.
(13) Reaction cycle	Ten reaction times between 1 and 10 min corresponding to measuring points between 4 and 34.
(14) Temperature control	Waterbath, 37 ± 0.1 °C
(15) Photometer	Single-beam photometer with 12 available wavelengths: 340, 376, 415, 450, 480, 505, 546, 570, 600, 660, 700 and 800 nm; mono- or bichromatic measurement with free selectable wavelength combinations. Light source: halogen lamp. Detector: silicone photodiode. Wavelength adjustment: fixed, via a grating chromator, inaccuracy at 340 ± 2 nm and at 405–800 ± 55 nm. Half band width: 4 nm in the UV range, 10 nm in the visible range. Photometric range of linearity: A = 0–3.0 at 340 nm. Photometric resolution: A = 0.0002. Photometric inaccuracy: max. 1% at 2.0 abs.
(16) Ion-selective electrodes	Indirect potentiometry; flow-through electrode with liquid membrane. Reference electrode, liquid membrane. Dilution ratio: 1:3 1. Incubation temperature: 37 ± 0.1 °C. Calibration: two-point with compensation. Measuring cycle: 18 s. Measuring range: Na+ in serum 80–180, in urine 10–250 mmol/l; K+ in serum 1.5–10, in urine 1–100 mmol/l; Cl− in serum 60–120, in urine 10–250 mmol/l Consumption of ISE solution per sample: Diluent: 450 µl Internal standard: 1050 µl KCl solution: 130 µl.
(17) Data processing	Data input: via touch screen or alpha numeric keyboard item select keys. Data control: CRT 14 inch colour monitor. Data output: matrix printer, 80 characters per line, 220 characters per second. CPU with 16 MB RAM, 270 MB HD and 1 FD drive, 3.5 inches. Interface: RS 232 C. Bidirectional link with a host computer.
(18) Water supply	Internal reservoir with an external supply. Quality: <1 s. Consumption during operation: 40 l/h
(19) Ambient temperature	15–32 °C.
(20) Relative humidity	45–85%.
(21) Physical dimensions	Analyser unit: Width 1.40 m, Depth 0.77 m, Height 1.17 m Operation unit: Width 0.65 m, Depth 0.85 m, Height adjustable.
(22) Weight	Approx. 400 kg.

Table 2. Analytes, methods and comparison instruments.

			Comparison instruments and methods different from H917							
	Methods on BM/Hitachi 917		*A*	*B*	*D*	*E*	*GB*	*I*	*NL*	*Study units*
ALAT	Alanine aminotransferase	IFCC, with PYP	H717 opt.	H747 no PYP	H747 opt.	H747			Chem I	U/l
ASAT	Aspartate aminotransferase	IFCC, with PYP		H747 no PYP	H747 opt.		H737 opt.	H747	Chem I	U/l
ALP_I	Akaline phosphatase	IFCC				H747				U/l
ALP_O	Alkaline phosphatase	DGKCh		H747						U/l
AMYLP	Pancreatic α-amylase	EPS		H747 CNP malt.	H747		H717		Chem I	U/l
AMYLT	Total α-amylase	EPS						H747		U/l
CK	Creatine kinase	NAC activ.		H747	H747		C. FARA Sigma	H747	ELAN	U/l
CK-MB	Creatine kinase, MB-isoform	Immuninhibition					C. FARA Sigma			U/l
GGT_I	γ-Glutamyl-transferase	IFCC				H747				U/l
GGT_S	γ-Glutamyl-transferase	Szasz	H717	H747	H747				Chem I	U/l
LDH_O	Lactate dehydrogenase	DGKCh	H717		H747				Chem I	U/l
LDH_S	Lactate dehydrogenase	SFBC		H747		H717				U/l
LIP	Lipase	Turbidimetric	H717							U/l
CHOL	Cholesterol	CHOD-PAP		H747	H747		H717	H747 Biotr. Abel Kend.	Chem I	mmol/l
CREAJ	Creatinine	Jaffé	H717	H747		H747			Chem I	µmol/l
CREAP	Creatinine	PAP			H747					µmol/l
GLU_HK	Glucose	HK		H747	H747		C. FARA	H747	Dimens.	mmol/l
TP	Total protein	Biuret		H747	H747		H737	H747	Chem I	g/l
UA	Uric acid	PAP	H717	H747	H747	H747			Chem I	µmol/l
UREA	Urea	UV	H717	H747	H747	H747			Chem I	mmol/l
CA	Calcium	OCPC		H747	H747		H717	H747	Chem I	mmol/l
FE	Iron	Ferrozine	H717	H747	H747	H747			EPOS	µmol/l
LACT	Lactate	UV		H911 PAP/Biom.						mmol/l
NA_I	Sodium	ISE	H717	H747	H747	H747	H737	H747	Chem I	mmol/l
K_I	Potassium	ISE	H717	H747	H747	H747	H737	H747	Chem I	mmol/l
CL_I	Chloride	ISE	H717	H747	H747	H747	H737	H747	Chem I	mmol/l
APOA1	Apolipoprotein A1	TIA, IFCC				H717		BNA	Array	g/l
APOB	Apolipoprotein B	TIA, UFCC				H717		BNA	Array	g/l
ASLO	Antistreptolysin O	LPIA	BN-II							IU/ml
CRP	C-reactive protein	TIA	H717	H911	BNA BNA	H717	FLX Abbott	BNA	Dimens.	mg/l
DDIM	D-Dimer	LPIA	Nycocard					Sclavo		mg/l
FERRI	Ferritin	LPIA	C. Core		ES 700				ES 600	µg/l
HBA1C	Haemoglobin A1c	TIA	HPLC Shimatsu	H911					HPLC Biorad	%
IGA	Immunoglobulin A	TIA		BNA					Array	g/l
IGG	Immunoglobulin G	TIA		BNA					Array	g/l
IGM	Immunoglobulin M	TIA		BNA					Array	g/l
RF	Rheumatoid factor	LPIA	BNA	BNA		H717				IU/ml
TRANS	Transferrin	TIA	H717	H911	BNA	H717			Array	g/l
DIG	Digoxin	LPIA	H717					STRATUS/ ELAN		µg/l
DIGIT	Digitoxin	CEDIAR assay	H717							µg/l
PHEBA	Phenobarbital	CEDIAR assay						ELAN SYVA		mg/l
THEO	Theophylline	CEDIAR assay						ELAN SYVA		mg/l
T4	Thyroxine	CEDIAR assay					ACS CIBA CORN.			nmol/l
A1MG	α-1 Microglobulin	TIA			—					mg/l
MAU	Albumin in urine	TIA		RIA	—				Array	mg/l
CREAJU	Creatinine (in urine)	Jaffé		H911			C. FARA		EPOS	mmol/l
CREAPU	Creatinine (in urine)	PAP	NOVA		H747					mmol/l
GLUHKU	Glucose (in urine)	HK		H911	H747				EPOS	mmol/l
UA_U	Uric acid (in urine)	PAP		H911	H747				EPOS	µmol/l
UREA_U	Urea (in urine)	UV	NOVA	H911	H747		H737		EPOS	mmol/l
CA_U	Calcium (in urine)	OCPC		H911	H747		H717		EPOS	mmol/l
MG_U	Magnesium (in urine)	Xylidyl blue			H747		H717		AAS	mmol/l
PHOS_U	Phosphate (in urine)	Molybdate, UV		H911	H747		H717		EPOS	mmol/l
NA_IU	Sodium (in urine)	ISE	NOVA	H911	H747		Flame		Dimens.	mmol/l
K_IU	Potassium (in urine)	ISE	NOVA	H911	H747		Flame		Dimens.	mmol/l
CL_IU	Chloride (in urine)	ISE	NOVA	H911	H747		Flame		Dimens.	mmol/l

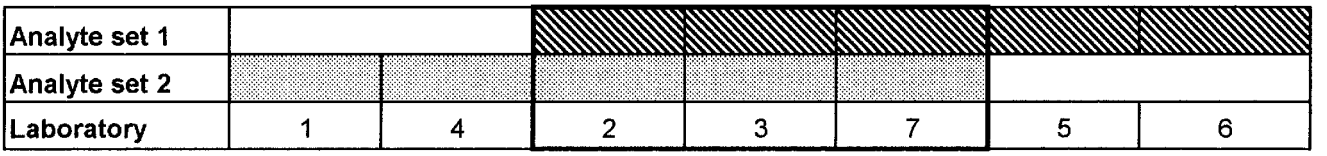

Figure 1. Contribution of analytes of the core programme over the evaluation sites.

analytes. Three laboratories took all analytes of the core programme (figure 1). The protocol was designed in that way where each analyte was processed in an odd number of laboratories so that the median of the statistics from the individual laboratories is related to the outcome of a single experiment. The ISE analytes were performed by all evaluation sites. The various analytes were split between the seven evaluation sites for the studies of linearity, drift and sample-related carry-over. Similarly, the testing for endogenous interferences was shared between the laboratories. Only the core programme covered the total evaluation phase with familiarization, initial trial and main trial. The initial trial consisted of a between-day imprecision experiment over 11 days. The evaluation protocol of the main trial is shown in table 3.

The satellite programme contained analytes from various laboratory segments, e.g. specific proteins, drugs and urinalysis. This programme was integrated into the main trial and included the experiments within-run and between-day imprecision, method comparison and in most cases analytical range limits and interference.

During a start-up meeting of the multicentre evaluation, all evaluators agreed upon the protocol and the quality specifications proposed by Boehringer Mannheim.

Software upgrade evaluation

The total evaluation of the analytical performance was carried out with software version V1. In addition to this evaluation a software functionality testing of the new version V2 was performed. This new version includes improvements of certain screen designs and new functions, e.g. enhanced data management capabilities, bar code sheets for convenient transfer of applications, calibrator and control material information, reagent exchange during operation, a new quality control package, usage of monoreagents either on reagent disk one or two in order to increase the number of tests on board, and a context sensitive help system.

The evaluation protocol comprised a familiarization phase with the new software, a within-run imprecision experiment with two control sera and a human specimen pool to provide the information that the new software version shows a comparable imprecision. Routine simulation experiments related to reproducibility and download experiments to test comparability and functionality testing of the bar code sheets for applications, calibrators and control materials should prove reliability and correct system functionality.

As for the other experiments of the study, the definition and performance of the routine simulation was carried out with the software package CAEv [10].

Reproducibility was tested in an experiment based on the within-run imprecision concept which consisted of two parts, a 'reference' part being performed as a usual imprecision run with two control materials and at least two human specimen pools in 15 repetitions, followed by the random part with variable numbers of requests (1–23) per sample and variable test pattern per sample type according to the routine situation of the laboratory [1]. In a second simulation imprecision experiment, provocation steps to the analytical system were integrated, e.g. sample short, STAT sampling, reagent interrupt, reagent bar code error, sample bar code error, additional test selection.

In two routine download experiments, ~100 samples from the daily routine runs were transferred to the BM Hitachi instrument. The sample sequence and the results were downloaded to the CAEv database, and a corresponding request for BM/Hitachi was generated [1].

Assessment of reliability and practicability

For the assessment of reliability, a logbook was kept throughout the total evaluation period (7 months, multicentre evaluation and software V2 testing). Any breakdown, defect, malfunction or unexpected incident of the analysis system was recorded.

Practicability was assessed with the aid of a questionnaire [11] comprising ~200 questions or attributes which covered all important aspects of an analysis system in the clinical laboratory. The attributes were summarized into 14 groups, as shown in figure 7. They were related to the installation of the analyser, organization of work, quality assurance and miscellaneous characteristics.

The assessment was based on a scale from 1 to 10 for the instrument under evaluation as well as for the present laboratory situation. A score of 1 meant unimportant, useless or poor, and a score of 10, absolutely necessary or excellent. The meaning of score 5 was acceptable or comparable with the present laboratory situation. Additionally, a weight factor was assigned to each of the attributes. The factor ranged from 0 to 3 with the following meanings: 0, the attribute was not used during this assessment; 1, the attribute was unimportant for the laboratory; 2, the attribute was of general importance for the assessment; and 3, the attribute is very important for the evaluation site.

Table 3. Evaluation protocol.

Imprecision

Within-run
On 3 days, each day one run with 21 aliquotes.

- Two control materials (serum, plasma, urine) with different concentrations of the analyte.
- One human specimen pool at the decision level.

Between-day

- Two control materials with different concentrations of the analyte and one human pool (deep frozen and thawed) at the decision level over 11 days and subsequent 10 days in the main trial combining the two parts into one experiment. Precision is derived from the second of triplicate measurements.

Drift

- Two control sera and the calibrator are determined every 30 min during 8 h.
- At zero hour the base value is determined as the median of triplicate measurements.
- The percentage recovery from the base value is taken as the measure for drift effects.

Linearity

Protocol is based on Ref. [3].
Mixing of a high level with a low level specimen leads to:

- a dilution series of 11 concentration steps with nine dilution steps plus two basic concentrations;
- triplicate measurements of samples from the 11 concentration steps and calculation of the median for each step;
- calculation of the regression line (P/B-regression [7] using values of five concentrations, the range of which is assumed to be linear;
- calculation of the target values for all concentration steps from the regression line.

Carry-over

Sample-related
Model of Broughton [8]

- Measurements of five aliquots of a high-concentration sample $(h_1 \ldots h_5)$.
- Followed by measurements of five aliquots of a low-concentration sample $(l_1 \ldots l_5)$.

The experiments are repeated 10 times.
If a carry-over effects exists, the l_1 is the most influenced, l_5 the least influenced aliquot.
The sample-related carry-over—median $(l_1–l_5)$—is compared with the imprecision of the low-concentration sample.

Reagent-dependent
Assay A influences assay B.

- Carry-over caused by the cuvettes.
  Test A is pipetted into 21 cuvettes and the analyser is stopped. Assay B is performed in 42 cuvettes; the first 21 determinations may be influenced by assay A, the last 21 determinations are uninfluenced. The difference of the medians of both series is the carry-over.
- Carry-over caused by reagents probes and stirrers.
  Assay B is carried out 21 times. In a second step, test A and B are requested 21 times. The carry-over is the difference between the medians of both series.
  The carry-over effects are compared with the imprecision and the diagnostic relevance of assay B.

Interference

Protocol of Glick [9].
A serum with concentrations at the relevant decision level is spiked with the interfering substance, and a dilution series of 10 dilution steps is prepared with the same baselinee serum. The different analytes are measured in triplicate. The concentration of the interfering substance is related to the serum index of the instrument. The percentage recovery of the baseline value from the corresponding analyte is calculated for each dilution step.
The serum indices characterize the specimens according to haemolytic, icteric and lipaemic interference. The index for bilirubin and haemoglobin corresponds approximately to the concentration of these interferents, and the lipaemic index is related to the turbidity at 660/700 nm expressed at absorbance $\times$ 10.000.

Accuracy

Calibration.

- The calibrators of BM/Hitachi 917 and of the comparison instrument are both run on each instrument.

Quality control in two control materials.

- Assigned values for several substrate and electrolyte methods are related to reference methods.
- Median, calculated from the second of triplicate measurements on 21 days.

Interlaboratory survey.

- One control material with concentrations not known to the evaluators; assigned values for several substrate methods are related to reference methods.
- Median, calculated from the second of triplicate measurements over 10 days.

Standard reference material.

- For certain enzymes, substrate and electrolyte methods analysed on 1 day in triplicate measurements.

Method comparison in fresh human specimens.

- Five–15 specimens pr day depending on analytes for 10 days on BM/Hitachi 917 and on the comparison instruments. The total number of specimens cover the entire analytical range.
- Comparison of the methods by calculation of the Passing/Bablok regression line [7].

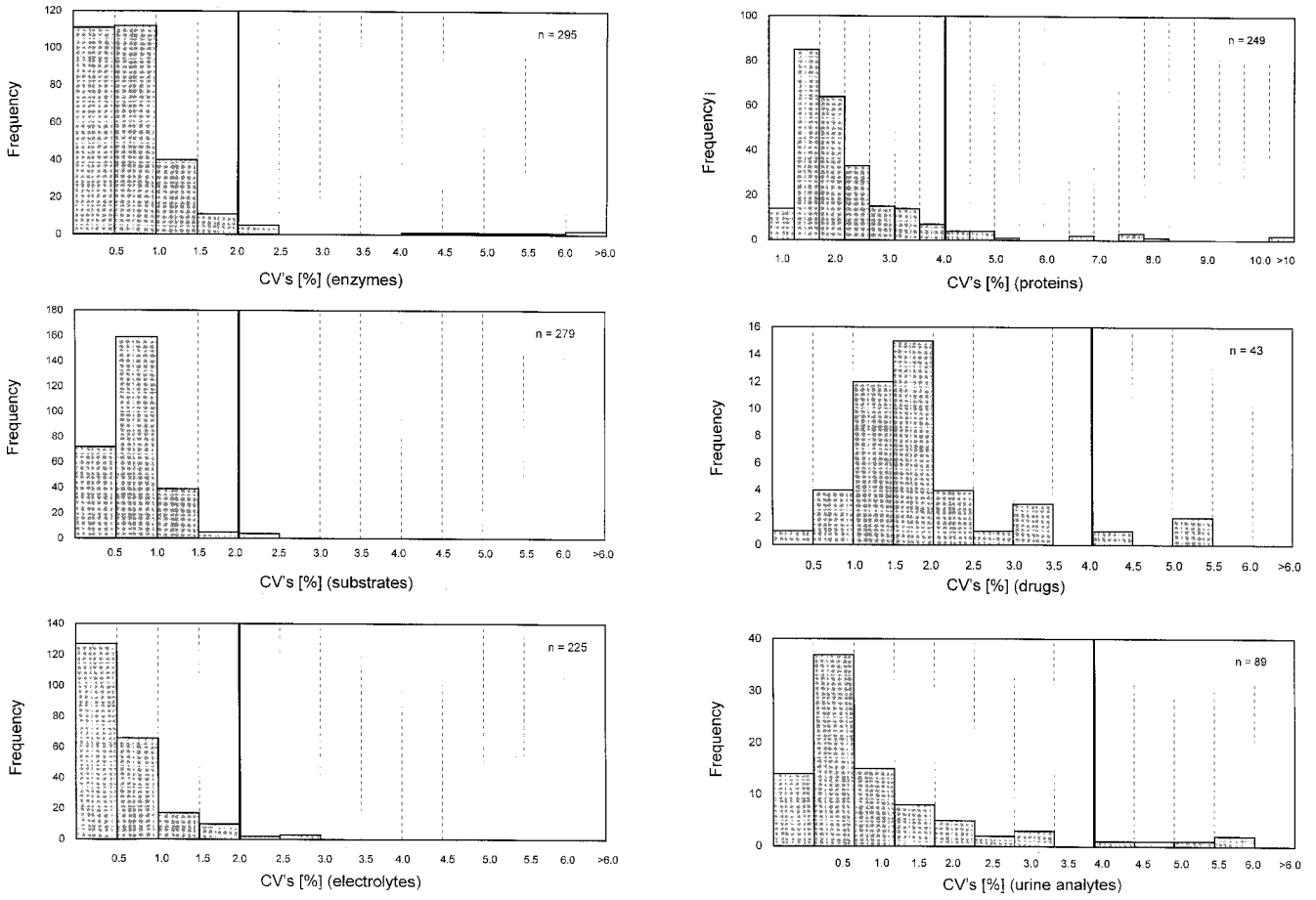

Figure 2. Within-run imprecision, frequency distribution of all CVs.

Quality specifications

The agreed acceptance criteria for imprecision are set up with a view to fulfilling requirements of the daily laboratory routine and statistical error propagation [12]; they are listed in table 4. Additionally, imprecision is judged on criteria based on within-subject biological variation according to Fraser *et al.* [13, 14]

The quality specifications for the within-run CV of the enzyme and substrate methods are derived from error propagation as shown in Ref. [12]. Due to the daily variation of the analysis system, one should expect a higher CV compared to the within-run CV. The ISE methods in general show a better reproducibility than the photometric assays. Drug and specific protein assays have very often low analytical sensitivity and many of them are calibrated by a non-linear mode; therefore, a CV twofold higher than that of the classical photometric determinations is reasonable. Because urine applications are performed in several cases with a sample predilution and are calibrated with the serum application volume ratio, which is not adequate for urine concentrations, an elevated CV can be expected.

Table 4. Acceptance limits for imprecision.

Analyte group	*Within-run CV(%)*	*Between-day CV(%)*
Enzymes	2	3
Substrates	2	3
ISE methods	1	2
Specific proteins	4	6
Drugs	4	6
Urine methods	4	6

The measuring range of a method should cover the greatest part of the physiological and pathophysiological range so that rerun analyses rarely will be necessary. In the upper range, a method is defined to be linear if the differences between the measured values and the target values from the dilution series are below 5%. In the lower range, the absolute differences are judged with respect to the diagnostic relevance. Methods with multipoint calibration are regarded as linear if a change in the target concentration leads to a corresponding change in the measured concentration [6].

Drift effects are not accepted if a systematic deviation from the initial value exceeds 3%.

Carry-over effects are assessed on the basis of the observed change in recovery of an analyte. Instead of adapting an individual deviation for each analyte, the within-run imprecision system performance is used which

Table 5. Within-run imprecision in a normal human serum, plasma or urine pool $(n = 21)$.

Analyte	*Unit*	*Concentration*	*CV (%)*
Alanine aminotransferase	U/l	49.4	0.5
Aspartate aminotransferase	U/l	44.9	1.0
Alkaline phosphatase	U/l	102	0.5
α-Amylase total	U/l	168	1.0
α-Amylase pancreatic	U/l	79.2	1.1
Creatine kinase	U/l	163	0.6
Creatine kinase MB	U/l	14.4	5.8
γ-Glutamyltransferase	U/l	42.2	1.2
Lactate dehydrogenase	U/l	446	0.3
Cholesterol	mmol/l	5.3	1.0
Creatinine	µmol/l	115	0.9
Glucose	mmol/l	6.32	1.0
Total protein	g/l	68.8	1.0
Uric acid	µmol/l	300	0.6
Urea	mmol/l	8.65	0.7
Calcium	mmol/l	2.33	0.6
Iron	µmol/l	13.7	2.0
Lactate	mmol/l	2.19	0.4
Sodium	mmol/l	143	0.4
Potassium	mmol/l	4.63	0.3
Chloride	mmol/l	106	0.9
Apolipoprotein A-1	g/l	1.29	1.4
Apolipoprotein B	g/l	1.05	0.5
Antistreptolysin O	IU/ml	85	1.8
D-dimer	mg/l	1.5	1.5
C-reactive protein	mg/l	7.6	3.0
Ferritin	µg/l	77.6	1.7
Haemoglobin A_{1c}	%	5.94	2.8
Immunoglobulin A	g/l	2.8	1.0
Immunoglobulin G	g/l	11.27	1.4
Immunoglobulin M	g/l	1.19	0.8
Rheumatoid factor	IU/ml	22.9	3.5
Thyroxine	nmol/l	104	2.2
Transferrin	g/l	3.2	0.7
Digoxin	µg/l	0.74	4.5
Digitoxin	µg/l	17.9	3.1
Phenobarbital	mg/l	24.6	0.8
Theophylline	mg/l	7.4	1.7
Albumin in urine	mg/l	16.3	3.0
α-1-Microalbumin	µg/l	7.2	2.2
Creatinine in urine	mmol/l	13	0.6
Glucose in urine	mmol/l	17.2	0.8
Uric acid in urine	µmol/l	2.5	1.4
Urea in urine	mmol/l	283	0.9
Magnesium in urine	mmol/l	3.7	1.4
Sodium in urine	mmol/l	43	0.5
Potassium in urine	mmol/l	68	0.3

means that a change of less than twice the standard deviation is accepted.

According to Glick *et al.* [9], a method is resistant to interference if the deviation between the baseline value and the measured value is less than 10%.

Accuracy is assessed in recovery experiments performed with certified reference materials, with control materials of which the assigned values are related to reference methods, and in method comparison experiments in which the comparison method is a reference method. A relative accuracy is obtained by the usual method comparison experiments related to the routine methods of the laboratory.

Results of the recovery experiments are defined as being acceptable if their deviations from the target values do not exceed more than $\pm$ 5% for enzymes and substrates, and $\pm$3% for the electrolyte methods calcium, chloride, potassium and sodium.

For the method comparisons, the acceptable range is defined for the slope and intercept of the regression equation. The slope should not deviate more than $\pm$5% from the identity line and the intercept should

Table 6. Linearity.

Analyte/Method	*Unit*	*Lab*	*Concentration tested*	*Linearity found*
Alanine aminotransferase	U/l	3	270	270
		BM*	440	310
Aspartate aminotransferase	U/l	3	340	340
		BM*	550	550
Alkaline phosphatase/IFCC	U/l	4	770	770
		BM*	2500	2500
α-Amylase total	U/l	6	1500	1500
		BM*	3200	3200
α-Amylase pancreatic	U/l	7	2100	2100
Creatine kinase	U/l	2	1750	1750
Creatine kinase MB	U/l	5	230	230
γ-Glutamyltransferase/IFCC	U/l	4	900	900
		BM*	1600	1600
γ-Glutamyltransferase/Szasz	U/l	7	1200	1200
		BM*	1800	1800
Lactate dehydrogenase/opt.	U/l	3	1060	1000
		BM*	1600	1300
Lactate dehydrogenase/SFBC	U/l	4	600	600
		BM*	1900	1900
Cholesterol	mmol/l	BM*	22.9	22.9
Creatinine	µmol/l	BM*	2100	2000
Glucose	mmol/l	6	53	53
Total protein	g/l	5	115	115
		BM*	190	190
Uric acid	µmol/l	1	1550	1550
		BM*	1800	1800
Urea	mmol/l	1	44	44
		BM*	70	70
Calcium	mmol/l	6	6.3	5.9
Iron	µmol/l	BM*	314	314
Lactate	mmol/l	2	16	15
Sodium	mmol/l	5	150	150
		BM*	300	300
Potassium	mmol/l	5	6.3	6.3
		BM*	15	15
Chloride	mmol/l	5	112	112
		BM*	270	270
Antistreptolysin O	IU/ml	1	580	560
C-reactive protein	mg/l	4	180	180
Ferritin	µg/l	3	400	400
Immunoglobulin A	g/l	2	8.6	8.6
Immunoglobulin G	g/l	2	40	40
		BM*	56	50
Immunoglobulin M	g/l	2	7.5	7.5
		BM*	10	10
Thyroxine	nmol/l	5	248	248
Transferrin	g/l	3	3.2	3.2
Digoxin	µg/l	6	7.5	7.5
Digitoxin	µg/l	1	44	44
Albumin in urine	mg/l	3	370	370
α-1-Microalbumin	µg/l	3	94	94
Calcium in urine	mmol/l	7	12	12
Creatinine in urine	mmol/l	7	32	32
Uric acid in urine	µmol/l	7	17	17
Urea in urine	mmol/l	7	950	950
Sodium in urine	mmol/l	7	220	220
Potassium in urine	mmol/l	7	93	93
Phosphorus in urine	mmol/l	7	100	100

* Evaluation data from Boehringer Mannheim.

be less than ±5% of the diagnostically important decision level. Due to the lower analytical sensitivity and the non-linear calibration mode of many of the homogeneous immunoassays, the acceptance limits for the method comparisons must be set higher. A deviation of ±10% for the slope is tolerated by the evaluators. Likewise, a deviation of ±10% from the decision or the detection limit is acceptable.

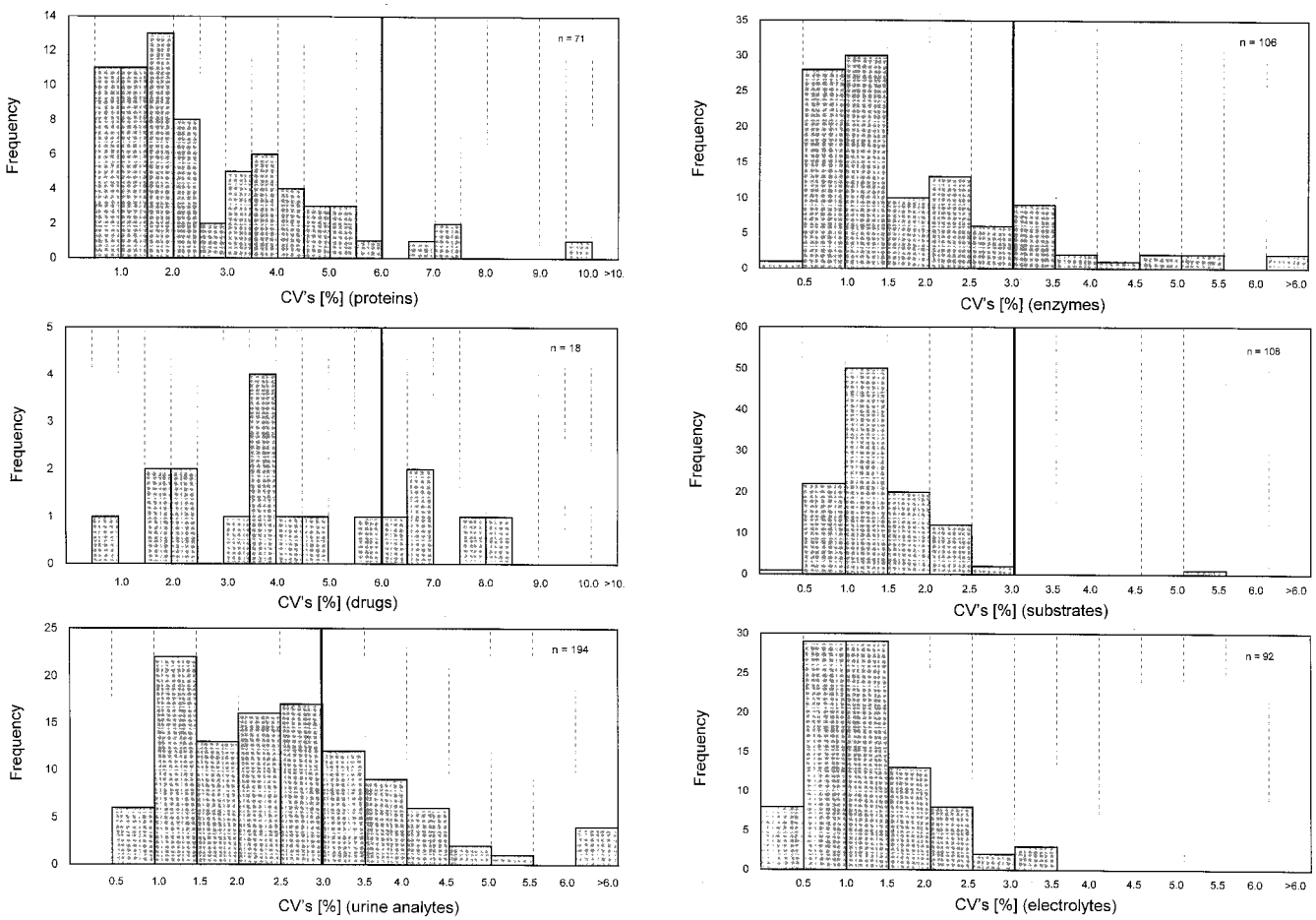

Figure 3. Between-day imprecision, frequency distribution of all CVs.

Table 7. Sample related carry-over.

Analyte	*Unit*	*Lab*	*Median high conc.*	*Median low conc.*	*Ratio h : l*	*Median* $I_1 - I_5$	*SD* I_3, I_4, I_5
Amylase total	U/l	6	10263	96	107	0	1.1
Creatine Kinase	U/l	7	3606	55	65.6	1	0.6
Ferritin	µg/l	1	7300	17.8	410	−0.3	0.5
Ferritin	µg/l	7	>900	80	>11	0.7	1.3
Albumin U/S	mg/l	3	40 000	27.2	1470	5.3	0.22
Creatinine U/S	mmol/l	3	15.2	0.12	127	0	0.003
Creatinine U/S	mmol/l	2	25.1	0.08	331	0	0.001
Creatinine U/S	mmol/l	5	20.1	0.1	201	0	0.003
Creatinine U/S	mmol/l	7	22.5	0.11	201	0	0.001
Potassium U/S	mmol/l	3	150	3.89	38	0.05	0.012
Potassium U/S	mmol/l	3	150	4.02	37	0.04	0.009
Potassium U/S	mmol/l	5	124	4.14	30	0.03	0.027

U = urine; S = serum.

Assessment of the ISE methods in serum or plasma cannot be achieved according to the above-mentioned criteria. Due to the narrow physiological range, especially of sodium and chloride, a relatively large confidence interval for the regression line is obtained. Therefore, method comparisons are judged by the concentration range in which the difference between the methods is less than 3%.

Sodium: 120–170 mmol/l.
Potassium: 2–10 mmol/l.
Chloride: 80–130 mmol/l.

Results

Imprecision

Acceptance criteria were based on statistical error propagation [12] (see table 4) . Within-run distribution of all CVs measured for all analytes are shown in figure 2, additionally the median CVs for within-run imprecision in a human serum and urine pool are presented in table 5. The medians of all analytes met the acceptance criteria, except for creatine kinase MB isoform (CV of 5.8% in the human serum pool), lipase (CV of 5.2% in the human

Table 8. Endogeneous interferences.

Analyte	*Haemolysis*	*Icterus*	*Lipaemia*
Alanine aminotransferase	↑		
Aspartate aminotransferase	↑↑↑*	↑	↑
α-Amylase total	↑		
α_Amylase pancreatic			↑
Creatine kinase	↑↑	↑	
Creatine kinase MB		↑↑	
γ-Glutamyltransferase	↑↑	↑	
Lipase	↑↑		
Lactate dehydrogenase	↑↑↑*		
Cholesterol		↑	
Creatinine PAP		↑↑↑	
Total protein	↑	↑	
Uric acid		↑↑	
Calcium		↑	
Iron	↑↑*		
Potassium	↑↑*		
D-dimer	↑↑		
C-reactive protein		↑	

* Present in erthyrocytes.

serum pool), digoxin (4.5% in the human serum pool) and albumin in urine (4.3%). In individual control sera results exceeding the acceptance limits were obtained for ALAT (2.1%), creatinine (2.4%), chloride (2.8%) and glycosylated haemoglobin (4.3%).

The distribution of all CVs measured in all sera for between-day imprecision are presented in figure 3. The medians met the defined quality specifications for the majority of analytes. The acceptance limits for median CV were exceeded for creatine kinase (3.3% in the human serum pool), creatine kinase MB isoform (9.4% in the human serum pool), lipase (4.5% in control serum 2 and 4.8% in the human serum pool), D-dimer (6.6% in control serum 1), glycosylated haemoglobin (6.9% in control serum 2), rheumatoid factors (9.8% in control serum 2), digoxin (7.8% in the human serum pool), digitoxin (6.6% in control serum 1 and 8.4% in the human serum pool), theophylline (6.7% in the human serum pool) and albumin in urine (up to 23% below 10 mg/l). In individual control sera, results exceeding the quality specifications could be seen for alkaline phosphatase (3.6%) and chloride (up to 3.2%).

Additionally, the data related to within-day imprecision are judged by the maximum allowable imprecision based on within-subject biological variation according to Fraser *et al.* [13, 14]. Median CVs for between-day imprecision were within these criteria for all analytes except for sodium (1.0%), chloride (1.6%), digoxin (8.4%) and phenobarbital (3.9%).

Analytical range limit

In table 6, the results of the assessment of linearity are presented. A wide linearity range was obtained for all clinical chemistry analytes, covering the greatest part of the clinical relevant range. All results were within the specifications of the manufacturer.

Drift

Drift effects were not accepted if a systematic deviation from the initial value exceeded 3%. No drift effects were observed over an 8 h period in any of the methods tested.

Carry-over

In table 7, the results of the sample carry-over testing are presented. If the carry-over is less than twice the standard deviation of the analyte tested, the results are judged as being acceptable. As can be seen from table 7, all results are acceptable except albumin in urine. The carry-over of 5.3 mg/l is not only exceeding twice the standard deviation (0.44 mg/l), but also the criteria of the manufacturer (1 mg/l). Considering the reagent-dependent carry-over, there was a significant probe carry-over in two out of seven laboratories (ALAT/LDH) and a cuvette carry-over (TG/LIP) in one out of seven laboratories. This could be explained by sub-optimal wash procedures in the analysers concerned.

Interferences

According to Glick *et al.* [9], a method is resistant to interferences if the deviation between the baseline value and the measured value is below 10%. The methods not fulfilling these criteria are presented in table 8.

Accuracy

The results of the recovery experiments in the certified reference materials are presented in figure 4. As can be seen, the results for enzymes (95.3–103.9%) are all within the 95–105% range. Considering the substrates and electrolytes there was a good performance except for creatinine, urea and chloride. Creatinine showed a recovery up to 120% in SRM 909 a-1 and a recovery of only 93% in SRM 909 a-2. The recovery for urea is only slightly above the tolerance limits (105.8%) and therefore not very relevant. The recovery for chloride is significantly different between the two laboratories concerned. This is possibly caused by a lot-to-lot variability.

The results for the recovery in the interlaboratory survey are presented in figure 5. The analytes outside the recovery limits for the reference materials also show results exceeding the limits in the interlaboratory survey. Additionally, results for alanine aminotranferase, aspartate aminotranferase, pancreatic amylase, cholesterol and glucose were not within the quality specifications for all laboratories.

Method comparison

In total, 160 method comparison studies were performed, using fresh human sera or urines; representative regression equations of each group of analytes are shown in figure 6. Additional regression data are available on request.

For cholesterol and creatinine, the results are compared to both routine and reference methods. As can be seen from figure 6, cholesterol meets the acceptance criteria if

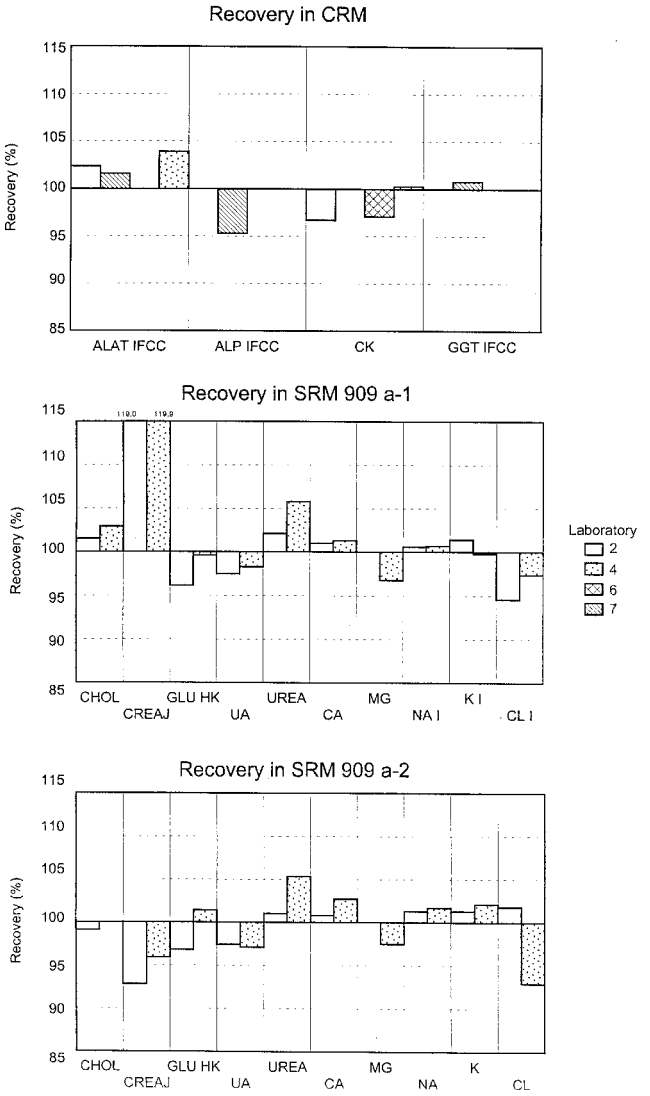

Figure 4. Accuracy CRM/NIST.

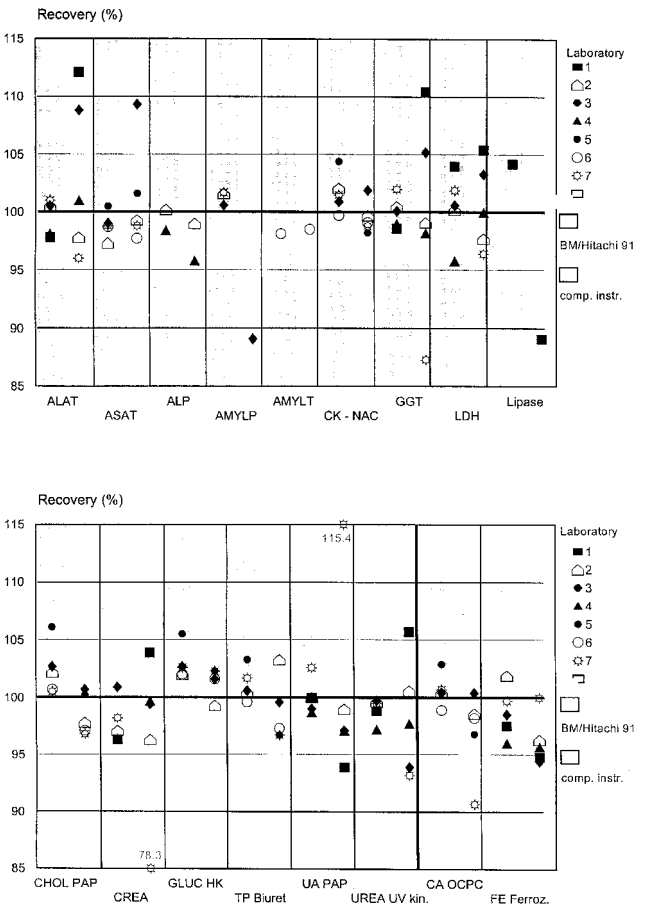

Figure 5. Interlaboratory survey.

compared to the Abell Kendall reference method, but creatinine on the BM/Hitachi 917 is inaccurate if compared to the HPLC reference method. For all other analytes, regression data do show an acceptable regression equation with the exception of ASAT, ALAT, sodium, chloride and glycosylated haemoglobin in some laboratories.

Reliability

Reliability during the evaluation phase was rated with the aid of a logbook in which all aspects of interest were recorded.

As a result of all logbooks, only a few problems or incidents have to be mentioned here. In one laboratory, the liquid level detection for reagent pipetting appeared to work incorrectly just before a reagent bottle change-over leading to an incorrect result without any flag. This error could not be reproduced during the further study.

The motor of the operation unit stand was defect at one site. As a consequence, the screen could not be adjusted correctly to the height of the operator. The defect was repaired by exchanging the motor. A further laboratory reported an alarm of abnormal ISE syringe movement which was observed only once.

Assessment of practicability

The practicability of the BM/Hitachi 917 was judged in comparison with the present situation in the evaluating laboratories. The median of all laboratories was calculated from the mean of all scores obtained from each group of attributes. These results are shown in figure 7. More detailed information on the distribution of scores in relation to the main topics is given in figure 8.

Discussion

The new selective access analysis system BM/Hitachi 917 was evaluated in an international multicentre study, mainly according to the ECCLS criteria for the evaluation of analysers in clinical chemistry. Forty-three different analytes, covering 56 different methods—enzymes, substrates, electrolytes, specific proteins, drugs and urine applications—were tested in seven European clinical chemistry laboratories. Additionally, the practicability of the BM/Hitachi 917 was tested according to a standardized questionnaire.

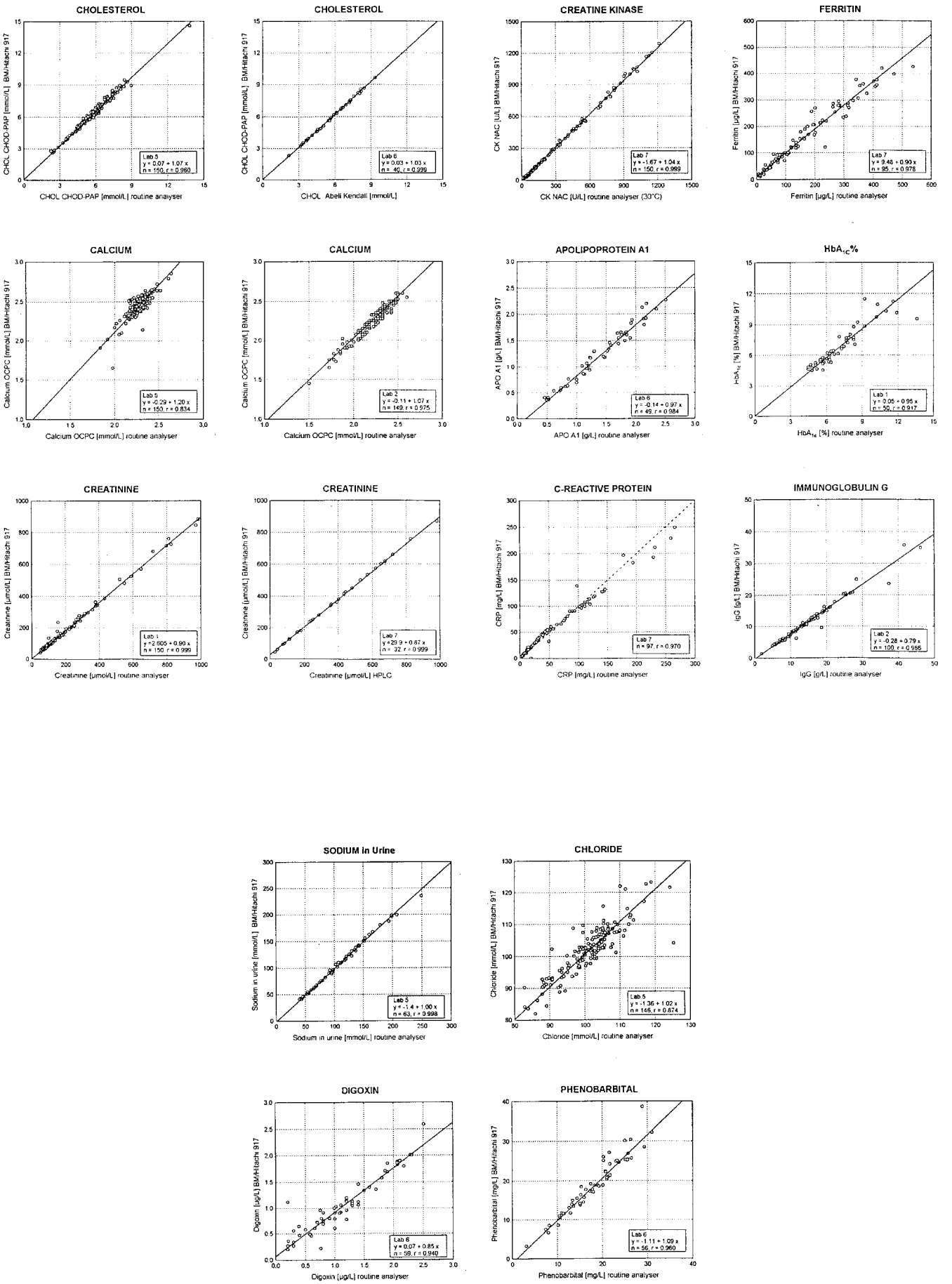

Figure 6. Method comparison.

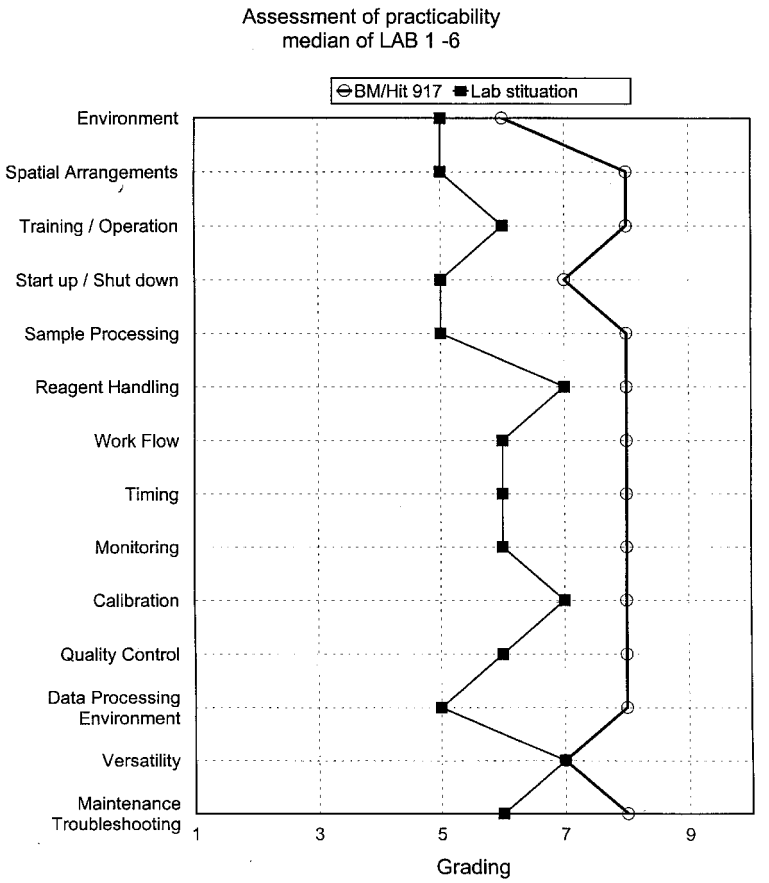

Figure 7. Assessment of practicability (median of scores).

A good performance was found for most of the analytes in all laboratory sections using different sample materials of serum, plasma and urine. Although some of the analytes did not fulfil the acceptance criteria, none could be rated as unacceptable. With more than 120 000 individual data, it is impossible to discuss all the results, we therefore selected mainly the results outside the acceptance criteria for discussion.

Regarding the analytical evaluation, and starting with the precision study, we found very satisfying results overall with only a few exceptions (see tables 4 and 5). In the enzyme, substrate and electrolyte section, we only found two outlying results with the human pool sample in measuring the within-run imprecision, maybe because of the (low) concentration of creatine-kinase MB and lipase. For proteins, drugs and urine analytes, all within-run median CV results were lower than 4%, except for digoxin (4.5%) and albumin in urine (4.3%)

Concerning the between-day CVs, here too, very few results exceeding the acceptance limits were observed, i.e. lipase, creatine-kinase and MB isoform, D-dimer, glycosylated haemoglobin, rheumatoid factor, digoxin, digitoxin, theophylline and albumin in urine in some materials. In all situations, the comparison methods gave equivalent results with the exception of glycosylated haemoglobin.

Comparing the results of the between-day imprecision measurements with the Fraser criteria based on within-subject biological variation [13, 14], it is justified to say that the BM/Hitachi 917 achieved these criteria for all analytes except sodium, chloride, digitoxin and phenobarbital. For sodium and chloride it should be stated that the biological varition is that low that no available technology of today can fulfil these criteria.

The linearity, drift and carry-over study showed results all satisfying the test specifications. One exception is the carry-over effect of 5.3 mg/l albumin in urine, which is beyond the acceptance limits of 1.0 mg/l specified by the manufacturer. Measurements performed on two instruments at Boehringer Mannheim resulted in a carry-over effect of 1.7 mg/l, which still requires the use of a evasion procedure.

The interference results are given in table 8, clearly showing that also for the BM/Hitachi 917 interference exists sometimes, as could be expected because of the chemistries applied. It is a situation that can be found in equivalent analysers as well [2].

The method comparisons were often performed with other Hitachi instruments except for the exoteric tests. Most of the 160 comparisons showed acceptable agreement. Nevertheless, some deviations were found, also caused by discrepancies in the evaluation group methods. Striking examples in this respect are ASAT, ALAT, chloride, sodium and HbA1c (results not shown). The question arises whether the tolerance limits (see Introduction) are applicable here.

Further, we want to point out some exceptional results. It was, e.g. remarkable that creatinine deviated in the

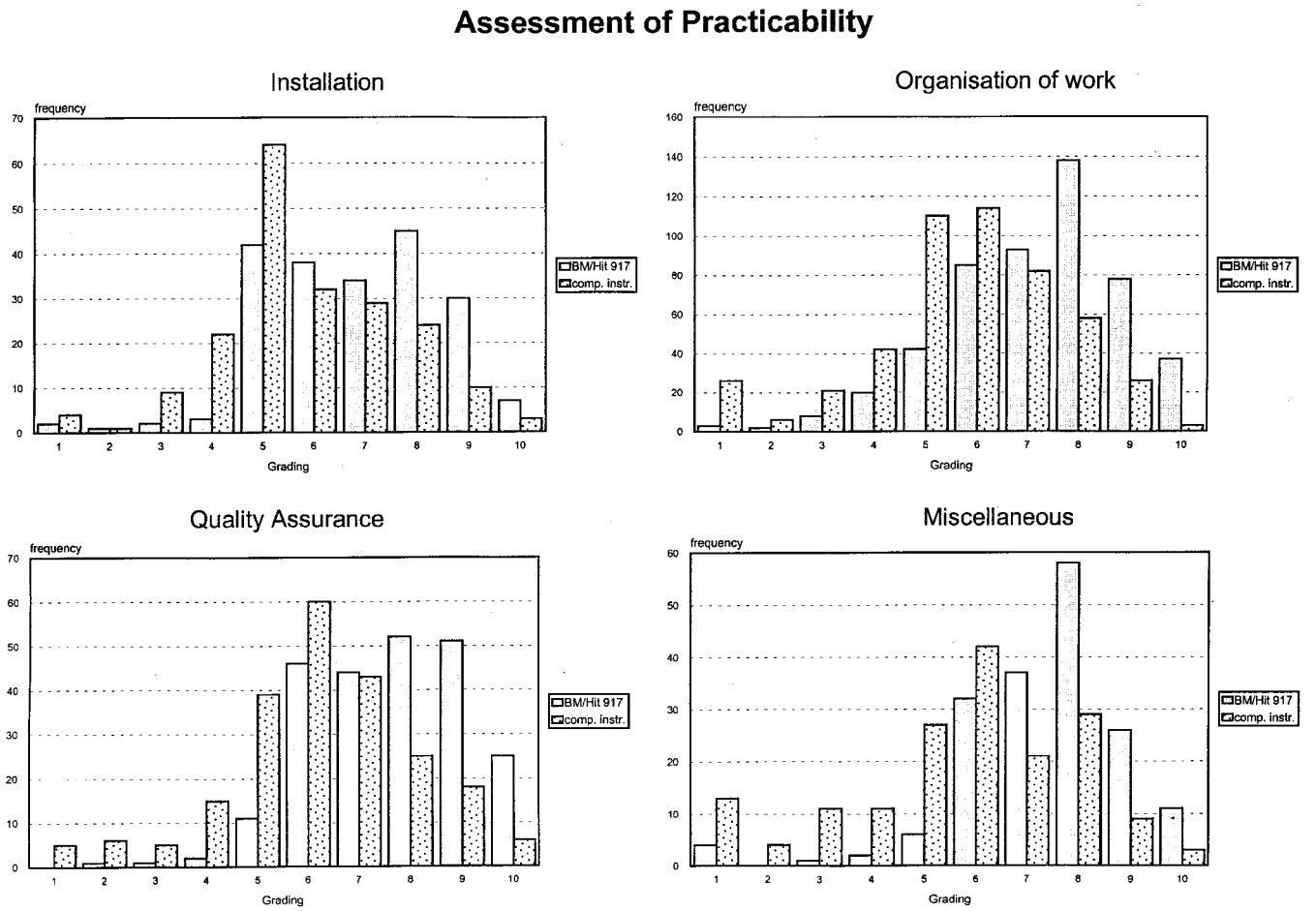

Figure 8. Assessment of practicability (distribution of scores of the main attribute groups).

comparison with the HPLC reference method (see figure 6). This deviation was also found in the NIST materials. According to the information of the manufacturer, this problem is under study now. C-reactive protein also showed a remarkable picture: results lower than 100 mg/l showed a different regression equation from results higher than 100 mg/l (see figure 6). We have no explanation for this phenomenon. The regression equations and figures of all additional analytes are available on request.

In a multicentre evaluation, usually the main interest is the evaluation of the analytical performance. Additional to that performance, we thoroughly tested reliability and practicability of the BM/Hitachi 917 as well. Particulary in those stages of the evaluation, the analyser appeared to be a multi-purpose analyser with benefits exceeding those of comparable analysis systems. As can be seen from figure 7, the assessment of practicability for 14 groups of attributes resulted in a grading of one–three scores better for BM/Hitachi 917 than the present laboratory situation.

The system offers features making it attractive to different purposes and different sections in clinical chemistry. It can either be used as a high-throughput analyser for the basic clinical chemistry tests, or as a consolidated workstation for the determination of at least 48 different analytes (on board), covering besides the classical routine assays, specific protein methods, drug methods in serum and urine, and urinalysis applications for enzymes, substrates, electrolytes and proteins.

In the opinion of the authors, laboratory consolidation in combination with laboratory automation is the future of clinical chemistry. The BM/Hitachi 917 therefore can not only be seen as a valuable analyser for the laboratories of today, but also fits in the organizational structures of the future.

Notes

(1) Most of the practical work was performed during 1996, part of it in early 1997.

(2) Despite the 1998 takeover of Boehringer Mannheim by Roche, we used the term BM/Hitachi 917 because of its wide international acceptance.

Acknowledgment

The authors would like to thank all technical personnel at the various locations for their valuable and dedicated support.

Table 9. Control and standard reference materials.

Short name	*Description*	*Lot. no.*	*Experiments*
CAL	Calibrator routine		BI
CFAS	Cfas, H917 calibrator	187184-01	BI, D
CFAS-PROT	Cfas Protein, H917 calibrator	187044-01	BI
COMP	Compensator for H917/ISE	186654-61	BI
COMP-R	Compensator for Routine		BI
PM RF	Precimat RF	653015-01	
PNU	Control Serum PNU	182658-01	WI, BI, D
PPU	Control Serum PPU	186269-02	WI, BI, D, CO-C/P
PN CK-MB	Precinorm CK-MB	184932-61	WI, BI, QC
PN PROT	Precinorm Protein	185861-03	WI, BI, QC
PP PROT	Precipath Protein	186653-01	WI, BI, QC
PN L	Precinorm Lipid	185597-01	WI, BI, QC
PP L	Pricipath Lipid	183253-64	WI, BI, QC
PN RF	Precinorm RF	654570-01	WI, BI, QC
PN S	Precinorm S	174973-72	WI, BI, QC
PP S	Precipath S	181413-64	WI, BI, QC
PN HBA1C	Precinorm HBA1C	187821-01	WI, BI, QC
PP HBA1C	Precipath HBA1C	187820-01	WI, BI
C1 D-DIMER	Control 1 D-Dimer	655266-01	WI, BI
C2 D-DIMER	Control 2 D-Dimer	655266-01	WI, BI
TDM II	PN TDM, level II	186618-01	WI, BI, QC
TDM III	PN TDM, level II	186618-01	WI, BI
SRM	Ring Trial sample for substrates and electrolytes	909A	QA
QC PNU	Control Serum PNU	185229-08	QC
QC PPU	Control Serum PPU	179000-05	QC
QC RT	QC Ring Trial	187746 Cfas	QA
CRM 426	Ring Trial sample for ALAT		QA
CRM 371	Ring Trial sample for ALP		QA
CRM 299	Ring Trial sample for CK		QA
CRM 319	Ring Trial sample for GGT		QA
HPP	Human plasma pool		WI, BI, Lin
HPP-SAT	Human plasma pool for satellite analytes		WI, BI
HSP	Human serum pool		WI, BI, Lin
HEMOLYSATE	Human hemolysed blood		WI, BI, Lin
HSP-CKMB	Human serum pool with CK-MB		WI, BI, Lin
HSP-DIGOX	Human serum pool with Digoxin		WI, BI, Lin
HSP-PHEBA	Human serum pool with Phenobarbital		WI, BI, Lin
HSP-SAT	Human serum pool for satellite experiments		WI, BI, Lin
HSP-THEO	Human serum pool with Theophylline		WI, BI
HP	Human plasma		MC, I, CO-S
HS	Human serum		MC, I, CO-S
HS-CKMB	Human serum with CK-MB		MC, I
HS-DIGIT	Human serum with digitoxin		MC, I
HS-DIGOX	Human serum with digoxin		MC, I
HS, PHEBA	Human serum with Phenobarbital		MC, I
HS-THEO	Human serum with Theophylline		MC, I
CT A1	Control alpha 1 Microglobulin	Eval. Lot.	WI, BI
PN A1	Precinorm alpha 1 Microglobulin	Eval. Lot.	WI, BI
LYPHO1	Lyphocheck 1	62021	WI, BI, QC
LYPHO2	Lyphocheck 2	62022	WI, BI, QC
PN ALB	Precinorm Albumin	186312-01	WI, BI, QC
PP ALB	Precipath Albumin	187289-01	WI, BI
HUP	Human urine pool		WI, BI
HU	Human urine		MC, CO-S

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