IGG-2

cobas®

Tina-quant IgG Gen.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
08057915190	08057915500	Tina-quant IgG Gen.2 (300 tests)	System-ID 2074 001	**cobas c** 303, **cobas c** 503, **cobas c** 703

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 20656	
03121305122	Calibrator f.a.s. PUC (5 x 1 mL)	Code 20489	
03121313122	Precinorm PUC (4 x 3 mL)	Code 20240	
03121291122	Precipath PUC (4 x 3 mL)	Code 20241	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 20391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 20391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 20392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 20392	
08063494190	Diluent NaCl 9 % (123 mL)	System-ID 2906 001	

English

System information

IGG2: ACN 20740 (Standard application for serum and plasma)

IGG2U: ACN 20743 (Sensitive application for urine)

IGG2C: ACN 20741 (Sensitive application for cerebrospinal fluid)

Specific applications for Reiber diagnostic*

IGG2-SR: ACN 20744 (application in serum/plasma)

*not available in all countries

Intended use

In vitro test for the quantitative determination of IgG in human serum, plasma, cerebrospinal fluid and urine on **cobas c** systems.

Intended use of the specific applications for Reiber diagnostic*

*not available in all countries

In vitro test for the quantitative determination of IgG specifically in human cerebrospinal fluid and corresponding human serum/plasma on **cobas c** system.

Summary

Immunoglobulin G (IgG) measurements performed with this assay in human serum and plasma are used as an aid in diagnosis of clinical conditions associated with increased IgG levels, such as infections and inflammatory diseases, and with decreased IgG levels, such as IgG deficiencies.

IgG measurements performed with this assay in human urine are used in the assessment of increase or decrease of IgG excretion, such as proteinuria.

IgG measurements performed with this assay in human cerebrospinal fluid (CSF) are used as an aid in diagnosis of neurological diseases.

Immunoglobulins (Ig) or antibodies are glycoproteins produced by plasma cells to protect the human body against invading organisms and agents. Human immunoglobulin molecules consist of one or more basic units built of two identical heavy (H) chains and two identical light (L) chains. Each of the four chains has one variable and one (L chain) or three to four (H chain) constant domains. Diversity in the variable domains is generated by somatic recombination and mutation of the immunoglobulin genes. Individual plasma cells or clonally expanded cells are committed to synthesis of a single variable domain sequence for H and L chains. The variable domains contain the antigen binding regions and the constant domains of the heavy chains contain sites for complement activation and receptor binding. Cleavage of immunoglobulins with pepsin or papain can yield antigen binding fragments (Fab) and constant region fragments (Fc). The Fab portion recognizes antigens in solution (e.g. toxins) and antigens associated with microorganisms (e.g. bacteria, viruses). The Fc portion interacts with cells of the immune system and complement factors. Antigen binding initiates the direct neutralization of toxins, the sensitization of immunocompetent cells, the reduction of viral infectivity, or the development of an inflammatory reaction. Variations in the Fc region result in the classes and subclasses into which immunoglobulins are grouped: IgM, IgG (four subclasses), IgA (two subclasses), IgD, and IgE, respectively. As a normal result of infections all immunoglobulin classes increase in serum.[1]

The molecular weight of IgG is approximately 150 kDa, including one N-linked oligosaccharide on each heavy chain.[1] IgG accounts for 70 to 75 % of the total immunoglobulins in plasma;[1] its main tasks are the defense against microorganisms, direct neutralization of toxins and induction of complement fixation.[2,3] IgG is the only immunoglobulin that can cross the placental barrier and provide passive immune protection for the fetus and newborn.[4,5] Passively derived maternal IgG is the source of virtually all of the IgG subclasses detected in the fetus and neonate. At 2 months of age, IgG synthesized by the neonate and that derived from the mother are approximately equal. By 10 to 12 months of age, the IgG is nearly all derived from synthesis by the infant, and by 1 year of age, the total IgG concentration is approximately 60 % of that in adults.[6]

Increases of polyclonal immunoglobulins (including IgG) in serum/plasma are the normal response to infections. IgG increases may additionally be associated with chronic inflammatory conditions, including systemic lupus erythematosus, cystic fibrosis, cirrhosis and autoimmune hepatitis.[1,7,8,9] Monoclonal IgG increases in diseases where neoplastic proliferation of secretory B cells is present, such as multiple myeloma.[1]

Decreased levels of IgG can be due to reduced synthesis, increased loss, hypercatabolism or a combination of causes. IgG deficiencies occur in congenital and acquired immunodeficiency syndromes, inherited deficiencies, hematologic malignancies.[1,10,11]

The determination of urine IgG aids, in combination with urinary albumin, to separate selective forms from unselective forms of tubular proteinuria, since IgG is markedly increased only in unselective forms of glomerular proteinuria (IgG/albumin > 0.03 mg/mg). Additionally, measurements of IgG in urine can be used in the monitoring and assessment of glomerular proteinuria.[12,13]

In CSF, disease-related changes of the immunoglobulin patterns (IgG, IgA, IgM with reference to albumin) allow for the differential diagnosis of neurological disorders. The diffusion of proteins through the blood-brain barrier normally occurs at a steady rate which is influenced by the permeability of the blood-brain barrier and CSF flow rate.[14] Changes in protein and immunoglobulins concentrations in the CSF can be an indication of infections involving the central nervous system (CNS), neoplasms or primary neurologic diseases. Specifically, elevated levels of IgG in CSF are often associated with opportunistic infections of the CNS, neurotuberculosis, or multiple sclerosis.[1,14,15] Increased CSF IgG concentrations may occur because of either increased permeability of the blood-brain barrier or local/intrathecal production of IgG, or both. Malfunction of the blood-brain barrier can be reliably quantified by means of the albumin CSF/serum ratio. An elevated albumin ratio is an indication of a disorder of the blood-brain barrier. If IgG and albumin are measured in CSF and serum simultaneously, differentiation between IgG originating from blood and IgG originating from intrathecal production is possible.[1,14,15]

To determine the intrathecal IgG production, several formulae have been proposed and evaluated. The linear IgG index has been broadly used in the past because of its simplicity, but it has been replaced by non linear formulae, such as Reiber's hyperbolic formula that better reflects human neurophysiology.[16] The most informative method indicating intrathecal synthesis of IgG is the qualitative demonstration of two or more CSF-specific oligoclonal bands.[17]

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This assay is based on the principle of immunological agglutination. In addition to the standard application (IGG2), there are sensitive applications (IGG2C and IGG2U) designed for the quantitative determination of IgG in CSF and urine.

It is known that the so-called paraproteins secreted in monoclonal gammopathies (monoclonal immunoglobulinemia) may differ from the respective immunoglobulins of polyclonal origin by amino acid composition and size.[1] This may impair the binding to antibody and hence impair accurate quantitation.

Test principle

Immunoturbidimetric assay.

Anti-IgG antibodies react with antigen in the sample to form an antigen/antibody complex. Following agglutination, this is measured turbidimetrically. Addition of PEG allows the reaction to progress rapidly to the end point, increases sensitivity, and reduces the risk of samples containing excess antigen producing false negative results.

Reagents - working solutions

R1	TRIS buffer: 20 mmol/L, pH 8.0; NaCl: 200 mmol/L; polyethylene glycol: 3.6 %; preservative; stabilizers
R3	Anti-human IgG antibody (goat): dependent on titer; TRIS buffer: 20 mmol/L, pH 8.0; NaCl: 150 mmol/L; preservative

R1 is in position B and R3 is in position C.

Precautions and warnings

For in vitro diagnostic use for health care professionals. Exercise the normal precautions required for handling all laboratory reagents.

Infectious or microbial waste:
Warning: handle waste as potentially biohazardous material. Dispose of waste according to accepted laboratory instructions and procedures.

Environmental hazards:
Apply all relevant local disposal regulations to determine the safe disposal.

Safety data sheet available for professional user on request.

This kit contains components classified as follows in accordance with the Regulation (EC) No. 1272/2008:

Danger

H318	Causes serious eye damage.

Prevention:

P280	Wear eye protection/ face protection.

Response:

P305 + P351 + P338 + P310	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.

Product safety labeling follows EU GHS guidance.

Contact phone: all countries: +49-621-7590

Reagent handling

Ready for use

Storage and stability

Shelf life at 2-8 °C:	See expiration date on **cobas c** pack label.
On-board in use and refrigerated on the analyzer:	26 weeks

Specimen collection and preparation

For specimen collection and preparation only use suitable tubes or collection containers.

Only the specimens listed below were tested and found acceptable.

For Reiber diagnostic, pairs of CSF/serum or CSF/plasma should be collected at the same time.

Serum/plasma application (IGG2, IGG2-SR)
Serum
Plasma: Li-heparin and K_2-EDTA plasma

Urine application (IGG2U)

Urine.

CSF application (IGG2C)
Cerebrospinal fluid

The sample types listed were tested with a selection of sample collection tubes that were commercially available at the time of testing, i.e. not all available tubes of all manufacturers were tested. Sample collection systems from various manufacturers may contain differing materials which could affect the test results in some cases. When processing samples in primary tubes (sample collection systems), follow the instructions of the tube manufacturer.

Centrifuge samples containing precipitates before performing the assay.

See the limitations and interferences section for details about possible sample interferences.

Serum and plasma

Stability:[18]	4 months at 15-25 °C
	8 months at 2-8 °C
	8 months at -20 °C (±5 °C)

Freeze only once.

Urine

Spontaneous, 24-hour urine or 2nd morning urine. Centrifuge the urine samples for 10 min at ≥ 800 g.

Stability:[19]	7 days at 15-25 °C
	1 month at 2-8 °C
	Storage at -20 °C (±5 °C) is not recommended.

CSF

Samples should be as fresh as possible. Centrifuge samples containing particles and/or cells before performing the assay.

Stability:[18]	1 day at 15-25 °C
	7 days at 2-8 °C
	Storage at -20 °C (±5 °C) is not recommended.

Materials provided

See “Reagents – working solutions” section for reagents.

Materials required (but not provided)

See “Order information” section

General laboratory equipment

Assay

For optimum performance of the assay follow the directions given in this document for the analyzer concerned. Refer to the appropriate operator’s manual for analyzer-specific assay instructions.

The performance of applications not validated by Roche is not warranted and must be defined by the user.

Application for serum and plasma (IGG2)

Test definition

Reporting time	10 min	
Wavelength (sub/main)	700/340 nm	
Reagent pipetting		Diluent (H_2O)

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R1	77 µL	–	
R3	24 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	3.2 µL	5 µL	100 µL
Decreased	2.3 µL	1.6 µL	133 µL
Increased	6.4 µL	15 µL	69 µL

Application for urine (IGG2U)

Test definition

Reporting time	10 min		
Wavelength (sub/main)	700/340 nm		
Reagent pipetting		Diluent (H_2O)	
R1	72 µL	–	
R3	23 µL	–	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	8.7 µL	–	–
Decreased	8.7 µL	10 µL	90 µL
Increased	8.7 µL	–	–

Application for CSF (IGG2C)

Test definition

Reporting time	10 min		
Wavelength (sub/main)	700/340 nm		
Reagent pipetting		Diluent (H_2O)	
R1	95 µL	–	
R3	8 µL	16 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	11.5 µL	–	–
Decreased	11.5 µL	20 µL	80 µL
Increased	11.5 µL	–	–

For further information about the assay test definitions refer to the application parameters screen of the corresponding analyzer and assay.

Specific applications for Reiber diagnostic*

*not available in all countries

Application for sample type serum and plasma (IGG2-SR)

Test definition

Reporting time	10 min		
Wavelength (sub/main)	700/340 nm		
Reagent pipetting		Diluent (H_2O)	
R1	95 µL	–	
R3	8 µL	16 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	2.3 µL	2 µL	98 µL
Decreased	2.3 µL	2 µL	98 µL
Increased	2.3 µL	2 µL	98 µL

For further information about the assay test definitions refer to the application parameters screen of the corresponding analyzer and assay.

Application for sample type CSF (IGG2C)

Test definition

Reporting time	10 min		
Wavelength (sub/main)	700/340 nm		
Reagent pipetting		Diluent (H_2O)	
R1	95 µL	–	
R3	8 µL	16 µL	
Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	11.5 µL	–	–
Decreased	11.5 µL	20 µL	80 µL
Increased	11.5 µL	–	–

Calibration

Application for serum/plasma (IGG2):

Calibrators	S1: H_2O S2-S6: C.f.a.s. Proteins
Calibration mode	Non-linear
Calibration frequency	Automatic full calibration - after reagent lot change Full calibration - as required following quality control procedures

Application for urine (IGG2U) and CSF (IGG2C) :

Calibrators	S1: H_2O S2-S6: C.f.a.s. PUC
Calibration mode	Non-linear
Calibration frequency	Automatic full calibration - after reagent lot change Full calibration - as required following quality control procedures

Calibration of the specific applications for Reiber diagnostic.

Application for serum/plasma (IGG2-SR)

Transfer of calibration from CSF application (IGG2C)

Calibration interval may be extended based on acceptable verification of calibration by the laboratory.

Traceability: This method has been standardized against the certified reference material in human serum of the IRMM (Institute for Reference Materials and Measurements) ERM-DA470k/IFCC.

Quality control

For quality control, use control materials as listed in the "Order information" section.

IGG2, IGG2-SR: (Serum/plasma): PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2

IGG2U : (Urine) Precinorm PUC, Precipath PUC

IGG2C , IGG-C: (CSF) Precinorm PUC, Precipath PUC

In addition, other suitable control material can be used.

The control intervals and limits should be adapted to each laboratory's individual requirements. Values obtained should fall within the defined limits. Each laboratory should establish corrective measures to be taken if values fall outside the defined limits.

Follow the applicable government regulations and local guidelines for quality control.

Calculation

Serum/plasma

cobas c systems automatically calculate the analyte concentration of each sample in the unit g/L (µmol/L, mg/dL, mg/L).

Conversion factors: g/L × 6.67 = µmol/L
g/L × 100 = mg/dL
g/L × 1000 = mg/L

Urine and CSF

Urine: **cobas c** systems automatically calculate the analyte concentration of each sample in the unit mg/L (nmol/L).

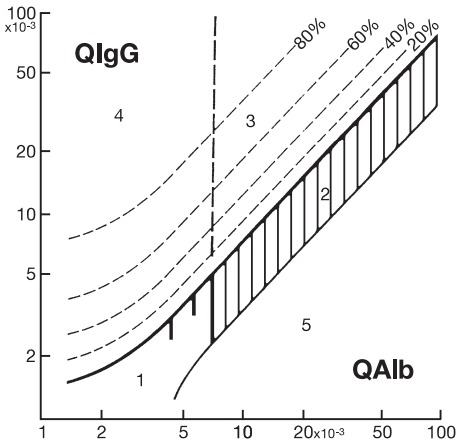
CSF: **cobas c** systems automatically calculate the analyte concentration of each sample in the units mg/L (nmol/L, g/L, mg/dL).

Conversion factors: mg/L × 6.67 = nmol/L
mg/L × 0.001 = g/L
mg/L × 0.1 = mg/dL

Reiber Quotient Graph

With the aid of commercially available software, Reiber Quotient Diagrams can be automatically generated.

The calculation employs a ratio diagram including hyperbolic functions as differential lines according to Reiber and Felgenhauer. Results from the determination of IgG and albumin in CSF and serum (IgG and albumin ratios)[20] are plotted.



1. Reference range. 2. Blood brain barrier functional disorder without local IgG synthesis. 3. Blood brain barrier functional disorder with concomitant IgG synthesis in the CNS. 4. IgG synthesis in the CNS without blood brain barrier functional disorder. 5. As confirmed empirically, there are no values in this region (i.e. values here are due to errors introduced by blood sampling or analytical errors). Generally speaking, cases not associated with local IgG synthesis in the CNS lie below the bold line (hyperbolic function). The percentage values indicate what percentage of the total IgG in CSF (minimum) originates in the CNS relative to the statistically-defined 0 % differential lines.

Limitations - interference

Serum/plasma application (IGG2, IGG2-SR)

Criterion: Recovery within ± 0.7 g/L of initial values of samples ≤ 7.0 g/L and within ± 10 % of samples > 7.0 g/L.

Icterus:[21] No significant interference up to an I index of 60 for conjugated and unconjugated bilirubin (approximate conjugated and unconjugated bilirubin concentration: 1026 µmol/L or 60 mg/dL).

Hemolysis:[21] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[21] No significant interference up to an L index of 2000 (approximate Intralipid concentration: 2000 mg/dL). There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors: No significant interference from rheumatoid factors up to a concentration of 1200 IU/mL.

High-dose hook effect: No false result occurs up to an IgG concentration of 400 g/L.

There is no cross-reaction between IgG and IgA or IgM under the assay conditions.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[22,23]

As with other turbidimetric or nephelometric procedures, this test may not provide accurate results in patients with monoclonal gammopathy, due to individual sample characteristics which can be assessed by electrophoresis.[24]

The Reiber diagnostic was designed for the determination of IgG in serum/CSF or plasma/CSF pairs only. This diagnostic shall not be used to determine IgG in serum or plasma alone, but always in combination with the matching CSF samples.

Urine application (IGG2U)

Criterion: Recovery within ± 2 mg/L of initial values of samples ≤ 10 mg/L and within ± 10 % of samples > 10 mg/L.

Icterus: No significant interference up to a conjugated bilirubin concentration of 257 µmol/L or 15 mg/dL.

Hemolysis: No significant interference up to an H index of 150 (approximate hemoglobin concentration: 93.2 µmol/L or 150 mg/dL).

High-dose hook effect: No false result occurs up to an IgG concentration of 6000 mg/L.

There is no cross-reaction between IgG and IgA or IgM under the assay conditions.

Drugs: No interference was found at therapeutic concentrations using common drug panels.[23]

Exception: N-acetyl cysteine and ascorbic acid cause artificially low IgG results.

No significant interference from h-albumin ≤ 5000 mg/L, glucose ≤ 111 mmol/L, creatinine ≤ 44 mmol/L, urea ≤ 900 mmol/L, uric acid ≤ 6 mmol/L, oxalate ≤ 2.2 mmol/L, calcium ≤ 40 mmol/L, citrate ≤ 10 mmol/L, magnesium ≤ 75 mmol/L and phosphate ≤ 40 mmol/L.

CSF application (IGG2C)

Criterion: Recovery within ± 1.5 mg/L of initial values of samples ≤ 15 mg/L and within ± 10 % of samples > 15 mg/L.

Icterus: No significant interference up to an I index of 15 for conjugated bilirubin (approximate conjugated bilirubin concentration: 257 µmol/L or 15 mg/dL).

Hemolysis: No significant interference up to an H index of 200 (approximate hemoglobin concentration: 124 µmol/L or 200 mg/dL).

High-dose hook effect: No false result without a flag was observed up to an IgG concentration of 2500 mg/L.

There is no cross-reaction between IgG and IgA or IgM under the assay conditions.

For diagnostic purposes, the results should always be assessed in conjunction with the patient's medical history, clinical examination and other findings.

ACTION REQUIRED

Special Wash Programming: The use of special wash steps is mandatory when certain test combinations are run together on **cobas c** systems. All special wash programming necessary for avoiding carry-over is available via the **cobas** link. The latest version of the carry-over evasion list can be found with the NaOHD/SMS/SCCS Method Sheet. For further instructions, refer to the operator's manual.

Limits and ranges

Measuring range

Serum/plasma application (IGG2):

3.0-50.0 g/L (20.0-334 µmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5.6 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.6.

Determine samples having lower concentrations via the rerun function. For samples with lower concentrations, the re-run function increases the

sample volume by a factor of 7.5. The results are automatically divided by this factor.

Serum/plasma application (IGG2-SR):

3.0-50.0 g/L (20.0-334 µmol/L)

Urine application (IGG2U):

4.00-200 mg/L (26.7-1334 nmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:10 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 10.

CSF application (IGG2C):

4.00-200 mg/L (26.7-1334 nmol/L)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:5 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 5.

Lower limits of measurement

Limit of Blank, Limit of Detection and Limit of Quantitation
Serum/plasma application (IGG2, IGG2-SR)

Limit of Blank	= 0.3 g/L (2.00 µmol/L)
Limit of Detection	= 0.5 g/L (3.34 µmol/L)
Limit of Quantitation	= 3.0 g/L (20.0 µmol/L)

Urine application (IGG2U)

Limit of Blank	= 3 mg/L (20.0 nmol/L)
Limit of Detection	= 4 mg/L (26.7 nmol/L)
Limit of Quantitation	= 7 mg/L (46.7 nmol/L)

CSF application (IGG2C, IGG-SR)

Limit of Blank	= 3 mg/L (20.0 nmol/L)
Limit of Detection	= 4 mg/L (26.7 nmol/L)
Limit of Quantitation	= 7 mg/L (46.7 nmol/L)

The Limit of Blank, Limit of Detection and Limit of Quantitation were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements.

The Limit of Blank is the 95th percentile value from n ≥ 60 measurements of analyte-free samples over several independent series. The Limit of Blank corresponds to the concentration below which analyte-free samples are found with a probability of 95 %.

The Limit of Detection is determined based on the Limit of Blank and the standard deviation of low concentration samples.

The Limit of Detection corresponds to the lowest analyte concentration which can be detected (value above the Limit of Blank with a probability of 95 %).

The Limit of Quantitation is the lowest analyte concentration that can be reproducibly measured with a total error of 20 %. It has been determined using low concentration IgG samples.

Expected values

Serum/plasma

Adults:[25] 7-16 g/L (46.7-107 µmol/L*)

Children/juveniles:[26]
0-14 days: 3.20-12.1 g/L (21.3-80.4 µmol/L*)
15 days - < 1 yr: 1.48-6.31 g/L (9.87-42.1 µmol/L*)
1 - < 4 yr: 3.17-9.94 g/L (21.1-66.3 µmol/L*)
4 - < 10 yr: 5.01-11.7 g/L (33.4-77.7 µmol/L*)
10 - < 19 yr: 5.95-13.1 g/L (39.7-87.2 µmol/L*)

Urine

The upper normal 97.5th percentile limit was found to be 8.5 mg/24 h for IgG (0.90 confidence interval: 7.7-10.1 mg/24 h).[27]

CSF[28]

10-30 mg/L (66.7-200 nmol/L*)

*calculated by unit conversion factor

Each laboratory should investigate the transferability of the expected values to its own patient population and if necessary determine its own reference ranges.

For Reiber diagnostic only, these values are only for orientation. The only relevant values are the CSF/serum ratios.

Specific performance data

Representative performance data on the analyzers are given below. These data represent the performance of the analytical procedure itself.

Results obtained in individual laboratories may differ due to heterogenous sample materials, aging of analyzer components and mixture of reagents running on the analyzer.

Precision

Precision was determined using human samples and controls in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP05-A3 requirements with repeatability (n = 84) and intermediate precision (2 aliquots per run, 2 runs per day, 21 days). Results for repeatability and intermediate precision were obtained on the **cobas c** 503 analyzer.

Serum/plasma application (IGG2)

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
PCCC1[a)]	6.81	0.0367	0.5
PCCC2[b)]	10.1	0.0573	0.6
Human serum 1	3.41	0.0206	0.6
Human serum 2	6.40	0.0352	0.6
Human serum 3	15.8	0.106	0.7
Human serum 4	25.0	0.169	0.7
Human serum 5	44.4	0.364	0.8

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
PCCC1[a)]	6.71	0.0771	1.1
PCCC2[b)]	10.1	0.131	1.3
Human serum 1	3.41	0.0396	1.2
Human serum 2	6.43	0.0761	1.2
Human serum 3	15.8	0.187	1.2
Human serum 4	25.0	0.298	1.2
Human serum 5	44.9	0.573	1.3

Urine application (IGG2U)

Repeatability	*Mean mg/L*	*SD mg/L*	*CV %*
Precinorm PUC	23.5	0.248	1.1
Precipath PUC	133	0.523	0.4
Urine 1	5.80	0.314	5.4
Urine 2	6.65	0.201	3.0
Urine 3	49.4	0.328	0.7
Urine 4	98.4	0.421	0.4
Urine 5	164	0.724	0.4

Intermediate precision	*Mean mg/L*	*SD mg/L*	*CV %*
Precinorm PUC	23.5	0.275	1.2
Precipath PUC	133	0.650	0.5

Urine 1	5.80	0.332	5.7
Urine 2	6.65	0.306	4.6
Urine 3	49.2	0.476	1.0
Urine 4	98.4	1.46	1.5
Urine 5	162	2.13	1.3

CSF application (IGG2C)

Repeatability	*Mean mg/L*	*SD mg/L*	*CV %*
Precinorm PUC	23.6	0.351	1.5
Precipath PUC	139	0.715	0.5
CSF 1	9.91	0.224	2.3
CSF 2	25.9	0.317	1.2
CSF 3	38.0	0.280	0.7
CSF 4	104	0.824	0.8
CSF 5	168	1.16	0.7

Intermediate precision	*Mean mg/L*	*SD mg/L*	*CV %*
Precinorm PUC	23.6	0.488	2.1
Precipath PUC	139	1.30	0.9
CSF 1	9.91	0.449	4.5
CSF 2	25.9	0.550	2.1
CSF 3	38.0	0.572	1.5
CSF 4	104	1.04	1.0
CSF 5	168	1.85	1.1

Serum/plasma (IGG2-SR):

Repeatability	*Mean g/L*	*SD g/L*	*CV %*
PCCC1[a)]	6.96	0.0906	1.3
PCCC2[b)]	10.7	0.0794	0.7
Human serum 1	3.40	0.0553	1.6
Human serum 2	6.93	0.0529	0.8
Human serum 3	16.0	0.105	0.7
Human serum 4	24.0	0.159	0.7
Human serum 5	42.5	0.352	0.8

Intermediate precision	*Mean g/L*	*SD g/L*	*CV %*
PCCC1[a)]	6.96	0.115	1.6
PCCC2[b)]	10.7	0.153	1.4
Human serum 1	3.40	0.0909	2.7
Human serum 2	6.66	0.112	1.7
Human serum 3	15.7	0.203	1.3
Human serum 4	24.0	0.299	1.2
Human serum 5	42.5	0.676	1.6

a) PreciControl ClinChem Multi 1

b) PreciControl ClinChem Multi 2

The data obtained on **cobas c** 503 analyzer(s) are representative for **cobas c** 303 analyzer(s) and **cobas c** 703 analyzer(s).

Method comparison

IgG values for human serum, plasma, urine, CSF and serum, plasma Reiber samples obtained on a **cobas c** 503 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Serum/plasma application (IGG2)
Sample size (n) = 87

Passing/Bablok[29]	Linear regression
y = 1.028x + 0.0539 g/L	y = 1.039x - 0.0701 g/L
τ = 0.985	r = 0.999

The sample concentrations were between 3.00 and 47.8 g/L.

Urine application (IGG2U)
Sample size (n) = 67

Passing/Bablok[29]	Linear regression
y = 0.976x + 0.857 mg/L	y = 0.964x + 1.69 mg/L
τ = 0.985	r = 0.999

The sample concentrations were between 4.90 and 189 mg/L.

CSF application (IGG2C)
Sample size (n) = 83

Passing/Bablok[29]	Linear regression
y = 1.003x + 1.37 mg/L	y = 0.971x + 2.66 mg/L
τ = 0.978	r = 0.998

The sample concentrations were between 4.19 and 193 mg/L.

Serum/plasma (IGG2-SR)
Sample size (n) = 84

Passing/Bablok[29]	Linear regression
y = 0.960x + 0.315 g/L	y = 0.943x + 0.525 g/L
τ = 0.976	r = 0.998

The sample concentrations were between 3.56 and 49.2 g/L.

IgG values for human serum, plasma, CSF and urine samples obtained on a **cobas c** 303 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 501 analyzer (x).

Serum/plasma application (IGG2)
Sample size (n) = 73

Passing/Bablok[29]	Linear regression
y = 1.022x + 0.0659 g/L	y = 0.994x + 0.486 g/L
τ = 0.991	r = 0.999

The sample concentrations were between 3.70 and 47.9 g/L.

Urine application (IGG2U)
Sample size (n) = 74

Passing/Bablok[29]	Linear regression
y = 0.977x + 0.00568 mg/L	y = 0.956x + 0.713 mg/L
τ = 0.977	r = 0.999

The sample concentrations were between 5.62 and 199 mg/L.

CSF application (IGG2C)
Sample size (n) = 81

Passing/Bablok[29]	Linear regression
y = 1.022x + 1.67 mg/L	y = 1.005x + 2.18 mg/L
τ = 0.988	r = 1.000

The sample concentrations were between 5.33 and 193 mg/L.

Serum/plasma (IGG2-SR)
Sample size (n) = 74

Passing/Bablok[29]	Linear regression

y = 0.944x + 0.661 g/L	y = 0.911x + 1.09 g/L
τ = 0.983	r = 0.997

The sample concentrations were between 3.73 and 47.1 g/L.

IgG values for human serum, plasma, CSF and urine samples as for others obtained on a **cobas c** 703 analyzer (y) were compared with those determined using the corresponding reagent on a **cobas c** 503 analyzer (x).

Serum/plasma application (IGG2)
Sample size (n) = 81

Passing/Bablok[29]	Linear regression
y = 1.000x - 0.100 g/L	y = 1.000x - 0.0455 g/L
τ = 0.984	r = 0.999

The sample concentrations were between 3.88 and 49.2 g/L.

Urine application (IGG2U)
Sample size (n) = 68

Passing/Bablok[29]	Linear regression
y = 1.033x - 1.12 mg/L	y = 1.029x - 0.898 mg/L
τ = 0.979	r = 1.000

The sample concentrations were between 4.73 and 187 mg/L.

CSF application (IGG2C)
Sample size (n) = 80

Passing/Bablok[29]	Linear regression
y = 1.013x + 0.0401 mg/L	y = 1.036x - 0.577 mg/L
τ = 0.971	r = 0.996

The sample concentrations were between 4.73 and 191 mg/L.

Serum/plasma application (IGG2-SR)
Sample size (n) = 83

Passing/Bablok[29]	Linear regression
y = 0.998x - 0.0662 g/L	y = 0.996x + 0.0546 g/L
τ = 0.984	r = 1.000

The sample concentrations were between 3.61 and 48.3 g/L.

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A point (period/stop) is always used in this Method Sheet as the decimal separator to mark the border between the integral and the fractional parts of a decimal numeral. Separators for thousands are not used.

Any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the Member State in which the user and/or the patient is established.

Symbols

Roche Diagnostics uses the following symbols and signs in addition to those listed in the ISO 15223-1 standard:

CONTENT	Contents of kit
→	Volume for reconstitution
GTIN	Global Trade Item Number
Rx only	For USA: Caution: Federal law restricts this device to sale by or on the order of a physician.

CE 0123

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