IGA-2

cobas®

Tina-quant IgA Gen.2

Order information

REF		CONTENT		Analyzer(s) on which **cobas c** pack(s) can be used
03507343190	03507343500	Tina-quant IgA Gen.2 (150 tests)	System-ID 07 6786 7	**cobas c** 311, **cobas c** 501/502

Materials required (but not provided):

11355279216	Calibrator f.a.s. Proteins (5 x 1 mL)	Code 656	
03121291122	Precipath PUC (4 x 3 mL)	Code 241	
05117003190	PreciControl ClinChem Multi 1 (20 x 5 mL)	Code 391	
05947626190	PreciControl ClinChem Multi 1 (4 x 5 mL)	Code 391	
05117216190	PreciControl ClinChem Multi 2 (20 x 5 mL)	Code 392	
05947774190	PreciControl ClinChem Multi 2 (4 x 5 mL)	Code 392	
04489357190	Diluent NaCl 9 % (50 mL)	System-ID 07 6869 3	

English

System information

For **cobas c** 311/501 analyzers:
IGA-2: ACN 458 (Standard application)
IGAP2: ACN 295 (Sensitive application)

For **cobas c** 502 analyzer:
IGA-2: ACN 8458 (Standard application)
IGAP2: ACN 8295 (Sensitive application)

Intended use

In vitro test for the quantitative determination of IgA in human serum and plasma on **cobas c** systems.

Summary

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

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]

Immunoglobulin A (IgA) has a molecular weight of 160 kDa and usually accounts for about 10 to 15 % of the total circulating immunoglobulins. IgA exists in monomeric, dimeric and polymeric forms. In CSF and blood the monomeric form is predominant. In bodily secretions, such as saliva, sweat, mucosa, milk and colostrum, IgA exists predominantly in dimeric form. IgA is an important component of mucosal immunity; in colostrum and milk it may aid in protection of neonates from intestinal infection, while the exact role of IgA in serum is not clear.[1] Due to the slow onset of IgA synthesis, the IgA concentration in serum of infants is lower than in adults.[1,2,3]

Increases of polyclonal immunoglobulins (including IgA) are the normal response to infections. IgA is increased in skin, gut, respiratory, and renal infections.[1] IgA increases may additionally be associated with chronic inflammatory conditions, including cirrhosis, rheumatoid arthritis, systemic lupus erythematosus and Wiscott-Aldrich syndrome.[1,4,5,6,7,8,9] Monoclonal IgA increases in diseases where neoplastic proliferation of secretory B cells is present, such as multiple myeloma.[1]

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

This assay is based on the principle of immunological agglutination. In addition to the standard application (test IGA-2), there is a sensitive application (test IGAP2) designed for the quantitative determination of low IgA concentrations, e.g. in pediatric samples.

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-IgA 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

R2 Anti-human IgA antibody (goat): dependent on titer; TRIS buffer: 20 mmol/L, pH 8.0; NaCl: 150 mmol/L; preservative

R1 is in position B and R2 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:	12 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.

Standard application (IGA-2)

Serum

Plasma: Li-heparin and K_2-EDTA plasma

Sensitive application (IGAP2)

Serum

Plasma: Li-heparin and K_2-EDTA plasma

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.

Partially filled K_2-EDTA plasma tubes can cause incorrect results.

Centrifuge samples containing precipitates before performing the assay.

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

Stability:[1,2]	8 months at 15-25 °C 8 months at 2-8 °C 8 months at (-15)-(-25) °C

Freeze only once.

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

Standard application (IGA-2)

cobas c 311 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 6-31
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	g/L (µmol/L, mg/dL)
Reagent pipetting	Diluent (H_2O)
R1	120 µL –
R2	38 µL –

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	5 µL	9 µL	180 µL
Decreased	2.7 µL	2 µL	180 µL
Increased	2.4 µL	–	–

cobas c 501/502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-46
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	g/L (µmol/L, mg/dL)
Reagent pipetting	Diluent (H_2O)
R1	120 µL –
R2	38 µL –

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	5 µL	9 µL	180 µL
Decreased	2.7 µL	2 µL	180 µL
Increased	2.4 µL	–	–

Sensitive application (IGAP2)

cobas c 311 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 6-22
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	g/L (µmol/L, mg/dL)
Reagent pipetting	Diluent (H_2O)
R1	120 µL –
R2	38 µL –

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	9 µL	75 µL
Decreased	7 µL	5 µL	93 µL
Increased	2.7 µL	–	–

cobas c 501/502 **test definition**

Assay type	2-Point End
Reaction time / Assay points	10 / 10-46
Wavelength (sub/main)	700/340 nm
Reaction direction	Increase
Units	g/L (µmol/L, mg/dL)
Reagent pipetting	Diluent (H_2O)
R1	120 µL –
R2	38 µL –

IGA-2

Tina-quant IgA Gen.2

Sample volumes	*Sample*	*Sample dilution*	
		Sample	*Diluent (NaCl)*
Normal	10 µL	9 µL	75 µL
Decreased	7 µL	5 µL	93 µL
Increased	2.7 µL	–	–

Calibration

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

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

Traceability: This method has been standardized against the reference preparation of the IRMM (Institute for Reference Materials and Measurements) BCR470/CRM470 (RPPHS - Reference Preparation for Proteins in Human Serum).[13]

Quality control

For quality control, use control materials as listed in the "Order information" section. In addition, other suitable control material can be used.

Standard application (IGA-2):	PreciControl ClinChem Multi 1, PreciControl ClinChem Multi 2
Sensitive application (IGAP2):	Precipath PUC, PreciControl ClinChem Multi 1

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

cobas c systems automatically calculate the analyte concentration of each sample.

Conversion factors:	g/L x 6.25 = µmol/L g/L x 100 = mg/dL g/L x 1000 = mg/L

Limitations - interference

Standard application (IGA-2):

Criterion: Recovery within ± 0.07 g/L of initial values of samples ≤ 0.7 g/L and within ± 10 % for samples > 0.7 g/L.

Icterus:[14] 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:[14] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors < 1200 IU/mL do not interfere.

High dose hook-effect: No false result up to an IgA concentration of 100 g/L (625 µmol/L, 10000 mg/dL) occurs due to an antigen excess within polyclonal specimens.

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

Drugs: No interference was found at therapeutic concentrations using common drug panels.[15,16]

Sensitive application (IGAP2):

Criterion: Recovery within ± 0.04 g/L of initial values of samples ≤ 0.4 g/L and within ± 10 % for samples > 0.4 g/L.

Icterus:[14] 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:[14] No significant interference up to an H index of 1000 (approximate hemoglobin concentration: 621 µmol/L or 1000 mg/dL).

Lipemia (Intralipid):[14] No significant interference up to an L index of 2000. There is poor correlation between the L index (corresponds to turbidity) and triglycerides concentration.

Rheumatoid factors < 500 IU/mL do not interfere.

High dose hook-effect: No false result up to an IgA concentration of 20 g/L (125 µmol/L, 2000 mg/dL) occurs due to an antigen excess within polyclonal specimens.

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

Drugs: No interference was found at therapeutic concentrations using common drug panels.[15,16]

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.[17]

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. The latest version of the carry-over evasion list can be found with the NaOHD-SMS-SmpCln1+2-SCCS Method Sheets. For further instructions refer to the operator's manual. **cobas c** 502 analyzer: All special wash programming necessary for avoiding carry-over is available via the **cobas** link, manual input is required in certain cases.

Where required, special wash/carry-over evasion programming must be implemented prior to reporting results with this test.

Limits and ranges

Measuring range

Standard application (IGA-2):

0.50-8.00 g/L (3.13-50 µmol/L, 50-800 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:8 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 8.

Determine samples having lower concentrations via the rerun function. For samples with lower concentrations, the rerun function increases the sample volume by a factor of 10. The results are automatically divided by this factor.

Sensitive application (IGAP2):

0.1-4.00 g/L (0.63-25 µmol/L, 10-400 mg/dL)

Determine samples having higher concentrations via the rerun function. Dilution of samples via the rerun function is a 1:3 dilution. Results from samples diluted using the rerun function are automatically multiplied by a factor of 3.

Determine samples having lower concentrations via the rerun function. For samples with lower concentrations, the rerun function increases the sample volume by a factor of 2.5. The results are automatically divided by this factor.

Lower limits of measurement

Standard application (IGA-2):

Limit of Blank and Limit of Detection

Limit of Blank	= 0.05 g/L (0.31 µmol/L, 5 mg/dL)
Limit of Detection	= 0.05 g/L (0.31 µmol/L, 5 mg/dL)

The Limit of Blank and Limit of Detection were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A 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 %).

Sensitive application (IGAP2):

Lower detection limit of the test

0.04 g/L (0.25 µmol/L, 4 mg/dL)

The lower detection limit represents the lowest measurable analyte level that can be distinguished from zero. It is calculated as the value lying 3 standard deviations above that of the lowest standard (standard 1 + 3 SD, repeatability, n = 21).

Expected values

Reference values according to CRM 470 Protein Standardization:[18,19]

Adults	0.7-4 g/L
Children and juveniles	
0 - < 1 year female	< 0.14 g/L
0 - < 1 year male	< 0.14 g/L
1 - < 3 years female	< 0.80 g/L
1 - < 3 years male	< 0.80 g/L
3 - < 6 years female	0.11-1.42 g/L
3 - < 6 years male	0.11-1.42 g/L
6 - < 14 years female	0.34-2.20 g/L
6 - < 14 years male	0.34-2.22 g/L
14 - < 19 years female	0.40-2.93 g/L
14 - < 19 years male	0.40-2.93 g/L

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

Specific performance data

Representative performance data on the analyzers are given below. Results obtained in individual laboratories may differ.

Precision

Precision was determined using human samples and controls in an internal protocol with repeatability (n = 21) and intermediate precision (3 aliquots per run, 1 run per day, 21 days). The following results were obtained on the **cobas c** 501 analyzer:

Standard application (IGA-2):

Repeatability	*Mean* *g/L (µmol/L, mg/dL)*	*SD* *g/L (µmol/L, mg/dL)*	*CV* *%*
Precinorm Protein	1.95 (12.2, 195)	0.02 (0.1, 2)	1.1
Precipath Protein	3.23 (20.2, 323)	0.02 (0.1, 2)	0.7
Human serum 1	1.55 (9.69, 155)	0.02 (0.13, 2)	1.0
Human serum 2	2.23 (13.9, 223)	0.02 (0.1, 2)	0.9
Intermediate precision	*Mean* *g/L (µmol/L, mg/dL)*	*SD* *g/L (µmol/L, mg/dL)*	*CV* *%*
Precinorm Protein	1.95 (12.2, 195)	0.03 (0.2, 3)	1.8
Precipath Protein	3.25 (20.3, 325)	0.04 (0.3, 4)	1.4
Human serum 3	1.93 (12.1, 193)	0.04 (0.3, 4)	1.8
Human serum 4	3.31 (20.7, 331)	0.04 (0.3, 4)	1.1

Sensitive application (IGAP2):

Repeatability	*Mean* *g/L (µmol/L, mg/dL)*	*SD* *g/L (µmol/L, mg/dL)*	*CV* *%*
Precipath PUC	0.27 (1.69, 27.0)	0.01 (0.06, 1.0)	1.8
Precinorm Protein	2.24 (14.0, 224)	0.02 (0.1, 2)	0.9
Human serum 1	0.37 (2.31, 37.0)	0.01 (0.06, 1.0)	1.3
Human serum 2	2.40 (15.0, 240)	0.02 (0.1, 2)	0.8
Intermediate precision	*Mean* *g/L (µmol/L, mg/dL)*	*SD* *g/L (µmol/L, mg/dL)*	*CV* *%*
Precipath PUC	0.27 (1.69, 27.0)	0.01 (0.06, 1.0)	3.2
Precinorm Protein	2.25 (14.1, 225)	0.04 (0.3, 4)	1.8
Human serum 3	0.36 (2.25, 36.0)	0.01 (0.06, 1.0)	2.4
Human serum 4	1.26 (7.89, 126)	0.02 (0.13, 2)	1.5

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

Method comparison

IgA values for human serum and plasma samples obtained on a **cobas c** 501 analyzer (y) were compared with those determined using the corresponding reagent on a Roche/Hitachi 917 analyzer (x).

Standard application (IGA-2):

Sample size (n) = 79

Passing/Bablok[20]	Linear regression
y = 1.035x - 0.019 g/L	y = 1.027x - 0.003 g/L
τ = 0.987	r = 0.999

The sample concentrations were between 0.500 and 7.74 g/L (3.13 and 48.4 µmol/L, 50.0 and 774 mg/dL).

Sensitive application (IGAP2):

Sample size (n) = 194

Passing/Bablok[20]	Linear regression
y = 0.981x + 0.002 g/L	y = 0.956x + 0.035 g/L
τ = 0.957	r = 0.998

The sample concentrations were between 0.166 and 4.00 g/L (1.06 and 25.0 µmol/L, 16.6 and 400 mg/dL).

The data obtained on **cobas c** 501 analyzer(s) are representative for **cobas c** 311 analyzer(s).

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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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