BECKMAN COULTER CE

SYNCHRON System(s)
Chemistry Information Sheet

Ig-A
Immunoglobulin A

REF 467920

For *In Vitro* Diagnostic Use

Rx Only

ANNUAL REVIEW

Reviewed by	Date	Reviewed by	Date

PRINCIPLE

INTENDED USE

Ig-A reagent, when used in conjunction with UniCel® DxC 600/800 System(s) and SYNCHRON® Systems CAL 1, is intended for quantitative determination of immunoglobulin a concentration in human serum or plasma.

CLINICAL SIGNIFICANCE

Measurements of immunoglobulin A are used in the diagnosis and treatment of immune deficiency states, protein-losing conditions, chronic infections, myeloma, cirrhosis and liver disease.

METHODOLOGY

Ig-A reagent is used to measure the immunoglobulin A concentration by an immuno-turbidimetric method.[1,2] In the reaction, immunoglobulin A combines with specific antibody to form insoluble antigen-antibody complexes.

The SYNCHRON System(s) automatically dilutes sample and dispenses the appropriate diluted sample volumes and reagent into a cuvette. The ratio used is one part diluted sample to 23 parts reagent. The system monitors the change in absorbance at 340 nanometers. This change in absorbance is proportional to the concentration of immunoglobulin A in the sample and is used by the System to calculate and express the immunoglobulin A concentration based upon a single-point calibration curve.

CHEMICAL REACTION SCHEME

Ig-A + Anti-Ig-A Antibody ⟶ Antigen-Antibody Complex

(Antigen)
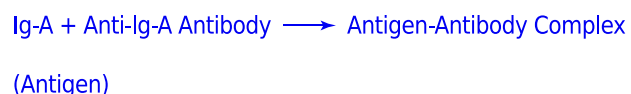
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SPECIMEN

TYPE OF SPECIMEN

Biological fluid samples should be collected in the same manner routinely used for any laboratory test.[3] Freshly drawn serum or plasma are the preferred specimens. Acceptable anticoagulants are listed in the PROCEDURAL NOTES section of this chemistry information sheet. Whole blood or urine are not recommended for use as a sample.

SPECIMEN STORAGE AND STABILITY

1. Tubes of blood are to be kept closed at all times and in a vertical position. It is recommended that the serum or plasma be physically separated from contact with cells within two hours from the time of collection.[4]

2. Separated serum or plasma should not remain at room temperature longer than 8 hours. If assays are not completed within 8 hours, serum or plasma should be stored at +2°C to +8°C. If assays are not completed within 48 hours, or the separated sample is to be stored beyond 48 hours, samples should be frozen at -15°C to -20°C. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.[4]

Additional specimen storage and stability conditions as designated by this laboratory:

SAMPLE PREPARATION

Sample preparation is not required. All samples are diluted automatically by the system using the DIL1 Cartridge.

SAMPLE VOLUME

The optimum volume, when using a 0.5 mL sample cup, is 0.3 mL of sample. For optimum primary sample tube volumes and minimum volumes, refer to the Primary Tube Sample Template for your system.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this chemistry information sheet for information on unacceptable specimens.

Criteria for sample rejection as designated by this laboratory:

PATIENT PREPARATION

Special instructions for patient preparation as designated by this laboratory:

SPECIMEN HANDLING

Special instructions for specimen handling as designated by this laboratory:

REAGENTS

CONTENTS

Each kit contains the following items:

Two Ig-A Reagent Cartridges (2 x 150 tests)
One lot-specific Parameter Card

VOLUMES PER TEST

Serum or Plasma

Sample Dilution Volumes

Sample Volume	15 µL
Diluent Volume	285 µL
Diluted Sample Volume (1:20 dilution)	10 µL

Total Reagent Volume   230 µL

Cartridge Volumes

A	200 µL
B	30 µL
C	– –

Serum or Plasma URDAC

Sample Volume (neat)	5 µL
Total Reagent Volume	230 µL
Cartridge Volumes	
A	200 µL
B	30 µL
C	– –

Serum or Plasma ORDAC

Sample Dilution Volumes	
Sample Volume	3 µL
Diluent Volume	297 µL
Diluted Sample Volume (1:100 dilution)	4 µL
Total Reagent Volume	230 µL
Cartridge Volume	
A	200 µL
B	30 µL
C	– –

REACTIVE INGREDIENTS

REAGENT CONSTITUENTS

Reaction Buffer	43 mL
Goat Antibody Monospecific for Human immunoglobulin a	7.2 mL

Also non-reactive chemicals necessary for optimal system performance.

⚠ **CAUTION**

Sodium azide preservative may form explosive compounds in metal drain lines. See NIOSH Bulletin: Explosive Azide Hazard (8/16/76).
To avoid the possible build-up of azide compounds, flush wastepipes with water after the disposal of undiluted reagent. Sodium azide disposal must be in accordance with appropriate local regulations.

GHS HAZARD CLASSIFICATION

Not classified as hazardous

[SDS]   Safety Data Sheet is available at techdocs.beckmancoulter.com.

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

SYNCHRON® Systems CAL 1
Diluent 1 Cartridge

At least two levels of control material

REAGENT PREPARATION

No preparation is required.

ACCEPTABLE REAGENT PERFORMANCE

The acceptability of a reagent is determined by successful calibration and by ensuring that quality control results are within your facility's acceptance criteria.

REAGENT STORAGE AND STABILITY

Ig-A reagent when stored unopened at +2°C to +8°C, will obtain the shelf-life indicated on the cartridge label. Once opened, the reagent is stable for 60 days at +2°C to +8°C unless the expiration date is exceeded. DO NOT FREEZE.

DIL 1 stored unopened at room temperature is stable until the expiration date indicated on each cartridge. Once opened, DIL 1 is stable for 60 days on instrument or until the expiration date, if sooner.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

SYNCHRON® Systems CAL 1

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

SYNCHRON® Systems CAL 1 is stable until the expiration date printed on the label if stored capped in the original container at +2°C to +8°C. DO NOT FREEZE.

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| ⚠ **CAUTION** |
| |
| **Because this product is of human origin, it should be handled as though capable of transmitting infectious diseases. Each serum or plasma donor unit used in the preparation of this material was tested by United States Food and Drug Administration (FDA) approved methods and found to be negative for antibodies to HIV and HCV and nonreactive for HbsAg. Because no test method can offer complete assurance that HIV, hepatitis B virus, and hepatitis C virus or other infectious agents are absent, this material should be handled as though capable of transmitting infectious diseases. This product may also contain other human source material for which there is no approved test. The FDA recommends such samples to be handled as specified in Centers for Disease Control's Biosafety Level 2 guidelines.[5]** |
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Calibrator storage location:

CALIBRATION INFORMATION

1. The system must have a lot-specific parameter card and a valid calibration adjustment in memory before controls or patient samples can be run.

2. Under typical operating conditions the Ig-A reagent cartridge must be calibrated every 14 days and also with certain parts replacements or maintenance procedures, as defined in the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual. This assay has within-lot calibration available. Refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual for information on this feature.

3. For detailed calibration instructions, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

4. The system will automatically perform checks on the calibration and produce data at the end of calibration. In the event of a failed calibration, the data will be printed with error codes and the system will alert the operator of the failure. For information on error codes, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

TRACEABILITY

For Traceability information refer to the Calibrator instructions for use.

QUALITY CONTROL

At least two levels of control material should be analyzed daily. In addition, these controls should be run with each new calibration, with each new reagent cartridge, and after specific maintenance or troubleshooting procedures as detailed in the appropriate system manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on good laboratory practices or laboratory accreditation requirements and applicable laws.

The following controls should be prepared and used in accordance with the package inserts. Discrepant quality control results should be evaluated by your facility.

Table 1.0 Quality Control Material

CONTROL NAME	SAMPLE TYPE	STORAGE

TESTING PROCEDURE(S)

1. If necessary, load the reagent onto the system. A lot-specific parameter card must be loaded one time for each lot.

2. After reagent load is completed, calibration may be required.

3. Program samples and controls for analysis.

4. After loading samples and controls onto the system, follow the protocols for system operations.

For detailed testing procedures, refer to the UniCel DxC 600/800 System *Instructions For Use* (IFU) manual.

CALCULATIONS

The SYNCHRON System(s) performs all calculations internally to produce the final reported result. The system will calculate the final result for sample dilutions made by the operator when the dilution factor is entered into the system during sample programming.

REPORTING RESULTS

Equivalency between the SYNCHRON LX and UniCel DxC 600/800 Systems has been established. Chemistry results between these systems are in agreement and data from representative systems may be shown.

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The reference intervals listed below were taken from literature and a study performed on SYNCHRON Systems.[6]

Table 2.0 Reference intervals

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S. I. UNITS
Literature	Serum or Plasma	40 – 350 mg/dL	0.4 – 3.5 g/L
SYNCHRON	Serum or Plasma	66 – 436 mg/dL	0.7 – 4.4 g/L

INTERVALS	SAMPLE TYPE	CONVENTIONAL UNITS	S. I. UNITS
Laboratory			

Refer to References (7,8,9) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

1. If plasma is the sample of choice, the following anticoagulants were found to be compatible with this method based on a study of 20 healthy volunteers:

Table 3.0 Compatible Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	AVERAGE PLASMA-SERUM BIAS (mg/dL)
Ammonium Heparin	14 Units/mL	NSI[a]
Lithium Heparin	14 Units/mL	NSI
Sodium Heparin	14 Units/mL	NSI

a   NSI = No Significant Interference (within ± 10.0 mg/dL or 10%).

2. The following anticoagulant was found to be incompatible with this method:

Table 4.0 Incompatible Anticoagulants

ANTICOAGULANT	LEVEL TESTED FOR IN VITRO INTERFERENCE	PLASMA-SERUM BIAS (mg/dL)[a]
Potassium Oxalate/Sodium Fluoride	2.0 / 2.5 mg/mL	- 73

a   Bias is based on worst case instead of average. Plus (+) or minus (-) signs in this column signify positive or negative bias.

LIMITATIONS

Samples containing a monoclonal immunoglobulin may result in a condition of antigen excess and artificially decreased values. Since the presence of an M-protein can normally be detected using protein electrophoresis, the validity of immunochemical results should be determined by observing consistency with an electrophoretic pattern.[10,11,12]

INTERFERENCES

1. The following substances were tested for interference with this methodology:

Table 5.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT
Bilirubin (unconjugated)	Bovine	30 mg/dL	NSI
Hemoglobin	RBC hemolysate	500 mg/dL	NSI
Lipemia	Intralipid	400 mg/dL	NSI

2. Refer to References (13,14,15) for other interferences caused by drugs, disease and preanalytical variables.

PERFORMANCE CHARACTERISTICS

ANALYTIC RANGE

The SYNCHRON System(s) method for the determination of this analyte provides the following analytical ranges:

Table 6.0 Analytical Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS
Serum or Plasma	40 – 700 mg/dL	0.4 – 7.0 g/L
Serum or Plasma (ORDAC Hi)	560 – 8000 mg/dL	5.6 – 80.0 g/L
Serum or Plasma (ORDAC Lo)	6 – 50 mg/dL	0.06 – 0.5 g/L

Samples with concentrations exceeding the high end of the analytical range should be diluted with saline and reanalyzed.

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 7.0 Reportable Range

SAMPLE TYPE	CONVENTIONAL UNITS	S.I. UNITS

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for Ig-A determination is 6 mg/dL (0.06 g/L).

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of patient samples to accepted clinical methods.

Serum or plasma (in the range of 29.0 to 592.0 mg/dL):

Y (SYNCHRON LX Systems)	= 0.924X + 0.686
N	= 78
MEAN (SYNCHRON LX Systems)	= 217.6
MEAN (Array®)	= 234.9
CORRELATION COEFFICIENT (r)	= 0.9962

Refer to References (16) for guidelines on performing equivalency testing.

PRECISION

A properly operating SYNCHRON System(s) should exhibit imprecision values less than or equal to the maximum performance limits in the table below. Maximum performance limits were derived by an examination of the imprecision of various methods, proficiency test summaries, and literature sources.

Table 8.0 Maximum Performance Limits

TYPE OF PRECISION	SAMPLE TYPE	1 SD		CHANGEOVER VALUE[a]		% CV
		mg/dL	g/L	mg/dL	g/L	
Within-run	Serum or Plasma	5	0.05	100	1.0	5.0
	Serum or Plasma (ORDAC)	NA[b]	NA	NA	NA	10.0
Total	Serum or Plasma	7.5	0.08	100	1.0	7.5
	Serum or Plasma (ORDAC)	NA	NA	NA	NA	15.0

a   When the mean of the test precision data is less than or equal to the changeover value, compare the test SD to the SD guideline given above to determine the acceptability of the precision testing. When the mean of the test precision data is greater than the changeover value, compare the test % CV to the guideline given above to determine acceptability. Changeover value = (SD guideline/CV guideline) x 100.

b   NA = Not applicable.

Comparative performance data for a SYNCHRON LX® System evaluated using the NCCLS Proposed Guideline EP5-T2 appears in the table below.[17] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 9.0 NCCLS EP5-T2 Precision Estimate Method

TYPE OF IMPRECISION	SAMPLE TYPE		No. Systems	No. Data Points[a]	Test Mean Value (mg/dL)	EP5-T2 Calculated Point Estimates	
						SD	%CV
Within-run	Serum	Control 1	1	80	109	1.8	1.7
	Serum	Control 2	1	80	242	4.0	1.7
Total	Serum	Control 1	1	80	109	2.0	2.0
	Serum	Control 2	1	80	242	4.6	1.9

a   The point estimate is based on the data from one system, run for twenty days, two runs per day, two observations per run on an instrument operated and maintained according to the manufacturer's instructions.

NOTICE

These degrees of precision and equivalency were obtained in typical testing procedures on a SYNCHRON LX® System and are not intended to represent the performance specifications for this reagent.

ADDITIONAL INFORMATION

For more detailed information on UniCel DxC Systems, refer to the appropriate system manual.

Beckman Coulter, the Beckman Coulter Logo, Synchron, UniCel and DxC are trademarks of Beckman Coulter, Inc and are registered in the USPTO.

SHIPPING DAMAGE

If damaged product is received, notify your Beckman Coulter Clinical Support Center.

REVISION HISTORY

Revision AF

Revised Quality Control section, and removed the sodium azide warning.

Revision AG

Updated corporate address; removed EDTA as an Acceptable Anticoagulant claim.

Revision AH

Added Revision History.

Revision AJ

Added new language requirement: Czech, and Korean.

Revision AK

Removed references to CX and LX systems as they are discontinued effective 12/2013.

Added Beckman Coulter trademark statement and disclaimer.

Revision AL

Added GHS Classification information

Revision AM

Added new language requirement: Romanian

REFERENCES

1. Boyden, A., Button, E., Germerog, D., "Precipitin Testing With Special Reference to the Measurement of Turbidity", *J. Immunol.*, 57:211 (1947).

2. Hellsing, K., "The Effects of Different Polymers for Enhancement of the Antigen-Antibody Reaction as Measured with Nephelometry", *Protides of the Biological Fluids*, 23:579 (1973).

3. Tietz, N. W., "Specimen Collection and Processing; Sources of Biological Variation", *Textbook of Clinical Chemistry*, 5th Edition, W. B. Saunders, Philadelphia, PA (2005).

4. National Committee for Clinical Laboratory Standards, *Procedures for the Handling and Processing of Blood Specimens* Approved Guideline, NCCLS publication H18-A, Villanova, PA (1990).

5. CDC-NIH, *Biosafety in Microbiological and Biomedical Laboratories,* 5th Edition, (Washington, D.C.: U.S. Government Printing Office, 2009). (CDC 21-1112)

6. Tietz, N. W., *Clinical Guide to Laboratory Tests*, 3rd Edition, W. B. Saunders Company, Philadelphia, PA (1995).

7. National Committee for Clinical Laboratory Standards, *How to Define, Determine, and Utilize Reference Intervals in the Clinical Laboratory* Approved Guideline, NCCLS publication C28-A, Villanova, PA (1995).

8. Tietz, N. W., ed., *Fundamentals of Clinical Chemistry*, 6th Edition, W. B. Saunders, Philadelphia, PA (2007).

9. Henry, J. B., *Clinical Diagnosis and Management by Laboratory Methods*, 22nd Edition, W. B. Saunders Company, Philadelphia, PA (2006).

10. Goeken, J. A., Keren, D. F., "Introduction to the Report of the Concensus Conference on Monoclonal Gammopathies", *Arch. Path. Lab. Med.*, 123:104 105, (1999).

11. Keren, D. F., Alexanian, R., Goeken, J. A., et al., "Guidelines for Clinical and Laboratory Evaluation of Patients with Monoclonal Gammopathies", *Arch Path. Lab. Med.*, 123:106 107, (1999).

12. Keren, D. F., "Procedure for the Evaluation of Mononclonal Immunoglobulins", *Arch. Path. Lab. Med.*, 123:126 132, (1999).

13. Young, D. S., *Effects of Drugs on Clinical Laboratory Tests*, 5th Edition, AACC Press, Washington, D. C. (2000).

14. Friedman, R. B., Young, D. S., *Effects of Disease on Clinical Laboratory Tests*, 4th Edition, AACC Press, Washington, D.C. (2001).

15. Young, D. S., *Effects of Preanalytical Variables on Clinical Laboratory Tests*, 3rd Edition, AACC Press, Washington, D. C. (2007).

16. National Committee for Clinical Laboratory Standards, *Method Comparison and Bias Estimation Using Patient Samples* Approved Guideline, NCCLS publication EP9-A, Villanova, PA (1995).

17. National Committee for Clinical Laboratory Standards, *Precision Performance of Clinical Chemistry Devices* Tentative Guideline, 2nd Edition, NCCLS publication EP5-T2, Villanova, PA (1992).