BECKMAN COULTER

IMMAGE Immunochemistry Systems
Instructions For Use

IGE
Total Immunoglobulin E

REF 474620 (150 tests)

For *In Vitro* Diagnostic Use

FOR PROFESSIONAL USE ONLY

Rx Only

PRINCIPLE

INTENDED USE

IGE reagent, when used in conjunction with IMMAGE Immunochemistry Systems and IGE Calibrator, is intended for quantitative determination of total immunoglobulin E (IgE) concentration in human serum or plasma by rate turbidimetry.

CLINICAL SIGNIFICANCE

IgE is a member of the immunoglobulin family of proteins that was first described in the 1960's.[1,2] IgE, like all immunoglobulins, is produced by plasma cells in response to antigenic stimuli. IgE is unique however in certain structural aspects and the role it plays in allergic diseases.

Measurement of total serum IgE is often used as a tool in the diagnosis and management of atopic diseases such as asthma, hay fever, atopic dermatitis and urticaria. It has been used to distinguish atopic from non-atopic individuals presenting allergy-like symptoms.[3] In addition, studies have also shown that increased levels of IgE in cord blood and infants may be predictive of future atopic tendencies.[4,5]

Normal levels of circulating IgE are extremely low in comparison to other immunoglobulins. Levels of IgE at birth are almost undetectable but increase in non-allergic adults.[6] Elevated levels are commonly seen in cases of allergic diseases, parasitic infections, pulmonary aspergillosis, Wiskott-Aldrich Syndrome, and myeloma.[7,8,9,10,11]

Serum IgE levels may vary as a result of diet, genetic background, geographical location and other factors. It is therefore recommended that total IgE measurements be used in conjunction with other clinical tests when establishing diagnoses.

METHODOLOGY

The IMMAGE IGE reagent is based on the sensitive Near Infrared Particle Immunoassay (NIPIA) rate methodology. An anti-IgE antibody-coated particle binds to IgE in the patient sample resulting in the formation of insoluble aggregates causing turbidity. The rate of aggregate formation is directly proportional to the concentration of IgE in the sample.

CHEMICAL REACTION SCHEME

E014854L.EPS

SPECIMEN

TYPE OF SPECIMEN

Serum samples are recommended. Plasma samples (EDTA, Lithium Heparin, and Sodium Heparin) can be used.

Serum or plasma samples should be collected in the manner routinely used for any clinical laboratory test.[12] Freshly drawn serum or plasma from a fasting individual is preferred. Anticoagulants tested are listed in the PROCEDURAL NOTES section of this instructions for use.

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.[13]
2. If serum and plasma samples are not assayed within 8 hours, the samples can be stored at +2°C to +8°C for up to 48 hours. Serum and plasma samples can be stored at -15°C to -20°C for up to 60 days. Frozen samples should be thawed only once. Analyte deterioration may occur in samples that are repeatedly frozen and thawed.[13]

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

SAMPLE VOLUME

For sample volumes refer to the Sampling Template.

CRITERIA FOR UNACCEPTABLE SPECIMENS

Refer to the PROCEDURAL NOTES section of this instructions for use.

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:

KIT COMPONENTS	QUANTITY
IGE Cartridge (Antibody and Reaction Buffer)	3
Evaporation Caps	6
IGE Calibrator, 2 mL	1
IGE Reagent Bar Code Card	1
IGE Calibrator Bar Code Card	1
IGE Calibrator Strips	2
Value Assignment Sheet	1

INITIAL VOLUMES OF SAMPLE AND REAGENTS IN THE CUVETTE

Sample Volume	20 µL
Total Reagent Volume	242 µL
Antibody-coated particle	47 µL
Reaction Buffer	140 µL
Diluent 1	55 µL

REACTIVE INGREDIENTS

REAGENT CARTRIDGE CONSTITUENTS	VOLUME
IgE Antibody (particle-bound mouse anti-IgE antibody)	3.0 mL
Reaction Buffer	7.7 mL
Sodium Azide (used as a preservative)	< 0.1% (w/w)

Also non-reactive chemicals necessary for optimal system performance.

CALIBRATOR CONSTITUENTS

Human IgE (diluted in a non-serum matrix)	2 mL
Sodium Azide (used as a preservative)	< 0.1% (w/w)
Bovine Serum Albumin (BSA)	6.0%

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.

⚠ 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.[14]

GHS HAZARD CLASSIFICATION

Not classified as hazardous

SDS	Safety Data Sheet is available at beckmancoulter.com/techdocs

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

IMMAGE Immunochemistry Systems Wash Solution
IMMAGE Immunochemistry Systems Diluent 1
Centrifuge capable of 90,000 x g
At least two levels of control material

REAGENT PREPARATION

1. Invert cartridge gently before removing screw caps.
2. Remove screw caps from reagent cartridges. Check each cartridge for bubbles and remove any bubbles present.
3. Place evaporation caps on both reagent cartridge compartments before loading the cartridge on the instrument.

4. Reagent cartridges should be stored upright and can be removed from the refrigerator and used immediately.
5. Mix all buffers and diluents thoroughly by inversion. Remove screw cap from container. Check each container for bubbles and remove any bubbles present. Place evaporation cap on container before loading the container on the instrument.

ACCEPTABLE REAGENT PERFORMANCE

Acceptability of a reagent is determined from the successful performance of quality control testing, as defined in the QUALITY CONTROL section of this instructions for use.

REAGENT STORAGE AND STABILITY

Storage conditions other than those recommended may cause erroneous results.

Reagent Cartridges

1. Return all reagent cartridges to the refrigerator (+2°C to +8°C) upon completion of the daily workload.
2. The IGE reagents are stable for 14 days with the evaporation caps in place.
3. The IGE reagents are stable until the expiration date on the label if the reagents are stored at +2°C to +8°C with the screw caps in place.

Diluent 1

1. Diluent 1 is stable on the system for 30 days with the evaporation caps in place.
2. Diluent 1 is stable until the expiration date on the label if stored at room temperature with the screw caps in place.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

IGE Calibrator (included in reagent kit)

CALIBRATOR PREPARATION

No preparation is required.

CALIBRATOR STORAGE AND STABILITY

The calibrator is stable until the expiration date printed on the calibrator bottle if stored capped in the original container at +2°C to +8°C.

Storage conditions other than those recommended may cause erroneous results.

Calibrator storage location:

CALIBRATION INFORMATION

1. The IMMAGE Immunochemistry Systems calibration is reagent lot specific.
2. The IGE reagent lot should be recalibrated following specific part replacements or maintenance procedures as defined in the IMMAGE *Operations Manual*.
3. The IMMAGE Immunochemistry System is designed for minimum calibration. Calibrations retained in system memory should be monitored by the performance of quality control procedures on each day of testing.
4. Calibration for IGE is stable for 30 days.
5. The system will automatically perform a verification check during calibration and produce a calibration report. The system will alert the operator of a failed calibration. An explanation of any accompanying error message can be found in the TROUBLESHOOTING Section of the IMMAGE Immunochemistry Systems *Operations Manual*.

CALIBRATOR ASSIGNED VALUES

The assigned value for IGE Calibrator was determined using a matrix of multiple instruments, runs and replicates. For calibrator assigned values, see the Value Assignment Sheet provided in the Reagent Kit.

CALIBRATOR SUMMARY

The IGE Calibrator is a preparation of human IgE serum diluted in a non-serum matrix containing BSA, salts and <0.1% sodium azide (w/w). Assay of the IGE Calibrator provides a response value utilized by the instrument for adjustment of a pre-programmed dose response curve from which concentration values are determined in test specimens.

ADDITIONAL BAR CODE INSTRUCTIONS

1. Locate the calibrator bar code label provided with the calibrator.
2. Place the appropriate label on an empty 13 x 100 mm or 16 x 100 mm test tube. The labeled test tube should be saved for re-use.
3. Place 150 µL of IGE Calibrator in a 0.5 mL sample cup.
4. Place the sample cup in the labeled test tube.
5. Place the labeled tube into a sample rack.
6. Open the sample compartment lid and place the rack on the carousel.
7. Close the sample compartment lid and run the test.

CALIBRATOR LIMITATIONS

IGE Calibrator is lot number specific. It must be used in conjunction with the same lot number of Total Immunoglobulin E reagent.

TRACEABILITY

IGE is traceable to the WHO 2nd International Reference Preparation for Immunoglobulin E (IgE) (IRP 75/502). The traceability process is based on ISO 17511.

QUALITY CONTROL

It is recommended that at least two levels of control material, normal and abnormal, be analyzed daily. Controls should also be run with each new calibration, with a new lot of reagent or buffer, and after specific maintenance or troubleshooting as detailed in the IMMAGE Immunochemistry Systems Operations Manual. More frequent use of controls or the use of additional controls is left to the discretion of the user based on work load and work flow.

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. After setup, load reagents onto the system as directed in the IMMAGE *Operations Manual*.
2. Select chemistries to be calibrated, if necessary. Load bar coded calibrators, controls, and samples or program and load non-bar coded controls and samples for analysis as directed in the IMMAGE *Operations Manual* .
3. Follow the protocols for system operation as directed in the IMMAGE *Operations Manual*.

CALCULATIONS

The IMMAGE Immunochemistry System will automatically calculate results.

REPORTING RESULTS

REFERENCE INTERVALS

Each laboratory should establish its own reference intervals based upon its patient population. The reference interval listed below was obtained from a study consisting of 134 non-allergic adults, performed on the Beckman Coulter ACCESS and verified by the IMMAGE IGE assay.[15]

Table 2.0 Reference intervals

	SAMPLE TYPE	NUMBER OF SAMPLES	95% RANGE (IU/mL)[a]
Beckman Coulter	Serum	134	< 165

a *Non-parametric estimate of 95% confidence interval.

	SAMPLE TYPE	NUMBER OF SAMPLES	95% RANGE (IU/mL)
Laboratory			

Refer to References (16,17) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

UNITS AND CONVERSION FACTOR

Results for the IGE test are reported in default units of IU/mL. Metric conversion within the same unit category will occur automatically if a new unit is selected. A conversion factor must be entered when selecting a unit category different from the default.

Beckman Coulter recommends a conversion factor of 2.4 to convert IU/mL to ng/mL (1 IU/mL = 2.4 ng/mL).[18]

1. From the Setup screen, select **<7>, Units**.
2. Select ng/mL as the unit for IGE.
3. Enter 2.4 as the conversion factor for IGE.

Refer to the System Setup section of the IMMAGE *Operations Manual* for more detailed information on units and conversion factors.

PROCEDURAL NOTES

ANTICOAGULANT TEST RESULTS

The following anticoagulants were assessed by Deming regression analysis with a minimum of 40 paired human serum and plasma samples. Values of serum (X) ranging from 5.01 IU/mL to 754 IU/mL were compared with the values for plasma (Y) yielding the following results:

Table 3.0 Anticoagulant Test Results

ANTICOAGULANT	LEVEL OF ANTICOAGULANT TESTED	DEMING REGRESSION ANALYSIS (IU/mL)
Lithium Heparin	14 Units/mL	Y = 1.013X + 2.55; r = 0.996
Sodium Heparin	14 Units/mL	Y = 0.996X + 4.93; r = 0.995
EDTA	1.5 mg/mL	Y = 0.956X + 3.55; r = 0.998

LIMITATIONS

Samples can be accurately measured within the reportable range of the assay (5 to 30,000 IU/mL). Samples less than 5 IU/mL should be reported as "<5 IU/mL". Samples with concentrations greater than 30,000 IU/mL may report false low results. Samples suspected to have concentrations of this magnitude should be diluted 1:100 and repeated.

Patients with high levels of rheumatoid factor or anti-human IgE autoantibodies may falsely elevate IgE results.[19]

INTERFERENCES

1. The following substances were tested in serum for interference with this methodology at the initial dilution:

Table 4.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT
Bilirubin	Porcine	5 – 60 mg/dL	None
Lipid	Human Triglyceride	180 – 1,126 mg/dL	None[a]
Hemoglobin	Human	100 – 750 mg/dL	None

a Quantitation of IGE by turbidimetry may not be possible in lipemic specimens or may produce inaccurate results, due to the extreme light scattering properties of the sample. Lipemic specimens should be delipidated by ultra centrifugation (90,000 x g for 10 minutes) prior to determination of IGE concentration.

Table 5.0 Rheumatoid Factor Interferences

SUBSTANCE	SOURCE	IGE Concentration (IU/mL)	OBSERVED EFFECT at levels of Interferent
Rheumatoid Factor	Human	46	+16% at 376 IU/mL
		149	None
		343	None

2. Dust particles or other particulate matter (i.e. debris and bacteria) in the reaction solution may result in extraneous light-scattering signals, resulting in variable sample analysis.
3. For assays employing mouse antibodies, the possibility exists for interference by human anti-mouse antibodies (HAMA) in the sample. Human anti-mouse antibodies may be present in samples from patients who have received immunotherapy or diagnostic procedures utilizing monoclonal antibodies or in individuals who have been regularly exposed to animals.[20,21] Additionally, other heterophile antibodies, such as human anti-goat antibodies may be present in patient samples. Interpretation of results should be done in the context of the overall clinical presentation of the patient, including symptoms, clinical history, data from additional tests and other appropriate information.

PERFORMANCE CHARACTERISTICS

NOTE ON PERFORMANCE CHARACTERISTICS

Performance characteristics are based on the initial analytical range. The instrument automatically dilutes samples to be within the initial analytical range. Refer to IMMAGE Immunochemistry Systems Operations Manual for more information.

ANALYTIC RANGE

The IGE test is designed to detect concentrations of this analyte using an initial undiluted (neat) sample.

Table 6.0 Analytical Range

SAMPLE TYPE	BECKMAN COULTER ANALYTICAL RANGE
Serum/Plasma	Initial: 5 – 500 IU/mL Extended: 5 – 30,000 IU/mL

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 7.0 Reportable Range

SAMPLE TYPE	LABORATORY REPORTABLE RANGE

ANALYTICAL SENSITIVITY

Analytical sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Analytical sensitivity for IGE determination is 5.0 IU/mL.

FUNCTIONAL SENSITIVITY

Functional sensitivity is defined as the lowest concentration that can be measured with an interassay CV of 20%. Functional sensitivity is estimated to be 5.0 IU/mL.

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of samples to an accepted clinical method. Values obtained for human IgE using the IMMAGE IGE Test were compared to the values obtained using a commercially available automated chemiluminesence method. Both normal and abnormal IgE serum samples were included in the analysis.

Table 8.0 Equivalency Values

	CHEMILUMINESENCE (EIA) METHOD
N	125
Slope	1.06
Intercept	2.76
Mean (IMMAGE)	79.4
Mean (EIA)	72.1
Correlation Coefficient (r)	0.991

The equivalency values were determined using patient samples ranging from 5.09 IU/mL to 431 IU/mL. Refer to References (22,23) at the end of this instructions for use for guidelines on performing equivalency testing.

PRECISION

A properly operating IMMAGE Immunochemistry Systems should exhibit imprecision values less than or equal to the maximum performance limits listed below. Maximum performance limits were derived by an examination of the precision of various methods, proficiency test summaries, and literature sources.

Table 9.0 Maximum Performance Limits

TYPE OF PRECISION	SAMPLE TYPE	SD (IU/mL)	% CV	CHANGEOVER VALUE (IU/mL)[a]
Within-run	Serum/Plasma	1.0	7.0	14.3
Total	Serum/Plasma	1.5	7.5	20

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.

Comparative performance data for the IMMAGE Immunochemistry Systems evaluated using the NCCLS Approved Guideline EP5-A appears in the table below.[24] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 10.0 Typical Imprecision Values

TYPE OF PRECISION	SAMPLE	Data Points[a]	Test Mean Value (IU/mL)	SD (IU/mL)	% CV
Within-run	Serum Level 1	80	16.5	0.97	5.8
	Serum Level 2	80	145	7.4	5.1
	Serum Level 3	80	383	19.9	5.2
Total	Serum Level 1	80	16.5	1.11	6.7
	Serum Level 2	80	145	9.1	6.3
	Serum Level 3	80	383	28.1	7.3

a The serum point estimate is based on the data from 1 system, run for 20 days, 2 runs per day, 2 observations per run on an instrument operated and maintained according to the manufacturer`s instructions.

Refer to References (22,24) for guidelines on performing precision testing.

NOTICE

These degrees of precision were obtained in typical testing procedures and are not intended to represent performance specifications for this test procedure.

ADDITIONAL INFORMATION

For more information, refer to the IMMAGE Immunochemistry Systems *Operations Manual*.

SHIPPING DAMAGE

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

REVISION HISTORY

Revision AE

Updated references to manual sections.

Revision AF

Updated corporate address.

Revision AG

Added Revision History

Revision AH

Added new language requirement: Czech, and Korean.

Revision AJ

Revised Traceability section.

Revision AK

Added GHS classification and Trademark statement.

Revision AL

Updates to comply with requirements per Beckman Coulter Global Labeling Policy.

Revision AM

Added new language requirement: Brazilian Portuguese.

Revision AN

Update to Symbols Key

Revision AP

Added new language requirement: Dutch, Romanian, and Slovak. Additional changes to comply with requirements per Beckman Coulter Global Labeling Policy.

Revision AR

Revised Interferences section.

Revision AT

Removed references to "Chemistry Reference Manual", CE mark and EC Rep name and address.

Revision of sample stability information, minor instructional clarification and corrections throughout, and updates to comply with requirements per Beckman Coulter Global Labeling Policy.

SYMBOLS KEY

Table 11.0

REF	Catalogue Number	IVD	In Vitro Diagnostic
CONTENTS	Contents		Temperature limit
	Manufacturer		Expiration Date
LOT	Batch code	SDS	Safety Data Sheet
CE	CE Mark		Consult Instructions for Use
EC REP	Authorized Representative in the European Community		Date of Manufacture
	Caution		Biological risks
REAGENT CART	Reagent Cartridges	BAR CODE STRIP	Bar Code Strip
CALIBRATOR	Calibrator	CAL CARD	Calibration Card
BAR CODE CARD	Bar Code Card	CAPS	Caps
VA SHEET	Value Assignment Sheet	SN	Serial Number
Made in USA of US and Foreign Components		Made in USA of US and Foreign Components	

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