BECKMAN COULTER

IMMAGE Immunochemistry Systems
Instructions For Use

DNB
Antideoxyribonuclease B

REF 447480 (150 tests)

For *In Vitro* Diagnostic Use

FOR PROFESSIONAL USE ONLY

Rx Only

PRINCIPLE

INTENDED USE

DNB reagent, when used in conjunction with IMMAGE Immunochemistry Systems and DNAse B Calibrator, is intended for the quantitative determination of antibodies to deoxyribonuclease B (DNB) in human serum by rate nephelometry.

CLINICAL SIGNIFICANCE

Deoxyribonuclease B (DNAse B) is one of several extracellular enzymes produced by group A beta-hemolytic streptococci. Since DNAse B is produced extensively by group A serotypes and is not produced in significant amounts by other serological groups (C and G), anti-DNAse B is a reliable streptococcal antibody test for both skin and throat infections. Testing for anti-DNAse B assists in the diagnosis and management of patients with acute rheumatic fever, acute glomerulonephritis, Sydenham's chorea, scarlet fever, pharyngitis, and many other group A streptococcal based illnesses.

Unlike anti-streptolysin O (ASO), anti-DNAse B is less susceptible to false positives caused by bacterial growth in the specimen, liver disease, and oxidation of the antigen. In determining the presence of group A streptococcal infection, it is highly recommended that ASO testing be performed in conjunction with anti-DNAse B, especially when the ASO titer is borderline.[1,2,3,4]

METHODOLOGY

The DNB test measures the rate of increase in light scattered from particles suspended in solution as a result of complexes formed during an antigen-antibody reaction.

CHEMICAL REACTION SCHEME

Antideoxyribonuclease B(sample) + Particle bound deoxyribonuclease B(antigen) → [Antideoxyribonuclease B(sample) - antigen Complex]

E014488L.EPS

SPECIMEN

TYPE OF SPECIMEN

Serum samples are the recommended specimens.

Samples should be collected in the manner routinely used for any clinical laboratory test.[5] Freshly drawn sample from a fasting individual is preferred.

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 be physically separated from contact with cells within two hours from the time of collection.[6]
2. If serum samples are not assayed within 8 hours, samples should be stored at +2°C to +8°C for up to 48 hours.[6]

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
DNB Reagent Cartridge (Antigen)	1
Evaporation Caps	2
DNB Reagent Bar Code Card	1
DNAse B Calibrator (1 mL)	1
DNAse B Calibrator Bar Code Card	1
DNAse B Calibrator Strips	2
Vigil DNAse B Control, Level 1 (4 mL)	2
Vigil DNAse B Control, Level 2 (4 mL)	2
Value-assignment Sheet	1

NOTICE

Only components of reagent kits of the same lot number may be combined for use.

INITIAL VOLUMES OF SAMPLE AND REAGENTS IN THE CUVETTE

Sample Volume	4.5 µL
Total Reagent Volume	347.5 µL
Antigen	25 µL
Buffer 3	300 µL
Diluent 1	22.5 µL

REACTIVE INGREDIENTS

REAGENT CARTRIDGE CONSTITUENTS	VOLUME
DNB Antigen (purified recombinant protein attached to polystyrene particles)	4.7 mL
Sodium Azide (used as a preservative)	< 0.1% (w/w)

Also non-reactive chemicals necessary for optimal system performance.

NOTICE

The recombinant-based Deoxyribonuclease B is **not classified as a Biohazard**.

⚠ 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 beckmancoulter.com/techdocs

MATERIALS NEEDED BUT NOT SUPPLIED WITH REAGENT KIT

IMMAGE Immunochemistry Systems Wash Solution
IMMAGE Immunochemistry Systems Buffer 3
IMMAGE Immunochemistry Systems Diluent 1
Centrifuge capable of 10,000 x g

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. Storage of reagent above +45°C will adversely affect performance.

Reagent Cartridges

1. Return all reagent cartridges to the refrigerator (+2°C to +8°C) upon completion of the daily workload.
2. The DNB reagents are stable for 30 days with the evaporation caps in place.
3. The DNB 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 and Buffer 3

1. Diluent 1 and Buffer 3 are stable on the system for 30 days with the evaporation caps in place.
2. Diluent 1 and Buffer 3 are stable until the expiration date on the label if they are stored at room temperature with the screw caps in place.

Reagent storage location:

CALIBRATION

CALIBRATOR REQUIRED

DNAse B Calibrator (DNB-CAL) - included in the DNB Reagent Kit.

DNAse B Calibrator is derived from defibrinated and processed fresh frozen human plasma with <0.1% sodium azide (w/w). Assay of DNAse B Calibrator provides a response value utilized for the adjustment of a pre-programmed calibrator curve from which concentration values are determined in test specimens.

NOTICE

The lot number on the DNAse B Calibrator bottle and bar code card must be the same.

CALIBRATOR PREPARATION

1. Allow contents of the bottle to thaw and come to room temperature.
2. Mix the contents by gently inverting the bottle.

⚠ 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.[7]

CALIBRATOR STORAGE AND STABILITY

DNAse B 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 DNB reagent lot should be recalibrated when changing Buffer 3 lot or 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 DNB 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

IMMAGE values are printed on the value assignment sheet.

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 the appropriate calibrator in a sample cup.
4. Place the appropriate cup in the labeled test tube.

5. Place the tube into a sample rack.
6. Repeat steps 1-5 for any additional calibrators. Continue placing calibrators into the same sample rack.
7. Open the sample compartment lid.
8. Place the rack(s) containing calibrators in positions A and B on the sample carousel.
9. Close the sample compartment lid.

TRACEABILITY

DNB is traceable to the Manufacturer's Working Calibrator. 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

CONTROLS REQUIRED

Vigil DNAse B Control, Levels 1 and 2 (included in the DNB Reagent Kit)

Vigil DNAse B assayed control is a stabilized liquid designed for monitoring the overall performance of antideoxyribonuclease B test systems in the clinical laboratory. The use of two levels of control enables the laboratorian to monitor changes in calibration, along with analytical error and impression. Vigil DNAse B Control is not intended for use as a standard.

Vigil DNAse B Control is derived from defibrinated and processed fresh frozen human plasma with <0.1% sodium azide (w/w). The preparation of these stabilized controls in liquid form eliminates errors commonly associated with filling, drying and the reconstitution of lyophilized control products.[8,9,10,11]

In order to assess system performance, it is essential that procedures in the IMMAGE *Operations Manual* be followed precisely while using these control materials.

CONTROL PREPARATION

1. Mix the contents with a gentle swirling motion before dispensing.
2. To prevent leakage into the cap, store upright and do not mix by inversion.

⚠ 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.[7]

CONTROL STORAGE AND STABILITY

The controls are stable until the expiration date printed on the label if stored capped in the original container at +2°C to +8°C.

To maximize stability, remove the bottle from the specified storage temperature, dispense the control required, and **immediately** return the bottle to the specified storage temperature.

Vigil DNAse B Control storage location:

ASSAY VALUES

IMMAGE values are printed on the value assignment sheet.

The MEAN VALUES were established through participating laboratories performing replicate analyses utilizing representative samples of control materials.

The PERFORMANCE RANGE was obtained by combining estimates of assay variance as determined by participating laboratory data and other currently available studies. Average values obtained in the laboratory should fall within the performance range, although the recovery may not be identical with the mean value listed. Those values outside the range may indicate unsatisfactory performance. The causes for such a discrepancy may be variations in the technique, equipment, calibrator, etc., which should be evaluated by the laboratorian and remedial action taken before the results are reported.

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

The reference interval values for this analyte were established using the IMMAGE Immunochemistry Systems for a population of 310 apparently healthy male and female adults from California.

Each laboratory should establish its own reference interval(s) based on its patient population.

Table 2.0 Reference intervals

	UPPER LIMIT OF NORMAL
Beckman Coulter	187 U/mL

	UPPER LIMIT OF NORMAL
Laboratory	

Because of the variability associated with population characteristics it is important to understand the need for each laboratory to establish its own upper limit of normal.[12,13]

The upper limit of normal is usually defined as the highest value that is exceeded by only 20% of a population.[4] Normal values may vary with season of the year, age, and geographical location of the patient.[12,13]

A single DNB analysis may not be meaningful due to the variability of DNB values within the normal population.[14] Both clinical and laboratory findings should be considered in reaching a diagnosis.

Refer to References (15,16) for guidelines on establishing laboratory-specific reference intervals.

Additional reporting information as designated by this laboratory:

UNITS AND CONVERSION FACTOR

Results for the DNB test are reported in default units of U/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.

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

PROCEDURAL NOTES

LIMITATIONS

1. Streptococcal infections already treated with antibiotics may not produce increased results.[14]
2. Abnormally high antideoxyribonuclease B test results should not be used as a single diagnostic indicator but should be correlated with other clinical findings.[14] Multiple results obtained at weekly or bi-weekly intervals are more relevant.

3. DNAse B Calibrator values are specific for IMMAGE Immunochemistry Systems only when using Beckman Coulter Reagents. Use of DNAse B Calibrator with other reagents or test procedures is not recommended.
4. 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 calibration rate units.
5. The viscosity of the control materials may be higher than that of normal serum. Care should be taken when pipetting small volumes of control. It is recommended that the pipet tip be held only slightly below the meniscus while aspirating control, to avoid adherence of excess amounts of material on the tip of the pipet. For automated systems, a slower speed setting is recommended.
6. Only components of reagent kits of the same lot number may be combined for use.

INTERFERENCES

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

Table 3.0 Interferences

SUBSTANCE	SOURCE	LEVEL TESTED	OBSERVED EFFECT
Rheumatoid Factor	Human	22 – 442 IU/mL	None
Bilirubin	Porcine	5 – 30 mg/dL	None
Lipid	Intralipid[a]	125 – 750 mg/dL	None[b]
Hemoglobin	Human	100 – 500 mg/dL	None

a Intralipid is a registered trademark of KabiVitrum, Inc., Clayton, NC 27250.

b Quantitation of DNB by nephelometry 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 (10,000 x g for 3 minutes) prior to determination of DNB concentration.

2. Nonspecific interference can occur between less dilute samples and polymer-enhanced buffer when off-line dilutions less than 1:6 are assayed.
3. 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.

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 DNB test is designed to detect concentrations of this analyte using an initial 1:6 sample dilution.

Table 4.0 Analytical Range

SAMPLE TYPE	BECKMAN COULTER ANALYTICAL RANGE
Serum	Initial: 50 – 600 U/mL Extended: 50 – 21,600 U/mL

REPORTABLE RANGE (AS DETERMINED ON SITE):

Table 5.0 Reportable Range

SAMPLE TYPE	LABORATORY REPORTABLE RANGE

SENSITIVITY

Sensitivity is defined as the lowest measurable concentration which can be distinguished from zero with 95% confidence. Sensitivity for DNB determination is 50 U/mL.

EQUIVALENCY

Equivalency was assessed by Deming regression analysis of samples to an accepted clinical method. Values obtained for DNB using the IMMAGE Immunochemistry Systems DNB test were compared to the values obtained using a commercially available automated nephelometric assay (NIA) method. Both normal and abnormal samples were included in the analysis.

Table 6.0 Methods Comparison Values

	NIA METHOD
N	101
Slope	0.885
Intercept	-99.0
Mean (IMMAGE)	383
Mean (NIA)	545
Correlation Coefficient (r)	0.897

The methods comparison values were determined using patient samples ranging from 50 to 2,375 U/mL U/mL. Refer to References (17,18) 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 7.0 Maximum Performance Limits

TYPE OF PRECISION	SAMPLE TYPE	SD (U/mL)	% CV	CHANGEOVER VALUE (U/mL)[a]
Within-run	Serum	12	5.0	240
Total	Serum	16	6.5	246

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.[19] Each laboratory should characterize their own instrument performance for comparison purposes.

Table 8.0 Typical Imprecision Values

TYPE OF PRECISION	SAMPLE	Data Points[a]	Test Mean Value (U/mL)	SD (U/mL)	% CV
Within-run	Serum Level 1	80	90.7	2.47	2.7
	Serum Level 2	80	319	6.6	2.1
	Serum Level 3	80	433	8.3	1.9
Total	Serum Level 1	80	90.7	2.47	2.7
	Serum Level 2	80	319	7.3	2.3
	Serum Level 3	80	433	9.3	2.1

a The 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 (17,20) 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 AJ

Revised Reagent Cartridge Constituents Volume.

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

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 9.0

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	CONTROL	Control
CALIBRATOR	Calibrator	BAR CODE STRIP	Bar Code Strip
CAL CARD	Calibration Card	CAPS	Caps
BAR CODE CARD	Bar Code Card	SN	Serial Number
VA SHEET	Value Assignment Sheet		
Made in USA of US and Foreign Components		Made in USA of US and Foreign Components	

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