SIEMENS Healthineers

N Latex IgG3

N IGG3

Revision bar indicates update to previous version.

BN II System / BN ProSpec® System

Intended Use

In-vitro diagnostic for the quantitative determination of IgG Subclass 3 in human serum and plasma by means of particle-enhanced immunonephelometry with the BN II and BN ProSpec® System.

Summary and Explanation

Human IgG antibodies are composed of the four subclasses IgG1, IgG2, IgG3 and IgG4. The structural differences between the IgG subclasses are reflected in different biologically important functions such as antigen recognition, complement activation and cell surface receptor binding[1].

While absolute concentrations of the IgG subclasses are subject to a large biological variance, their relative proportions with regard to total IgG content is regulated within relatively narrow limits, with about 60 to 75 % for IgG1, 15 to 25 % for IgG2 and < 10 % each for IgG3 and IgG4. A deficiency of IgG subclasses is often observed in patients with recurring infections of the upper and lower respiratory passages[1,2]. A decreased concentration of IgG1 is more likely to be traced back to a general immune deficiency than to a specific subclass deficiency. Decreased IgG2 concentrations are associated with respiratory tract infections as well as autoimmune disorders. Polyclonal increases of IgG subclass concentrations may occur with chronic antigen stimulation, but have only a secondary diagnostic role[1]. Monoclonal IgG increases are due to the increased production of one IgG subclass. The determination of IgG subclasses is indicated for diagnostic clarification in patients with increased susceptibility to infection. A determined IgG subclass deficiency is an indication of a malfunctioning immune defense and requires additional diagnostic investigation[1].

Principles of the Procedure

Polystyrene particles coated with specific antibodies to human IgG3 form aggregates that cause irradiated light to be scattered when mixed with samples containing IgG3. The intensity of the scattered light is dependent on the concentration of the respective protein in the sample. The evaluation is performed by comparison with a standard of known concentration.

Reagents

Reagent	Description	Storage	Stability

N Latex IgG3
N IGG3 REAGENT
	Ready to use liquid containing:
	• suspension of polystyrene particles coated with specific antibodies (sheep) against IgG3 (< 1 g/L)
	• Preservative:
	  • Amphotericin B (0.625 mg/L)
	  • Gentamicin sulfate (6.25 mg/L)
		2–8 °C
		May be used up to the expiry date indicated on the label if stored unopened.
		Do not freeze!
			2–8 °C:
			once opened, 2 weeks[a]

[a] if re-closed tightly immediately following use and stored at 2 to 8 °C

On-board stability
At least 5 days at 8 hours each or a comparable period of time (maximum 40 hours).

Note: On-board stability may vary, depending on the system used and laboratory conditions. For further details, refer to the respective Assay Protocols document.

Warnings and Precautions

For *in-vitro* diagnostic use only.

For laboratory professional use.

Safety data sheets (MSDS/SDS) available on siemens-healthineers.com/sds.

CAUTION!
Federal (USA) law restricts this device to sale by or on the order of licensed healthcare professionals.

Caution
This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with all government requirements.

Preparing Reagents

N IGG3 is ready-for-use as supplied and requires no additional preparation.

Specimen Collection and Handling

For testing, use the freshest possible (stored for a maximum of 8 days at 2 to 8 °C) or frozen human serum samples as well as heparinized and EDTA plasma samples. If samples are frozen within 24 hours after collection, they may be stored below –20 °C for up to one month, if repeated thawing and freezing are avoided. Serum samples must be fully coagulated and must not contain any particles or traces of fibrin after centrifuging. Lipemic samples or frozen samples that are cloudy after thawing must be clarified prior to the assay by centrifuging (10 minutes at approx. 15 000 × g).

Procedure

Materials Provided

REF	Contents		
OPAV03	N Latex IgG3 N IGG3	1 ×	2 mL

Materials Required but not Provided

Item	Description
REF OQIM19	N PROT STANDARD SL, N Protein Standard SL (human)
REF OQIN19	N/T PROT CONTROL SL/L, N/T Protein Control SL/L (human)
REF OQIO19	N/T PROT CONTROL SL/M, N/T Protein Control SL/M (human)
REF OQIP19	N/T PROT CONTROL SL/H, N/T Protein Control SL/H (human)
REF OUMT65	N DILUENT, N Diluent
REF OUMU15	N SUPPLEMENT P, N Supplementary Reagent/Precipitation
REF OQUB21	Cleaner SCS (for BN II System)
REF OVLE21	BN II Evaporation Stoppers (optional)
Instruments, such as:	• BN II System • BN ProSpec® System

Disposable supplies and equipment as described in the BN System's Instruction Manual.

Notes

Consult the respective BN System Instruction Manual for detailed instructions.

Reagents and samples stored at 2 to 8 °C may be used immediately for testing in the BN II and BN ProSpec® System.

Assay Protocols on the BN Systems

The assay protocols for N IGG3 are included in the Assay Protocols document as well as the software for the respective device. All steps are performed automatically by the system.

Performing Calibration

Reference curves are plotted by multiple point calibration. The calculation is automatically performed by producing dilution series of the N PROT STANDARD SL with N DILUENT. The dilutions must be used within 4 hours. The reference curves may be used as long as accuracy controls, e.g. N/T PROT CONTROL SL/L, N/T PROT CONTROL SL/M and N/T PROT CONTROL SL/H, remain within the respective range. A new reference curve must be generated for each change in reagent lot.

The exact measuring range depends upon the concentration of the protein in each lot of N PROT STANDARD SL. Typical measuring ranges are given in the respective Assay Protocols document.

Measuring patient samples

Samples are automatically diluted 1:2 000 with N DILUENT. The dilutions must be measured within 4 hours. For results that lie outside the measuring range, the measurement may be repeated with a higher or lower sample dilution.

Repeat measurements from further sample dilutions are described in the BN System's Instruction Manual.

Internal Quality Control

The N/T PROT CONTROL SL/L, N/T PROT CONTROL SL/M and N/T PROT CONTROL SL/H should be analyzed after each calculation of a reference curve, after the first time a reagent vial is used, as well as with each series of samples.

The controls are assayed and evaluated like patient samples. The target value and range for the controls are given in the corresponding Table of Assigned Values.

The values can be entered via data storage device on the BN ProSpec® System.

Follow government regulations or accreditation requirements for quality control frequency.

If a result of the control measurements lies outside of the range, the control determination must be repeated. If the deviation is confirmed by the repeat measurement, a new reference curve should be calculated. Patient results should not be released until the cause of the deviation is identified and corrected.

Results

The evaluation is performed automatically in g/L or in a derived unit selected by the user on the BN System.

Limitations

Samples containing particles must be centrifuged prior to testing. Lipemic samples that cannot be clarified by centrifuging (10 minutes at approx. 15 000 × g) must be excluded from testing. In individual cases, monoclonal immunoglobulins may exhibit reactions that deviate from that of the polyclonal standard, with the possibility of lower or nonlinear results. In case of suspicious results, the measurement should be repeated with a higher sample dilution.

As an additional control, the determination of all four IgG subclasses (N AS IgG1, REF OQXI09, N AS IgG2, REF OQXK09 and N Latex IgG4, REF OPAU03) and the comparison of their sum to the total IgG (determined with N Antiserum to Human IgG, REF OSAS19) is recommended. The sum of subclasses 1 - 4 should fall within 80 to 120 % of the total IgG; otherwise, the presence of a monoclonal component or another disturbance should be tested.

Results of this test should always be interpreted in conjunction with the patient's medical history, clinical presentation and other findings.

Due to matrix effects, inter-laboratory survey samples and control samples may yield results that differ from those obtained with other methods. It may therefore be necessary to assess these results in relation to method-specific target values.

Siemens Healthineers has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. User defined modifications are not supported by Siemens Healthineers as they may affect performance of the system and assay results. It is the responsibility of the user to validate modifications to these instructions or use of the reagents on analyzers other than those included in Siemens Healthineers Reference Guides (Application Sheets) or these Instructions for Use.

Expected Values

The following reference ranges (2.5th to 97.5th percentile in g/L) were established by testing samples from 405 apparently healthy children from North America and Central Europe as well as 279 apparently healthy adults from Central Europe with N IGG3 on a BN System:

Age Group	IgG3 (g/L)
≤ 1 year	0.093 – 0.920
> 1 to ≤ 3 years	0.087 – 0.864
> 3 to ≤ 6 years	0.129 – 0.789
> 6 to ≤ 12 years	0.158 – 0.890
> 12 to ≤ 18 years	0.138 – 1.058
> 18 years	0.11 – 0.85

In addition, each laboratory should determine its own reference ranges, since these are subject to many variables that may be different for each population tested.

Performance Characteristics

Note: The values indicated for the Specific Performance Characteristics represent typical results and are not to be regarded as specifications for N IGG3.

Specificity

There are no known cross reactivities with the antibodies used.

Sensitivity

The sensitivity of the test is determined by the lower limit of the reference curve and is therefore dependent on the concentration of analytes in the N PROT STANDARD SL.

Precision

The precision was calculated by measuring samples with different analyte concentrations and calculating the coefficients of variation (CV) of the results by means of variance analysis (n = 40):

IgG3	Mean Value (g/L)	Run-to-Run CV (%)	Within-Run CV (%)	Total CV (%)
N/T PROT CONTROL SL/L	0.224	2.4	5.3	5.2
N/T PROT CONTROL SL/M	0.344	2.4	4.0	4.2
N/T PROT CONTROL SL/H	0.45	3.3	3.3	4.4
Serum pool 1	0.108	3.6	3.8	4.9
Serum pool 2	0.84	3.8	5.3	6.0

Method Comparison

72 serum samples were tested with N IGG3 in the BN System (y). For comparison, these samples were also tested by radial immunodiffusion methods (RID, x) found on the market. Correlation of the results provided the following data:

Protein	Regression line comparison	Correlation Coefficient
IgG3	y (BNS) = 1.01 × (RID) - 0.014 g/L	r = 0.98

Technical Assistance

For customer support, contact your local technical support provider or distributor.

siemens-healthineers.com

Current Version of Assay Protocols

N IGG3 can be used in combination with various automated analyzers. Siemens Healthineers provides Assay protocols for instruments listed in section "Materials Required but not Provided", page 3 under the dedicated link below:

siemens-healthineers.com/ap

As Siemens Healthineers continuously monitors the product performance and safety, the users are required to ensure that they work with the correct revision of the instructions for the product lots in use. Please periodically review the availability of new electronic labeling revisions to ensure safe use of the product.

The IFU version number is visible on each product box label. Siemens Healthineers ensures that all products lots bearing the same IFU version number are compatible with the electronic labeling provided via siemens-healthineers.com/eIFU.

References

1. Zielen S, Thomas L. IgG subclasses. In: Thomas L, ed. Clinical Laboratory Diagnostics. Frankfurt: TH-Books Verlagsgesellschaft, 1998: 678-81.
2. Morell A. Clinical relevance of IgG subclass deficiencies. Ann Biol Clin (Paris) 1994; 52: 49-52.

Definition of Symbols

The following symbols may appear on the product labeling:

	Do not reuse		Use By
LOT	Batch Code	REF	Catalogue Number
	Caution		Manufacturer
EC REP	Authorized representative in the European Community		Contains sufficient for <n> tests
	Biological Risks	IVD	*In Vitro* Diagnostic Medical Device
	Temperature Limitation		Consult instruction for Use
	Non-sterile		CE marking of conformity
CE 0197	CE marking of conformity with notified body ID number. Notified body ID number can vary.	CONTENTS	Contents
	Reconstitution volume	LEVEL	Level
	Keep away from sunlight and heat	WARNING	Warning
DANGER	Danger	RxOnly	Prescription device (US only)
UDI	Device Identification (UDI) barcode	REACH xx/xx/xx	REACH Authorization Number

Legal Information

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