SIEMENS Healthineers

N AS IgG1

N AS IGG1

CE 0197

Revision bar indicates update to previous version.

Atellica® NEPH 630 System / BN II System / BN ProSpec® System

Intended Use

N AS IGG1 is an in vitro diagnostic reagent for the quantitative determination of IgG subclass 1 as aid to diagnosis and monitoring of immune deficiencies in individuals with suspected immune deficiency in human serum, heparin and EDTA plasma by means of automated Siemens Healthineers immuno-nephelometry systems.

For IgG1 testing no international reference preparation or method is available.

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[1,2].

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. Diminished serum IgG subclass concentrations can be linked to different disease states[3–6].

A deficiency of IgG subclasses is often observed in patients with recurring infections of the upper and lower respiratory passages. 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. 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.

Principles of the Procedure

Proteins contained in human body fluids form immune complexes in an immunochemical reaction with specific antibodies. These complexes scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the relevant protein in the sample. The result is evaluated by comparison with a standard of known concentration.

Reagents

Reagent	Description	Storage	Stability
N AS IgG1 N AS IGG1	Ready to use liquid containing: • animal serum produced by immunization of sheep with highly purified human IgG subclasses (concentration of active antibodies: < 60 g/L) • Preservative: • Sodium azide (< 1 g/L)	2–8 °C May be used up to the expiry date indicated on the label if stored unopened.	2–8 °C: once opened, 2 weeks[a,b]

[a] if securely capped immediately after use
[b] if contamination (e.g. by microorganisms) is precluded

During storage, N AS IGG1 can develop precipitates or turbidity which are not caused by microbial contamination and which do not affect their activity.

In such cases, the antiserum should be clarified by centrifugation (10 minutes at approximately 15 000 × g) or filtered prior to use.

Disposable filters with a pore size of 0.45 µm are suitable for this purpose.

On-board stability
3 days at 8 hours each or comparable period of time (maximum 24 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.

According to EU regulation 2017/746, any serious incident that has occurred in relation to the device shall be reported to the manufacturer and the competent authority of the EU Member State in which the user and/or patient is established.

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

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

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

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 AS IGG1 is ready-for-use as supplied and requires no additional preparation.

Specimen Collection and Handling

Storing the Specimen

Suitable samples are human serum, heparinized or EDTA plasma, as fresh as possible (stored no more than 8 days at 2 to 8 °C) or stored deep-frozen. Serum and plasma samples can be stored at below –20 °C for up to one month, if they are frozen within 24 hours after collection and if repeated freezethaw cycles are avoided. The serum samples must be completely coagulated and, after centrifugation, must not contain any particles or traces of fibrin. Lipemic samples or frozen samples which became turbid after thawing must be clarified by centrifugation (10 minutes at approximately 15 000 × g) prior to testing.

Procedure

Materials Provided

REF	Contents		
OQXI09	N AS IgG1 N AS IGG1	1 ×	1.5 mL

Materials Required but not Provided

Item	Description
REF OQIM13	N PROT STANDARD SL, N Protein Standard SL (human)
REF OQIN13	N/T PROT CONTROL SL/L, N/T Protein Control SL/L (human)
REF OQIO13	N/T PROT CONTROL SL/M, N/T Protein Control SL/M (human)
REF OQIP13	N/T PROT CONTROL SL/H, N/T Protein Control SL/H (human)
REF OUMS65	N BUFFER, N Reaction Buffer
REF OUMT65	N DILUENT, N Diluent
REF OVLE21	BN II Evaporation Stoppers (optional)
Instruments[c], such as:	• Atellica® NEPH 630 System • BN II System • BN ProSpec® System

Additional materials and supplies as described in the respective System's Instruction Manual.

[c] Availability of analyzers may vary by country.

Notes

Consult your respective System's Instruction Manual for details regarding operation of the instrument.

Reagents and samples stored at 2 to 8 °C can be used immediately on the Atellica® NEPH 630 System, BN II System or BN ProSpec® System.

Assay Protocols on the Atellica® NEPH 630 System and the BN Systems

The assay protocols are given in the Assay Protocols document and software of the instrument. All the steps are performed automatically by the system.

Performing Calibration

Reference curves are constructed by multi-point calibration. Serial dilutions of N PROT STANDARD SL are automatically prepared by the instrument using N DILUENT. The standard dilutions are to be used within four hours. The reference curves can be used for as long as the accuracy controls, e.g. N/T PROT CONTROL SL/L, N/T PROT CONTROL SL/M and N/T PROT CONTROL SL/H, are reproduced within their respective range. If a different lot of antiserum is used, as well as a different lot of N BUFFER, a new reference curve must be recorded. 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.

Assay of Specimens

Samples are automatically diluted 1:100 with N DILUENT and measured. The dilutions must be measured within 4 hours. If the readings obtained are outside the measuring range, the assay can be repeated using a higher or lower dilution of the sample. Refer to respective System's Instruction Manual for information on repeat measurements using other dilutions.

Internal Quality Control

Assay N/T PROT CONTROL SL/L, N/T PROT CONTROL SL/M and N/T PROT CONTROL SL/H after each establishment of a reference curve, the first opening of an antiserum vial as well as with each run of samples. The controls are assayed and evaluated as for patient samples. The assigned values and range are listed in the Table of Assigned Values for the respective control.

The values can be entered via data storage device on the Atellica® NEPH 630 System and 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

Evaluation is performed automatically in g/L or in a unit selected by the user.

Limitations

Turbidity and particles in the samples may interfere with the determination. Therefore, 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.

As an additional control, the determination of all four IgG subclasses (N AS IgG2, REF OQXK09, N Latex IgG3, REF OPAV03 and N Latex IgG4, REF OPAU03) and the comparison of their sum to the total IgG (determined with N Antiserum to Human IgG, REF OSAS15) 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.

Siemens Healthineers has validated use of these reagents on various analyzers to optimize product performance and meet product specifications. Please note that the applications on other analyzers can be validated by the instrument manufacturer in accordance with the requirements of the REGULATION (EU) 2017/746 under their responsibility as long as the intended purpose and performance are not modified. 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 Application Sheets or these Instructions for Use.

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.

Expected Values

The following reference ranges (2.5th to 97.5th percentile in g/L) were established by testing samples from 417 apparently healthy individuals from North America and Central Europe as well as 279 apparently healthy adults from Central Europe with N AS IGG1 on a BN System:

Age Group	[g/L]
≤ 1 year	1.51–7.92
> 1–≤ 3 years	2.65–9.38
> 3–≤ 6 years	3.62–12.28
> 6–≤ 12 years	3.77–11.31
> 12–≤ 18 years	3.62–10.27
> 18 years	4.05–10.11

Equivalency for the Atellica® NEPH 630 System has been confirmed.

Nevertheless, each laboratory should determine its own reference intervals since values may vary depending on the population studied.

Performance Characteristics

Note: The values cited for specific performance characteristics of the assay represent typical results and are not to be regarded as specifications for N AS IGG1.

Measuring Range

The measuring range of the N AS IGG1 assay is established by the lower limit of the reference curve and depends therefore upon the concentration of the protein in the N PROT STANDARD SL. Typical measuring ranges are given in the respective Assay Protocols document.

Specificity

There are no known cross-reactivities of the antiserum used.

Sensitivity

The analytical sensitivity of the assay is determined by the lower limit of the reference curve and depends therefore upon the concentration of IgG1 in the N PROT STANDARD SL. A typical Limit of Detection (LoD) for IgG1 is < 0.047 g/L.

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):

IgG1	Mean [g/L]	Repeatability CV [%]	Within-Device/Lab Precision CV [%]
N/T PROT CONTROL SL/L	3.6	2.1	3.0
N/T PROT CONTROL SL/M	6.8	1.9	2.9
N/T PROT CONTROL SL/H	9.1	2.1	2.5
Serum pool 1	15.6	1.5	1.8
Serum pool 2	5.8	1.6	2.5

Equivalency for the Atellica® NEPH 630 System to a BN System has been confirmed.

The reproducibility was assessed by Siemens Healthineers for N AS IGG1 based on publicly available proficiency testing information in 2019/2020. The overall reproducibility median CV% was found to be < 10 % including lot, instrument, laboratory and operator variability factors.

Method Comparison

Thirty (30) serum samples were assayed with N AS IGG1 on the BN System (y) and also with a commercial method (x) of radial immunodiffusion. Correlation of the results yielded the following data:

Protein	n	Regression line comparison	Correlation Coefficient
IgG1	30	y (BN) = 0.93 x (RID) + 0.50 g/L	0.98

Equivalency for the Atellica® NEPH 630 System to a BN System has been confirmed.

Antigen Excess

The N AS IGG1 reagent shows no high-dose hook effect in the assay for IgG1 up to 78.6 g/L.

Technical Assistance

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

siemens-healthineers.com

Current Version of Assay Protocols

N AS IGG1 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. Vlug A, et al. The structure and function of human IgG subclasses. Eur Clin Lab 1989; 8: 26.
2. Jefferis R, Kumararatne DS. Selective IgG subclass deficiency: quantification and clinical relevance. Clin Exp Immunol 1990; 81: 357-67.
3. Morell A. Clinical relevance of IgG subclass deficiencies. Ann Biol Clin (Paris) 1994; 52: 49-52.
4. Stiehm ER. The four most common pediatric immunodeficiencies. J Immunotoxicol. 2008; 5: 227-34.
5. Herrod HG. Clinical significance of IgG subclasses. Curr Opin Pediatr. 1993; 5: 696-9.
6. Hamilton RG. Human IgG subclass measurements in the clinical laboratory. Clin Chem 1987; 33: 1707-25.

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	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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