SIEMENS Healthineers

N Latex SAA

N SAA

CE 0197

Revision bar indicates update to previous version.

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

Intended Use

N SAA is an in vitro diagnostic reagent for the quantitative, WHO-standardized determination of serum amyloid A (SAA) as an aid in diagnosis and monitoring of inflammatory and infectious disorders in human serum and heparin plasma by means of automated Siemens Healthineers immuno-nephelometry system.

Summary and Explanation

Serum amyloid A (SAA) is an acute-phase protein mainly produced by the liver in response to proinflammatory cytokines secreted by the activated monocytes. However, SAA also can be produced by macrophages, endothelial cells, cancer cells, smooth muscle fiber cells and adipocytes at the sites of atherosclerotic lesions. SAA plasma levels can increase ep to 1 000-fold; first elevations are seen 3 to 6 hours after an inflammatory stimulus, reaching a peak concentration in 2 to 3 days[1,2].

SAA is associated with the high-density lipoproteins (HDL) and plays a major role as a modulator of inflammation, is involved in carcinogenesis, in metabolism and in transport of cholesterol[3]. One particularly important aspect of SAA is that its degradation products can be deposited in various organs as amyloid A (AA) fibrils[4]. Secondary AA amyloidosis is a serious complication in chronic inflammatory diseases primarily affecting kidney function.

Like C-reactive protein (CRP), SAA determination can be used in the diagnosis and monitoring of inflammatory and infectious processes; in contrast to CRP SAA levels also show a moderate increase in response to viral infections[1]. Furthermore, SAA can help in the assessment of different lung disorders, acute renal transplant rejection, and cardiovascular risk assessment[2,5–7]

Principles of the Procedure

Polystyrene particles coated with specific antibodies to human SAA are aggregated when mixed with samples containing SAA. These aggregates scatter a beam of light passed through the sample. The intensity of the scattered light is proportional to the concentration of the respective protein in the sample. The result is evaluated by comparison with a standard of known concentration.

Reagents

Reagent	Description	Storage	Stability
N Latex SAA N SAA			

REAGENT	Lyophilized reagent containing:
	• polystyrene particles coated with specific antibodies (sheep) to human SAA
	• Albumin, human
	• Preservatives:
	  • Gentamicin sulfate (reconstituted: 6.25 mg/L)
	  • Amphotericin B (reconstituted: 0.625 mg/L)
		2–8 °C
		May be used up to the expiry date indicated on the label if stored unopened.
			2–8 °C: reconstituted, 4 weeks[a,b]
			Do not freeze!

STANDARD	Lyophilized reagent containing: • human sera with elevated levels of SAA • Preservative: • Sodium azide (reconstituted: < 1 g/L)	2–8 °C May be used up to the expiry date indicated on the label if stored unopened.	2–8 °C: reconstituted, 4 weeks[a,b] Do not freeze!
CONTROL	Lyophilized reagent containing: • human sera with elevated levels of SAA • Preservative: • Sodium azide (reconstituted: < 1 g/L)	2–8 °C May be used up to the expiry date indicated on the label if stored unopened.	2–8 °C: reconstituted, 4 weeks[a,b] Do not freeze!
SUPPLEMENT	Ready to use liquid containing: • glycine • Sodium chloride • 2-Pyrrolidone • Detergent • 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, 4 weeks[a,b] Do not freeze!

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

Standardization

N SAA STANDARD: The SAA concentration of the reconstituted standard is indicated in the enclosed table. The SAA concentration of N SAA STANDARD was calibrated with reference to the 1st International Standard Serum Amyloid A Protein Lot No. 92/680[8] and is lot-dependent.

N SAA CONTROL: The SAA concentration of the reconstituted control is indicated in the enclosed table. The concentration of the listed analyte is calibrated by reference to a protein standard preparation of Siemens Healthineers in the appropriate method and is lot-dependent.

On-board stability

A minimum of 5 days, at 8 hours per day or comparable period of time.

Note: On-board stability may vary, depending on the system used and laboratory conditions. For further details, refer to the respective Assay Protocols document.
On-board stability of the N SAA CONTROL on the Atellica® NEPH 630 System and on the BN ProSpec® System is stated in 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.

Danger! N SAA REAGENT
Hazardous ingredient: Imidazole (7.19 % [w/w]).
H314: Causes severe skin burns and eye damage. **H360D**: May damage the unborn child.
P260: Do not breathe dust. **P264**: Wash hands thoroughly after handling. **P201**: Obtain special instructions before use. **P280**: Wear protective gloves/protective clothing/eye protection/face protection. **P301 + P330 + P331**: IF SWALLOWED: rinse mouth. Do NOT induce vomiting. **P303 + P361 + P353**: IF ON SKIN (or hair): Remove/Take off immediately all contaminated clothing. Rinse skin with water/shower. **P363**: Wash contaminated clothing before reuse. **P310**: Immediately call a POISON CENTER or doctor/physician. **P305 + P351 + P338**: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. **P308 + P313**: IF exposed or concerned: Get medical advice/attention. **P501**: Dispose of contents and container in accordance with all local, regional, and national regulations.

Danger! N SAA SUPPLEMENT
Hazardous ingredient: 2-Pyrrolidone (9.76 % [w/w]), epsilon-Caprolactam (8.09 % [w/w]).
H319: Causes serious eye irritation. **H360D**: May damage the unborn child.
P201: Obtain special instructions before use. **P280**: Wear protective gloves/protective clothing/eye protection/face protection. **P308 + P313**: IF exposed or concerned: Get medical advice/attention.
P337 + P313: If eye irritation persists: Get medical advice/attention.

Warning! N SAA STANDARD, N SAA CONTROL
Hazardous ingredient: Sodium azide (1.34 % [w/w]).
H312: Harmful in contact with skin. **H412**: Harmful to aquatic life with long lasting effects.
P280: Wear protective gloves/protective clothing/eye protection/face protection. **P273**: Avoid release to the environment. **P312**: Call a POISON CENTER or doctor/physician if you feel unwell.
P501: Dispose of contents and container in accordance with all local, regional, and national regulations.

CAUTION! POTENTIAL BIOHAZARD
N SAA REAGENT, N SAA STANDARD, N SAA CONTROL
Each donor or donor unit was tested and found to be negative for human immunodeficiency virus (HIV) 1 and 2, hepatitis B virus (HBV) and hepatitis C virus (HCV) using either tests that are CE marked or FDA approved for this purpose. Because no known test can offer complete assurance of the absence of infectious agents, all human derived products should be handled with appropriate caution.

Caution
N SAA REAGENT, N SAA STANDARD, N SAA CONTROL
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 SAA REAGENT: Resuspend the lyophilized vial contents with 2 mL of distilled water. The reagent can be used 15 minutes after reconstitution. Shake gently to mix before first use.

N SAA STANDARD and N SAA CONTROL: Dissolve the lyophilized vial contents in 0.5 mL of distilled water. Shake gently to mix. The standard as well as the control are ready for use 60 minutes after reconstitution.

N SAA SUPPLEMENT: The solution is supplied ready-for-use.

Specimen Collection and Handling

Collecting the Specimen

Suitable samples are human serum and heparinized plasma, either as fresh as possible (stored for no more than 7 days at 2 to 8 °C) or stored frozen.

Storing the Specimen

Samples can be stored at below – 20 °C for up to 3 months, if they are frozen within 24 hours after collection and if repeated freeze-thaw cycles are avoided. Serum samples must be completely coagulated and, after centrifugation, must not contain any particles or traces of fibrin. Lipemic samples or frozen samples which are turbid after thawing, must be clarified by centrifugation (10 minutes at approximately 15 000 × g) prior to testing.

Procedure

Materials Provided

REF	Contents	
OQMP11	N Latex SAA N SAA	
	N SAA Reagent N SAA REAGENT	3 × → 2 mL
	N SAA Standard SY (human) N SAA STANDARD	3 × → 0.5 mL
	N SAA Control SY (human) N SAA CONTROL	4 × → 0.5 mL
	N SAA Supplementary Reagent N SAA SUPPLEMENT	3 × 1.3 mL

Materials Required but not Provided

Item	Description
REF OUMT65	N DILUENT, N Diluent
REF OQUB19	Cleaner SCS
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.

Only components (reagent, standard, control and supplementary reagents) from kits of the same lot may be used together; do not combine kit components from kits of different lots.

The lyophilized reagents must not be used until properly reconstituted, (at least 15 minutes for N SAA REAGENT, and at least 60 minutes for N SAA STANDARD and N SAA CONTROL).

A separate cuvette rotor must be used for the SAA assay on the BN II System. The assay can be combined with CardioPhase® hsCRP and N CYSC.

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

The assay protocol for serum and plasma is given in the Assay Protocols document and software of the respective instrument. All steps are performed automatically by the system.

Performing Calibration

Reference curves are generated by multi-point calibration. Serial dilutions of the N SAA STANDARD are automatically prepared by the instrument using N DILUENT. The standard dilutions must be used within half an hour. The analytical value is given in the enclosed table.

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

The reference curve is valid for one week and can be used beyond this period of time as long as a control with corresponding method-depending target values, e.g., N SAA CONTROL, is reproduced within its respective confidence interval. If a different lot of reagent is used, a new reference curve must be generated.

The exact measuring range depends upon the concentration of the protein in each lot of N SAA STANDARD SY. Typical measuring ranges are provided in the respective Assay Protocols document.

Assay of Specimens

Samples are automatically diluted 1:400 with N DILUENT. The diluted samples must be used within two hours.

If the results obtained are outside the measuring range, the assay can be repeated using a higher or lower dilution of sample. Details on repeat measurements using further sample dilutions are described in the respective System's Instruction Manual.

Internal Quality Control

Assay N SAA CONTROL after each establishment of a reference curve, after the first use of a reagent vial as well as with each run of samples. Like the patient samples, the N SAA CONTROL is automatically diluted 1:400 with N DILUENT and must be measured within 30 minutes. The assigned value and the confidence range of the N SAA CONTROL are indicated in the enclosed table.

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 is outside the confidence interval, the determination must be repeated. If the repeated determination confirms the deviation, a new reference curve should be established. Do not release patient results until the cause of the deviation has been identified and corrected.

Results

Evaluation is performed automatically in mg/L or in a unit selected by the user on the respective system.

Limitations

No interference was detected for concentrations of triglycerides up to 20 g/L, of bilirubin up to 0.6 g/L, and of free hemoglobin up to 10 g/L.

Turbidity and particles in the samples may interfere with the determination. Therefore, samples containing particles must be centrifuged prior to testing. Lipemic or turbid samples which cannot be clarified by centrifugation (10 minutes at approximately 15 000 × g) must not be used.

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

In a population with normal serum CRP levels (95th percentile = 5.0 mg/L, n = 483), the 95th percentile for N SAA was found to be at 6.4 mg/L.

Reference intervals vary from laboratory to laboratory depending on the population served and the technique, method, equipment and reagent lot used. Therefore, each laboratory must establish its own reference intervals or verify them whenever one or more of the aforementioned variables are changed.

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 SAA.

Measuring Range

The measuring range of the assay is established by the lower limit of the reference curve and depends therefore upon the concentrations of the proteins in the N SAA STANDARD SY. Typical measuring ranges are given in the respective Assay Protocols document.

Specificity

No cross-reactivity of the applied antibodies is known.

Sensitivity

The analytical sensitivity of the assay is determined by the lower limit of the reference curve and depends therefore on the concentration of the protein in N SAA STANDARD SY.

A typical Limit of Detection (LoD) for SAA < 0.714 mg/L.

The exact assay ranges depend upon the concentration of the protein in each lot of N SAA STANDARD SY. For typical ranges refer to your respective Assay Protocols document.

Precision

For determinations of SAA concentrations within the initial measuring range of 2 to 64 mg/L on a BN System following coefficients of variation (CV), calculated by analysis of variance (n = 40) according to the CLSI Guideline EP05-A[9], were found.

Sample	n	Mean [mg/L]	Repeatability CV [%]	Within-Device/Lab Precision CV [%]
N SAA CONTROL SY	40	13.6	4.2	5.3
Serum sample 1	40	6.60	6.2	6.1
Serum sample 2	40	55.1	4.3	5.4
Serum sample 3	40	192	4.9	6.4

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

The reproducibility was assessed by Siemens Healthineers for N SAA based on analysis of the batch to batch variability. The overall batch to batch variability CV% was found to be < 10 % including lot, instrument and operator variability factors.

Method Comparison

The SAA assay was compared to a commercially available nephelometric SAA method by evaluating 54 serum samples ranging from 3.54 to 163 mg/L. A correlation coefficient of 0.994 was obtained, with an intercept value of − 0.310 mg/L and a slope of 1.07.

Antigen Excess

The N SAA REAGENT shows no high-dose hook effect in the SAA assay up to concentrations of: 2 300 mg/L SAA

Technical Assistance

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

siemens-healthineers.com

Current Version of Assay Protocols

N SAA 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 4 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

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5. Perez JD, Sakata MM, Colucci JA, et al. Plasma proteomics for the assessment of acute renal transplant rejection. Life Sci. 2016;158:111-20.
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7. Zewinger S, Drechsler C, Kleber ME, et al. Serum amyloid A: high-density lipoproteins interaction and cardiovascular risk. Eur Heart J. 2015;36:3007-16.
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9. NCCLS. Evaluation of Precision Performance of Clinical Chemistry Devices; Approved Guideline. NCCLS document **EP05-A** [ISBN 1-56238-368-X]. NCCLS, 940 West Valley Road, Suite 1400, Wayne, PA 19087-1898, USA, 1999.

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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