SIEMENS Healthineers

N α_1-Microglobulin Kit

N A1M

CE 0197

Revision bar indicates update to previous version.

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

Intended Use

N A1M is an in vitro diagnostic reagent for the quantitative determination of α1-microglobulin as aid to diagnosis and monitoring of kidney disease in patients at risk or with signs of kidney disease in human urine by means of automated Siemens Healthineers immuno-nephelometry systems.

N A1M uses a calibration against an internal protein reference preparation.

Summary and Explanation

α1-microglobulin (A1M, protein HC) is a 27 kDa glycoprotein produced by the liver. In the circulation, A1M exists in free form or complexed with other plasma proteins. The free form is filtered by the glomerulus into primary urine, from which it is reabsorbed by the proximal tubulus, where catabolization occurs[1].

Urinary A1M levels are a sensitive marker of tubular function. In normal urine only trace amounts of A1M are present. Any damage to the tubular system interferes with the reabsorption from the primary urine and leads to an increased A1M excretion with the urine. Such tubular proteinuria can result from nephrotoxic substances, such as heavy metals (lead, cadmium) or drugs (e.g. certain analgesics, cytostatics, or antibiotics), acute kidney failure, acute or chronic pyelonephritis, renal vascular diseases, Fanconi syndrome, Balkan nephropathy or kidney transplant rejection[1–3].

Via a mathematical model the quantitation of urinary A1M in relation to albuminuria allows the calculation of the degree of tubulointestinal involvement in proteinuria and helps in differential diagnosis between tubular and glomerular proteinuria[4].

Principles of the Procedure

In an immunochemical reaction, the proteins contained in the human urine sample form immune complexes 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 α_1-Microglobulin Kit N A1M			
N AS A1M	Ready to use liquid containing: • animal serum produced by immunization of rabbits with highly purified human A1M (α_1-Microglobulin) (concentration of active antibodies: < 1.0 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, 4 weeks[a,b] Do not freeze!
N SUPPLEMENT A	Ready to use liquid containing: • Detergent • Buffer • Preservative: • reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one / 2-methyl-2H-isothiazol-3-one (3:1)	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

During storage, N Antisera 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 filtered prior to use. Disposable filters with a pore size of 0.45 µm are suitable for this purpose.

On-board stability
A minimum of three days at eight hours per day or a 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.

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.

N SUPPLEMENT A
Hazardous ingredient: reaction mass of 5-chloro-2-methyl-2H-isothiazol-3-one / 2-methyl-2H-isothiazol-3-one (3:1) (0.00105 % [w/w]).
May produce an allergic reaction.

Caution
N AS A1M
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

The N Antiserum and N Supplementary Reagent A are ready-for-use as supplied and require no additional preparation.

Specimen Collection and Handling

Collecting the Specimen

Suitable samples are human urine, as fresh as possible (stored no more than 8 days at 2 to 8 °C). Random and timed urine collections are suitable specimens for the assay. Urine samples must not be frozen. Each urine sample must be centrifuged prior to testing (10 minutes at approximately 15 000 × g).

Procedure

Materials Provided

REF	Contents		
OWLA11	N α_1-Microglobulin Kit N A1M		
	N Antiserum to Human α_1-Microglobulin N AS A1M	1 ×	2 mL
	N Supplementary Reagent A N SUPPLEMENT A	1 ×	2 mL

Materials Required but not Provided

Item	Description
REF OQLV05	N PROT STANDARD UY, N Protein Standard UY
REF OQLW13	N/T PROT CONTROL LC, N/T Protein Control LC (human)
REF OPFT03	N CON LC1, N Protein Control LC1
REF OPFU03	N CON LC2, N Protein Control LC2
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.

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

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 steps are performed automatically by the system.

Performing Calibration

Reference curves are constructed by multi-point calibration. Serial dilutions of N PROT STANDARD UY 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 controls with corresponding methoddepending target values, e.g. N/T PROT CONTROL LC, N CON LC1 and N CON LC2 are reproduced within their respective range. If a different lot of antiserum is used, 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 UY. Typical measuring ranges are given in the respective Assay Protocols document.

Assay of Specimens

Samples are assayed in undiluted form. If the readings obtained are outside the measuring range, the assay can be repeated using a higher dilution of the sample. Refer to the respective System's Instruction Manual for information on repeat measurements using other dilutions.

Internal Quality Control

Assay N/T PROT CONTROL LC, N CON LC1, N CON LC2 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 ranges are listed in the Table of Assigned Values for the respective controls.

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 control value is outside the range, 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 deviation has been identified and corrected.

Results

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

Limitations

Turbidity and particles in the sample may interfere with the determination. Therefore, all urine samples must be centrifuged prior to testing. Samples which cannot be clarified by centrifugation (10 minutes at approximately 15 000 × g) must not be used. At pH values below 6 a measurable fall in the α_1-microglobulin concentration may occur in some cases if the urine samples are stored for several days[5].

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 concentration of α_1-microglobulin in second morning urine specimen of healthy adults is below 12 mg/L[6]. The reference interval was established based on 115 urine specimens. Different reference intervals apply for other types of urine specimen (first morning specimen, 24 hour specimen).

Nevertheless, each laboratory should determine its own reference intervals since values may vary depending on the individual 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 A1M.

Measuring Range

The measuring range of the assays is established by the lower limit of the reference curve and depends therefore upon the concentrations of the proteins in the N PROT STANDARD UY. 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 assays is determined by the lower limit of the reference curve and depends therefore upon the concentration of A1M in the N PROT STANDARD UY. A typical Limit of Detection (LoD) for a1MU is < 5.36 mg/L.

Precision

The following coefficients of variation (CV) were obtained with the N Antiserum to Human α_1-Microglobulin on a BN II System:

a1MU	n	Mean [mg/L]	Repeatability CV [%]	CV Within-Device/Lab Precision CV%
N/T PROT CONTROL LC	40	36.0	2.3	2.6
Pool Low	40	8.6	3.2	3.2
Pool High	40	58.6	2.6	3.2

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

The reproducibility was assessed by Siemens Healthineers for N A1M based on publicly available proficiency testing information in 2019/2020. The overall reproducibility median CV% was found to be < 15.5 % including lot, instrument, laboratory and operator variability factors.

Method Comparison

Fiftytwo (52) urine samples were assayed with the N AS A1M on the BN System (y) and radial immunodiffusion (x) (LC Partigen®). Correlation of the results yielded the following data:

Protein	Linear Regression	Coefficient of Correlation
α_1-Microglobulin	y (BN) = 1.08 x (RID) - 2.36 mg/L	0.996

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

Antigen Excess

The N AS A1M reagent shows no high-dose hook effect in the assay for a1MU up to 1 062 mg/L.

Technical Assistance

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

siemens-healthineers.com

Current Version of Assay Protocols

N A1M 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. Penders J, Delanghe JR. Alpha 1-microglobulin: clinical laboratory aspects and applications. Clin Chim Acta 2004;346(2):107-18.
2. Terzi I, Papaioannou V, Papanas N, et al. Alpha1-microglobulin as an early biomarker of sepsis-associated acute kidney injury: a prospective cohort study. Hippokratia 2014;18(3):262-8.
3. Guder WG, Hofmann W. Clinical role of urinary low molecular weight proteins: their diagnostic and prognostic implications. Scand J Clin Lab Invest Suppl 2008;241:95-8.
4. Hofmann W, Ehrich JH, Guder WG, et al. Diagnostic pathways for exclusion and diagnosis of kidney diseases. Clin Lab 2012;58(9-10):871-89.
5. Donaldson MD, Chambers RE, Woolridge MW, et al. Stability of alpha 1-microglobulin, beta 2-microglobulin and retinol binding protein in urine. Clin Chim Acta 1989; 179: 73-7.
6. Hofmann W, Guder WG. Präanalytische und analytische Faktoren bei der Bestimmung von IgG, Albumin, α_1-Mikroglobulin und Retinol-bindendem Protein im Urin mit dem Behring Nephelometer System (BNS). Lab med 1989; 13: 470-8.

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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