SIEMENS

CE

ADVIA® 1800
ADVIA® 2400
Chemistry Systems

Ammonia (AMM)

Current Revision and Date[a]	Rev. L, 2020-02	
Product Name	ADVIA® Chemistry Ammonia (AMM) Reagents	REF 04802290
Systems	ADVIA 1800 Chemistry System ADVIA 2400 Chemistry System	
Materials Required but Not Provided	Siemens ToxAmmonia Calibrator Reagent container adapters Commercially available controls	REF 06549444
Specimen Types	Plasma (heparin, EDTA)	
Assay Principle	Enzymatic	
Assay Range	Plasma: 8.8–1300.0 µg/dL (5.2–763.1 µmol/L)	
Reagent Storage	2–8°C	
Reagent On-System Stability	30 days	
Reagent Code	74047	

[a] In Rev. H or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

This *in vitro* diagnostic method is intended to quantitatively measure the concentration of ammonia in human plasma (heparin or EDTA) on ADVIA® Chemistry systems.

Summary and Explanation

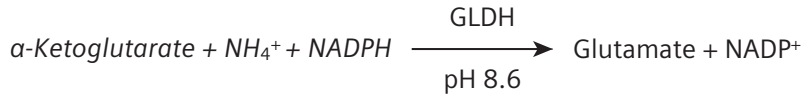
The major source of circulating ammonia is the gastrointestinal (GI) tract. Under normal conditions, ammonia is metabolized to urea by liver enzymes. Several diseases, both inherited and acquired, cause elevated ammonia (hyperammonemia). The inherited deficiencies of urea cycle enzymes are the major cause of hyperammonemia in infants. The acquired hyperammonemia diseases are caused by liver disease, renal failure, and Reye's syndrome. Elevated ammonia is toxic to the central nervous system.

Plasma ammonia is measured by either chemical or enzymatic methods. The enzymatic assay, which is simple and specific, is the most frequently used. The ADVIA Chemistry Ammonia (AMM) assay is an enzymatic method that uses glutamate dehydrogenase and reduced nicotinamide adenine dinucleotide phosphate (NADPH). The enzymatic reaction, which generates an optical density change, is measured as an endpoint. The advantage of using NADPH is that it has less interference from intrinsic plasma constituents than does reduced nicotinamide adenine dinucleotide (NADH).[1–3]

Principles of the Procedure

The ammonia concentration in plasma is measured by using the enzyme glutamate dehydrogenase (GLDH) and the coenzyme NADPH. GLDH catalyzes the conversion of ammonia and α-ketoglutarate to glutamate and H_2O together with the conversion of NADPH to NADP. In the excess of α-ketoglutarate and NADPH, the reaction rate of NADPH to NADP is proportional to the concentration of ammonia in the sample. The corresponding optical decrease in absorbance is measured at 340/694 nm.

Reaction Equation



Reagents

Reagent	Description	Storage	Reagent Stability
REF 04802290	**ADVIA Chemistry Ammonia (AMM) Reagents**		
Ammonia Reagent 1 - buffer AMM R1	16 mL in 20-mL containers Triethanolamine buffer, pH 8.6 (0.15 mol/L) NaN_3 (0.09%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days
Ammonia Reagent 1 Mix - substrate AMM R1 MIX	2.4 g in 5-mL bottles Reduced nicotinamide adenine dinucleotide phosphate (NADPH) (0.26 mmol/L) α-Ketoglutarate (3.88 mmol/L)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days
Ammonia Reagent 2 - buffer AMM R2	6 mL in 20-mL container Triethanolamine buffer, pH 8.6 (0.15 mol/L) NaN_3 (0.09%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days
Ammonia Reagent 2 Mix - enzyme AMM R2 MIX	0.5 mL in 5-mL bottles Glutamate dehydrogenase (GLDH) (≥ 1200 U/L) NaN_3 (≤ 0.2%, weight/volume)	2–8°C	**Unopened:** Stable until the expiration date on product. **On-system:** 30 days

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

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 prevailing regulatory requirements.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For *in vitro* diagnostic use.

Storing and Stability

Unopened reagents are stable until the expiration date printed on the product label when stored at 2–8°C. Do not freeze reagents.

Specimen Collection and Handling

Siemens Healthcare Diagnostics validated plasma (heparin and EDTA) for the ADVIA Chemistry AMM assay.

Follow these guidelines for specimens used for this assay:

- Immediately after collection, centrifuge and assay the specimen.
- The specimen should be kept on ice.
- The use of lipemic samples may cause a significant interference with this assay.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Procedure

Materials Provided

The following materials are provided:

Item	Contents	Number of Tests
REF 04802290	Reagent 1: 2 × 20-mL containers Reagent 1 Mix: 2 × 5-mL containers Reagent 2: 2 × 20-mL containers Reagent 2 Mix: 2 × 5-mL containers	2 × 138

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description
REF 06549444	Siemens ToxAmmonia Calibrator
REF 02404085	20-mL reagent container adapter for 40-mL slot (ADVIA 1800)
REF 00771668	20-mL reagent container adapter for 70-mL slot (ADVIA 2400)
	Commercially available control materials

Assay Procedure

Sampling, reagent delivery, mixing, and processing are automatically performed by the ADVIA Chemistry system.

For detailed information on performing the procedure, refer to the system operating instructions.

Preparing the System

Prepare the ADVIA Chemistry AMM reagents using the instructions listed in the *Preparing the Reagents* section.

For detailed information on preparing the system, refer to the system operating instructions.

Preparing the Reagents

Use the following steps to prepare the ADVIA Chemistry AMM reagents:

Reagent 1

1. Add approximately one-half of the contents of the R1 buffer container into the R1 mix vial.
2. Mix the vial contents to ensure homogeneity.
3. Pour the solution back into R1 buffer container.
4. Mix well.
5. Rinse the R1 mix vial again using part of R1 buffer container content.
6. Pour the R1 buffer back into the R1 buffer container.
7. Mix the contents well to ensure homogeneity.

The R1 reagent is ready for use.

Reagent 2

1. Add the contents of the R2 buffer container to the contents of the R2 concentrate vial.
2. Mix the concentrate vial contents to ensure homogeneity.
3. Pour the solution back into the R2 buffer container.
4. Mix well.
5. Using the R2 buffer contents, carefully rinse the R2 concentrate vial several times.
6. Empty the contents into the R2 container.
7. Mix the contents well to ensure homogeneity.

The R2 reagent is ready for use.

Preparing the Samples

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles.

On-System Stability

The ADVIA Chemistry AMM reagents are stable on the system for 30 days.

Do not use reagents beyond the expiration date.

Performing Calibration

To calibrate the ADVIA Chemistry AMM assay, use the Siemens ToxAmmonia Calibrator, REF 06549444.

Enter the lot-specific calibrator values that are provided with each lot of calibrator. Perform the calibration as described in the calibrator instructions for use.

Calibration Frequency

Calibrate the assay every 30 days.

Calibrate the assay after the following events:

- When the reagent lot number changes
- When a reagent pack is replaced by a new reagent pack with the same lot number, and the previous reagent pack was recalibrated during use

- After replacing critical optical or hydraulic components
- When indicated by quality control procedures

Individual laboratory quality control programs and procedures may require more frequent calibration.

Reagent Blank (RBL) Frequency

The ADVIA Chemistry system measures the RBL during assay calibration.

Run an additional RBL on the same reagent pack every day.

Run an additional RBL when the reagent pack on the system is replaced with a new reagent pack.

Note Use deionized water as the sample for the RBL in the ADVIA Chemistry AMM assay.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

At least once each day of use, analyze 2 levels (low and high) of a commercially available quality control (QC) material with known ammonia concentrations.

A satisfactory level of performance is achieved when the analyte values obtained are within the expected control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

The actual frequency of control in a laboratory is based on many factors, such as workflow, system experience, and government regulation. Each laboratory should evaluate the controls based on the frequency established by their laboratory guidelines.

Also, assay controls under the following conditions:

- Whenever you use a new reagent lot
- Following any system maintenance, cleaning, or troubleshooting procedure
- After performing a new calibration or an additional reagent blank

Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Taking Corrective Action

If the quality control results do not fall within the expected control range or within the laboratory's established values, do not report results. Take the following actions:

1. Determine and correct the cause of the unacceptable control results:
    a. Verify that the assay was performed according to the instructions for use.
    b. Verify that the materials are not expired.
    c. Verify that required maintenance was performed.
    d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
    e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat the prior step.
    f. If necessary, contact your local technical support provider or distributor for assistance.
2. After corrective action is complete, repeat required testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

The system calculates and reports results based on the absorbance measurements of the test sample during the test, and of the calibrator(s) from calibration.

The instrument calculates the concentration of ammonia in µg/dL (common units) or µmol/L (SI units).

Conversion factor: µg/dL × 0.587 = µmol/L

Interpretation of Results

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

Limitations

Avoid the use of hemolyzed or lipemic samples.

A number of substances cause physiological changes in plasma analyte concentrations. A comprehensive discussion of possible interfering substances, their plasma concentrations, and their possible physiological involvements is beyond the scope of this document. Consult the listed reference for specific details on known potential interfering substances.[4,5]

As with any chemical reaction, you must be alert to the possible effect on results of unknown interferences from medications or endogenous substances. The laboratory and physician must evaluate all patient results in light of the total clinical status of the patient.

Venipuncture should occur prior to sulfasalazine administration due to the potential for falsely elevated results and sulfapyridine administration due to the potential for falsely depressed results.

Expected Values

The reference range for ammonia is 19.0–60.0 µg/dL (11–35 µmol/L).[6]

Siemens provides this information for reference. As with all *in vitro* diagnostic assays, each laboratory should determine its own reference ranges for the diagnostic evaluation of patient results. Consider these values as a guideline only.

Performance Characteristics

Analytical Measuring Range

This assay is linear from 10.0–1300.0 µg/dL (5.9–767.0 µmol/L).

Results that are below the assay range are flagged **L**. You should report the test result as < 10.0 µg/dL (< 5.9 µmol/L).

Results that are above the assay range are flagged **H**. You should report the test result as > 1300.0 µg/dL (> 767.0 µmol/L).

Precision

The precision of the ADVIA Chemistry AMM assay was analyzed as described in CLSI protocol EP05-A2.[7] Each sample was assayed 2 times per run, 1 or 2 runs per day, for at least 10 days.

ADVIA 1650/1800

Specimen Type	Mean	Repeatability (Within-Run) SD[a]	Repeatability (Within-Run) CV[b] (%)	Within-Lab (Total) SD	Within-Lab (Total) CV (%)
Common Units (µg/dL)					
Control 1	121.0	4.20	3.5	7.04	5.8
Control 2	257.9	3.53	1.4	6.14	2.4
Control 3	672.4	3.95	0.6	10.00	1.5
SI Units (µmol/L)					
Control 1	71.4	2.48	3.5	4.16	5.8
Control 2	152.2	2.08	1.4	3.62	2.4
Control 3	396.7	2.33	0.6	5.90	1.5

[a] SD = standard deviation
[b] CV = coefficient of variation

ADVIA 2400

Specimen Type	Mean	Repeatability (Within-Run) SD[a]	Repeatability (Within-Run) CV[b] (%)	Within-Lab (Total) SD	Within-Lab (Total) CV (%)
Common Units (µg/dL)					
Control 1	120.6	4.29	3.6	9.34	7.7
Control 2	258.3	5.81	2.3	12.05	4.7
Control 3	678.1	27.94	4.1	34.69	5.1
SI Units (µmol/L)					
Control 1	71.1	2.53	3.6	5.51	7.7
Control 2	152.4	3.43	2.3	7.11	4.7
Control 3	400.1	16.48	4.1	20.47	5.1

[a] SD = standard deviation
[b] CV = coefficient of variation

Actual results will vary depending on the study design, and on the sample and sample population used. Results obtained at individual laboratories may vary from the data provided.

Accuracy / Method Comparison

The performance of the ADVIA Chemistry AMM assay (y) was compared with the performance of the comparison assay on the indicated system (x).

ADVIA 1650/1800

Specimen Type	Comparison Assay (x)	N	Regression Equation	Sy.x	r	Sample Range
Plasma (EDTA)	DCL on ADVIA 1650	43	y = 0.94x - 7.2 y = 0.94x - 4.2	12.6 7.4	0.994	7.7–466.3 µg/dL 4.5–273.7 µmol/L

ADVIA 2400

Specimen Type	Comparison Assay (x)	N	Regression Equation	Sy.x	r	Sample Range
Plasma (EDTA)	ADVIA 1800	43	y = 0.99x - 1.7 y = 0.99x - 1.0	5.8 3.4	0.999	21.0–449.2 µg/dL 12.3–263.7 µmol/L

The correlation of the assay may vary depending on the study design, comparable method, and sample population. Results obtained at individual laboratories may vary from the data provided.

Interferences

Siemens tested the following potential interferents and found the results shown below.

ADVIA 1650/1800

Interferent	Interferent Level	Ammonia Sample Concentration	Interference
Bilirubin (conjugated and unconjugated)	25.0 mg/dL (427.5 µmol/L)	97.8 µg/dL (57.4 µmol/L)	NSI[a]
Hemolysis (hemoglobin)	375 mg/dL (3.75 g/L)	84.6 µg/dL (49.7 µmol/L)	NSI
	500 mg/dL (5.0 g/L)	133.4 µg/dL (78.3 µmol/L)	NSI
Lipemia[b] (from Intralipid)	120.0 mg/dL (1.3 mmol/L)	113.0 µg/dL (66.3 µmol/L)	-21.3%

[a] NSI = No significant interference. A percentage effect ≥ 10% is considered a significant interference.

[b] SI units calculated as triolein

ADVIA 2400

Interferent	Interferent Level	Ammonia Sample Concentration	Interference
Bilirubin (conjugated and unconjugated)	25.0 mg/dL (427.5 µmol/L)	97.8 µg/dL (57.4 µmol/L)	NSI[a]
Hemolysis (hemoglobin)	125 mg/dL (1.25 g/L)	83.6 µg/dL (49.1 µmol/L)	NSI
	125 mg/dL (1.25 g/L)	123.6 µg/dL (72.6 µmol/L)	NSI
Lipemia[b] (from Intralipid)	150.0 mg/dL (1.7 mmol/L)	125.0 µg/dL (73.4 µmol/L)	NSI

[a] NSI = No significant interference. A percentage effect ≥ 10% is considered a significant interference.

[b] SI units calculated as triolein

Note There is poor correlation between turbidity and triglyceride concentration in a lipemic sample.[8]

Actual results will vary depending on the study design, the levels of the potential interferences tested, and the samples used. Results obtained at individual laboratories may vary from the data provided.

Standardization

The ADVIA Chemistry AMM assay standardization is traceable to an internal standard manufactured using highly purified material. Assigned values of Siemens ToxAmmonia Calibrator are traceable to this standardization.

Technical Assistance

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

siemens.com/healthcare

References

1. Burtis CA, Ashwood ER, eds. *Tietz Fundamentals of Clinical Chemistry*. 5th ed. Philadelphia, PA, WB Saunders Company; 2001:417–418.
2. Van Anken HC, Schiphorst ME. A Kinetic Determination of Ammonia in Plasma. *Clinica Chimica Acta*. 56:151–157 (1974).
3. Neeley WE, Phillipson J. Automated Enzymatic Method for Determining Ammonia in Plasma, with 14-Day Reagent Stability, *Clin Chem*. 34:1868–1869 (1988).
4. Martin EW. Hazards of medication, Alexander SF, Farage DJ, Hassan WE, Jr, eds., J.B. Lippincott Company, Philadelphia, PA and Toronto, Canada; 169-189 (1971).
5. Young DS. *Effects of Drugs on Clinical Laboratory Tests*. 5th ed. Washington, DC: AACC Press; 2000.
6. Wu AHB, ed. *Tietz Clinical Guide to Laboratory Tests*, 4th ed. St. Louis, MO: WB Saunders Company; 2006:98–99.
7. Clinical and Laboratory Standards Institute (formerly NCCLS). *Evaluation of Precision Performance of Quantitative Measurement Methods; Approved Guideline—Second Edition.* CLSI document EP05-A2. Wayne, PA: Clinical and Laboratory Standards Institute; 2004.
8. Twomey PJ, Don-Wauchope AC, McCullough D. Unreliability of triglyceride measurement to predict turbidity induced interference. *J Clin Pathol.* 2003 Nov;56(11):861–862.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Keep away from sunlight and heat		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Do not freeze (> 0°C)		Up
	Use by	Σ (n)	Contains sufficient for (n) tests
	Recycle	PRINTED WITH SOY INK	Printed with soy ink
Rev.	Revision	YYYY-MM-DD	Date format (year-month-day)
LOT	Batch code	**RxOnly**	Prescription Device (US only)

Trademarks

Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591 USA

Global Siemens Headquarters
Siemens AG
Wittelsbacherplatz 2
80333 Muenchen
Germany

Global Siemens Healthcare Headquarters
Siemens AG
Healthcare Sector
Henkestrasse 127
91052 Erlangen
Germany
Phone: +49 9131 84-0
siemens.com/healthcare

Global Division
Siemens Healthcare Diagnostics Inc.
511 Benedict Avenue
Tarrytown, NY 10591
USA
siemens.com/healthcare