

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k123320

B. Purpose for Submission:

New Device

C. Measurand:

Ammonia

D. Type of Test:

Quantitative, enzymatic

E. Applicant:

Siemens Healthcare Diagnostics

F. Proprietary and Established Names:

Dimension Ammonia Flex reagent cartridge (AMM)

G. Regulatory Information:

1. Regulation section:

21 CFR 862.1065

2. Classification:

Class I

3. Product code:

JIF

4. Panel:

75 (Chemistry)

H. Intended Use:

1. Intended use(s):

Refer to Indications for Use.

2. Indication(s) for use:

The AMM method is an in vitro diagnostic test for the quantitative measurement of ammonia in human plasma on the Dimension® clinical chemistry system. Ammonia measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Dimension RxL Max

I. Device Description:

The reagent consists of α -ketoglutarate (10 mmol/L), glutamate dehydrogenase (24 KU/L), NADPH analog (0.2 mmol/L) and preservatives.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Dimension Ammonia Flex reagent cartridge (AMON)

2. Predicate 510(k) number(s):

k863840

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Same	Quantitative measurement of ammonia in human plasma
Format	Same	Prepackaged for use on an automated system
Measurement	Same	Bichromatic Rate

Differences		
Item	Device	Predicate
Measuring Range	17 – 1277 µg/dL	0 – 1703 µg/dL
Sample Size	44 µL	53 µL
Sample Type	Plasma (Lithium Heparin and EDTA)	Plasma (Lithium Heparin, EDTA, and Sodium Fluoride)
Reagent Form	Liquid	Tablet

K. Standard/Guidance Document Referenced (if applicable):

EP5-A2: Evaluation of Precision Performance of Quantitative Measurement Methods

EP6-A: Evaluation of the Linearity of Quantitative Measurement Procedures; A Statistical Approach

EP7-A2: Interference Testing In Clinical Chemistry

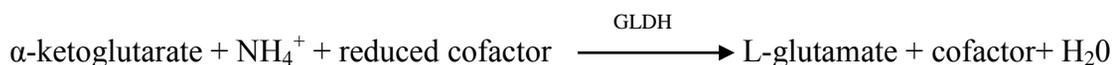
EP9-A2: Method Comparison and Bias Estimation Using Patient Samples

EP17-A: Protocols for Determination of Limits of Detection and Limits of Quantitation

C28-A3: Defining, Establishing, and Verifying Reference Intervals in The Clinical Laboratory

L. Test Principle:

The Dimension® Ammonia assay (AMM) is an enzymatic method that uses glutamate dehydrogenase (GLDH) and a stabilized NADPH analog. Ammonia reacts with α -ketoglutarate and reduced cofactor to form L-glutamate and the cofactor. The reaction is catalyzed by glutamate dehydrogenase. The decrease in absorbance due to the oxidation of the reduced cofactor is monitored at 340/700 nm and is proportional to the ammonia concentration.



M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision was evaluated in accordance with CLSI EP5-A2. The testing was performed over 20 days, with two separate runs per day and two results per run, resulting in a total n of 80. Three levels of commercial control materials were evaluated. The results are summarized in the following table:

Material	Mean (µg/dL)	Repeatability		Within Lab	
		Standard Deviation	% CV	Standard Deviation	% CV
Level 1	40	2.1	5.2	3.7	9.3
Level 2	187	2.6	1.4	3.7	2.0
Level 3	565	3.3	0.6	7.3	1.3

b. *Linearity/assay reportable range:*

Linearity was evaluated in accordance with CLSI EP-6A on the Dimension RxL Max analyzer.

Seventeen levels were prepared using Dimension Vista CHEM 3 CAL B (887 µg/dL) diluted by sequential mixing with CHEM 3 CAL A (0 µg/dL). The mean of 3 replicates was used to evaluate linearity at each level. The range of samples tested was 0 – 1380 µg/dL.

Linear regression of the data produced the following:

$$y = 1.00x + 0.95$$

$$r^2 = 1.00$$

Based on the results of this testing and the Limit of Quantitation testing, the analytical measurement range was determined to be 17 – 1277 µg/dL.

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The calibrators for this assay were cleared under k123321. Please refer to that submission for more information.

d. *Detection limit:*

The **Limit of Detection** (LoD) for AMM is 11 µg/dL, determined consistent with CLSI guideline EP17-A 11 and with proportions of false positives (α) less than 5%

and false negatives (β) less than 5%; based on 96 determinations, with 4 blank and 4 low level samples. The Limit of Blank (LoB) is 5 $\mu\text{g/dL}$.

LoD is the lowest concentration of analyte that can be detected reliably. LoB is the highest concentration that is likely to be observed for a blank sample.

The **Limit of Quantitation** (LoQ) for AMM is 17 $\mu\text{g/dL}$ determined consistent with CLSI Guideline EP17-A and an inter-assay imprecision of <20 % Coefficient of Variation (CV).

e. Analytical specificity:

Interference was evaluated according to CLSI EP7-A2. Bias is the difference in the results between the control sample (without the interferent) and the test sample (contains the interferent) expressed in percent. Bias exceeding 10% is considered interference. The concentrations in the table below represent the highest concentration of the potential interferent tested that did not cause bias greater than +/- 10% at ammonia concentrations of 85 and 426 $\mu\text{g/dL}$.

Substance	Test Concentration
Acetaminophen	20 mg/dL
Amikacin	8.0 mg/dL
Ampicillin	5.3 mg/dL
Ascorbic Acid	6.0 mg/dL
Caffeine	6.0 mg/dL
Carbamazepine	3 mg/dL
Cefoxitin	300 $\mu\text{g/mL}$
Chloramphenicol	5.0 mg/dL
Chlordiazepoxide	1.0 mg/dL
Chlorpromazine	0.2 mg/dL
Cimetidine	2 mg/dL
Diazepam	0.51 mg/dL
Digoxin	6.1 ng/mL
Erythromycin	6 mg/dL
Ethanol	400 mg/dL
Ethosuximide	25 mg/dL
Furosemide	6 mg/dL
Gentamicin	1.0 mg/dL
Heparin	3 U/mL
Ibuprofen	50 mg/dL
Lidocaine	1.2 mg/dL
Lithium	2.2 mg/dL
Nicotine	0.1 mg/dL
Penicillin G	25 U/mL

Pentobarbital	8 mg/dL
Phenobarbital	10 mg/dL
Phenytoin	5 mg/dL
Primidone	4 mg/dL
Propoxyphene	0.16 mg/dL
Protein: Total	14 g/dL
Salicylic Acid	60 mg/dL
Theophylline	4 mg/dL
Urea	500 mg/dL
Valproic Acid	50 mg/dL
Vancomycin	10 mg/dL

For some endogenous substances, the sponsor performed a dose-response study to evaluate interference. The following substances did not cause bias greater than +/- 10% at the concentrations listed:

Substance Tested	Test Concentration	AMM concentration (µg/dL)
Albumin	5.4 g/dL	170
Bilirubin (unconjugated)	60 mg/dL	85
	80 mg/dL	426
Bilirubin (conjugated)	80 mg/dL	85
	80 mg/dL	426
Cholesterol	489 mg/dL	341
Creatinine	21.1 mg/dL	230
Triglyceride	1102 mg/dL	363
Uric Acid	9.3 mg/dL	145

One endogenous substance, hemoglobin, produced a bias of + 11% at 75 mg/dL hemoglobin and 85 µg/dL ammonia. Hemoglobin at 500 mg/dL produced a bias of < +/- 10% at an ammonia concentration of 426 µg/dL ammonia. The sponsor states in their labeling that hemolyzed samples should not be used.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

A method comparison study between the Dimension® Ammonia (AMM) assay and the Dimension® Ammonia (AMON) was performed using 127 patient plasma

samples anticoagulated with lithium heparin on the Dimension RxL Max analyzer. The linear regression is summarized below.

Slope	0.98
Intercept	9 µg/dL
Correlation Coefficient (r)	1.00
Concentration Range:	20 – 1265 µg/dL

b. Matrix comparison:

To demonstrate the relationship between results from lithium heparin plasma and EDTA plasma samples, the sponsor compared 50 matched lithium heparin and EDTA plasma samples on the Dimension RxL Max analyzer. The linear regression is summarized below:

Slope	0.96
Intercept	1.6 µg/dL
Correlation Coefficient (r)	1.00
Concentration Range:	19 – 1153 µg/dL

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

19 – 54 µg/dL

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.