

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

A. 510(k) Number:

k051114

B. Purpose for Submission:

Clearance to market an ammonia assay and control material

C. Measurand:

Ammonia

D. Type of Test:

Quantitative spectrophotometric

E. Applicant:

Sentinel CH SRL

F. Proprietary and Established Names:

Sentinel Ammonia Ultra

Sentinel Ammonia Controls

G. Regulatory Information:

1. Regulation section:

21CFR862.1065: Ammonia test system.

21CFR862.1660: Quality control material (assayed and unassayed).

2. Classification:

Class I (reserved)

3. Product code:

JIF

JJX

4. Panel:

(75) Chemistry

H. Intended Use:

1. Intended use(s):

The Ammonia Ultra is intended for the in vitro quantitative determination of Ammonia (NH₃) in human plasma.

Ammonia measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome.

2. Indication(s) for use:

The Ammonia Ultra is intended for the in vitro quantitative determination of Ammonia (NH₃) in human plasma.

Ammonia measurements are used in the diagnosis and treatment of severe liver disorders such as cirrhosis, hepatitis and Reye's syndrome.

The Ammonia Controls are intended as a means of monitoring Sentinel Ammonia Ultra Assay.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

Abbott ARCHITECT c8000 analyzer

I. Device Description:

The Ammonia Ultra assay described in this bundled submission is composed of a reagent, calibrator and control materials. The device is intended to be sold as an in-vitro diagnostic test for professional use.

The Ammonia Ultra is an enzymatic in vitro diagnostic assay for the quantitative determination of ammonia in human plasma. Ammonia in a patient plasma sample reacts with alpha-ketoglutarate in the presence of glutamate dehydrogenase and NADH to yield glutamate and NAD⁺. The decrease in absorbance due to the NADH oxidation, monitored at 340 nm, is proportional to the ammonia concentration in the patient plasma. The assay eliminates interference from endogenous pyruvate by reaction with lactate dehydrogenase prior to NADH oxidation. The actual

concentration of ammonia is determined multiplying the rate of change in absorbance by a calibration factor obtained during calibration with the ammonia standard included in the kit.

Ammonia controls which are sold separately from the reagent are provided at three different concentrations as quality control material. They are provided in liquid form containing bovine albumin and are designed to mimic human plasma samples. The ammonia controls are used to verify the performance of the Ammonia Ultra assay.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Ammonia-Incorporating Dynamic Stabilization Technology

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

k974620

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Sample	Human plasma	Human Plasma
Method of Action	Enzymatic	Enzymatic
Reaction type	Kinetic	Kinetic
Calibration	Aqueous standard	Aqueous standard
Observation Wavelength	340 nm	340 nm

Differences		
Item	Device	Predicate
Reading Time	54-126 seconds	30-120 seconds
Sample:Reagent Ratio	1:6.7	1:11
Initial Delay	72 seconds	90 seconds

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

CLSI EP05-A2: Evaluation of Precision Performance of Clinical Chemistry Devices;
Approved Guideline-Second Edition

CLSI EP06-A: Evaluation of the Linearity of Quantitative Analytical Methods;
Approved Guideline

CLSI EP09-A2: Method Comparison and Bias Estimation Using Patient Samples;
Approved Guideline - Second Edition

L. Test Principle:

Ammonia reacts with alpha-ketoglutarate and reduced cofactor to form L-glutamate and the cofactor. The reaction is catalyzed by glutamate dehydrogenase. The decrease in absorbance at 340 nm due to the oxidation of the NADH is proportional to the ammonia concentration

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Inter-assay imprecision was determined on an ARCHITECT c8000 for three levels of control materials assayed in 4 replicates twice a day over a period spanning 5 days (n=40 for each level). Calibration was performed every day.

The lowest concentration of ammonia investigated, 56 ug/dL, demonstrated a 4.76% CV inter-assay precision. At 269 ug/dL, the inter-assay precision was 1.3% CV while at 369 ug/dL ammonia, the inter-assay precision was 0.6% CV.

Intra-assay imprecision was determined on 20 replicates of three levels of control materials assayed in one run in one day. The intra-assay imprecision for the low concentration, 54 ug/dL, was 3.2% CV. The intra-assay imprecision for the intermediate concentration, 267 ug/dL, was 0.76% CV. The intra-assay imprecision for the highest concentration used in this test, 373 ug/dL, was 0.46% CV.

b. Linearity/assay reportable range:

Following CLSI EP06-A, the company measured 12 different concentrations of ammonia in duplicate spanning the concentration range of the assay. A linear regression of the expected vs. observed concentration of ammonia yielded a slope of 0.9999 with a R-squared value of 0.9996. Inclusion of a quadratic term in the regression did improve the fit marginally. However, this improvement was not deemed to be clinically relevant.

The analytical range for the assay is 4 to 1700 ug/dL.

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

The calibrators and controls bundled with the assay are prepared gravimetrically from available, high purity ammonium sulfate.

The shelf life of the assay, calibrator, and controls were determined from

actual real-time performance data on materials stored at room temperature. Based on these real-time studies, the shelf life of the Ammonia Ultra assay kit (reagent, standard, and controls) is 18 months.

d. Detection limit:

The sensitivity was determined from 20 replicates of blank material measured in one run in one day and calculated as “the mean of the zero value + 2.547 x Standard Deviation, rounded to 3 x Standard Deviation”. Using this procedure, the sensitivity was found to be 4 ug/dL.

e. Analytical specificity:

Interference from hemoglobin, triglycerides, conjugated and free bilirubin, and pyruvate was evaluated on an Abbott ARCHITECT c8000 analyzer using a significance criterion of >10% variance from control. The controls used had an ammonia concentration of approximately 60 ug/dL.

Concentrations of hemoglobin up to 94 mg/dL did not cause interference at the 10% level. Free bilirubin did not interfere with the assay at the 10% level up to 296 mg/dL, the highest concentration tested. Conjugated bilirubin did not interfere with the assay at the 10% level at concentrations up to 20 mg/dL. Triglycerides did not impact the assay at concentrations up to 2000 mg/dL. Plasma pyruvate levels up to 0.75 mmol/L (6.6 mg/dL) did not cause interference.

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

The performance of this assay was compared to its predicate on an Abbott ARCHITECT c8000. To insure coverage across the full concentration range of their assay, the company supplemented the 40 clinical samples used in this study with 15 additional clinical samples spiked with added ammonia. Samples ranged in ammonia concentration from 40 ug/dL to 1646 ug/dL.

Using the full set of clinical samples, the company demonstrated that their device linearly correlated with their predicate with a correlation coefficient of 0.9972, a slope of 0.9927 and an intercept of 2.526.

b. Matrix comparison:

Not applicable.

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):

Not applicable.

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

Plasma: 31 - 123 µg/dL (18 - 72 µmol/L)

In the package insert, the company states: "It is recommended that each laboratory establish its own expected range. For diagnostic purposes, results obtained for Ammonia should always be evaluated taking into consideration the patient's medical history and all other clinical findings."

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.