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

A. 510(k) Number:

k171482

B. Purpose for Submission:

Modification of an existing device

C. Measurand:

The test reports an AKIRisk score derived from the measurement of insulin-like growth factor-binding protein (IGFBP7) and tissue-inhibitor of metalloproteinases 2 (TIMP2).

D. Type of Test:

Quantitative Immunoassay

E. Applicant:

Astute Medical, Inc.

F. Proprietary and Established Names:

NEPHROCHECK Test System

G. Regulatory Information:

1. Regulation section:

   21 CFR 862.1220

2. Classification:

   Class II

3. Product code:

   PIG

4. Panel:

   75, Clinical Chemistry

H. Intended Use:

1. Intended use(s):

   See Indication(s) for use below.

2. Indication(s) for use:

   The Astute Medical NEPHROCHECK Test System is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and or respiratory compromise and are ICU patients as an aid in the risk assessment for moderate or severe acute kidney injury (AKI) within 12 hours of patient assessment. The NEPHROCHECK Test System is intended to be used in patients 21 years of age or older.

3. Special conditions for use statement(s):

   The NEPHROCHECK Test should not be used as a "standalone test"; test results should be evaluated in the context of all clinical and laboratory data available.

   Test results should be used in patients 21 years of age and older.

   For prescription use only.

   This test system is for central laboratory use only. It is not for point-of-care use.

4. Special instrument requirements:

   ASTUTE140 Meter

I. Device Description:

The Astute NEPHROCHECK Test System is comprised of the NEPHROCHECK Test Kit, the ASTUTE 140 Meter Kit, NEPHROCHECK Liquid Controls Kit and the NEPHROCHECK Calibration Verification (Cal Vers) Kit. The system is designed to be used by trained medical professionals in the central laboratory.

The NEPHROCHECK Test Kit, includes the NEPHROCHECK Test which is a single-use cartridge comprised of two immunoassays for the protein biomarkers, insulin-like growth factor-binding protein (IGFBP7) and tissue-inhibitor of metalloproteinases 2 (TIMP-2) on a membrane test strip enclosed in a plastic housing. The concentrations of the TIMP-2 and IGFBP-7 proteins are used to derive an AKIRISK Score. The test procedure involves the

operator applying a clinical urine sample mixed with labeled fluorescent conjugate to the NEPHROCHECK Test cartridge, and then inserting the Test cartridge into the ASTUTE 140 Meter for incubation, reading, result calculation and result display. Internal positive and negative procedural controls in each NEPHROCHECK Test cartridge monitor the function of each test cartridge. If the automatic check of these procedural controls shows that the control value results are not within pre-defined limits, the ASTUTE 140 Meter will display an error message and the Test result will not be reported.

Included in the NEPHROCHECK Test is test buffer and the NEPHROCHECK Test Conjugate Vial which contains murine monoclonal and goat polyclonal antibodies against TIMP-2 and IGFBP-7, fluorescent dye, stabilizers and excipients. Each kit has the materials necessary to perform 25 tests. Each NEPHROCHECK Test Kit also contains a lot-specific radio-frequency identification (RFID) card containing lot and calibration information. The RFID card information must be loaded prior to using a new test kit lot.

The ASTUTE 140 Meter is a bench-top analyzer that converts the fluorescent signal from each of the two immunoassays contained within the NEPHROCHECK Test cartridge into the AKIRisk score. Only the AKIRisk score appears on the meter display. The ASTUTE 140 Meter contains an internal printer that can print the AKIRisk score.

The NEPHROCHECK Low Liquid Control and NEPHROCHECK High Liquid Control are bi-level, lyophilized control materials prepared from human urine containing human TIMP-2 and human IGFBP7 proteins with protein stabilizers. TIMP-2 and IGFBP-7 proteins have been added to the urine to achieve specified target concentration levels. Each NEPHROCHECK Liquid Controls Kit also contains a high and low RFID encoded with the Liquid Control Kit lot number, expiration date, and the expected range of concentration values based on + two standard deviations in the measurement of each protein biomarker (TIMP-2 and IGFBP-7) in each Liquid Control level. Each NEPHROCHECK Liquid Control Kit Vial is intended for single use only.

The NEPHROCHECK Calibration Verification Kit includes five levels of lyophilized material prepared from human urine, containing TIMP-2 and human IGFBP-7 to achieve specified target concentration levels that evenly span the reportable range of the AKIRisk Score. The expected concentrations and standard deviations of the individual biomarkers are printed on an enclosed Expected Values Card.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   NEPHROCHECK Test System

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

   k153165

3. Comparison with predicate:

Similarities and Differences		
Item	Device Astute Medical NEPHROCHECK Test System	Predicate Astute Medical NEPHROCHECK Test System (k153165)
Indications for Use	The Astute Medical NEPHROCHECK Test System is intended to be used in conjunction with clinical evaluation in patients who currently have or have had within the past 24 hours acute cardiovascular and or respiratory compromise and are ICU patients as an aid in the risk assessment for moderate or severe acute kidney injury (AKI) within 12 hours of patient assessment. The NEPHROCHECK Test System is intended to be used in patients 21 years of age or older.	Same
Electronic Quality Control (EQC) Cartridge	>1000 micron dye dispense rate	~700 micron dye dispense rate

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

CLSI EP09-A3, Measurement Procedure Comparison and Bias Estimation Using Patient Samples; Approved Guideline —Third Edition.

L. Test Principle:

The NEPHROCHECK Test is a sandwich fluorescent immunoassay. Test Buffer Solution and centrifuged urine supernatant are manually added by the operator to the Test Conjugate Vial containing the labeled fluorescent conjugate. A 100 µL aliquot of the urine/fluorescent conjugate mixture is dispensed into the sample port on the NEPHROCHECK Test cartridge where it diffuses across a membrane containing the capture antibodies for TIMP-2 and IGFBP-7. After a brief waiting period, the NEPHROCHECK Test Cartridge is inserted into the ASTUTE 140 Meter for incubation, reading, result calculation and result display. The fluorescent signals from both biomarkers are incorporated into an algorithm to derive the

AKIRisk Score. The NEPHROCHECK Test result is displayed as a single value (AKIRisk score). The AKIRisk Score result is displayed on the Meter LCD screen in approximately 20 minutes from the addition of the specimen.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Performance previously established in DEN130031.

   b. *Linearity/assay reportable range:*

      Performance previously established in DEN130031.

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

      The ASTUTE 140 Meter is factory calibrated. ASTUTE 140 Meter calibration is based on two parameters: fluorescent intensity and linear positioning of the Meter's optics. Calibration is verified by the operator with an Electronic Quality Control (EQC) cartridge and with liquid calibration verifiers. In this submission, the dye dispense rate during production was changed to achieve an increased line width in the EQC cartridge to mitigate potential effects of a cyclic positioning error of the optic block of the ASTUTE 140 Meter during reading of an EQC device.

   d. *Detection limit:*

      Performance previously established in DEN130031.

   e. *Analytical specificity:*

      Performance previously established in DEN130031.

   f. *Assay cut-off:*

      The assay cut-off was previously established in DEN130031.

2. Comparison studies:

   a. *Method comparison with predicate device:*

      42 patient urine samples sourced from the DEN130031 clinical study with a range of AKI Risk scores from 0.04 to 6.87 were tested in duplicate on eight ASTUTE 140 Meters calibrated with the previously cleared EQC cartridge and on eight ASTUTE 140 Meters calibrated with the modified EQC cartridge. Results were analyzed using

Passing-Bablok regression and are as follows:

$y = 1.005x + 0.001432$

b. Matrix comparison:

Not applicable. The NEPHROCHECK Test is for human urine only.

3. Clinical studies:

Performance previously established in DEN130031.

a. Clinical Sensitivity:

See section M3.

b. Clinical specificity:

See section M3.

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

Not applicable.

4. Clinical cut-off:

The assay cut-off was previously established in DEN130031.

5. Expected values/Reference range:

The reference range was previously established in DEN130031.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable and the special controls for this device type under 21 CFR 862.1220.

O. Conclusion:

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