

The NEPHROCHECK® Test System

Intended Use

The Astute 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 intensive care unit (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.



Filling an Unmet Medical Need

Each year in the United States, hospital ICUs admit more than 5.7 million patients.¹ Studies show that up to half of these individuals will develop AKI, turning the situation from bad to worse. In fact, AKI can double or triple ICU length of stay, cost of care and readmission rates.^{2,3} In addition, post-cardiac surgery AKI has been linked to a ten-fold increase in mortality.⁴

There is a consensus that better diagnostic and predictive tools are needed to reduce the burden of this deadly complication.^{5,6} Astute Medical developed the NEPHROCHECK® Test System to address this unmet clinical need. Clinicians can test patients to identify those at risk of developing moderate to severe AKI within the following twelve hours, so that kidney-sparing strategies can be implemented in order to reduce the threat of severe damage.

The Renal “Alarm System”

The NEPHROCHECK® Test quantitatively measures tissue inhibitor of metalloproteinase 2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP-7) – two urinary biomarkers that signal risk of AKI.

When exposed to inflammation, toxicity or other potential sources of injury, certain kidney cells release TIMP-2 and IGFBP-7, temporarily halting the regeneration of cells at the early G1 phase.⁷ This disruption, called G1-cell-cycle arrest, prevents cells with possible damage from dividing. This interruption may be protective in the short term,⁷ however when it involves multiple cells and leads to increases in TIMP-2 and IGFBP-7 that can be detected in urine AKI often

follows.⁸ In a multi-center clinical study the test measuring the combination of TIMP-2 and IGFBP-7 accurately identified risk of moderate to severe AKI within 12 hours of assessment.⁹

Key Clinical Studies

The NEPHROCHECK[®] Test System is a “first of its kind” Urine Biomarker Test. It received FDA clearance in the United States in September 2014. The FDA’s review included a multi-center clinical study comparing the clinical diagnoses of more than 500 subjects to NEPHROCHECK[®] Test results.⁹ Currently, in the United States, no other *in vitro* diagnostic device is marketed for the same intended use as the NEPHROCHECK[®] Test System.

For information regarding trademarks and other intellectual property applicable to this product, including international trademarks, please see AstuteMedical.com/about/intellectual-property. PN0334 Rev C 2016/2/29

¹ Critical Care Statistics. Society of Critical Care Medicine [accessed January 25, 2016]. Available at www.sccm.org.

² Dasta JF, Kane-Gill SL, Durtschi AJ, Pathak DS, Kellum JA. [Costs and outcomes of acute kidney injury \(AKI\) following cardiac surgery](#). *Nephrol Dial Transplant*. 2008;23:1970-1974.

³ Brown JR, Parikh CR, Ross CS, et al. [Impact of perioperative acute kidney injury as a severity index for thirty-day readmission after cardiac surgery](#). *Ann Thorac Surg*. 2014;97(1):111-7.

⁴ Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, et al. Cost and mortality associated with postoperative acute kidney injury. *Ann Surg*. 2014;00:1-8.

⁵ Lewington AJP, Certa J, Mehta RL [Raising Awareness of Acute Kidney Injury: A Global Perspective of a Silent Killer](#). *Kidney Int*. 2013;84(3):457-467.

⁶ American Society of Nephrology Renal Research Report. *J Am Soc Nephrol*. 2005;16:1886-1903.

⁷ Kashani K, Al-Khafaji A, Ardiles T, et al. [Discovery and validation of cell cycle arrest biomarkers in human acute kidney injury](#). *Crit Care*. 2013;17:R25.

⁸ Kellum JA, Chawla LS. Cell-cycle arrest and acute kidney injury: the light and dark sides. *Nephrol Dial Transplant* (2015) 0: 1–7doi: 10.1093/ndt/gfv130

⁹ Bihorac A, Chawla L, Shaw A, et al. [Validation of Cell-Cycle Arrest Biomarkers for Acute Kidney Injury Using Clinical Adjudication](#). *Am J Respir Crit Care Med*. Vol 189, Iss 8, pp 932–939, Apr 15, 2014.