The NephroCheck® Test System

The NephroCheck® Test System received FDA clearance in the United States in September 2014. Currently, in the United States, no other in vitro diagnostic device is marketed for the same intended use as the NephroCheck® Test System. The NephroCheck® Test System consists of the ASTUTE140® Meter, NephroCheck® Test Kit, NephroCheck® Liquid Controls Kit, and NephroCheck® Calibration Verification (Cal Vers) Kit.

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 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

If you are critically ill and are hospitalized you are at risk for developing AKI. If you get AKI everything could be twice as bad. When comparing patients with AKI to patients without AKI, length of stay in both the hospital and the intensive care unit (ICU) doubles,\(^1,2\) the cost of care doubles\(^2\) and you have more than double the readmission rates.\(^3\) Moreover, death rates at one year are higher among those patients with AKI alone, compared to those patients with MI alone.\(^4\)

U.S. hospital ICUs admits more than 5 million critically ill patients/yr.\(^5\) Studies suggest that approximately 50 percent of these patients will develop acute kidney injury (AKI).\(^6\)

There has been a growing consensus that better diagnostic and predictive tools are needed to reduce the burden of AKI.\(^7\) The identification of novel AKI biomarkers has been designated a top priority by the American Society of Nephrology (ASN).\(^8\)
Astute Medical’s NEPHROCHECK® Test System was developed to address this critical unmet clinical need. The test is performed on the ASTUTE140® Meter by fluorescence immunoassay using a human urine sample.

A Renal “Alarm System”
The NEPHROCHECK® Test quantitatively measures two urinary biomarkers -- tissue inhibitor of metalloproteinase 2 (TIMP-2) and insulin-like growth factor binding protein 7 (IGFBP-7), which are thought to be involved in G1 cell cycle arrest in the earliest phases of injury.\(^9,10,11,12\) Recently, it has been shown that, similar to other epithelia, renal tubular cells enter a short period of G1 cell-cycle arrest following injury from experimental sepsis\(^13\) or ischemia\(^14\). It is believed that this prevents cells from dividing when the DNA may be damaged and arrests the process of cell division until the damage can be repaired lest resulting in the cell’s demise or senescence.\(^10\) TIMP-2 and IGFBP-7 are known to be involved in the response to a wide variety of insults (inflammation, oxidative stress, ultraviolet radiation, drugs, and toxins).\(^15,11,12\) This may help explain why they correspond to risk of AKI.

TIMP-2 is a soluble protein of about 22K Dalton molecular weight that is expressed in kidney and other tissues.\(^16\) TIMP-2 binds to and inhibits the activity of various metalloproteinases (MMPs).\(^17\) TIMP-2 also activates MMP2. Through its action on the MMPs, TIMP-2 is thought to be involved or induced in several processes associated with leukocyte infiltration, cellular injury and disruption of cell contacts.\(^18,19,20,21,22,23\)

IGFBP-7 is a soluble protein of about 26K Dalton molecular weight that is expressed in kidney and other tissues.\(^24\) IGFBP-7 is thought to be involved or induced in several types of processes that have been associated with cellular injury.\(^13,25,26,27,28,29,30\)

Key Clinical Studies
The FDA’s review included two multi-center clinical studies comparing the clinical diagnoses of more than 500 subjects to NEPHROCHECK® Test results.

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Criteria
http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx

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