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SUMMARY OF 510(K) SAFETY AND EFFECTIVENESS INFORMATION

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

HiChem BUN/Urea Reagent (product no. 70006) is for the quantitative determination of urea nitrogen in serum, plasma and urine. Plasma urea levels are affected by a wide variety of factors including diet, increased protein catabolism and mild dehydration as well as many renal diseases. The major value of plasma urea measurement is in distinguishing between renal and non-renal related causes.

The HiChem BUN/Urea Reagent determines urea nitrogen through enzymatic hydrolysis by urease. The rate of this reaction, and the quantity of urea nitrogen in the specimen is monitored through the measurement of the resulting ammonia which oxidizes NADH to NAD in the presence of α-keto-glutarate and glutamate dehydrogenase.

The HiChem BUN/Urea Reagent is intended to be used with the HiChem Chemistry Standard, product no. 70023 or other compatible NIST traceable calibration standard either as a manual procedure or on clinical analyzers which can automate the required manipulations. The reagent is supplied as two liquid-stable reagent components which are intended to be combined, either before or during use, in the approximate ratio of 1 part BUN/Urea Enzyme Reagent and 5 parts BUN/Urea Buffer. The BUN/Urea Enzyme Reagent can also be used as a start reagent and combined with the reagent buffer after sample addition.

The HiChem BUN/Urea Reagent calibrated with the HiChem Chemistry Standard, product 70023 is substantially equivalent to the BMD BUN Reagent, product no. 704092 calibrated with Precical Calibrator Serum and Diluent, product no. 620213, both manufactured by Boehringer Mannheim Corp., Indianapolis, IN. and the Sigma BUN (Rate) Reagent, procedure no. 67-UV calibrated with Glucose/Urea Nitrogen Standard, product no. 16-300, both manufactured by Sigma Diagnostics, St. Louis, MO. Substantial equivalence between the HiChem and other calibrators for the purpose of calibrating urea nitrogen methods is also shown. All three reagent/calibrator pairs support the same intended use (with the exception of the specimen limitations for the Sigma reagent) and produce equivalent results with the same clinical purpose. In addition, they are all based on the same methodology which determines urea nitrogen through the rate of NADH depletion. Finally, all reagents are sold in a generic format with their use on various instruments supported through procedure supplements (application sheets).

The effectiveness of the manual procedure is shown by the recovery of linearity standards, the precision of control recoveries, a comparison of serum and plasma recoveries to the Sigma BUN (Rate) Reagent and a comparison of urine recoveries to the BMD BUN Reagent.

Precision, demonstrated by replicate assay of commercially available control sera and urine pools, is shown below.

Specimen	n	mean	within run SD	total SD
Low serum control	30	8.7 mgN/dL	0.48 mgN/dL	0.58 mgN/dL
Mid. serum control	30	25.7 mgN/dL	0.73 mgN/dL	0.70 mgN/dL
High serum control	30	52.1 mgN/dL	0.93 mgN/dL	1.02 mgN/dL
Low urine pool	30	15.4 mgN/dL	0.71 mgN/dL	0.90 mgN/dL
High urine pool	30	53.3 mgN/dL	1.20 mgN/dL	1.54 mgN/dL

The recovery of urea nitrogen using HiChem BUN/Urea Reagent as a manual method is linear to at least 150 mgN/dL as shown by the recovery of linearity standards which span the claimed linear range. Regression statistics are shown below.

(*HiChem Results*) = 0.1 mgN/dL + 0.986 × (*Standard Value*), $r^2 = 1.000$, $s_{y.x} = 0.5$ mgN/dL.

Urea nitrogen recoveries of 80 mixed serum and plasma specimens are compared between the HiChem and Sigma reagents. Urea nitrogen recoveries of 39 urine specimens diluted with 20 parts normal saline are compared between the HiChem BUN/Urea Reagent and the BMD BUN Reagent used on the Hitachi 704. All reagents were calibrated with their recommended calibrators. Least squares regression statistics are shown below.

ELAN
Diagnostics Division

HiChem
231 North Puente Street, Brea, California 92621
Telephone: (714) 871-8360 / (800) 422-3526 / Fax: (714) 871-2439

Serum/Plasma Comparison

(*HiChem Results*) = 0.7 mgN/dL + 0.977 x (*Sigma Results*) $r^2 = 0.996$, $s_{y.x} = 1.00$ mgN/dL.

Urine Comparison

(*HiChem Results*) = 1.9 mgN/dL + 0.966 x (*BMD Results*) $r^2 = 0.990$, $s_{y.x} = 1.82$ mgN/dL.

The use of sodium and lithium heparin, EDTA, citrate, and iodoacetate are also shown to be acceptable chemical additives by comparison of spiked and unspiked serum pools. In all cases, the biases observed were less than 1% and statistically insignificant.

The stability of the combined working reagent over 1 month at 2-8°C and 4 days at 18-25°C are documented through the recovery of linearity standards which span the claimed linear range of the method. In all cases, the observed shifts in standard recovery were less than the greater of 3 mgN/dL or 3%.

The effectiveness of the automated Hitachi 704 procedure is shown by the precision of control recoveries, the recovery of linearity standards, and comparison of mixed serum and plasma and urine recoveries to the BMD BUN Reagent.

Precision, demonstrated by replicate assay of commercially available control sera and urine pools, is shown below.

Specimen	n	mean	within run SD	total SD
Low serum control	60	13.9 mgN/dL	0.59 mgN/dL	0.81 mgN/dL
Mid. serum control	60	52.7 mgN/dL	0.60 mgN/dL	0.77 mgN/dL
High serum control	60	78.8 mgN/dL	0.70 mgN/dL	1.09 mgN/dL
Low urine pool	60	21.9 mgN/dL	0.54 mgN/dL	0.52 mgN/dL
High urine pool	60	75.3 mgN/dL	0.85 mgN/dL	2.91 mgN/dL

The recoveries of urea nitrogen standards, which span the claimed linear range of 0 to 150 mgN/dL, are equivalent between the HiChem and BMD BUN Reagents. Regression statistics are shown below.

(*HiChem Results*) = 0.0 mgN/dL + 1.005 x (*BMD Results*), $r^2 = 1.000$, $s_{y.x} = 0.6$ mgN/dL.

Urea nitrogen recoveries of 190 mixed serum and plasma specimens and 60 urine specimens diluted with 20 parts normal saline compared between the HiChem and BMD reagents using least squares regression, yield the following statistics.

Serum/Plasma Comparison

(*HiChem Results*) = 0.0 mgN/dL + 1.009 x (*BMD Results*) $r^2 = 0.999$, $s_{y.x} = 0.6$ mgN/dL.

Urine Comparison

(*HiChem Results*) = 0.1 mgN/dL + 1.027 x (*BMD Results*) $r^2 = 0.999$, $s_{y.x} = 0.7$ mgN/dL.

The calibration stability claim of 48 hours is documented through the recovery of serum controls which span from 8 to 132 mgN/dL urea nitrogen. In all cases, the observed shifts in recoveries over the calibration period are less than the greater of 2 mgN/dL or 2%.

The HiChem BUN/Urea Reagent, calibrated with the HiChem Chemistry Standard, is shown to be safe and effective and substantially equivalent to the Sigma BUN (Rate) Reagent, procedure no. 67-UV calibrated with Sigma Glucose/Urea Nitrogen Standard, product no. 16-300 and the BMD BUN Reagent, product no. 704092 calibrated with Precical Calibrator Serum and Diluent, product no. 620213.

Wynn Starkey
Manager, Regulatory Affairs.