HiChem

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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 CK/NAC Reagent (product no. 70003) is intended for the quantitative determination of creatine kinase in serum and plasma. The principal diagnostic indications of elevated serum creatine kinase are diseases of the heart and skeletal muscle.

The HiChem CK/NAC Reagent determines creatine kinase by enzymatic phosphorylation of adenosine diphosphate in the presence of creatine phosphate to form adenosine triphosphate. The rate of this reaction, and the activity of creatine kinase in the specimen, is determined through the measurement of NADH which is formed through a series of linked enzymatic reactions.

The HiChem CK/NAC Reagent is intended to be used either as a manual procedure or on clinical analyzers which can automate the required manipulations. The reagent is supplied as two liquid-stable components which are combined, either before or during use, in the approximate ratio of 1 part CK/NAC Substrate and 8 parts CK/NAC Reagent Buffer. The CK/NAC Substrate can also be used as a start reagent and combined with the Reagent Buffer following sample addition.

The HiChem CK/NAC Reagent is substantially equivalent to the BMD CK/NAC Reagent, product no. 816360, manufactured by Boehringer Mannheim Corp., Indianapolis, IN., and the Sigma Diagnostics Creatine Kinase (CK) Reagent, procedure no. 47-UV manufactured by Sigma Diagnostics, St. Louis, MO. All three reagents support the same intended use and produce equivalent results with the same clinical purpose. In addition, they are all based on the same methodology which determines creatine kinase (CK) through the measurement of NADH production. Finally, all reagents are sold in a generic format which supplies the reagent with a manual procedure and supports its use on various instruments through procedure supplements (application sheets).

The effectiveness of the manual procedure is shown by the recovery of linearity standards, the precision of control recoveries, the comparison of serum and plasma recoveries to the Sigma Creatine Kinase (CK) Reagent and the validation of the chemical additives and reconstituted stability claims.

The recovery of creatine kinase using HiChem CK/NAC Reagent as a manual method at both 30°C and 37°C reaction temperatures is linear to at least 2000 U/L as shown by the recovery of linearity standards which span the claimed linear range. Regression statistics are shown below.

$$(\text{Recoveries at } 30^\circ C) = 6.1\ U/L + 0.9918 \times (\text{Standard Activity}), \quad r^2 = 0.9998, \quad s_{yx} = 8.1\ U/L.$$

$$(\text{Recoveries at } 37^\circ C) = 2.5\ U/L + 0.9867 \times (\text{Standard Activity}), \quad r^2 = 0.9998, \quad s_{yx} = 10.7\ U/L.$$

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

Specimen	n	mean	within-run SD	total SD
Serum control 1	30	50 U/L	1.5 U/L	1.6 U/L
Serum control 2	30	378 U/L	5.3 U/L	7.8 U/L
Serum control 3	30	1048 U/L	10.3 U/L	18.6 U/L

Creatine kinase recoveries of 90 mixed serum and plasma specimens are compared between the HiChem and Sigma reagents. Least squares regression statistics are shown below.

$$(\text{HiChem Results}) = 0.6\ U/L + 0.990 \times (\text{Sigma Results}) \quad r^2 = 0.991, \quad s_{yx} = 8.5\ U/L.$$

The use of heparin and EDTA are shown to be acceptable chemical additives by comparison of spiked and unspiked serum pools. In all cases, the biases observed were less than 2% and statistically insignificant at the 95% confidence level.

The stability of the combined working reagent over 2 weeks at 2-8°C and 1 day at 18-25°C are documented through the recovery of serum controls which range from 50 to 1200 U/L CK at 37°C. In all cases, the observed shifts in standard recovery were less than the greater of 4 U/L or 5%.

The effectiveness of the automated Hitachi 704 procedure is shown by the recovery of linearity standards, the precision of control recoveries, the recovery of serum controls over both the calibration stability period and the on-board stability claim, and the comparison of patient specimen recoveries to the BMD CK/NAC Reagent.

The recovery of creatine kinase using HiChem CK/NAC Reagent as an automated method is linear to at least 2,400 U/L as shown by the recovery of eleven linearity standards which span the claimed linear range. Regression statistics are shown below.

$$(\text{HiChem Recoveries}) = -0.2\ U/L + 1.0013 \times (\text{Activity}), \quad r^2 = 1.0000, \quad s_{yx} = 3.4\ U/L.$$

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

Specimen	*n*	*mean*	*within-run SD*	*total SD*
Serum control 1	*60*	*53 U/L*	*0.9 U/L*	*1.2 U/L*
Serum control 2	*60*	*415 U/L*	*1.4 U/L*	*3.0 U/L*
Serum control 3	*60*	*1183 U/L*	*3.4 U/L*	*6.9 U/L*

Creatine kinase recoveries of 126 mixed serum and plasma specimens compared between the HiChem and BMD reagents using least squares regression, yield the following statistics.

$$\textit{(HiChem Results)} = 0.0\ \text{U/L} + 1.048 \times \textit{(BMD Results)} \qquad r = 0.9994, \qquad s_{y,x} = 3.05\ \text{U/L}.$$

The 24 hour calibration stability claim is documented through the recovery of serum controls which span from approximately 50 to 1,200 U/L CK. In all cases, the observed shifts in recoveries over 24 hours without calibration are less than the greater of 1 U/L or 0.25%. The on-board stability claim is documented through the recovery of the same serum controls. The observed shifts in recoveries over the 21 day stability claim are no greater than 3.5%.

The HiChem CK/NAC Reagent is shown to be safe and effective and substantially equivalent to the BMD CK/NAC Reagent, product no. 816360, manufactured by Boehringer Mannheim Corp., Indianapolis, IN., and the Sigma Diagnostics Creatine Kinase (CK) Reagent, procedure no. 47-UV manufactured by Sigma Diagnostics, St. Louis, MO.

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