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DIAGNOSTICS

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 ALP/AMP Reagent (product no. 70001) is intended for the quantitative determination of alkaline phosphatase in serum and plasma. The principal diagnostic indications of elevated serum alkaline phosphatase are diseases of the liver, bone, parathyroid and intestine.

The HiChem ALP/AMP Reagent determines alkaline phosphatase by enzymatic hydrolysis of p-nitrophenyl-phosphate to p-nitrophenoxide at alkaline pH. The HiChem ALP/AMP 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 ALP/AMP Substrate and 5 parts ALP/AMP Reagent Buffer. The ALP/AMP Substrate can also be used as a start reagent and combined with the Reagent Buffer following sample addition.

The HiChem ALP/AMP Reagent is substantially equivalent to the BMD Alkaline Phosphatase/AMP Reagent, product no. 704093, manufactured by Boehringer Mannheim Corp., Indianapolis, IN., and the MAS ALP Reagent, product no. 139-154 manufactured by Medical Analysis Systems, Inc., Camarillo, CA. 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 alkaline phosphatase (ALP) through the measurement of liberated p-nitrophenoxide. 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 MAS ALP Reagent and the validation of the chemical additives and reconstituted stability claims.

The recovery of alkaline phosphatase using HiChem ALP/AMP Reagent as a manual method at both 30°C and 37°C reaction temperatures is linear to at least 900 U/L as shown by the recovery of linearity standards ranging from 0 to over 1,350 U/L. Regression statistics are shown below.

$$\text{(Recoveries at 30°C)} = -1.7\ \text{U/L} + 1.005 \times \text{(Standard Activity)}, \quad r^2 = 0.9998, \quad sy.x = 6.5\ \text{U/L}.$$

$$\text{(Recoveries at 37°C)} = 2.9\ \text{U/L} + 0.969 \times \text{(Standard Activity)}, \quad r^2 = 0.9998, \quad sy.x = 8.0\ \text{U/L}.$$

Precision, demonstrated by replicate assay of control sera at 37°C, is shown below.

Specimen	n	mean	within-run SD	total SD
Serum control 1	30	55 U/L	2.1 U/L	2.2 U/L
Serum control 2	30	225 U/L	3.7 U/L	3.9 U/L
Serum control 3	30	765 U/L	6.6 U/L	9.0 U/L

Alkaline phosphatase recoveries of 83 mixed serum and plasma specimens are compared between the HiChem and MAS reagents. Least squares regression statistics are shown below.

$$\text{(HiChem Results)} = -0.2\ \text{U/L} + 1.058 \times \text{(MAS Results)} \quad r^2 = 0.9986, \quad sy.x = 5.5\ \text{U/L}.$$

The use of heparin and lithium iodoacetate as anticoagulants is shown by the assay of spiked serum pools. In all cases, the bias due to the addition of anticoagulant is less than 2% and statistically insignificant at a 95% confidence level.

The stability of the combined working reagent over 1 month at 2-8°C and 3 days at 18-25°C are documented through the recovery of serum controls which range from approximately 50 to 750 U/L AMP at 37°C. For all controls, the observed shifts in recovery were less than the greater of 3 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 Alkaline Phosphatase/AMP Reagent.

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The recovery of alkaline phosphatase using HiChem ALP/AMP Reagent as an automated method is linear to at least 1,200 U/L as shown by the recovery of ten linearity standards which span the claimed linear range. Regression statistics are shown below.

(HiChem Recoveries) = 3.6 U/L + 0.981 x (Activity), $r^2 = 1.000$, $sy.x = 3.6$ *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	60	49 U/L	0.4 U/L	0.6 U/L
Serum control 2	60	196 U/L	0.8 U/L	1.1 U/L
Serum control 3	60	692 U/L	2.5 U/L	3.0 U/L

Alkaline phosphatase recoveries of 178 mixed serum and plasma specimens compared between the HiChem and BMD reagents using least squares regression, yield the following statistics.

(HiChem Results) = 1.2 U/L + 1.974 x (BMD Results) $r^2 = 1.000$, $sy.x = 1.4$ *U/L.*

The 24 hour calibration stability claim is documented through the recovery of serum controls which span from approximately 50 to 750 U/L ALP. In all cases, the observed shifts in recoveries over 24 hours without calibration are less than 0.25%. The on-board stability claim of 2 weeks is documented by the recovery of serum controls using the same reagent, left on the analyzer, over 15 days. The largest observed control shift over the 15 day period was only 2%.

The HiChem ALP/AMP Reagent is shown to be safe and effective and substantially equivalent to the BMD Alkaline Phosphatase/AMP Reagent, product no. 704093, manufactured by Boehringer Mannheim Corp., Indianapolis, IN., and the MAS ALP Reagent, product no. 139-154 manufactured by Medical Analysis Systems, Inc., Camarillo, CA.

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