Summary of Test Results

The data presented in Sections 14, 15, 16 and 17 of this document demonstrate the substantial equivalence between the BM/H cholinesterase test system and the Test-mate ChE Cholinesterase Test System. The Test-mate ChE is as safe and effective as the predicate system, when measuring either erythrocyte cholinesterase (AChE) or plasma cholinesterase (PChE) in blood samples.

The BM/H cholinesterase test system and the Test-mate ChE Cholinesterase Test System are both based upon the kinetic measurement of thionitrobenzoate. All of the critical components of enzymatic analysis, such as the concentration of reagents, type of reagent, pH, buffer, and measurement window are very similar or identical in both systems. The BM/H system uses *separated* whole blood obtained from a venipuncture sample, while the Test-mate ChE uses whole blood obtained from a fingerstick sample. The BM/H system operates at an assay temperature of 37°C, while the Test-mate ChE runs at ambient room temperature and is temperature compensated to 25°C. Because of these two minor differences in the assay procedure, the absolute values obtained from the two systems will not be the same. Expressed in the same measurement of units per liter of sample, the BM/H plasma cholinesterase levels are about three times that of the Test-mate ChE, and the BM/H erythrocyte cholinesterase levels are about four times that of the Test-mate ChE. Although the absolute values obtained from the two systems are somewhat different, the test values will still be highly correlated.

An analysis of the Clinical Accuracy Study (Section 14) shows that the Test-mate ChE system is highly correlated with the BM/H system for both AChE and PChE. The AChE incorporates a red cell correction factor (hematocrit correction is used by the BM/H system and hemoglobin correction is used by the Test-mate ChE system), thus decreasing the inherent error of measurement for both methods by adjusting for the red cell variability. An excellent correlation is observed for AChE when all same-sample data is considered (same-sample, N = 86; $r = 0.98$). A significantly lower - but very acceptable - correlation is observed for AChE over a fingerstick sample normal range (normal population, N = 44; $r = 0.78$). This lower correlation is largely due to the statistical artifact of narrow range. An excellent correlation is observed for PChE when all same-sample data is considered (same-sample, N = 87; $r = 0.98$). For PChE, even over a fingerstick sample normal range, an excellent correlation is observed (normal population, N = 44; $r = 0.96$). Because the PChE normal range is twice that of the AChE normal range, the PChE fingerstick correlation is much better than the AChE fingerstick correlation.

An analysis of the Clinical Precision Study (Section 15) shows further comparability between the BM/H cholinesterase test system and the Test-mate ChE Cholinesterase Test System. Although neither between-day precision nor AChE precision is listed in the product information for the BM/H system, the within-run precision is stated as approximately 1%. The between-day precision of 2 - 3% for the Test-mate ChE system

is similar to the "total" specified precision of 1 - 2% for serum cholinesterase, using the BM/H system.

An analysis of the Clinical Linearity Study (Section 16) demonstrates that the BM/H system and the Test-mate ChE system are both perfectly linear ($r = 1.00$) over the same range (0 - 200% normal).

Statistical analysis of the Clinical Operator Study (Section 17) demonstrates that the intended operators of the Test-mate ChE can achieve a precision of 1 - 6% CV which is comparable to the precision of the BM/H and commercial automated Drabkin hemoglobin methods. This precision is well within CAP (College of American Pathologists) user-group proficiency criteria of ±20% of mean for all enzymatic analyses (including cholinesterase), and compares favorably with 1996 CAP Survey data for cholinesterase testing (Chemistry Survey p.84, specimen C7-02) among all instruments, including the BM/H 717 (N = 15, CV = 27.9%), a successor of the BM/H 704 analyzer (the BM/H 704 was not reported). The World Health Organization, as well as the states of California and Texas, have made the specific recommendation of testing for erythrocyte cholinesterase (hemoglobin-corrected AChE) when testing for pesiticide poisoning. The between-operator precision of the hemoglobin-corrected AChE, reported in this study (N = 100, CV = 2.4%), is superior to the mean of any of the 1996 CAP cholinesterase instrument/reagent system user groups.

These analyses show that the mechanics of the measurement systems (including blood sampling), and the reagent systems (including the red cell correction factors), are substantially equivalent for the BM/H and the Test-mate ChE cholinesterase assays. The data is of high quality, as no outliers were observed or taken, and only a few samples were lost due to clotting of venipuncture tubes or capillaries. The *ex vivo* addition of paraoxon (the active metabolite of the typical organophosphate pesticide, parathion), accurately reproduces the effect of cholinesterase depression in real patients over an evenly distributed range of moderate (25 - 50% inhibition) to severe (50 - 100% inhibition) poisoning. Therefore, the data includes a balanced representation of the widest range of both normal and pathological samples, and is consequently a convincing demonstration of the equivalence between the BM/H cholinesterase test system and the Test-mate ChE Cholinesterase Test System.

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