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LEAD BIOAVAILABILITY IN RATS
MR 9660

An experiment was run to monitor absolute lead bioavailability in rats under four conditions. Group A received a single IV dose and was then sampled for 10 days. Group B received a single gavage and was then sampled for 10 days. Groups C and D were fed for 30 days, then received an IV and gavage, respectively. Both groups were sampled for 10 days. The rats in each study were caged in groups of 5. The rats in any one cage were tested at three time points. With few exceptions, all rats in a cage are tested at the same three time points. At most time points, only one group of rats was tested. At each time point, the blood drawn from a rat is divided and placed in two aliquats.

This is a departure from the recommended design and under this protocol, it is impossible to separate the effects of time from those of cage for groups C and D. The model fit to each data set was of the form

$$\text{LEAD} = A * \text{TIME}^{**}D * \text{EXP}(-B*\text{TIME}^{**}C),$$

where $A^{**}B$ means A raised to the power B. In all four data sets, an adequate fit to the data was obtained, although, for group A, lead is consistently underestimated after 12 hours.

Primary interest is in the area under the fitted curve, which can be computed from the formula

$$\text{AUC} = (A/(C*B^{**}F)) * \text{GAMMA}(F),$$

where $F = (D + 1)/C$ and Gamma is the gamma function.

The fitted curves are:

- (A) $\text{LEAD} = 492.11 * \text{TIME}^{**}.004 * \text{EXP}(-2.778 * \text{TIME}^{**}.25)$
- (B) $\text{LEAD} = .1087 * \text{TIME}^{**}1.426 * \text{EXP}(-.869 * \text{TIME}^{**}.5)$
- (C) $\text{LEAD} = 68.67 * \text{EXP}(-1.512 * \text{TIME}^{**}.252)$
- (D) $\text{LEAD} = .0910 * \text{TIME}^{**}.3667 * \text{EXP}(-.2377 * \text{TIME}^{**}.5).$

The areas under the curve, according to the formula cited, are 780.4, 21.7, 312.8 and 14.7, respectively.

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In the appendix following, the fitted values and upper and lower 95 % confidence values for the mean blood lead level are reported. Neither there nor in the above formulas are the factors 1.27, for groups A and C, and .62 for groups B and D incorporated in the computations. The fitted curves are obtained by multiplying the given equations by the appropriate factors.

To determine whether the computed areas for A compared to B and for C compared D are significantly different, the approximate area under the lower 95% confidence bound for A is computed and compared to the area under the upper 95% confidence bound for B. In each case, a trapezoidal approximation is computed over the interval on which the fitted value differs significantly from 0. The resulting computed areas will thus be different from the exact mathematical formula reported above. The comparisons are nevertheless valid.

The area under the curve A is significantly greater than the area under B. Likewise, the area under C is significantly greater than that under D.

This report supplements a report submitted to you on October 18, 1993. The results are consistent with the findings reported there, but are intended to answer the question of how the areas under the indicated pairs of curves compare.

If you have any question about these results, please do not hesitate to contact me.

Quality Management & Technology Center


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*Few values changed
after doing Stats, however
this change will not
effect the significance
of the results. BAC/9/93.*