

## MEETING ABSTRACTS

# BENCHMARK DOSE APPROACH IN EVALUATION OF *IN VIVO* AChE-REACTIVATING EFFICACY OF PROMISING EXPERIMENTAL OXIMES K203 AND K027

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Benchmark dose (BMD) approach, as an advanced statistical methodology for dose-effect analysis in toxicological research (1) was used to quantitatively characterize *in vivo* efficacy of two experimental bispyridinium oximes K203 and K027, following promising findings on their low acute toxicity and potential to reactivate acetylcholinesterase (AChE) inhibited by organophosphorus (OP) pesticides and nerve agents *in vitro* and *in vivo* (2). Immediately after DDVP challenge (75% LD<sub>50</sub>, s.c.), male Wistar rats were treated with oxime (0/1.25/2.5/5/25/50% LD<sub>50</sub>, i.m.). Erythrocyte and diaphragm AChE activity was determined by Ellman's method 60 min after the treatment. Benchmark analysis was done in PROAST software ver. 65.5 (RIVM, The Netherlands). Derived BMD<sub>01</sub> were K203 = 194 (153, 243) and K027 = 100 (81, 125) μmol/kg bw, BMD<sub>diaph</sub> were K203 = 117 (56, 209) and K027 = 21 (10, 37) μmol/kg bw, indicating that oxime K027 induces the same effect size with 2 and 5.5-times lower dose compared to oxime K203 in erythrocytes and diaphragm, respectively. Quantification of equieffective doses of oxime reactivators would enable more reliable definition of their therapeutic widths, which further contributes to better determination of therapeutic dosage regimens and, finally, increases the relevance of results obtained in animal models for the human population.

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**Keywords:** benchmark response; organophosphates; oximes; rat

## References

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