

Dose-Response Modeling for the Assessment of Cumulative Risk Due to Exposure to *N*-Methyl Carbamate Pesticides

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The US EPA's *N*-Methyl Carbamate Cumulative Risk Assessment (NMCRA) assesses the effect on acetylcholine esterase (AChE) activity of exposure to 10 *N*-methyl carbamate (NMC) pesticides through dietary, drinking water, and residential exposures. Similarly to the Agency's organophosphate cumulative risk assessment, the NMCRA is based on the relative potency factor (RPF) approach. However, unlike organophosphate-induced AChE inhibition, NMC inhibition is short-lived, with half-lives in animals on the order of hours. Thus, the risk assessment for NMC pesticides needs to take account not only of peak inhibition but the recovery of inhibition after exposure. This information was estimated from animal studies using dose-time-response modeling of gavage studies. As there were multiple data sets for each chemical, statistical methodology was used that allowed all the data to contribute to the overall dose-response estimate. Relative potencies were calculated as the ratios of benchmark doses for 10% AChE inhibition. The half-life for recovery of AChE activity was estimated simultaneously with BMDs. Dose-response shapes for the NMCs were not all perfectly consistent with the RPF approach. Comparison of dose-responses for mixtures of NMC based on expectations under the RPF approach with those based on a more general approach to dose-additivity indicate that the RPF-based dose-response estimates are reasonable approximations to those for the more general formulation. [Although this work was reviewed by EPA and approved for publication, it may not necessarily reflect official Agency policy.]