

Points for the Letter to the Administrator

- The Panel believes that it is important for the Agency to consider sensitive life stages explicitly in the development of a Maximum Contaminant Level Goal for perchlorate.
 - The mode of action of perchlorate is well understood and involves the potential for disturbance of thyroid homeostasis. Interference with thyroid is known to produce adverse effects on neurodevelopment in humans, with the fetus and infants most vulnerable. Although adverse neurodevelopmental effects of perchlorate in infants and children have not been reported in the literature, their risk can be reasonably inferred from other lines of evidence.
- The Panel recommends that the Agency derive perchlorate MCLGs that address sensitive life stages through PB/PK modeling based upon its mode of action. The Panel believes that this approach is a more facile, transparent, and rigorous way to address differences in biology and exposure between adults and sensitive life stages than is possible with the traditional approach for deriving an MCLG.
 - The Panel notes that Agency already has a PB/PK model for perchlorate that could be used for this purpose.
 - The model could be used in its present form, although expansion of the model to address important aspects of vulnerability to perchlorate is strongly recommended. In particular, expanding the model beyond prediction of inhibition of thyroid uptake to effects on thyroid hormone levels will be especially important to capture factors that could contribute to perchlorate sensitivity, such iodine intake, underlying thyroid disease, etc. As a long-term goal, additional research could be used to extent the model to prediction of adverse effects resulting from specific concentrations of perchlorate in drinking water.
 - The Panel has made specific recommendations on ways in which information from clinical and epidemiological studies can be used to inform the model.
 - The Panel notes that as perchlorate research continues, studies in animals may provide important insights into neurobehavioral

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consequences of perchlorate exposure. A PB/PK framework is well suited to help place these findings in the context of human perchlorate exposure.

- Although this approach is a departure from the usual method for MCLG calculation, it is consistent with the Agency's increasing use of PB/PK modeling in support of risk assessment.
- The Agency will need to develop a technical document for the approach and have it peer reviewed.