

The MCLG is intended to be protective – provide an adequate margin of safety considering the sensitive life stages.

Issue 4 Question 1: Pertaining to Integration of Information

Recommend use of the MOA of perchlorate to form the basis of MCLG as derived from the body of literature.

Qualitative presentation of MOA model with available data relevant to each piece (include all types of data in vitro, animal, human) this exercise will help organize available info

Quantitative approach

1. Use the PBPK model to get to NIS inhibition
 - a. Need clarification on exactly how this will work
 - b. EPA needs to provide justification for using the PBPK. Include robust, accessible and transparent documentation for each piece of the model; describe the role of the Greer study in development of the model; clearly identify and address limitations

2. Use Group #1 to get from NIS inhibition to serum free T4 & TSH based on the iodine deficiency human and animal literature

3. Use Group #1 to get from Free T4 & TSH to neurobiological outcome – specifically defining an adverse event or effect, using recognizing that these range from changes in gene expression, neurophysiology, and behavior and learning.

4. Use Group #2 (Epi) to extract from the non-ecologic data a dose-reconstruction to relate perchlorate levels to hormone changes (rationale – in support of the parallel approaches (PBPK & RfD)).

Procedure/Structure

Recommend that EPA develop a structured framework to capture the evaluation of each type of data [refer to draft offered in pre-meeting comments] this framework should be incorporated into their main text at the end of each section

Articulating the 'ideal' situation - Future Directions/Research

Do not Cite or Quote –

Draft Panel Responses for Discussion on July 19, 2012- Public Session

1. The qualitative presentation of full MOA model (see above) will point to research needs
2. Continue work on PD aspects of modeling

Question #2 – Benefits

1. EPA must define the adverse effects (range from changes in gene expression, neurophysiology, and behavior and learning.
2. EPA must define the sensitive population (pregnant women who are iodine insufficient?)
Shifts in exposure to sensitive population can begin to address impact and benefit
Quantitative procedure described above may also be helpful in describing dose response
3. Agency can look to Science and Decisions report –
 - a. Conceptual models for unified dose-response may be useful
 - b. Also refer to their discussion of better quantifying impact and benefit