Centers for Disease Control and Prevention (CDC)/Agency for Toxic Substances and Disease Registry (ATSDR) Comments on the Interagency Science Consultation Draft IRIS Assessment of RDX (dated September 2014)

Date: December 9, 2014

CDC/ATSDR appreciates the opportunity to participate in the EPA's IRIS Program. We have reviewed and provided comments on the draft Toxicology Review of RDX.

The attached comments were provided by The Division of Toxicology and Human Health Sciences.

General comments

Overall, the toxicology review of RDX appears complete. We are not aware of any additional data. The dose response analysis is well done; however, the details provided in the supplemental information make the discussion difficult to follow. It would be helpful to recommend adding additional detail in the review, particularly when summarizing the selection of the proposed overall reference dose. It should be noted that ATSDR used the Crouse et al (2006) study and the Sweeney model to derive the acute and intermediate-duration minimal risk levels (MRLs).

Minor comments

1. **Page XXX Line 14 "Selection of the Proposed Overall Reference Dose"**

For chronic duration, please note that the ATSDR MRL value is 1 x 10-1 mg/kg/day vs the proposed RfD of 9 x 10-4 mg/kg/day.

The chronic-duration MRL was derived based on the NOAEL of 8 mg/kg/day for tremors/convulsions in the 2-year Levine et al. (1983) study. BMD modeling could not be utilized because the investigators did not report incidence data for the neurological effects. The Sweeney model was used to predict the peak brain concentrations in the rat and to estimate the HED. The NOAELHED of 4.223 mg/kg/day was divided by an

uncertainty factor of 30 (3 for extrapolation from animals to humans and 10 for human variability), resulting in a chronic-duration oral MRL of 0.1 mg/kg/day.

Please see: http://www.atsdr.cdc.gov/ToxProfiles/tp.asp?id=412&tid=72

2. **Page XXX Line 3 "Other Toxicological Effects"**

The musculoskeletal effects entries are missing from Tables 1-14 and 1-15. The entries consisted of five or six case studies and a few animal studies which were negative. Please consider if these entries should be included.

For questions pertaining to CDC/ATSDR's comments please contact Michele Howard at (770) 488-3989 or mhoward@cdc.gov