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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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OFFICE OF
RESEARCH AND DEVELOPMENT

MEMORANDUM

DATE: January 28, 1999

FROM: Ralph J. Smialowicz (MD-92) RJ Smialowicz

TO: Annie Jarabek (MD-52)
National Center for Environmental Assessment

SUBJECT: Review of 90-Day Ammonium Perchlorate Exposure on the Antibody Response to SRBC in Mice

As indicated in the external review draft of the NCEA document entitled *Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization Based on Emerging Information*, an evaluation of the potential effects of ammonium perchlorate on humoral immunity was not performed as part of the original immunotoxicity testing protocol. This raised concern that a significant component of the immune system was not assessed in perchlorate-exposed animals. Consequently, the sponsor and contract laboratory agreed to perform 14-day and 90-day studies in which the antibody response to sheep red blood cells (SRBC) would be determined.

Results of a 90-day study were received on January 23,1999. In this study, B6C3F1 female mice, 12 mice per group, were exposed to ammonium perchlorate (0, 0.1, 1.0, 3.0, or 30 mg/kg/day) via drinking water for 90 days. Mice where immunized intravenously with SRBC on day 75. Serum was collected on day 79 (4 days post-immunization) and on day 90 (15 days post-immunization), and the SRBC-specific IgM and IgG antibody levels were determined using an enzyme-linked immunosorbent assay (ELISA) "based on a protocol provided by L. Temple of the Medical College of Virginia". Analysis of the ELISA data, which was expressed as the O.D. 50, indicated that neither the IgM nor IgG titers were affected by ammonium perchlorate exposure. In the report, the contract laboratory indicated limitations which were the following: 1) a kinetic study to determine the day of peak levels of IgM and IgG was not performed; and 2) since specialized software (e.g., Softmax®) was not available, serum antibody titers were calculated as the O.D. 50 or midpoint "as described by a SOP provided by L. Temple", rather than the conventional "titer to achieve 0.5 O.D.".

The results of a 14-day exposure study on SRBC-specific antibody responses in mice is expected on February 3, 1999. In addition, because of concern expressed in the external review draft about the infectivity data (i.e., *L. monocytogenes* challenge model) additional studies are currently in progress. The expected due date for the report of these data is June 1, 1999.