females, the serum levels were 0.37±0.0805 and 1.02±0.425 ug/l, respectively for the 10 and 30 mg/kg/day groups. In F1 animals, there was a significant reduction in mean body weight (sexes combined) during lactation in the 30 mg/kg/day group. In F1 females, there was a significant increase in post weaning mortality, a significant decrease in mean body weight, and a significant delay in sexual maturation at 30 mg/kg/day. In F1 males, significant decreases in body weights and body weight gains, and significant changes in absolute liver and spleen weights and in the ratios of liver, kidney, and spleen weights-to-brain weights were observed in all treated groups. The increase in post weaning mortality and the delay in sexual maturation was also noted in F1 males at 30 mg/kg/day. Reproductive indices were not affected in the F1 animals. The LOAEL for the F1 females was 30 mg/kg/day, and the NOAEL was 10 mg/kg/day; the LOAEL for F1 males was 1 mg/kg/day and a NOAEL was not determined. The difference in sensitivity is presumed to be related to the gender difference in elimination of APFO. No treatment-related effects were observed in the F2 generation. However, the F2 pups were sacrificed at weaning, and thus it was not possible to ascertain if the post-weaning effects that were noted in the F1 generation occurred in the F2 animals.

Preliminary Risk Assessment

This preliminary risk assessment focused on the potential risks for developmental toxicity associated with exposure to PFOA and its salts. A margin of exposure (MOE) approach was used; the MOE is calculated as the ratio of the NOAEL, LOAEL, or BMD for a specific endpoint to the estimated human exposure level. The MOE does not provide an estimate of population risk, but simply describes the relative "distance" between the exposure level and the NOAEL, LOAEL, or BMD. For many risk assessments, the MOE is calculated as the ratio of the administered dose from the animal toxicology study to the estimated human exposure level. The human exposure is estimated from a variety of potential exposure scenarios, each of which requires a variety of assumptions. A more accurate estimate of the MOE can be derived if measures of internal dose are available for humans and the animal model. In this preliminary risk assessment, serum levels of PFOA, which are a measure of internal dose, were available for the rat two-generation reproductive toxicology study and from human biomonitoring studies. Thus, internal dose was used for the calculation of MOEs in this assessment.

For this preliminary risk assessment, the endpoints from the two-generation reproductive toxicity study that were considered relevant included the significant reduction in F1 mean body weight during lactation (sexes combined). For F1 females, postweaning mortality and delayed sexual maturation were noted at 30 mg/kg/day APFO; the NOAEL for F1 females was 10 mg/kg/day. Postweaning mortality, delayed sexual maturation and a significant reduction in postweaning body weights were noted in F1 males at 30 mg/kg/day, and a significant reduction in postweaning body weight was noted at 10 mg/kg/day. For F1 males, the LOAEL for developmental effects was 10 mg/kg/day and the NOAEL was 3 mg/kg/day.

In the rat two-generation reproductive toxicity study, serum levels of PFOA were only measured in the F0 animals. In order to use these serum levels as surrogates for the serum levels in the F1