

TOXICOLOGICAL PERSPECTIVES ON PERFLUORINATED COMPOUNDS IN AVIAN SPECIES

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Introduction

Perfluorinated chemicals have been widely used in commerce for the last few decades. Until recently little was known about their environmental fate and even less was known about their potential environmental effects. Since Giesy and co-workers¹ first demonstrated the widespread occurrence of perfluorooctane sulfonic acid (PFOS) in wildlife there has been renewed interest in determining the biological and possible ecological effects of these compounds. The assessment of possible effects of these chemicals has been hampered by a limited understanding of their mode of action and by a lack of toxicological data for wildlife species. Here we summarize recently obtained toxicological studies available for perfluorinated compounds (PFCs) in two avian species and use this information and environmental concentration data to evaluate the potential for environmental risk that these compounds pose.

Recent Avian Toxicological Studies

Several recent toxicological studies have examined the acute and chronic effects of a dietary exposure of PFOS on two avian species, Mallards (*Anas platyrhynchos*) and Northern bobwhite quail (*Colinus virginianus*). In these studies, toxicological endpoints that were evaluated included mortality, altered behavior and appearance, body weight, growth, feed consumption, gross pathology and histopathology in adult birds. Reproductive endpoints included egg production, measures of egg fertility and hatchability, and survival, growth and health of the surviving offspring. PFOS concentrations were also measured in the liver and serum of adults and offspring at study termination and in eggs.

Bobwhite Reproductive Study

In a reproductive study with northern bobwhites, birds were exposed to PFOS at nominal concentrations of 0, 10, 50, or 150 mg PFOS/kg in the diet². However, due to overt signs of toxicity noted in both 50 and 150 mg PFOS/kg treatment by Week 5, these treatment levels were terminated. No treatment-related mortalities were observed in the 10 ppm treatment, nor were there any significant alterations in body weight or feed consumption in adult birds. The gross necropsy at study termination indicated that adult males had an increase in the incidence of small testes in the 10 ppm treatment. This increase in the incidence in small testes was not accompanied by any morphological change in spermatogenesis. While PFOS may have accelerated post-reproductive regression, a normal physiological process, the toxicological significance of this phenomenon is

unknown. Liver weights in adult male and female quail exposed to 10 ppm were not statistically significantly different from control values at study termination. No other treatment-related lesions were noted in the study.

There were no effects on egg production in the 10 mg/kg treatment when compared to controls. However, there were slight, but not statistically significant reductions in several parameters including the number of viable embryos, live 3-week embryos, hatchlings, and 14-day old offspring survivors. There were also slight but not statistically significant, reductions in most of the normalized reproductive values except for the percentage of 14-day old survivors as number of egg set that was significantly reduced ($p < 0.05$) from the controls. These results are indicative of an overall effect on chick health that can be defined as “failure to thrive” (Austin et al. 2003; Lau et al. 2003). No treatment related effects were observed in offspring body or liver weights. Based on these results, the female and male LOAEL was determined to be 10 ppm in the diet (or 0.77 mg PFOS/kg body weight/day). A NOAEL was not determined in the study. Female serum and liver PFOS concentrations corresponding to the LOAEL were 8.7 µg PFOS/ml and 4.9 µg PFOS/g, respectively. For males, the PFOS concentrations in serum and liver corresponding to the LOAEL were 141 µg PFOS/ml and 86 µg PFOS/g, respectively. PFOS concentration in egg yolk from the 10 mg/kg treatment averaged 62 mg PFOS/ml.

Mallard Reproductive Study

In a reproductive study with mallards, birds were exposed to PFOS at nominal concentrations of 0, 10, 50, or 150 mg PFOS/kg in the diet³. However, due to overt signs of toxicity noted in both 50 and 150 mg PFOS/kg treatments by Week 5, these treatment were terminated and only the control and 10 ppm treatments were maintained until the end of the study. No treatment-related mortalities were observed in the 10 ppm treatment nor were there any PFOS-related effects on body weight or feed consumption in adult male and female mallards. At study termination, gross necropsy of adult birds revealed that males from the 10 ppm treatment had a statistically significantly greater incidence of small testes. The increased incidence of small testes was suggestive of an accelerated post-reproductive regression of testes. No treatment related effects were noted on liver weights in either sex. In addition, there were no treatment-related effects on any reproductive parameter or on offspring survival, body or liver weight. Based on these results, the female LOAEL was determined to be 50 ppm in the diet (or 6.4 mg PFOS/kg body weight/day) while the NOAEL was determined to be 10 ppm in the diet (or 1.5 mg PFOS/kg body weight /day). For males, the LOAEL was determined to be 10 ppm in the diet (or 1.5 mg PFOS/kg body weight/day), while a NOAEL was not determined in the study. Female serum and liver PFOS concentrations corresponding to the NOAEL were 17 µg PFOS/ml and 11 µg PFOS/g, respectively. For males, the PFOS concentrations in serum and liver corresponding to the LOAEL were 87 µg PFOS/ml and 61 µg PFOS/g, respectively. PFOS concentration in egg yolk averaged 53 µg PFOS/ml.

Avian Risk Assessment

TRV Calculation

In a global monitoring study of PFOS residues in biota, fish-eating water birds were found to have some of the greatest liver and serum PFOS concentrations⁴. Top avian aquatic predators such as eagles and cormorants accumulated the greatest concentrations of PFOS when compared to other lower trophic level bird species. To be protective of all avian species, an avian TRV for PFOS was derived based on the characteristics of trophic level 4 fish-eating birds^{5,6}.

TRVs were developed from the laboratory studies by applying uncertainty factors to toxicity data based on an approach that results in very conservative estimates of the threshold effect levels and encourages the collection of additional information, especially for site-specific Ecological Risk Assessments (ERAs) ⁷. Based on the avian toxicity tests, northern bobwhites were selected to derive a TRV based on their overall greater sensitivity to PFOS compared to mallards. The assignment of uncertainty factors to the threshold dose for the calculation of a TRV for a Level 4 Avian predator exposed to PFOS is as follows:

Intertaxon Variability Extrapolation (Category A): This factor is used to estimate an effect concentration or dose for a receptor from laboratory test data from surrogate species. Values range from 1 to 5.

Exposure Duration Extrapolation (Category B): This factor is used to estimate LOAEL or dose of a chemical when only acute (short-term) toxicity test data are available. Values range from 1 to 15.

Toxicologic Endpoint Extrapolation (Category C): This factor is used to estimate NOAEL and/or LOAEL values from studies that report other endpoints. Values range from 0.75 to 15.

Modifying Factors (Category D): These factors incorporate other sources of uncertainty, including:

- Threatened, or listed, and endangered species, (d1): Values range from 0 to 2.
- Relevance of endpoint to ecological health, (d2): Values range from 0 to 2.
- Extrapolation from laboratory to field, (d3): Values range from -1 to 2.
- Study conducted with relevant co-contaminants, (d4): Values range from -1 to 2.
- Endpoint is mechanistically unclear (vs. clear), (d5): Values range from 0 to 2.
- Study species is either highly sensitive or highly resistant, (d6): Values range from -1 to 2.
- Ratios used to estimate whole body burden from tissue, (d7): Values range from 0 to 2.
- Intraspecific variability, (d8): Values range from 0 to 2.

$$\text{Overall UF} = (A * B * C * D) \quad \text{where : } D = (d1 + d2 + d3 + \dots + dn)$$

TRVs were estimated by application of uncertainty factors to Test Dose values. The Test Dose in this analysis was the LOAEL derived based on the toxicity results from the bobwhite quail reproduction study:

$$\text{TRV} = \frac{\text{Test Dose or LOAEL}}{\text{Overall UF}}$$

Dietary and tissue-specific (liver and serum) TRV values were then compared to serum and liver concentrations measured in avian species as part of the global monitoring program ¹.

Summary

Results from global monitoring programs have shown that concentrations of PFOS in birds vary depending on location and species. In most circumstances, the concentrations of PFOS found in bird tissues do not seem to pose a significant threat based on the results of this hazard assessment. While hazard quotient values at some locations suggest that further investigations would be

prudent, it is important to note that many of these locations were sampled prior to 2000 when, PFOS production essentially ceased, and so may not accurately represent current conditions.

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