Derivation of Toxicity Reference Values for PFOS and PFNA in a mammalian wildlife model

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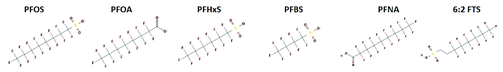
TEST MATERIALS

- Six per- and polyfluoroalkyl substances (PFAS).



MODEL SPECIES: *Peromyscus leucopus* (white-footed mouse)

- Represent a native, unique rodent taxon;
- Breed year-round in laboratory conditions;
- Have successfully been used for toxicity studies;
- Have a known genetic/disease background.

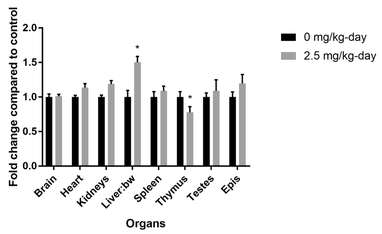
RANGE FINDING METHODS

1. PFAS were administered orally to white-footed mice for 28 days.
2. Blood samples were collected every 7 days via facial/submandibular venipuncture.
3. Tissues and blood samples were collected at termination.

PFOS RANGE FINDING RESULTS

1. 100% mortality at 20 and 40 mg/kg-day.
2. Dose-dependent increase in liver weights.
3. Serum analysis [PFOS] pending.

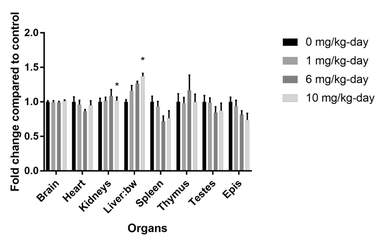
Organ weights of *P. leucopus* exposed to PFOS



PFNA RANGE FINDING RESULTS

1. Reduction of body weights (15%) in high dose females compared to controls.
2. Dose-dependent increase in liver weights.
3. Serum analysis [PFNA] pending.

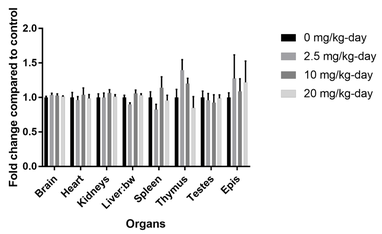
Organ weights of *P. leucopus* exposed to PFNA



6:2 FTS RANGE FINDING REULTS

1. No observed adverse effects.
2. Serum analysis [6:2 FTS] pending.

Organ weights of *P. leucopus* exposed to 6:2 FTS



Prenatal exposure to PFOS is associated with pup mortality in white-footed mice.
$BMDL_{10}$ = 0.09 mg/kg-day

Oral exposure to PFNA is associated with decreased immune response in white-footed mice.
$BMDL_{10}$ = 1.2 mg/kg-day

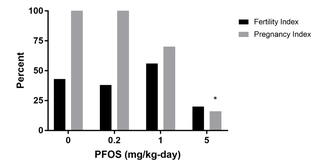
REPRODUTIVE AND DEVELOPMENTAL TEST METHODS

1. PFOS or PFNA was administered via oral gavage to white-footed mice for 28 days.
2. Breeding pairs were initiated and oral exposure continued.
3. Tissues and blood samples were collected at termination.

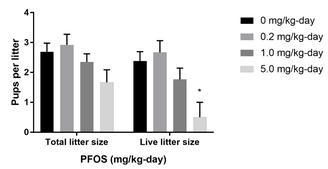
PFOS REPRODUCTIVE AND DEVELOPMENTAL TEST RESULTS

1. Decreased pregnancy at 5 mg/kg-day PFOS. No effect of PFOS on fertility.
2. No effect on total litter size, but decreased live litter size at 5 mg/kg-day PFOS.
3. Increased total litter loss (by PND1) at 5 mg/kg-day PFOS.
4. Increased liver weights (Parental generation).

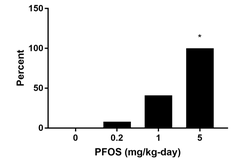
Fertility and pregnancy indices



Total and live litter sizes



Total litter loss – PND1

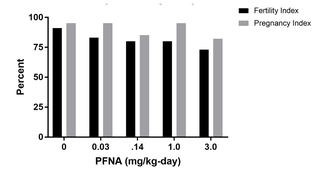


Critical effect = total litter loss by PND100	
LOAEL = 5.0 mg/kg-day	NOAEL = 1.0 mg/kg-day
BMD_{10} = 0.31 mg/kg-day	$BMDL_{10}$ = 0.09 mg/g-day

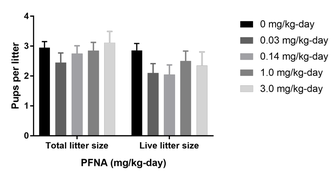
PFNA REPRODUCTIVE AND DEVELOPMENTAL TEST RESULTS

1. No effect of PFNA on fertility, pregnancy, live litter size or total litter size.
2. No effect of PFNA on pup survivability.
3. Increased liver and kidney weights (Parental generation).
4. Decreased immune response at 3 mg/kg-day PFNA (Parental generation).

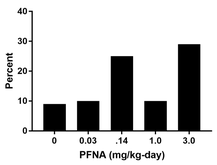
Fertility and pregnancy indices



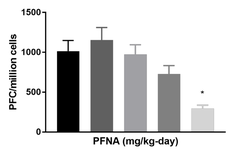
Total and live litter sizes



Total litter loss – PND1



Plaque Forming Cells



Critical effect = decreased immune response	
LOAEL = 3.0 mg/kg-day	NOAEL = 1.0 mg/kg-day
BMD_{10} = 2.2 mg/kg-day	$BMDL_{10}$ = 1.2 mg/kg-day

FUTURE DIRECTIONS

1. Reproductive and developmental tests will ultimately be conducted with all six PFAS investigated in our range finding studies.
2. *Peromyscus maniculatus* (deer mouse) will be used in the conduct of some future reproductive and developmental studies, as APHC acquired a breeding colony.
3. Comparison studies are planned using CD-1 mice exposed to 6:2 FTS, PFNA, and PFHxS.