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Document Processing Center (7407M)
(Attn: TSCA Section 8(e) Coordinator)
Office of Pollution Prevention and Toxics
Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Re: 2,3,7,8-tetrachlorodibenzo-p-dioxin, CASRN 1746-01-6
2,3,7,8-tetraclorodibenzofuran, CASRN 51207-31-9
2,3,4,7,8-pentachlorodibenzofuran, CASRN 57117-31-4

Dear Sir/Madam:

The following information is being submitted by The Dow Chemical Company (Dow) pursuant to current guidance issued by EPA indicating EPA's interpretation of Section 8(e) of the Toxic Substances Control Act. Dow has made no determination as to whether a significant risk of injury to health or the environment is actually presented by the findings.

Results of egg injection (Japanese Quail) and CYP1A1 (Chicken and Japanese Quail) induction studies, evaluating 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), 2,3,7,8-tetrachlorodibenzofuran (TCDF) and 2,3,4,7,8-pentachlorodibenzofuran (4-PeCDF), were submitted as abstracts by the university research groups performing this research to the upcoming 2008 Society of Environmental Toxicology (SETAC) meeting in Tampa Florida. LD50 and EC50 estimates for egg hatchability and EROD induction, respectively, along with relative potency estimates relative to TCDD, were included in the abstract information. The abstracts submitted by the university research groups involved in the studies are attached for further review.

No written report of these results is yet available.

Sincerely,

Linda C. Burgert
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CONTAINS NO CBI

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Contains No CBI

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Abstract Proof

CONTROL ID: 505999

SESSION CATEGORY: Terrestrial or Wildlife Toxicology and Ecology

SESSION: Wildlife Ecotoxicology

PRESENTATION TYPE: Poster preferred

Abstract

TITLE: Effects of TCDD, TCDF, and PeCDF injected into the air cell of Japanese quail (*Coturnix japonica*) prior to incubation

AUTHORS (FIRST NAME, LAST NAME): Andrew Cohen-Barnhouse¹, Steve Bursian¹, Jane Link¹, John Giesy², Paul Jones², Yi Wan², Steve Wiseman², Sean Kennedy³, John Newsted⁴, Matthew Zwiernik⁵

INSTITUTIONS (ALL): 1. Animal Science, Michigan State University, East Lansing, MI, USA.

2. Veterinary Biomedical Sciences and Toxicology Centre, University of Saskatchewan, Saskatoon, SK, Canada.

3. National Wildlife Research Centre, Environment Canada, Ottawa, ON, Canada.

4. Entrix, Okemos, MI, USA.

5. Zoology, Michigan State University, East Lansing, MI, USA.

ABSTRACT BODY: A molecular basis for distinguishing differences in sensitivity to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)-like compounds among avian species has been suggested. Amino acid substitutions in the ligand-binding domain of the aryl hydrocarbon receptor are presumed to be responsible, in part, for this differential sensitivity. Subsequent studies suggested that avian species may be classified into one of three TCDD-sensitivity categories: very sensitive Type 1 (chicken), moderately sensitive Type 2 (ringneck pheasant), and insensitive Type 3 (Japanese quail). A series of egg injection studies are being conducted to confirm the proposed avian sensitivity classification. The effect of TCDD, 2,3,7,8-tetrachlorodibenzofuran (TCDF) and 2,3,4,7,8-pentachlorodibenzofuran (PeCDF) on hatchability of Japanese quail eggs and growth and survival of hatchlings is reported here. Doses ranging from 0.1 to 61.5 ng/g egg were injected into the air cell prior to incubation. Hatchlings were maintained for 10 days to assess growth and survivability. A sample of the chicks was weighed, euthanized, and necropsied on day of hatch and at 10 days of age. Selected tissues of 10-day-old chicks were removed, weighed and processed for histological assessment. Subsamples of the liver were processed for chemical analysis and assessment of cytochrome P4501A induction. LD50 values for TCDD, TCDF and PeCDF based on hatchability data are 16.5 (12.7 - 22.5; 95% confidence intervals), 5.07 (4.05 - 6.35) and 0.84 (0.657 - 1.06) ng/g egg, respectively. The relative potencies (REPs) of TCDF and PeCDF compared to TCDD are 3.3 and 19.6, respectively. The REP of PeCDF based on hatchability of Japanese quail eggs is

similar to an REP value of 18 based on induction of CYP1A activity in cultured Japanese quail hepatocytes determined in a complimentary study. To our knowledge, this is the first in vivo study indicating that a TCDD-like compound is substantially more toxic in an avian species than TCDD. It would be of interest to determine if dietary exposure of Japanese quail to TCDD-like compounds results in similar REP values as determined in the enzyme induction and egg injection studies.

KEYWORDS: Avian, Toxicity, Dioxins, Development.

Abstract Details

Presentation Type Preference: Willing to present if preferred presentation type choice is not met.

Requested Submission:

Student Presentation Award:

Public E-Mail Address: bursian@msu.edu

CONTROL ID: 499066

SESSION CATEGORY:

SESSION:

PRESENTATION TYPE: Poster preferred

Abstract

TITLE: Sensitivity of chicken and Japanese quail embryo hepatocyte cultures to cytochrome P4501A induction upon exposure to TCDD, PeCDF, and TCDF

AUTHORS (FIRST NAME, LAST NAME): Jessica C. Hervé^{1, 2}, Stephanie P. Jones², Lukas J. Mundy², Steven J. Bursian³, John P. Giesy⁴, Paul D. Jones⁴, Matthew J. Zwiernik³, Sean W. Kennedy^{2, 1}

INSTITUTIONS (ALL): 1. Biology, University of Ottawa, Ottawa, ON, Canada.
2. Environment Canada, NWRC, Ottawa, ON, Canada.
3. Michigan State University, East Lansing, MI, USA.
4. University of Saskatchewan, Saskatoon, ON, Canada.

ABSTRACT BODY: The responsiveness of primary cultures of avian embryo hepatocytes to induction of cytochrome P4501A (CYP1A) is useful for predicting the sensitivity of avian species to the embryo-toxic effects of polychlorinated dibenzo-*p*-dioxins, dibenzofurans, and 'dioxin-like' polychlorinated biphenyls. CYP1A catalytic activity is conveniently measured by use of the ethoxyresorufin *O*-deethylase (EROD) assay. In the present study, EROD-inducing potencies of 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD), 2,3,4,7,8-pentachlorodibenzofuran (PeCDF) and 2,3,7,8-tetrachlorodibenzofuran (TCDF) were determined for domestic chicken (*Gallus domesticus*) and Japanese quail (*Coturnix japonica*) primary hepatocyte cultures. Hepatocytes were cultured in 48-well plates and exposed to serial dilutions of TCDD, PeCDF or TCDF for 24 h. In chicken hepatocytes, the potencies of the three compounds were similar - maximal EROD responses were nearly identical, and the concentrations that elicited fifty percent of the maximal response (EC50s) were 0.018 nM, 0.019 nM and 0.022 nM for TCDD, PeCDF and TCDF, respectively. The relative potencies (REPs - relative to TCDD) were 0.8 and 0.9 for PeCDF and TCDF, respectively. The results for TCDD and TCDF were similar to earlier findings, but prior to this work PeCDF had not been studied in detail. In contrast, the REPs for PeCDF and TCDF in Japanese quail were 18 and 0.1, respectively. EC50s for TCDD, PeCDF and TCDF were 0.19 nM, 0.014 nM and 1.5 nM, respectively. The fact that PeCDF is a more potent inducer of EROD than TCDD in Japanese quail was surprising. It was also surprising that the EC50s for TCDD in chicken hepatocytes (0.018 nM) and PeCDF in Japanese quail (0.014 nM) were essentially equivalent. Until this study, it had been assumed that the chicken was more sensitive than any other avian species to EROD induction by all dioxin-like compounds (DLCs). However, this research with cultured hepatocytes, along with our complementary research using egg-injection techniques and aryl hydrocarbon receptor (AHR) binding assays with chicken, Japanese quail and other avian species raises interesting questions regarding mechanisms of action of DLCs, as well as questions regarding tax-specific toxic equivalency factors (TEFs) assigned by the World Health Organization.

KEYWORDS: Dioxins, Cytochrome P450, Avian, Bioassay.

Abstract Details

Presentation Type Preference: Willing to present if preferred presentation type choice is not met.

Requested Submission:

Student Presentation Award: SNA Best Student Presentation Award (Masters)

Public E-Mail Address: