



**NTP**  
National Toxicology Program

# **NTP Board of Scientific Counselors Technical Reports Review Subcommittee**

**Report from the May 16-17, 2007 Meeting**

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**Subcommittee Chair**





## **Sodium Dichromate Dihydrate**

**Used as a corrosion inhibitor, in electroplating, leather tanning, wood preservation, textile manufacturing and in the production of pigments**

**Based on a 2-year drinking water study, the subcommittee unanimously approved (6-0) the conclusions:**

<b>Sex/Species</b>	<b>Evidence</b>	<b>Neoplastic lesions</b>
<b>Male Rats</b>	<b>CE</b>	<b>Oral squamous cell carcinoma</b>
<b>Female Rats</b>	<b>CE</b>	<b>Oral squamous cell carcinoma</b>
<b>Male Mice</b>	<b>CE</b>	<b>Neoplasms of the small intestine</b>
<b>Female Mice</b>	<b>CE</b>	<b>Neoplasms of the small intestine</b>

CE = clear evidence



## Formamide

**Used as a solvent and water softener, in water-soluble inks and as an intermediate in organic syntheses**

The Subcommittee accepted the report's conclusions on a 6-0 vote.

<b>Sex/Species</b>	<b>Evidence</b>	<b>Neoplastic lesions</b>
<b>Male Rats</b>	<b>NE</b>	-
<b>Female Rats</b>	<b>NE</b>	-
<b>Male Mice</b>	<b>CE</b>	<b>Hemangiosarcoma of the liver</b>
<b>Female Mice</b>	<b>EE</b>	<b>Hepatocellular adenoma and carcinoma (combined)</b>

The subcommittee also concluded that formamide exposure was associated with bone marrow hyperplasia in male rats

NE = no evidence

CE = clear evidence

EE = equivocal evidence



## Cumene

Used as a solvent and in the production of phenol, acetone and  $\alpha$ -methylstyrene

Based on results of 2-year inhalation studies, the Subcommittee unanimously accepted (6-0) the conclusions of the report:

<b>Sex/Species</b>	<b>Evidence</b>	<b>Neoplastic lesions</b>
<b>Male Rats</b>	<b>CE</b>	<b>Nasal epithelial adenoma; renal tubule adenoma and carcinoma (combined)</b>
	<b>EE</b>	<b>interstitial cell adenoma of the testes</b>
<b>Female Rats</b>	<b>SE</b>	<b>Nasal epithelial adenoma</b>
<b>Male Mice</b>	<b>CE</b>	<b>Alveolar/bronchial neoplasms</b>
	<b>EE</b>	<b>hemangiosarcoma of the spleen; thyroid follicular cell adenoma</b>
<b>Female Mice</b>	<b>CE</b>	<b>Alveolar/bronchial neoplasms; hepatocellular adenoma and carcinoma (combined)</b>

CE = clear evidence

SE = some evidence

EE = equivocal evidence = may have been related



## **Cresols (60:40m/p)**

**Used as a solvent, disinfectant and preservative, and in the production of fragrances, antioxidants, dyes, pesticides and resins**

Based on results of 2-year feeding studies, the subcommittee unanimously agreed (6-0) with the report's conclusions:

### **Sex/Species**

**Male Rats**

**Female Mice**

### **Evidence**

**EE**

**SE**

### **Neoplastic lesions**

**Renal tubule adenoma**

**Forestomach squamous cell papilloma**

SE = some evidence

EE = equivocal evidence



# Propargyl Alcohol

**Chemical intermediate, corrosion inhibitor, solvent stabilizer and polymer modifier**

On the basis of 2-year inhalation studies, the subcommittee voted 4-2\* to accept the conclusions.

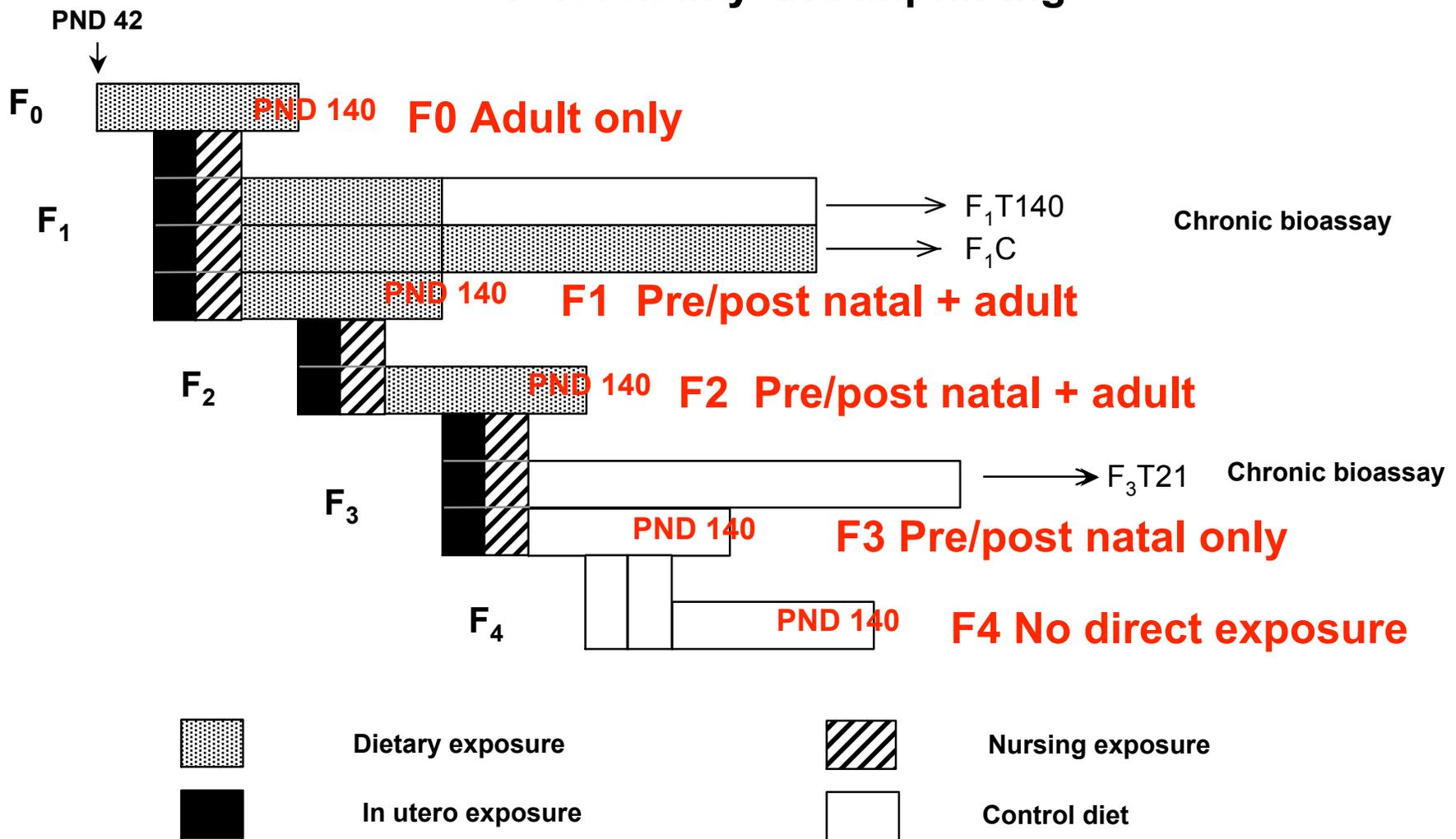
<b>Sex/Species</b>	<b>Evidence</b>	<b>Neoplastic lesions</b>
<b>Male Rats</b>	<b>SE</b>	<b>Nasal epithelial adenoma; mononuclear cell leukemia</b>
<b>Female Rats</b>	<b>NE</b>	<b>-</b>
<b>Male Mice</b>	<b>SE*</b> <b>EE</b>	<b>Nasal epithelial adenoma Harderian gland adenoma</b>
<b>Female Mice</b>	<b>SE*</b>	<b>Nasal epithelial adenoma</b>

NE = no evidence  
SE = some evidence



# Ethinyl estradiol - Multigenerational Dosing Scheme

1. Chronic effects (PND140) : cumulative over generations, reversibility and imprinting





## Ethinyl Estradiol (Multigenerational study)

Chronic effects (PND140)

2, 10 or 50 ppb in a low phytoestrogen diet

### Adverse Effects

Decreased body weight

Accelerated puberty in females

Perturbation of estrous cycle  
(aberrant cycles, time in estrus)

Increased mammary gland hyperplasia

Mild mineralization of nephrons

Delay of preputial separation

### Male

during exposure

F<sub>0</sub> - F<sub>3</sub>

F<sub>1</sub> and F<sub>2</sub>

F<sub>2</sub>\*

### Female

during exposure

F<sub>1</sub> - F<sub>3</sub>

F<sub>1</sub> and F<sub>2</sub>

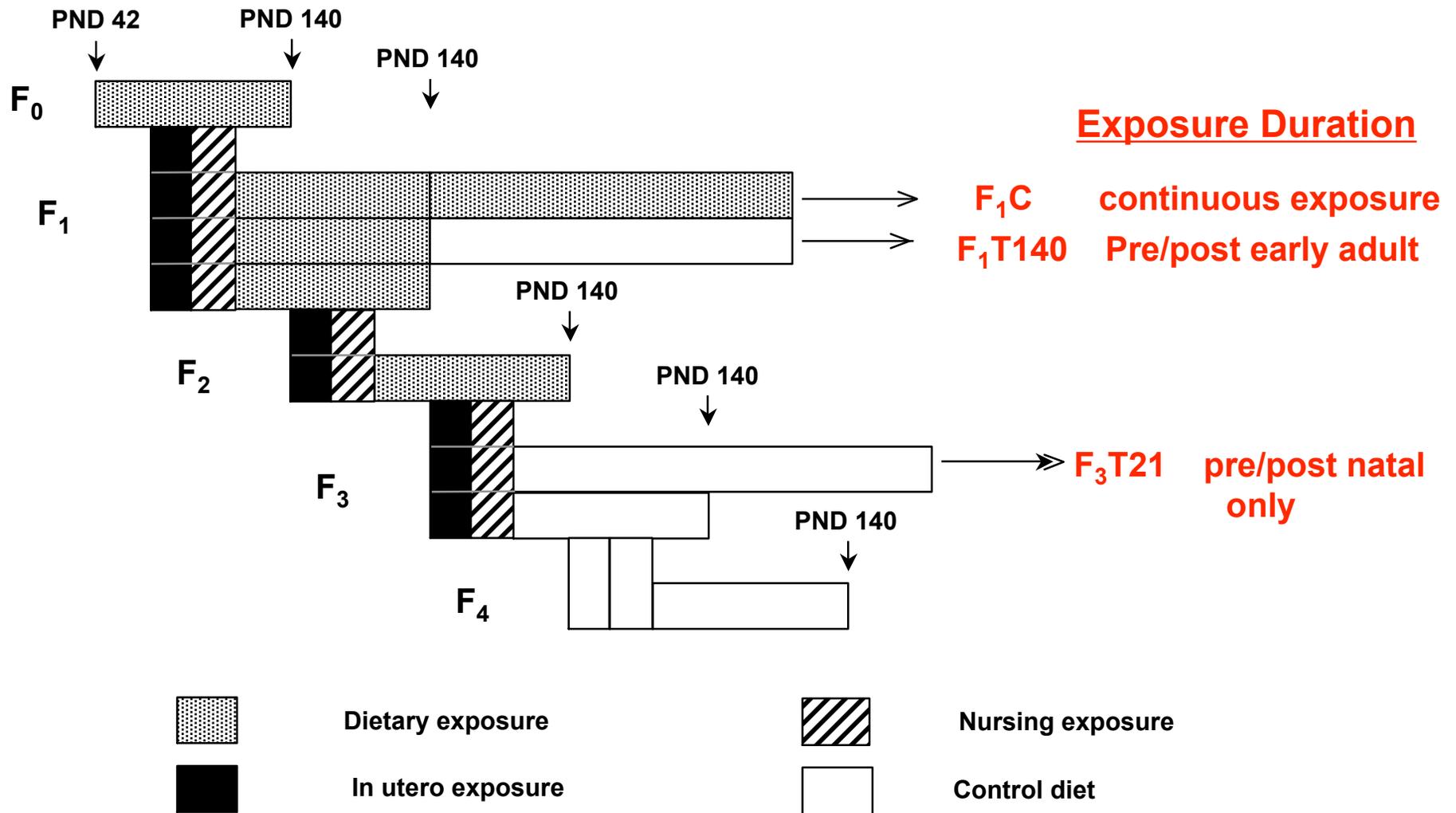
\* Possible cumulative effect, not seen in F1 gen

No effect in F4 generation with no direct exposure



# Ethinyl estradiol- Multigeneration Dosing Scheme

## 2. Carcinogenicity – 2 yr bioassays





## **Ethinyl Estradiol (2-year bioassay)** **2, 10 or 50 ppb in a low phytoestrogen diet**

**Conclusions accepted by subcommittee (7-0)**

<b>Times of Exposure</b>	<b>Sex</b>	<b>Evidence</b>	<b>Neoplastic Lesions</b>
<b>F<sub>1</sub> Conception to 2yrs. old</b>	<b>M</b>	<b>NE*</b>	-
	<b>F</b>	<b>NE*</b>	-
<b>F<sub>1</sub> Conception to 20 weeks old</b>	<b>M</b>	<b>NE</b>	-
	<b>F</b>	<b>EE</b>	<b>Uterine stromal polyps</b>
<b>F<sub>3</sub> Conception to PND 21</b>	<b>M</b>	<b>EE</b>	<b>Preputial gland epithelial neoplasms; mammary gland adenocarcinoma</b>
	<b>F</b>	<b>EE</b>	<b>Uterine stromal polyps</b>

\*EE previously classified as a carcinogen at higher doses

NE = no evidence  
EE = equivocal evidence