



**NTP**  
National Toxicology Program

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

## **Report from the August 28, 2006 Meeting**





## Genetically Modified Models - Allyl bromide

Chemical intermediate in the manufacture of polymers

<b>Mouse model</b>	<b>Exposure route</b>	<b>Sex</b>	<b>Evidence</b>	<b>Lesions</b>
<b>p53<sup>+/-</sup></b>	<b>Gavage</b>	<b>F</b>	<b>NE</b>	<b>-</b>
<b>Tg.AC</b>	<b>Gavage</b>	<b>F</b>		<b>Squamous cell papillomas of the vulva</b>



## Genetically Modified Models - Dicyclohexylcarbodiimide

Chemical and pharmaceutical reagent

<b>Mouse model</b>	<b>Exposure route</b>	<b>Sex</b>	<b>Evidence</b>	<b>Lesions</b>
p53 <sup>+/-</sup>	Dermal	F	NE	-
Tg.AC	Dermal	F		Squamous cell papilloma of the skin



## Genetically Modified Models - p16<sup>Ink4a</sup>/p19<sup>Arf</sup> mice

Substance	Exposure Route	Sex	Evidence	Lesions
Solvent				
Benzene	Gavage	M	CE	Malignant lymphoma
Benzene	Gavage	F	NE	-
Chemical intermediate and stabilizer				
Glycidol	Gavage	M	CE	Histiocytic sarcoma
Gycidol	Gavage	F	SE	Alveolar/bronchiolar adenoma
Laxative				
Phenolphthalein	Feed	M and F	NE	-



## Concordance of GMM to Bioassay Data

<b>Classification</b>	<b>p53</b>	<b>Tg.AC</b>	<b>p16<sup>Ink4a</sup>/p19<sup>Arf</sup></b>
<b>Known human carcinogens</b>	<b>12</b>	<b>9</b>	<b>1</b>
<b>Identified human carcinogens</b>	<b>10</b>	<b>8</b>	<b>1</b>
<b>Suspected human carcinogens</b>	<b>19</b>	<b>15</b>	<b>2</b>
<b>Identified human carcinogens</b>	<b>11</b>	<b>9</b>	<b>1</b>
<b>Probable human non carcinogens</b>	<b>28</b>	<b>12</b>	<b>1</b>
<b>Identified human non carcinogens</b>	<b>27</b>	<b>10</b>	<b>0*</b>
<b>Overall concordance</b>	<b>81%</b>	<b>74%</b>	

\* unclassified chemical; negative in the model



## Use of Genetically Modified Models (GMMs) in NTP Cancer Hazard Identification

The NTP proposes to utilize GMMs as needed, for example:

- when there is compelling prior evidence that suggests that a particular agent or class of agents could be adequately studied in a particular model, or
- when there is insufficient test agent available to employ conventional 2-year or lifetime exposure cancer models, or
- when studying the effects of mixtures of agents if the response of the particular model chosen is known for at least one component of the mixture.

The NTP proposes to continue to develop and/or refine GMMs for the study of agents when appropriate.

The NTP concludes that there is insufficient evidence to support the routine replacement of the 2-year mouse bioassay with GMMs.



## Technical Reports for Review on May 16 - 17, 2007

- **Cresol**
- **Cumene**
- **Ethinyl Estradiol (multigenerational) in Sprague Dawley rats**
- **Formamide**
- **Isoeugenol**
- **Propargyl Alcohol**
- **Sodium Dichromate Dihydrate (VI)**