National Toxicology Program  
Board of Scientific Counselors  
Technical Reports Review Subcommittee  

September 27-28, 2005  
NIEHS, Research Triangle Park, NC  

Summary Minutes

<table>
<thead>
<tr>
<th>Contents</th>
<th>Page Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attendees</td>
<td>1</td>
</tr>
<tr>
<td>Peer Review Meeting - September 27, 2005</td>
<td>2</td>
</tr>
<tr>
<td>Simulated Solar Light Studies</td>
<td>2</td>
</tr>
<tr>
<td>Dibromoacetic Acid</td>
<td>3</td>
</tr>
<tr>
<td>Peer Review Meeting - September 28, 2005</td>
<td>4</td>
</tr>
<tr>
<td>Dichloroacetic Acid</td>
<td>5</td>
</tr>
<tr>
<td>Bromodichloromethane</td>
<td>7</td>
</tr>
<tr>
<td>Sodium Bromate</td>
<td>8</td>
</tr>
<tr>
<td>Divinylbenzene-HP</td>
<td>9</td>
</tr>
<tr>
<td>Methyl Isobutyl Ketone</td>
<td>10</td>
</tr>
<tr>
<td>Public Comments</td>
<td>11</td>
</tr>
<tr>
<td>September 28, 2005</td>
<td>11</td>
</tr>
<tr>
<td>Diisopropylcarbodiimide</td>
<td>11</td>
</tr>
<tr>
<td>Diisopropylcarbodiimide - GMM Report</td>
<td>13</td>
</tr>
<tr>
<td>4-Methylimidazole</td>
<td>13</td>
</tr>
</tbody>
</table>

Attachment 1 – Federal Register Meeting Announcement
Attachment 2 – Agenda
Attachment 3 – Committee Roster
Attendees

Members:
Charlene McQueen (chair)
Diane Birt (absent on 09/28/05)
Michael Elwell
Thomas Gasiewicz
John Giesy
Stephen Roberts
Mary Vore

Ad Hoc Attendees:
Kenneth Crump
Harish Sikka
Keith Soper

NIEHS Attendees:
Douglas Bristol
John Bucher
Po C. Chan
Rajendra Chhabra
John French
Burhan Ghanayem
Ronald Herbert
Dojung Kim
Grace Kissling
David Malarkey
Gail Pearse
John Peckham
Christopher Portier
Barbara Shane
Fernando Suarez
Greg Travlos
Molly Vallant
Kristine Witt
Mary Wolfe

Agency Attendees:
William Allaben, FDA
Paul Howard, FDA
Andrija Kornhauser, FDA
Ronald Lorentzen, FDA
Mark Toraason, NIOSH
Wayne Warner, FDA

Public Attendees:
Stephen Brecker, Dynamac Corp.
Patricia Crockett, Constella Health Sciences
Michael Easterling, Constella Group
Sanford Garner, Constella Group
Ralph Gingell, Shell Chemical LP
William Gulledge, American Chemistry Council
Beom-sook Han, NITR Korea
Jessica Matthews, Constella Group
Joel Parker, Constella Health Sciences
Peer Review Meeting - September 27, 2005

The meeting began at 8:30 a.m. on September 27, 2005, in the Rodbell Conference Center, David P. Rall Building, National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, North Carolina. The following members of the National Toxicology Program (NTP) Board of Scientific Counselors Technical Reports Review Subcommittee (TRR Subcommittee) were present: Drs. Charlene McQueen (chairperson), Diane Birt, Michael Elwell, Thomas Gasiewicz, John Giesy, Jr., Stephen Roberts, and Mary Vore. Attending the meeting as ad hoc (non-voting) members to the subcommittee were Drs. Kenneth Crump, Keith Soper, and Harish Sikka.

Dr. Christopher Portier, Associate Director of the NTP, NIEHS, welcomed the TRR Subcommittee to the meeting. Dr. Charlene McQueen asked the TRR Subcommittee and public attendees to identify themselves. Dr. Barbara Shane, Executive Secretary, NIEHS, read the conflict of interest statement and asked for any conflicts. No TRR Subcommittee members had a conflict. She said Drs. Crump, Soper and Sikka were attending the meeting as ad hoc members and could participate in the discussions, but not vote.

Simulated Solar Light Studies
Dr. Paul C. Howard, National Center for Toxicological Research (NCTR), described the NCTR’s program for phototoxicity and photocarcinogenicity studies and their facilities for exposure of rodents to simulated solar light. This facility has been designated as the National Toxicology Program Center for Phototoxicology. Dr. Howard then described the rationale, design, and results for two studies to test the effects of an alpha hydroxy acid (glycolic acid) and a beta hydroxy acid (salicylic acid) on the photocarcinogenicity of simulated solar light (SSL). The proposed conclusions were:

These experiments investigated the impact of topical application of a cosmetic formulation containing 4% or 10% glycolic acid (pH 3.5) or 2% or 4% salicylic acid (pH 4) on the photocarcinogenesis of filtered 6.5 kW xenon arc simulated SSL in SKH-1 hairless mice. Taking into consideration the survival data, time to tumor, and the pathology results, glycolic acid did not alter the photocarcinogenesis of SSL, while salicylic acid was photoprotective reducing the carcinogenicity of a 0.3 minimal erythema dose (MED) of SSL.
Dr. Roberts, a principal reviewer, had no scientific criticisms. He suggested adding more description of the animal exposure procedures and the survival analysis. He also suggested that data on tumor multiplicity shown in Dr. Howard’s presentation be included in the report.

Dr. Soper, a principal reviewer, noted that the poly-3 statistical test does not require lethality assumptions. He agreed that inclusion of the tumor multiplicity data in the report would be helpful. He asked whether the tumor incidence in the 10% group might be a false positive result.

Dr. Birt, a principal reviewer, noted the higher incidences of tumors in animals exposed to SSL and receiving the control cream alone compared to those only receiving the SSL. She asked whether the control cream might have an additive effect on the rate of skin cancers caused by SSL and whether these creams could be contributing to skin cancer in the human population.

Dr. Howard agreed to augment the description of the study’s methodology. He said the two major reasons for removing animals from the study were either a tumor reached 10 mm in size or discrete tumors were likely to merge into a larger tumor that could have confounded the multiplicity of the tumor counts. Dr. Howard responded to the effect of the control cream and noted that a large variety of cream formulations are used in various cosmetic preparations. In a review of 12 coded “control” formulations studied at a similar facility, some of the formulations enhanced and some protected against photocarcinogenicity by SSL. Dr. Howard explained that the principal effect of creams could be alteration of the optical scattering and UV absorption properties of the skin itself.

Dr. John Bucher, NIEHS, said the tumor multiplicity data had only been developed recently. They would not be part of the report’s conclusions considered at this review, but could be presented as an appendix in this report or in a separate publication. Dr. Roberts thought the data were important enough to warrant inclusion in the technical report. He felt that the tumor multiplicity data did not contradict the conclusions from the tumor incidence data. Dr. Portier proposed that the “p” values for tumor multiplicity be included in the tables in the appendix, but not in the results section.

Dr. Roberts moved and Dr. Birt seconded that the conclusions be accepted as written. The motion was accepted unanimously with six yes votes.

**Dibromoacetic Acid**

Dr. Ronald Melnick, NIEHS, described the occurrence of dibromoacetic acid as a water disinfection byproduct, the design and results of the NTP studies, the metabolism of dihaloacetic acids, and a pharmacokinetic model for the behavior of the chemical in rats and mice. The proposed conclusions were:

Under the conditions of these studies, there was *some evidence of carcinogenic activity* of dibromoacetic acid in male rats based on an increased incidence of malignant mesothelioma. There was *some evidence of carcinogenic activity* of dibromoacetic acid in female rats based on an increased incidence and positive trend of mononuclear cell leukemia. There was *clear evidence of carcinogenic*
activity of dibromoacetic acid in male and female mice based on increased incidences of hepatocellular neoplasms and hepatoblastomas (males only). Increased incidences of lung neoplasms in male mice were also considered to be exposure related. The slight increased incidence of lung neoplasms in female mice may have been related to dibromoacetic acid exposure.

Exposure to dibromoacetic acid for two years caused increased incidences of cystic degeneration of the liver in male rats, increased incidences of alveolar epithelial hyperplasia and nephropathy in female rats, and increased incidences of splenic hematopoiesis in male mice.

Dr. Vore, a principal reviewer, felt the study was well conducted. She had no scientific criticisms and agreed with the proposed conclusions.

Dr. Elwell asked for more explanation of the reasons for classifying the mononuclear cell leukemia in female rats as some evidence. He noted that rather similar values formed the basis for an equivocal evidence call in a different study presented at this review. Dr. Crump said another study with a similar increase in mononuclear cell leukemia was considered as no evidence. Drs. Roberts and Vore expressed a desire for consistency in the conclusions relating to the variability in occurrence of mononuclear cell leukemia in rats.

Dr. Bucher urged the subcommittee to consider each study as unique, and base the conclusions on that study’s results rather than comparing incidences across separate studies.

Drs. Portier and Roberts both commented on the high rates of mononuclear cell leukemia in the mid-range dose groups of male rats.

Dr. Vore moved and Dr. Roberts seconded that the conclusion for male rats be modified by adding “the increased incidences in mononuclear cell leukemia in male rats may have been related to chemical exposure.” The motion was carried with five affirmative votes, one negative vote (Dr. Elwell), and no abstentions.

September 28, 2005

Dr. Roberts asked the TRR Subcommittee to revisit the conclusions for dibromoacetic acid in relation to mononuclear cell leukemia. This request followed the subcommittee’s review of several other draft-technical reports for this meeting including two studies that involved conclusions based on mononuclear cell leukemia in female rats. Dr. Roberts wanted to ensure that the conclusions from all the studies were being considered consistently. Dr. Birt was not present for this discussion.

Dr. Bucher restated the arguments for calling the female rat leukemia response in the dibromoacetic acid study as some evidence including a statistically significant trend, a doubling of the incidence in the high dose group, and the mean incidence in the control group matching the mean for the historical controls.
Dr. Roberts questioned why the conclusion for female rats exposed to dibromoacetic acid was different from that proposed in the 4-methylimidazole study and suggested *equivocal evidence* might be more appropriate for the former. Dr. Elwell noted that the statistical support was slightly stronger for the female rats exposed to 4-methylimidazole. Dr. Crump suggested that the historical range for mononuclear cell leukemia in female rats from only four drinking water studies might be artificially tight, given the variability seen in other studies. Dr. Soper also suggested *equivocal evidence* might be more appropriate for the dibromoacetic acid study.

Dr. Portier noted that the incidence of mononuclear cell leukemia in the concurrent control group in the 4-methylimidazole study was lower than in the historical controls, whereas in the dibromoacetic acid study, the incidence of mononuclear cell leukemia in the concurrent controls was similar to the historical mean.

Dr. Melnick said he consulted some previously printed NTP Technical Reports where similar increases in incidence of mononuclear cell leukemia in female rats across the treatment groups were part of the conclusion of *some evidence*, while this effect was not evident in males. Dr. Roberts suggested that to maintain transparency in the calls, the report on dibromoacetic acid should contain an explanation regarding how the NTP arrived at its conclusion of *some evidence* of carcinogenicity.

Following further discussion by the subcommittee, no motion was made to revise the conclusions for dibromoacetic acid approved the previous day. The TRR Subcommittee recommended adding an enhanced discussion of the supporting logic for the conclusions to the report.

**Dichloroacetic Acid**

Dr. Bucher reviewed the history of the use of genetically modified mouse models in NTP studies and the interpretation and reporting of study findings. He said based upon guidance provided previously by the NTP Board of Scientific Counselors the results for p53 models are described using the Levels of Evidence of Carcinogenic Activity while conclusions for the Tg.AC model are presented descriptively.

Dr. Gary Boorman, NIEHS, introduced the studies of the water disinfection byproduct dichloroacetic acid in the Tg.AC and p53 mouse models by various routes of administration. The proposed conclusions were:

- **Under the conditions of these drinking water studies, there was no evidence of carcinogenic activity of dichloroacetic acid in male or female p53 haploinsufficient mice exposed to 500, 1,000, or 2,000 mg/L for 26 or 41 weeks.** The incidences and/or severities of cytoplasmic vacuolization of the hepatocyte were increased in males and females exposed to dichloroacetic acid for 26 or 41 weeks.

- **Under the conditions of these dermal studies, there were increased incidences of squamous cell papillomas at the site of application in male and female Tg.AC hemizygous mice exposed to 500 mg/kg for 39 weeks.** There were dose-related
increased incidences of epidermal hyperkeratosis and hyperplasia at the site of application in both male and female mice exposed to dichloroacetic acid for 26 or 39 weeks.

Under the conditions of these drinking water studies, there was an increase in the incidence of alveolar/bronchiolar adenoma in male Tg.AC hemizygous mice exposed to 1,000 mg/L for 41 weeks. There were a few bronchiolar/alveolar carcinomas in male and female exposed to dichloroacetic acid in the drinking water for 26 weeks and a few bronchiolar/alveolar adenomas in females exposed to dichloroacetic acid in the drinking water for 41 weeks. There were increased incidences and/or severities of cytoplasmic vacuolization of the hepatocyte in male and female Tg.AC hemizygous mice exposed to dichloroacetic acid in the drinking water for 26 or 41 weeks.

The marginally increased incidences of pulmonary adenomas and/or carcinomas compared to the unexposed groups in both the dermal and drinking water studies at 26, 39, or 41 weeks were considered to be related to dichloroacetic acid exposure.

Dr. Elwell, a principal reviewer, had no scientific criticism of the study and agreed with the proposed conclusions.

Dr. Crump, a principal reviewer, thought the small differences in body weight might have been overemphasized. He noted some inconsistencies between the language in the results section and the data in the tables in that section and in the summary table. He inquired if statistical analyses were available for water consumption and the severity of nonneoplastic lesions.

Dr. Giesy, a principal reviewer, inquired if more information about thresholds or No Observed Adverse Effect Levels (NOAELs), dose selection, or non-cancer endpoints such as hematology might be presented in NTP Technical Reports.

Dr. Boorman agreed with the reviewers that the dermal studies were not very revealing. He explained that some tables presented in-life observations and some presented histological diagnoses and any apparent discrepancies would be clarified. He also explained that water consumption is not a very precise measure due to animal behavior and perhaps does not warrant formal statistical analysis.

Dr. Birt asked for a discussion of the gene silencing issue in the Tg.AC mice and clarification of when these animals were obtained relative to the process of re-deriving the mouse strain. She also felt historical control values would be more useful in studies like these with small numbers of animals per group.

Dr. Boorman said historical control values are generally not kept for nonneoplastic lesions because they do not receive the same degree of histopathologic review.
Dr. Giesy inquired if any conclusion should be made about the evaluation of the mouse models themselves. Dr. Bucher said the NTP Board of Scientific Counselors would probably conduct such an evaluation once a number of individual studies using these models are completed.

Dr. Elwell moved and Dr. Vore seconded that the conclusion be accepted as written with the deletion of reference to the dermal study in Tg.AC mice in the final paragraph. The motion carried with five affirmative votes, one no vote (Dr. Giesy), and no abstentions.

**Bromodichloromethane**

Dr. Boorman introduced the studies of the water disinfection byproduct bromodichloromethane in Tg.AC and p53 mice by different routes of administration. The proposed conclusions were:

Under the conditions of these drinking water studies, there was *no evidence of carcinogenic activity* of bromodichloromethane in male or female p53 haploinsufficient mice exposed to 175, 350, or 700 mg/L for 26 or 42 weeks.

Under the conditions of these gavage studies, there was *no evidence of carcinogenic activity* of bromodichloromethane in male or female p53 haploinsufficient mice exposed to 25, 50, or 100 mg/kg body weight five days per week for 26 or 41 weeks.

In both the drinking water and the gavage studies in p53 haploinsufficient mice, there were increased incidences of renal tubule degeneration in male mice and fatty change of the hepatocyte in female mice exposed to bromodichloromethane.

No treatment-related neoplasms or nonneoplastic lesions were seen in male or female Tg.AC hemizygous mice exposed dermally to 64, 128, or 256 mg bromodichloromethane/kg body weight, five days per week, for 26 or 39 weeks.

No treatment related neoplasms were seen in male or female Tg.AC hemizygous mice exposed by drinking water to 175, 350, or 700 mg bromodichloromethane/L for 26 or 42 weeks.

No treatment related neoplasms were seen in male Tg.AC hemizygous mice exposed by gavage to 25, 50, or 100 mg bromodichloromethane/kg body weight, five days per week, for 26 or 41 weeks. An increased incidence of multiple forestomach papillomas was seen in female Tg.AC hemizygous mice exposed to bromodichloromethane by gavage for 26 or 41 weeks.

In the drinking water and gavage studies in Tg.AC hemizygous mice, there were increased incidences of nephropathy and/or renal tubule degeneration in male mice and fatty changes and/or cytoplasmic vacuolization of the hepatocyte in female mice exposed to bromodichloromethane.
Dr. Birt, a principal reviewer, thought the studies were well designed and conducted appropriately. She suggested adding details about the source of the animals and also providing historical control data particularly for forestomach papillomas.

Dr. Vore, a principal reviewer, also felt the study was well conducted and had no scientific criticisms. She agreed with the conclusions.

Dr. Birt moved and Dr. Vore seconded that the conclusions be accepted as written. The motion was carried unanimously with six yes votes.

**Sodium Bromate**

Dr. Michelle Hooth, NIEHS, introduced the studies of the drinking water disinfectant sodium bromate in genetically modified mice by describing the uses of the chemical, the study design, and the effects of the chemical on survival, body weight, and nonneoplastic lesions in the animals. The proposed conclusions were:

Under the conditions of these drinking water studies there was *no evidence of carcinogenic activity* of sodium bromate in male or female p53 haploinsufficient mice exposed to 80, 400, or 800 mg/L for 27 or 43 weeks.

No treatment-related neoplasms were seen in male or female Tg.AC hemizygous mice exposed dermally to 64, 128, or 256 mg sodium bromate/kg body weight for 26 or 39 weeks.

No treatment-related neoplasms were seen in male or female Tg.AC hemizygous mice exposed by drinking water to 80, 400, or 800 mg sodium bromate/L for 27 or 43 weeks.

In drinking water and dermal studies in Tg.AC hemizygous mice, there were increased incidences of nonneoplastic lesions in the thyroid gland and kidney.

Dr. Giesy, a principal reviewer, said the studies were well designed and performed appropriately. He said he would like to see more discussion of the other non-cancer endpoints and possibly some discussion of the perceived utility of the model.

Dr. Gasiewicz, a principal reviewer, thought the conclusions were appropriate. He noted that while the chemical is a carcinogen in other rodent models, it was not in these models. He suggested that this issue be highlighted in the discussion. He emphasized that the description of tissue weights should distinguish between absolute and relative weights. Likewise, the report should be clear regarding the statistical and biological significance in the descriptions of the incidence of lesions.

Dr. Birt, a principal reviewer, asked for a discussion of the gene silencing issue in the Tg.AC mice and clarification of when these animals were obtained relative to the process of re-deriving the mouse strain. Overall, she agreed with the study’s conclusions.
Dr. Hooth noted that while thyroid or kidney neoplasms were not seen in these studies as they were in the traditional 2-year bioassays, those sites were targets of toxicity in these studies.

Dr. Roberts noted that different forms of conclusion statements are used for different model strains. Dr. Portier explained that the title of the NTP Technical Reports for studies in the p53 model identifies them as carcinogenesis tests and the title for studies in the Tg.AC models identifies them as toxicity studies. The NTP applies the Levels of Evidence for Carcinogenic Activity to the findings in the p53 model, but not the Tg.AC model. Dr. Roberts suggested that text be added to technical reports on studies with transgenic animals so that the reader can understand the basis for the distinction in conclusions.

Dr. Ronald Lorentzen, NCTR, said the results of the studies in the Tg.AC mice are consistent with other studies performed on brominated compounds that showed kidney toxicity.

Dr. Gasiewicz moved and Dr. Giesy seconded that the conclusions be accepted as written. The motion was carried unanimously with six yes votes.

**Divinylbenzene-HP**

Dr. Daniel Morgan, NIEHS, introduced the toxicology and carcinogenesis studies of divinylbenzene by describing the uses and metabolism of the chemical and the nomination, design, and results of the studies. The proposed conclusions in the draft report were:

Under the conditions of these 2-year inhalation studies, there was *equivocal evidence of carcinogenic activity* of divinylbenzene-HP in male F344/N rats based upon the occurrence of carcinomas in the kidney and glial tumors in the brain. There was *no evidence of carcinogenic activity* in female 344/N rats exposed to 100, 200, or 400 ppm divinylbenzene-HP. There was *no evidence of carcinogenic activity* in male B6C3F1 mice exposed to 10, 30, or 100 ppm divinylbenzene-HP. There was *equivocal evidence of carcinogenic activity* of divinylbenzene-HP in female B6C3F1 mice based on the incidences of alveolar/bronchiolar adenoma or carcinoma (combined) in the lung.

Exposure to divinylbenzene-HP caused nonneoplastic lesions in the nasal cavity of male and female rats including degeneration of the olfactory epithelium and basal cell epithelial hyperplasia. Nonneoplastic lesions were observed in the lung and nasal cavity of exposed mice. Atypical bronchiolar hyperplasia and hyperplasia of the alveolar epithelium were observed in the lung of male and female mice. In the nasal cavity of mice, suppurative inflammation, metaplasia of the respiratory and olfactory epithelium, and degeneration of the olfactory epithelium were present at all concentrations.

Dr. Gasiewicz, a principal reviewer, generally agreed with the conclusions. However, he expressed concern about the use of historical control data rather than control data from the study. In the case of mononuclear cell leukemia, apparently different conclusions were proposed in different studies, despite similar incidences in this tumor type.
Dr. Soper, a principal reviewer, suggested that the highly variable lung neoplasms in female mice might have merited *no evidence* since the control incidence is high.

Dr. Bucher explained that while the concurrent control group is the primary basis of comparison for each study, historical data could help by adding some perspective to the nature of particular tumor types. Historical control data are grouped within a 5-year moving window including the present studies. Over time, rare tumors remain rare, but more common tumors become more frequent and have a wider distribution of incidence.

Dr. Crump noted that the rates for mononuclear cell leukemia in female rats, which were called *no evidence*, were similar to those in a different study where the conclusion was *some evidence*. He said sometimes the historical ranges might appear artificially wide because of an outlier. He called for a formal statistical test incorporating historical controls.

Dr. Grace Kissling, NIEHS, said a statistical test that incorporates considerations of survival and tumor lethality is being developed for historical control incidences.

Dr. Elwell noted that non-neoplastic lesions in the kidney were not included in the summary table although they were mentioned in the text.

When the TRR Subcommittee began consideration of the conclusions, a revised version of the second paragraph was projected on the display screen:

Exposure to divinylbenzene-HP caused nonneoplastic lesions of the nasal cavity in male and female rats and of the lung and nasal cavity in male and female mice.

Dr. Birt moved and Dr. Vore seconded that the first paragraph of the conclusions be accepted as written. Dr. Roberts noted a disparity in the levels of evidence applied in different studies with mononuclear cell leukemia as the endpoint and inquired about the criteria used. In one study, similar incidences in female rats were called *some evidence*, but the present study was called *no evidence*. Dr. Bucher said the difference in study interpretations was based on the fact that inhalation studies consistently have a higher incidence of mononuclear cell leukemia in controls than studies by other routes. Dr. Elwell noted that the control incidence in the present study was the highest of all those in the historical set, which might diminish the apparent difference with the exposed groups. The motion was approved with five yes votes, and one abstention (Dr. Giesy).

Dr. Birt moved and Dr. Vore seconded a motion to accept the revised second paragraph as shown on the display screen. The motion was accepted unanimously with six yes votes.

**Methyl Isobutyl Ketone**

Dr. Fernando Suarez, NIEHS, introduced the toxicology and carcinogenesis studies of methyl isobutyl ketone by describing the uses of the chemical, reviewing the literature that was the basis for dose selection, and presenting the study design and results. The proposed conclusions were:
Under the conditions of these 2-year studies, there was some evidence of carcinogenic activity of methyl isobutyl ketone in male F344/N rats based on increased incidences of renal tubule neoplasms. Increased incidences of mononuclear cell leukemia in 1,800 ppm male F344/N rats may have been related to methyl isobutyl ketone exposure. There was equivocal evidence of carcinogenic activity of methyl isobutyl ketone in female F344/N rats based on the occurrence of renal mesenchymal tumors in the 1,800 ppm group. There was some evidence of carcinogenic activity of methyl isobutyl ketone in male and female B6C3F$_1$ mice based on increased incidences of liver neoplasms. Exposure to methyl isobutyl ketone resulted in nonneoplastic lesions of the kidney characteristic of a2u-globulin accumulation in male rats and nephropathy in female rats.

Dr. Elwell, a principal reviewer, had no scientific criticisms. He noted that as far as he was aware this was the first study in which a renal mesenchymal tumor effect has been considered as being related to treatment in NTP studies, and he requested a more detailed discussion of this finding in the report.

Dr. Giesy, a second principal reviewer, also agreed with the conclusions. He inquired whether the doses might have been too high.

Dr. Suarez noted that while the dose selection was based on literature values, some other studies performed elsewhere also used similar doses, and the present doses seemed appropriate.

Public Comments
Dr. Ralph Gingell, speaking on behalf of the American Chemistry Council Ketones Panel, said this group felt the studies were well performed and the conclusions appropriate. The Panel suggested that qualifying statements about mode of action be added to the discussion.

Dr. Elwell moved and Dr. Giesy seconded that the conclusions be accepted as written. The motion was accepted unanimously with six yes votes.

September 28, 2005
The following members of the subcommittee were present: Drs. Charlene McQueen (chairperson), Michael Elwell, Thomas Gasiewicz, John Giesy, Jr., Steve Roberts, and Mary Vore. Ad hoc (non-voting) members to the subcommittee present at the meeting included Drs. Kenneth Crump, Keith Soper, and Harish Sikka.

Diisopropylcarbodiimide
Dr. Raj Chhabra, NIEHS, introduced the technical report on the toxicology and carcinogenesis studies of diisopropylcarbodiimide by describing the nomination and rationale for the study of carbodiimides and the design and results of the long-term studies of diisopropylcarbodiimide. The proposed conclusions in the draft report were:
Under the conditions of these 2-year dermal studies, there was no evidence of carcinogenic activity of diisopropylcarbodiimide in male or female F344/N rats or B6C3F1 mice administered 10, 20, or 40 mg/kg.

Diisopropylcarbodiimide was associated with clinical signs of neurotoxicity and with brain hemorrhage in male rats.

Dr. Roberts, a principal reviewer, had no scientific criticisms with the study’s conduct and appreciated the inclusion of toxicokinetic data. He did not feel the occasional background seizures affected interpretation of the neurotoxicity. He wondered if inhalation might have been another route of exposure given the low dermal absorption rate. He also inquired if alveolar/bronchiolar carcinomas in female mice were discounted as an effect because of comparison with historical values.

Dr. Sikka, a principal reviewer, had no scientific criticisms and agreed with the conclusions. He noted that although the chemical was negative for carcinogenicity in rats and mice, it yielded a positive response in the mouse micronucleus test.

Dr. Elwell, a principal reviewer, inquired whether a statement that mice could have tolerated higher doses was warranted.

Dr. Chhabra explained that dermal exposure was chosen for the study, in part, because of reports of accidental human exposure that resulted in dermatitis. He explained that the alveolar/bronchiolar carcinomas were discounted because when combined with adenomas no significant effect was observed. Dr. Chhabra also defended the dose selection, noting that the high dose of 40 mg/kg was not far from the dose (70 mg/kg) that produced chronic necrosis and inflammation in the 3-month studies.

Dr. Crump noted that the historical control range for alveolar/bronchiolar carcinomas in female mice was somewhat misleading; with one study out of twenty-eight being an outlier with a response twice as high as any other study. He said he agreed with the conclusions despite the control data.

The proposed replacement text for the second paragraph of the conclusions was displayed on the screen:

Clinical and histological signs of neurotoxicity in male rats were associated with diisopropylcarbodiimide administration.

Dr. Roberts moved and Dr. Elwell seconded that the conclusions be accepted as displayed. The motion was accepted unanimously with five yes votes.
Diisopropylcarbodiimide - GMM Report
Dr. Chhabra introduced the studies of diisopropylcarbodiimide in genetically modified mice by explaining that the NTP was exploring the use of transgenic mice as a possible alternative test model and comparing results in the genetically modified mouse model with the standard 2-year bioassay. He described the design and results of tests of diisopropylcarbodiimide in two transgenic mouse strains (p53 and Tg.AC). In both the genetically modified mice and the bioassay, no carcinogenic responses were noted. The proposed conclusions were:

Under the conditions of this 27-week dermal exposure study, there was no evidence of carcinogenic activity of diisopropylcarbodiimide in female p53 haploinsufficient mice administered 4.38, 8.75, 17.5, 35, or 70 mg/kg in ethanol.

There were no treatment-related neoplasms or nonneoplastic lesions in female Tg.AC hemizygous mice administered 4.38, 8.75, 17.5, 35, or 70 mg/kg in ethanol for 21 weeks.

Dr. Vore, a principal reviewer, thought the study was well conducted and well written and had no scientific or editorial criticisms.

Dr. Sikka, a principal reviewer, noted that the p53 protein appeared protective against carcinogenesis, rather than enhancing malignancy, as stated in the background information. He asked why the study duration was shorter than in some other reported GMM studies.

Dr. Crump, a principal reviewer, also agreed with the conclusions. He inquired why one of the transgenic mouse studies was called a carcinogenicity study and the other a toxicity study.

Dr. Chhabra replied that the optimum study duration was being developed at the time this study started; often papillomas were seen in the Tg.AC model as early as nine weeks in positive controls. Dr. Bucher added that subsequent information has indicated that nine months is closer to the optimum duration for maximizing study sensitivity.

Dr. Chhabra explained that previous peer review panels were uncertain about the Tg.AC mouse model as a definitive indicator of carcinogenicity while the p53 model might be; hence studies with the former are called toxicity studies and the latter carcinogenicity studies.

Dr. Vore moved and Dr. Elwell seconded that the conclusions be accepted as written. The motion was accepted unanimously with five yes votes.

4-Methylimidazole
Dr. Po Chan, NIEHS, described the nomination, design, and results of the toxicology and carcinogenesis studies of 4-methylimidazole. The proposed conclusions were:

Under the conditions of these 2-year feed studies, there was no evidence of carcinogenic activity of 4-methylimidazole in male F344/N rats exposed to 625, 1,250, or 2,500 ppm. There was equivocal evidence of carcinogenic activity of
4-methylimidazole in female F344/N rats based on increased incidences of mononuclear cell leukemia. There was clear evidence of carcinogenic activity of 4-methylimidazole in male and female B6C3F1 mice based on increased incidences of alveolar/bronchiolar neoplasms.

Exposure to 4-methylimidazole resulted in nonneoplastic lesions in the liver of male and female rats and the lung of female mice and in clinical findings of neurotoxicity in female rats.

Dr. Gasiewicz, a principal reviewer, said this was another study where mononuclear cell leukemia was increased in female rats suggesting equivocal evidence of carcinogenicity. He urged an explanation of how the conclusions regarding the calls relating to mononuclear cell leukemia in other studies were reached, and a clear discussion of the comparison of the incidence of this tumor type with historical control rates to ensure consistency between studies. He agreed with all the other conclusions and appreciated the inclusion of the toxicokinetic studies.

Dr. Roberts, a principal reviewer, also called for consistency between studies in formulating conclusions. He felt that the description of the kinetics contradicted the findings of the physiologically based pharmacokinetic (PBPK) model and thought the kinetics in the rats were Michaelis-Menten rather than first-order. He found several problems with the toxicokinetic model, possibly related to assumptions made about the time-course of absorption, saturation, and elimination of 4-methylimidazole.

Dr. Chan explained that because the increased incidence of mononuclear cell leukemia in female rats was statistically significant, but only marginally, it was considered equivocal evidence. He noted also that there was an earlier onset of this tumor in the exposed females. Dr. Chan said there is a difference in its metabolism between rats and ruminants. Metabolism appears to be limited in rats and absorption is faster in gavage studies than in feeding studies. Dr. Bucher agreed this version of the model does not fit the data well and it would need to be revised. Dr. Portier said the models are usually derived from data from short-term toxicokinetic studies and are often difficult to apply to chronic exposures.

Dr. Crump said this was the third study reviewed with rather similar increases in mononuclear cell leukemia in female rats and suggested the conclusions should be similar in all the cases, perhaps equivocal evidence. Dr. Soper agreed. Dr. Bucher explained that staff debated between some evidence and equivocal evidence. He added that inhalation studies, which consistently have higher background rates for this leukemia, are considered somewhat differently from studies using other routes of exposure. Dr. Elwell said he considered the pattern in this study at least as strong as any of the others reviewed and felt equivocal evidence was appropriate. However, in his opinion, the incidence of mononuclear cell leukemia in the dibromoacetic acid should be classified as equivocal rather than some evidence and the divinylbenzene study was insufficient to be considered an equivocal effect.

Dr. Gasiewicz moved and Dr. Roberts seconded that the conclusions be accepted as written with addition of the word “marginally” before the words “increased incidences of mononuclear cell leukemia” in the conclusion for female rats. Dr. Crump suggested that this word might not be
appropriate. Drs. Gasiewicz and Roberts agreed that the response itself was not marginal, and the basis for the equivocal conclusion seemed related to the highly variable background frequency of this lesion. Dr. Roberts moved and Dr. Vore seconded a motion to remove the word “marginally.” The vote to accept the conclusions as originally drafted was approved unanimously with five yes votes.
Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Natcher Building, 45 Center Drive, Conference Room F1/F2, Bethesda, MD 20892.

Closed: September 15, 2005, 8 a.m. to 9:30 a.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Natcher Building, 45 Center Drive, Conference Room F1/F2, Bethesda, MD 20892.

Contact Person: Brent B. Stanfield, PhD, Director, Division of Extramural Activities, National Institute of Diabetes and Digestive and Kidney Diseases, 6707 Democracy Blvd., Room 715, Bethesda, MD 20892, (301) 594-8843, stanfieldb@extra.niddk.nih.gov.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

In the interest of security, NIH has instituted stringent procedures for entrance into the building by non-government employees. Persons without a government I.D. will need to show a photo I.D. and sign-in at the security desk upon entering the building.

Information is also available on the Institute's home page: http://www.niddk.nih.gov/fnd/divisions/DEA/Councils/contdesc.htm, where an agenda and any additional information for the meeting will be posted when available.

Catalogue of Federal Domestic Assistance Program Nos. 93.845, Diabetes, Endocrinology and Metabolic Research; 93.846, Digestive Diseases and Nutrition Research; 93.847, Kidney Diseases, Urology and Hematology Research, National Institutes of Health, HHS.

Dated: July 29, 2005.

Anthony M. Coelho, Jr., Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05-15537 Filed 8-4-05; 8:45am]
BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Allergy and Infectious Diseases; Notice of Closed Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the following meeting.

The meeting will be closed to the public in accordance with the provisions set forth in sections 552b(c)(4) and 552b(c)(6), Title 5 U.S.C., as amended. The grant applications and the discussions could disclose confidential trade secrets or commercial property such as patentable material, and personal information concerning individuals associated with the grant applications, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

Name of Committee: National Institute of Allergy and Infectious Diseases Special Emphasis Panel, Review of an Unsolicited POI Application.

Date: September 8, 2005.

Time: 11 a.m. to 2 p.m.

Agenda: To review and evaluate grant applications.

Place: National Institutes of Health, Rockledge 6700B, Rockledge Drive, Bethesda, MD 20892, (Telephone Conference Call).

Contact Person: Sujata Vih, PhD, Scientific Review Administrator, Scientific Review Program, Division of Extramural Activities, NIAID/NIH/DHHS, 6700B Rockledge Drive, MSC 7616, Bethesda, MD 20892, (301) 594-0993, vijha@niaid.nih.gov.

(Catalogue of Federal Domestic Assistance Program Nos. 93.845, Allergy, Immunology, and Transplantation Research; 93.856, Microbiology and Infectious Diseases Research, National Institutes of Health, HHS)

Dated: August 1, 2005.

Anthony M. Coelho, Jr., Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05-15537 Filed 8-4-05; 8:45am]
BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Institute of Child Health and Human Development; Notice of Meeting

Pursuant to section 10(a) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of a meeting of the National Children's Study Advisory Committee.

The meeting will be open to the public, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

Name of Committee: National Children's Study Advisory Committee, Ethics Subcommittee.

Date: September 7, 2005.

Time: 1:30 p.m. to 3 p.m.

Agenda: Discussions will focus on the development of preliminary recommendations regarding the dissemination of Study findings to the public.

Place: National Institutes of Health, 6100 Executive Boulevard, Rockville, MD 20852, (Telephone Conference Call).

Dated: August 1, 2005.

Anthony M. Coelho, Jr., Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05-15537 Filed 6-4-05; 8:45am]
BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Toxicology Program (NTP); Liaison and Scientific Review Officer; Meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee

AGENCY: National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH).

ACTION: Meeting announcement and request for comments.

SUMMARY: Pursuant to Public Law 92-463, notice is hereby given of a meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee (TRR Subcommittee).

The primary agenda topic is the peer review of the findings and conclusions of ten draft NTP Technical Reports (TR) of rodent toxicity and carcinogenicity studies conducted by the NTP (see Preliminary Agenda below). TRR Subcommittee meeting is open to the public with time scheduled for oral public comment. The NTP also invites written comments on any draft technical report discussed at the meeting. The TRR Subcommittee deliberations on the draft technical reports will be reported to the NTP Board of Scientific Counselors (NTP Board) at a future date.

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Toxicology Program (NTP); Liaison and Scientific Review Officer; Meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee

AGENCY: National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH).

ACTION: Meeting announcement and request for comments.

SUMMARY: Pursuant to Public Law 92-463, notice is hereby given of a meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee (TRR Subcommittee). The primary agenda topic is the peer review of the findings and conclusions of ten draft NTP Technical Reports (TR) of rodent toxicity and carcinogenicity studies conducted by the NTP (see Preliminary Agenda below). TRR Subcommittee meeting is open to the public with time scheduled for oral public comment. The NTP also invites written comments on any draft technical report discussed at the meeting. The TRR Subcommittee deliberations on the draft technical reports will be reported to the NTP Board of Scientific Counselors (NTP Board) at a future date.
DATES: The TRR Subcommittee meeting will be held on September 27-28, 2005. Written comments should be received by September 13, 2005, to enable review by the TRR Subcommittee and NIEHS/ NTP staff prior to the meeting. Individuals wishing to make oral public comments are asked to contact Dr. Barbara Shane (see FOR FURTHER INFORMATION CONTACT below) by September 11, 2005, and if possible, also to send a copy of the statement or talking points at that time. Persons needing special assistance, such as sign language interpretation, or other reasonable accommodation in order to attend, are asked to notify Dr. Shane at least 7 business days prior to the meeting (see FOR FURTHER INFORMATION CONTACT below).

ADDRESSES: The TRR Subcommittee meeting will be held in the Rodbell Auditorium, Rail Building at the NIEHS, 111 T. W. Alexander Drive, Research Triangle Park, NC 27709. A copy of the preliminary agenda, committee roster, and any additional information, when available, will be posted on the NTP Web site (http://ntp.niehs.nih.gov/select/"Advisory Boards and Committees") and provided upon request from the NTP (see FOR FURTHER INFORMATION CONTACT below).

FOR FURTHER INFORMATION CONTACT: Public comments and any other correspondence should be submitted to Dr. Barbara Shane, Executive Secretary for the NTP Board (NTP Liaison and Scientific Review Office, NIEHS, P.O. Box 12233, MD AA-01, Research Triangle Park, NC 27709; telephone: 919-541-4233, fax: 919-541-0295; or e-mail: shane@niehs.nih.gov).

SUPPLEMENTARY INFORMATION:

Background

The primary agenda topic is the peer review of the findings and conclusions of ten draft NTP Technical Reports (TR) of rodent toxicology and carcinogenicity studies conducted by the NTP (see Preliminary Agenda below). Five of the reports are on studies with conventional strains of rats and mice (TR 523, TR 534, TR 535, TR 537, TR 538); four reports are on studies performed in genetically modified models (GMM) including Tg.AC hemizygous and p53 haploinsufficient mice (GMM 5, GMM 6, GMM 10 and GMM 11), and one study is with Crl:SKH-1 hairless mice (TR 524). There will also be a presentation on background seizures in the F344/N rats used by the NTP.

Attendance and Registration

The meeting is scheduled for September 27-28, 2005, from 8:30 a.m. to adjournment and is open to the public with attendance limited only by the space available. Individuals who plan to attend are encouraged to register online at the NTP Web site by September 13, 2005, at http://ntp.niehs.nih.gov/select/"Advisory Boards and Committees" to facilitate access to the NIEHS campus. Please note that a photo ID is required to access the NIEHS campus. The NTP is making plans to videocast the meeting through the Internet at http://www.niehs.nih.gov/external/video.htm.

Availability of Meeting Materials

A copy of the preliminary agenda, committee roster, and any additional information, when available, will be posted on the NTP Web site (http://ntp.niehs.nih.gov/select/"Advisory Boards and Committees") or may be requested in hardcopy from the NTP (see FOR FURTHER INFORMATION CONTACT above). Following the meeting, summary minutes will be prepared and made available on the NTP Web site.

Request for Comments

Public input at this meeting is invited and time is set aside for the presentation of public comments on any draft technical report. Each organization is allowed one time slot per agenda topic. At least 7 minutes will be allotted to each speaker, and if time permits, may be extended to 10 minutes. Registration for oral comments will also be available on-site, although time allowed for presentation by on-site registrants may be less than that for pre-registered speakers and will be determined by the number of persons who register at the meeting.

Persons registering to make oral comments are asked, if possible, to send a copy of their statement to Dr. Shane (see FOR FURTHER INFORMATION CONTACT above) by September 13, 2005, to enable review by the TRR Subcommittee and NIEHS/NTF staff prior to the meeting. Written statements can supplement and extend to 10 minutes. Registration for oral comments will also be available on-site, although time allowed for presentation by on-site registrants may be less than that for pre-registered speakers and will be determined by the number of persons who register at the meeting.

Persons registering to make oral comments are asked, if possible, to send a copy of their statement to Dr. Shane (see FOR FURTHER INFORMATION CONTACT above) by September 13, 2005, to enable review by the TRR Subcommittee and NIEHS/NTF staff prior to the meeting. Written statements can supplement and extend to 10 minutes. Registration for oral comments will also be available on-site, although time allowed for presentation by on-site registrants may be less than that for pre-registered speakers and will be determined by the number of persons who register at the meeting.

Background Information on the NTP Board of Scientific Counselors

The NTP Board is a technical advisory body comprised of scientists from the public and private sectors who provide primary scientific oversight to the overall program and its centers. Specifically, the NTP Board advises the NTP on matters of scientific program content, both present and future, and conducts periodic review of the program for the purposes of determining and advising on the scientific merit of its activities and their overall scientific quality. The TRR Subcommittee is a standing subcommittee of the NTP Board. NTP Board members are selected from recognized authorities knowledgeable in fields, such as toxicology, pharmacology, pathology, biochemistry, epidemiology, risk assessment, carcinogenesis, mutagenesis, molecular biology, behavioral toxicology and neurotoxicology, immunochemistry, reproductive toxicology or teratology, and biostatistics. The NTP strives for equitable geographic distribution and minority and female representation on the NTP Board. Its members are invited to serve overlapping terms of up to four years. NTP Board meetings are held annually or biannually.

Dated: July 28, 2005.

Samuel H. Wilson,
Deputy Director, National Institute of Environmental Health Sciences.

Preliminary Agenda

National Toxicology Program (NTP) Board of Scientific Counselors, Technical Reports Review Subcommittee Meeting, September 27-28, 2005, Rodbell Auditorium, Rail Building, National Institute of Environmental Health Sciences, 111 T. W. Alexander Drive, Research Triangle Park, NC.

NTP Technical Reports (TR) Scheduled for Review

- TR 524: a- and b-Hydroxy acids (glycolic and salicylic acids, respectively) in combination with solar light (CAS Nos. 79-14-1 and 69-72-7, respectively)
- TR 537: Dichloroacetic acid (CAS No. 79-43-6)
- TR 538: a-Hydroxy acids (glycolic and salicylic acids, respectively) in combination with solar light (CAS Nos. 79-14-1 and 69-72-7, respectively)
- TR 538: Water disinfection by-product
- TR 538: Dichloroacetic acid (CAS No. 79-43-6)
- TR 538: Water disinfection by-product
DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Notice of Meeting

Pursuant to section 10(d) of the Federal Advisory Committee Act, as amended (5 U.S.C. Appendix 2), notice is hereby given of the National Institutes of Health Peer Review Advisory Committee.

The meeting will be open to the public, with attendance limited to space available. Individuals who plan to attend and need special assistance, such as sign language interpretation or other reasonable accommodations, should notify the Contact Person listed below in advance of the meeting.

Name of Committee: National Institutes of Health Peer Review Advisory Committee.

Date: September 26, 2005.

Time: 8:30 a.m. to 5 p.m.

Venue:

National Institutes of Health Peer Review Advisory Committee.

Place: Bethesda Marriott, 5151 Pooks Hill Road, Bethesda, MD 20814.

Contact Person: Karl Malik, Ph.D., Executive Secretary, Center for Scientific Review, National Institutes of Health, 6701 Rockledge Drive, Room 3110, MSC 7776, Bethesda, MD 20892, (301) 594-6800, malikk@csr.nih.gov.

Any interested person may file written comments with the committee by forwarding the statement to the Contact Person listed on this notice. The statement should include the name, address, telephone number and when applicable, the business or professional affiliation of the interested person.

Dated: July 28, 2005.

Anthony M. Coelho, Jr.,
Acting Director, Office of Federal Advisory Committee Policy.

[FR Doc. 05-15510 Filed 8-4-05; 8:45 am]

BILLING CODE 4140-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

Center for Scientific Review; Amended Notice of Meeting

Notice is hereby given of a change in the meeting of the Center for Scientific Review Special Emphasis Panel, August 11, 2005, 11 a.m. to August 11, 2005, 12:30 p.m. National Institutes of Health, 6701 Rockledge Drive, Bethesda, MD 20892 which was published in the Federal Register on July 13, 2005, 70 FR 40392-40393.

The meeting will be held August 18, 2005, from 2 p.m. to 3:30 p.m. The meeting location remains the same. The meeting is closed to the public.
### Chemical/CAS #

<table>
<thead>
<tr>
<th>Chemical/CAS #</th>
<th>Report #</th>
<th>Primary Use, Route &amp; Species</th>
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<tr>
<td>Photocarcinogenesis Study of Glycolic acid and Salicylic acid in SKH-1 Mice</td>
<td>TR 524</td>
<td>Study of Glycolic acid and Salicylic acid in SKH-1 Mice (Simulated solar light and topical application studies) / 79-14-1 and 69-72-7 respectively.</td>
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<tr>
<td>Dibromoacetic acid/631-64-1</td>
<td>TR 537</td>
<td>Water disinfection by-product; Drinking water, male and female rats and mice.</td>
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<tr>
<td>Dichloroacetic acid/79-43-6</td>
<td>GMM 11</td>
<td>Water disinfection by-product; Drinking water, male and female Tg.AC hemizygous mice and p53 haploinsufficient mice; Dermal exposure, male and female Tg.AC hemizygous mice.</td>
</tr>
<tr>
<td>Bromodichloromethane/75-27-4</td>
<td>GMM 5</td>
<td>Water disinfection by-product; Drinking water and gavage in male and female Tg.AC hemizygous mice and p53 haploinsufficient mice; Dermal exposure in male and female Tg.AC hemizygous mice.</td>
</tr>
<tr>
<td>Sodium bromate/7789-38-0</td>
<td>GMM 6</td>
<td>Water disinfection by-product; Drinking water and dermal exposure, male and female Tg.AC hemizygous mice and p53 haploinsufficient mice.</td>
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**Discussion on background seizures seen in rats**

**Divinylbenzene - High Purity/1321-74-0**

Production of vinyl polymers; Inhalation, male and female rats and mice.
<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS Number</th>
<th>Use</th>
<th>Testing</th>
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<tbody>
<tr>
<td>Methyl isobutyl ketone</td>
<td>108-10-1</td>
<td>Denaturant in rubbing alcohol, solvent for paints, industrial extraction processes, dry cleaning preparations and in synthetic reactions; Inhalation, male and female rats and mice</td>
<td>Day 2 September 28 8:30AM TR 538</td>
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<tr>
<td>Diisopropylcarbodiimide</td>
<td>693-13-0</td>
<td>Reagent for peptide synthesis, chemical intermediate and preparation of coatings; Dermal, male and female rats and mice</td>
<td>Day 2 September 28 8:30AM TR 523</td>
</tr>
<tr>
<td>Diisopropylcarbodiimide</td>
<td>693-13-0</td>
<td>Reagent for peptide synthesis, chemical intermediate and preparation of coatings; Dermal, p53 haploinsufficient female mice</td>
<td>Day 2 September 28 8:30AM GMM 10</td>
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<tr>
<td>4-Methylimidazole</td>
<td>822-36-6</td>
<td>Manufacture of pharmaceuticals, dyes, agricultural chemicals and rubber; Diet, male and female rats and mice</td>
<td>Day 2 September 28 8:30AM TR 535</td>
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