

**National Toxicology Program  
Board of Scientific Counselors  
Technical Reports Review Subcommittee Meeting**

May 22, 2003  
NIEHS, Research Triangle Park, NC

*Summary Minutes*

**National Toxicology Program  
Board of Scientific Counselors  
Technical Reports Review Subcommittee Meeting**

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**Summary Minutes – May 22, 2003**  
**NTP Board of Scientific Counselors Technical Reports Review Subcommittee Meeting**

**Attendees**

**Members**

Mary Anna Thrall (chair)  
Kim Boekelheide  
Hillary Carpenter  
Michael Elwell  
Walter Piegorsch  
Stephen Roberts  
Richard Storer  
Mary Vore  
Cheryl Lyn Walker

**Members Absent**

Shuk-Mei Ho  
James E. Klaunig

**NIEHS Attendees**

Mary Wolfe	Dean Woody
Christopher Portier	Michael Wyde
John Bucher	Grace Kissling
Charles Alden	Nneka George
Po Chan	Neil Allison
Gregory Travlos	Amy Brix
Bill Jameson	Glen Marrs
Kristine Witt	Wayne Batts
Rodney Miller	Erroll Parker
David Malarkey	John Trench
William Eastin	Georgina Christenson
Michael Cunningham	Ronald Cannon
Georgette Hill	Kylie Mordych
Rajendra Chhabra	Lorri Jones
Gail Pearse	Krystal Speight
John Peckham	Patrick Crockett
William Schrader	Michael Easterling
Molly Vallant	Gene McConnell
Jack Bishop	Adriana Doi
Chris Koivisto	Robert Sills
Joseph Haseman	Fernando Suarez
James Hailey	John French
Richard Irwin	Gabrielle Willson

**Agency Attendees**

William Allaben  
Mark Toraason  
Ron Lorentzen

**Public Attendees**

Andrew M. Ballard, BNA Inc.  
W.G. Flamm, AAC Consulting Group  
Marcy Banton, Lyondell Chemical Company

**Summary Minutes – May 22, 2003**

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

Roland Rossbacher, BASF AG Corp.  
Susan Felter, Procter & Gamble  
Arlean Medeiros, Exxon Mobil Biomedical Sciences  
Ryuji Yamaguchi, Ajinomoto USA  
Eric Morinello, Southern Research Institute  
Charles D. Hebert, Southern Research Institute  
Willem Faber, Lyondell Chemical Company  
Amy Poythress, Triangle Reporting  
Carol Eisenmann, Cosmetic, Toiletry and Fragrance Association  
Robert Bursey, Ajinomoto USA

The meeting began at 8:30 a.m. on May 22, 2003 in the Rodbell Conference Center of the David P. Rall Building, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina. Members of the subcommittee were Drs. Mary Anna Thrall (chairperson), Richard Storer, Cheryl Walker, Michael Elwell, Stephen Roberts, Mary Vore, Kim Boekelheide, Hillary Carpenter, and Walter Piegorsch. For further information, contact Dr. Mary S. Wolfe, Executive Secretary, at 919-541-3971 or [wolfe@niehs.nih.gov](mailto:wolfe@niehs.nih.gov).

**Propylene Glycol Mono-*t*-butyl Ether**

Dr. Adriana Doi, NIEHS, introduced the toxicology and carcinogenesis studies of propylene glycol mono-*t*-butyl ether by describing the commercial uses of the chemical, the design of the short- and long-term inhalation studies, and the survival, body weight, and kidney toxicity effects of chemical exposure. The proposed conclusions were:

Under the conditions of these 2-year inhalation studies, there was *equivocal evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in male F344/N rats based on marginally increased incidences of renal tubule and liver neoplasms. Renal tubule neoplasms occurred at concentrations where there was evidence of  $\alpha_{2u}$ -globulin nephropathy. There was *no evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in female F344/N rats exposed to 75, 300, or 1,200 ppm. There was *clear evidence of carcinogenic activity* of propylene glycol mono-*t*-butyl ether in male and female B6C3F<sub>1</sub> mice based on increased incidences of liver neoplasms.

Exposure to propylene glycol mono-*t*-butyl ether resulted in nonneoplastic lesions of the kidney in male rats, the liver and nose in male and female rats, the liver in male and female mice, and the eyes in female rats and mice.

Dr. Roberts, the first principal reviewer, questioned whether *equivocal evidence* was the most appropriate conclusion for the male rat study but agreed with the other conclusions. He thought the inclusion of NBR rats and the special attention to the question of  $\alpha_{2u}$ -globulin was useful.

Dr. Boekelheide, the second principal reviewer, said the studies had been carefully analyzed and he agreed with the proposed conclusions.

Dr. Walker, the third principal reviewer, questioned the significance of the renal tumors and liver adenomas in male rats and the liver neoplasms in mice.

Dr. Doi explained that renal tumors are rare in rats and the potential trend in liver adenomas, though not dose related, was consistent with *equivocal evidence*. Dr. Joseph Haseman, NIEHS, noted that the significance of the trend test derived from the spacing of the doses, with the lowest dose being close to the control value. He also observed that the control rate was at the upper end of the historical range.

Dr. Doi then explained the reasons for the choice of *clear evidence* for the mouse studies. The incidences of liver adenomas, and of multiple adenomas, were markedly increased in the top dose groups. The incidences of carcinomas were also elevated, and uncommon malignant hepatoblastomas were also seen in exposed mice.

Dr. Willem Faber, representing Lyondell Chemical Co., argued that propylene glycol mono-*t*-butyl ether should not be considered genotoxic because of a positive response in one *Salmonella* strain and a small increase in the micronucleus test. He also suggested that the 1,200 ppm concentration exceeded the maximum tolerated dose.

Dr. Roberts noted that the Technical Report made no overall conclusions of genotoxicity beyond listing individual test results. Dr. John Bucher, NIEHS, defended the dose selection, noting that any clinical signs of toxicity observed were brief and transient and that the 1200 ppm groups did not exceed the criteria of survival, body weight changes, or other toxicity.

Dr. Bucher also described two additions proposed to the concluding statement: a comment that the nonneoplastic lesions in male rats were “characteristic of  $\alpha_{2u}$ -globulin accumulation” and a statement that kinetic and biomarker studies indicated that clearance was saturated at the 1,200 ppm exposure both for rats and for mice.

Dr. Roberts moved, and Dr. Vore seconded, that these proposed conclusions be accepted. Dr. Walker proposed an amendment that the conclusion for female mice be changed to *some evidence of carcinogenic activity*. That amendment failed for lack of a second. The original motion was then approved unanimously with eight votes.

## **2-Methylimidazole**

Dr. Po Chan, NIEHS, introduced the toxicology and carcinogenicity studies of 2-methylimidazole by describing the uses of the chemical and the design of the previous short-term studies and the results of the current 2-year feed studies. The proposed conclusions were:

Under the conditions of these 2-year feed studies, there was *some evidence of carcinogenic activity* of 2-methylimidazole in male F344/N rats based on increased incidences of thyroid follicular cell neoplasms. The increased incidences of hepatocellular neoplasms in males may have been related to chemical exposure. There was *clear evidence of carcinogenic activity* of 2-methylimidazole in female F344/N rats based on increased incidences of thyroid gland follicular cell neoplasms. The increased incidences of hepatocellular adenomas in females may have been related to chemical exposure. There was *some evidence of carcinogenic activity* in male B6C3F<sub>1</sub> mice based on increased incidences of thyroid gland follicular cell adenomas and hepatocellular

neoplasms. There was *some evidence of carcinogenic activity* in female B6C3F<sub>1</sub> mice based on increased incidences of hepatocellular adenoma.

Exposure to 2-methylimidazole resulted in nonneoplastic lesions in the thyroid gland and liver of male rats; the thyroid gland, liver, and spleen of female rats; the thyroid gland, liver, spleen, bone marrow, kidney, epididymis and testes of male mice; and the thyroid gland and spleen of female mice.

Dr. Piegorsch, the first principal reviewer, agreed with the proposed conclusions for rats and female mice but suggested the weight of evidence for male mice might be considered *clear evidence*.

Dr. Elwell, the second principal reviewer, agreed with the overall conclusions and suggested some enhancements to the discussion about the possible relationship of the various proliferative lesions that occurred in the thyroid gland and further discussion on the granulomatous changes in the liver.

Dr. Vore, the third principal reviewer, also concurred with the conclusions but questioned directly linking the thyroid neoplasms to the induction of liver UDP-glucuronosyl transferase.

Dr. Chan described the reasoning that led to the conclusion for the male mouse study, noting that there was not a dose-related increase in neoplasms and that the neoplasm incidences in all groups were within the historical control range. Responding to Dr. Vore's question, he said that the T<sub>4</sub> related mechanism was mentioned because data on those measures were gathered in these studies, but the entire spectrum of the thyroid synthesis pathways and secretion were mentioned in the discussion as possible causes of the liver carcinogenesis.

Dr. Robert Sills, NIEHS, addressed the pathogenesis of the thyroid gland lesions and, following a review of other NTP studies, concluded that there was no relationship between liver hypertrophy and subsequent development of thyroid gland hyperplasia or neoplasms. Dr. Sills also indicated that the granulomatous inflammation of the liver and spleen were considered treatment related, and that a similar effect was seen in a preliminary review of tissues from studies on the related chemical 4-methylimidazole.

Dr. Storer suggested that the possible confounding effects of anemia and hematopoietic cell proliferation be added to the discussion of increases in micronuclei.

Dr. Piegorsch asked if the liver tumors and thyroid gland neoplasms in male mice might warrant a conclusion of *clear evidence*. He also suggested that formal statistical analyses incorporating historical incidences, rather than just noting whether incidences occurred within the historical range, might be another useful metric for study evaluation.

Dr. Carpenter inquired if relatively more importance was attached to carcinomas than to adenomas in evaluating the response. Dr. Bucher, noted that the studies are truncated at two years, and that progression or earlier onset of neoplasms are contributors to evidence of carcinogenic activity.

Dr. Boekelheide questioned the linking of testicular atrophy to epididymal alterations and suggested they could be independent responses to the chemical.

Dr. Piegorsch moved that the conclusions be accepted as drafted, with the exception that the conclusion for male mice be *clear evidence*. The motion failed for lack of a second. Dr. Piegorsch then moved that the conclusions be accepted as originally written. Dr. Boekelheide seconded the motion, which was approved unanimously with eight votes.

### **Triethanolamine**

Dr. Fernando Suarez, NIEHS, introduced the toxicology and carcinogenesis studies of triethanolamine by describing the uses of the chemical. In an earlier NTP report on triethanolamine (NTP TR 449), the mouse studies were considered inadequate because the mice were infected with *Helicobacter hepaticus*, and the male mice had an associated hepatitis that confounded interpretation of a possible liver tumor response. Thus, the mouse studies were repeated with the same protocol. The proposed conclusions were:

Under the conditions of this 2-year dermal study, there was *equivocal evidence of carcinogenic activity* of triethanolamine in male B6C3F<sub>1</sub> mice based on the occurrence of liver hemangiosarcoma. There was *some evidence of carcinogenic activity* in female B6C3F<sub>1</sub> mice based on increased incidences of hepatocellular adenoma.

Exposure to triethanolamine by dermal application resulted in increased incidences of eosinophilic foci of the liver in males and females. Dosed mice developed treatment-related nonneoplastic lesions at the site of application.

Drs. Walker, Roberts, and Carpenter, the three principal reviewers, all concurred with the conclusions. Dr. Carpenter asked for an expansion in the discussion on the relative certainty regarding the hemangiosarcomas. Dr. James Hailey, NIEHS, agreed to add more detail.

Dr. William Allaben, NCTR, inquired about the extent of ulceration of the skin at the site of application. Dr. Hailey explained that even the most severe were characterized as occasional pinpoint focal crusts, with most of the skin relatively unaffected.

Dr. Walker moved, and Dr. Carpenter seconded, that the conclusions be accepted as written. The motion was accepted unanimously with eight votes.

### **Stoddard Solvent IIC**

Dr. Rajendra Chhabra, NIEHS, introduced the toxicology and carcinogenesis studies of Stoddard solvent IIC by describing the uses, human exposure, and nomination rationale for the chemical and the designs and results of the 2-week, 3-month, and 2-year inhalation studies. The proposed conclusions were:

Under the conditions of these 2-year inhalation studies, there was *some evidence of carcinogenic activity* of Stoddard solvent IIC in male F344/N rats based on increased incidences of adrenal medulla neoplasms; the slightly increased

incidences of renal tubule adenoma may have been related to Stoddard solvent IIC exposure. There was *no evidence of carcinogenic activity* of Stoddard solvent IIC in female F344/N rats exposed to 550, 1,100, or 2,200 mg/m<sup>3</sup>. There was *no evidence of carcinogenic activity* of Stoddard solvent IIC in male B6C3F<sub>1</sub> mice exposed to 550, 1,100, or 2,200 mg/m<sup>3</sup>. There was *equivocal evidence of carcinogenic activity* of Stoddard solvent IIC in female B6C3F<sub>1</sub> mice based on increased incidences of hepatocellular adenoma; this slight increase was associated with increased body weight in exposed females.

Exposure of male rats to Stoddard solvent IIC resulted in nonneoplastic lesions of the kidney characteristic of  $\alpha_{2u}$ -globulin accumulation.

Dr. Vore, the first principal reviewer, said the study design was adequate, with the highest dose physically possible being used, and she agreed with the conclusions.

Dr. Carpenter, the second principal reviewer, inquired about the specificity or variability of toxicity assessment for a solvent that is a mixture of over 80 compounds. Dr. Chhabra replied that the composition of the mixture is well defined and the overall solvent fits within a narrow range of physical specifications.

Dr. Boekelheide, the third principal reviewer, suggested that the observation of sperm motility alterations in both species be given more attention. Dr. Chhabra noted that the changes were fairly small but more would be added to the discussion.

Dr. Arlean Medeiros, representing the American Chemical Council's Hydrocarbons Solvents Panel, suggested that the formation of adrenal gland pheochromocytomas in male mice may have been a secondary effect of the observed  $\alpha_{2u}$ -globulin induced kidney nephropathy and cited concurrent increases in pheochromocytomas and nephropathy from a review of some NTP studies. Dr. Haseman, replied that a logistic regression analysis performed on the same data set provided only a very weak correlation between the two lesions, whereas dose and survival did affect the incidences of both lesions after adjustment for other factors.

Dr Vore moved, and Dr. Carpenter seconded, that the conclusions be accepted as written. The motion was approved unanimously with eight votes.

### **Aspartame**

Dr. Bucher introduced a new Technical Report series consisting of studies performed with genetically modified mice. The toxicity and carcinogenicity studies of aspartame are the first report in that series. Dr. John French, NIEHS, presented an overview of the p53 and p16 haploinsufficient mouse models used in this study. Dr. Bucher proceeded to describe the uses of aspartame, the rationale for study nomination, the design of the transgenic mouse studies, the pathology evaluation, and the body weight, survival, and neoplasm incidence results. For the new report series the traditional Levels of Evidence of Carcinogenic Activity categories would be used to frame conclusions for the p53 model, but not for the Tg.AC or the p16 model. The proposed conclusions were:



Under the conditions of this 9-month feed study, there was *no evidence of carcinogenic activity* of aspartame in male or female p53 haploinsufficient mice exposed to 3,125, 6,250, 12,500, 25,000, or 50,000 ppm.

Dr. Elwell, the first principal reviewer, agreed that the studies did not show evidence of a carcinogenic effect. He also stated that the report clearly described the relevance and uncertainties of positive and negative findings in these models. He inquired why positive controls were not used in the p53 model studies and suggested clarification in the text based on cited literature reporting brain tumors, and the uncertainty of their relationship to the effect of treatment.

Dr. Storer, the second principal reviewer, questioned the statistical criteria used to score the micronucleus test, noting that in virtually every study some positive response was reported. He agreed with the overall conclusions.

Dr. Piegorsch, the third principal reviewer, inquired about design considerations such as the number of animals per group and the spacing of doses, particularly for studies with negative findings. He felt the conclusion statement was appropriate.

Dr. Bucher replied that for the p53 model positive controls were not used because historically variations in response to positive control agents were seen due to dosing irregularities rather than to a lack of responsiveness from the mouse model. He indicated that the procedure for scoring micronuclei was being changed from scoring slide smears to flow cytometry, which would enhance the power of the test. Dr. Christopher Portier, NIEHS, commented that one of the motivations for adopting the transgenic mouse models was the ability to use smaller numbers of animals, which will be justified for testing purposes if the background incidence rates for neoplasms prove to be low.

Dr. Elwell moved, and Dr. Storer seconded, that the conclusions be accepted as written. Dr. Roberts and Dr. Walker expressed concern that there was not sufficient historical information to determine whether the study design, particularly the number of animals per group, was adequate. Dr. French observed that in studies in these models groups of 10 to 20 mice had been used, and considerations of study duration and potency of the chemical were also factors in eliciting positive responses. He suggested that in the absence of preneoplastic lesions, larger group sizes would not reveal any differences in response. Dr. Storer suggested there were two different questions of adequacy: one about the validity of the study protocol, the other about the conduct and results of the study within that protocol. Deficiencies in the latter might fit the criteria for *inadequate study*, whereas questions about the overall validity of the study model might be addressed in other arenas, such as the Report on Carcinogens.

Dr. Carpenter suggested that some caveat be added to the conclusion reflecting reservations about the significance of a negative result in this type of study. Drs. Walker and Vore also endorsed adding some qualifying statement to the conclusions. The panel explored a variety of phrasings, and then agreed unanimously to add the following sentence:

Because this is a new model, there is uncertainty whether the study possessed sufficient sensitivity to detect a carcinogenic effect.

The subcommittee then unanimously approved the original conclusion, with this sentence added. There was subsequent discussion about adding results from the Tg.AC and p16/19 studies to the abstract table, to accompany the results from the p53 model upon which the conclusions were based. Following discussion, it was agreed that results from the other models could be summarized in the abstract table but with no reference to levels of evidence of carcinogenic activity.

### **Acesulfame Potassium**

Dr. Richard Irwin, NIEHS, introduced the studies of acesulfame potassium in genetically modified mice by describing the uses of the sweetener, its nomination as a presumptive negative control for evaluation of the transgenic mouse models, the study design, and the survival, body weight, and histopathology observations. The proposed conclusion was:

Under the conditions of this 9-month feed study, there was *no evidence of carcinogenic activity* of acesulfame K in male or female p53 haploinsufficient mice exposed to 0.3%, 1%, or 3%. Because this is a new model, there is uncertainty whether the study possessed sufficient sensitivity to detect a carcinogenic effect.

Dr. Storer, the first principal reviewer, agreed with the conclusions. He felt it more appropriate to characterize the Tg.AC mouse model as a zeta-globin promoter activation model with an oncogenic *H-ras* reporter phenotype than as a gain of oncogenic function *H-ras* model.

Dr. Elwell, the second principal reviewer, agreed with the conclusions and inquired if the mice might have been able to tolerate a higher dose. Dr. Irwin replied that in another study with CD-1 mice a mild weight gain depression was seen at the 3% dose.

Dr. Piegorsch, the third principal reviewer, also agreed with the conclusions.

Dr. Storer moved, and Dr. Elwell seconded, that the conclusions be accepted as written. Dr. Boekelheide inquired if the units would be changed from percentages to parts per million. Dr. Irwin agreed. The motion was then approved unanimously with eight votes.

Dated: April 7, 2003.

**Steven M. Ferguson,**  
Acting Director, Division of Technology  
Development and Transfer, Office of  
Technology Transfer.

[FR Doc. 03-9286 Filed 4-15-03; 8:45 am]

BILLING CODE 4140-01-P

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Public Health Service

#### National Toxicology Program (NTP) Board of Scientific Counselors Technical Reports Review Subcommittee Meeting; Review of Draft NTP Technical Reports

Pursuant to Pub. L. 92-463, notice is hereby given of the next meeting of the NTP Board of Scientific Counselors Technical Reports Review Subcommittee on May 22, 2003 in the Rodbell Auditorium, Rall Building, South Campus, National Institute of Environmental Health Sciences (NIEHS), 111 T.W. Alexander Drive, Research Triangle Park, North Carolina. The meeting will begin at 8:30 a.m.

#### Agenda

The primary agenda topic is the peer review of six draft NTP Technical Reports of rodent toxicology and carcinogenesis studies conducted by the NTP. The reports are listed in the table below in the tentative order of their review. There will be a brief presentation describing the p53 (+/-) and the p16 (+/-) haploinsufficient transgenic mouse models for short-term cancer bioassays prior to the reviews of the aspartame and acesulfame potassium reports.

The agenda and roster of Subcommittee members will be available prior to the meeting on the NTP Web homepage at <http://ntp-server.niehs.nih.gov> and upon request to the NTP Executive Secretary, Dr. Mary S. Wolfe, PO Box 12233, 111 T.W. Alexander Dr., MD A3-01, Research Triangle Park, NC 27709, T: 919-541-0530; F: 919-541-0295; e-mail: [wolfe@niehs.nih.gov](mailto:wolfe@niehs.nih.gov). Following the meeting, summary minutes will be available on the NTP Web site and in hard copy upon request to the Executive Secretary. Plans are underway for making this meeting available for viewing on the Internet (<http://www.niehs.nih.gov/external/video.htm>).

The NTP Board of Scientific Counselors Technical Reports Review Subcommittee meeting is open to the public. Attendance at this meeting is limited only by the space available. Individuals who plan to attend are

asked to register with the NTP Executive Secretary (see contact information above). The names of those registered will be given to the NIEHS Security Office in order to gain access to the campus. Persons attending who have not pre-registered may be asked to provide pertinent information about the meeting, i.e., title or host of meeting before gaining access to the campus. All visitors (whether or not you are pre-registered) will need to be prepared to show 2 forms of identification (ID) (e.g., driver's license, government ID). Persons needing special assistance, such as sign language interpretation or other reasonable accommodation in order to attend, are asked to notify the NTP Executive Secretary at least seven business days in advance of the meeting (see contact information above).

#### Draft Reports Available for Public Review and Comment

Approximately one month prior to the meeting, the draft reports will be available for public review, free of charge, through ehpOnline (<http://ehp.niehs.nih.gov>). Printed copies of the draft NTP Technical Reports can be obtained, as available, from Central Data Management (CDM), NIEHS, PO Box 12233, MD EC-03, Research Triangle Park, NC 27709, T: 919-541-3419, F: 919-541-3687, e-mail: [CDM@niehs.nih.gov](mailto:CDM@niehs.nih.gov).

Comments on any of the NTP Technical Reports are welcome. Time will be provided at the meeting for oral public comment on the reports. Persons requesting time for an oral presentation on a particular report are asked to notify the Executive Secretary (contact information given above) by May 14, 2003 and provide their contact information (name, affiliation, mailing address, phone, fax, e-mail), and supporting organization (if any). Persons registering to make comments are asked to provide a written copy of their statement to the Executive Secretary on or before May 14, 2003, to enable review by the Subcommittee and NTP staff prior to the meeting. These statements can supplement or expand an oral presentation. Each speaker will be allotted at least 7 minutes and, if time permits, up to 10 minutes for presentation of oral comments. Each organization is allowed one time slot per report being reviewed. Registration for making public comments will also be available on-site. If registering on-site to speak and reading comments from printed text, the speaker is asked to provide 25 copies of the statement. These copies will be distributed to the Subcommittee and NTP staff and will supplement the record.

Written comments without an oral presentation at the meeting are also welcome. Comments should include contact information for the submitter (name, affiliation, mailing address, phone, fax, and e-mail) and supporting organization (if any). Written comments should be received by the Executive Secretary on or before May 14, 2003, to enable distribution to the Subcommittee and NTP staff for their review and consideration prior to the meeting.

#### Request for Additional Information

The NTP would welcome receiving toxicology and carcinogenesis information from completed, ongoing or planned studies as well as current production data, human exposure information, and use patterns for any of the chemicals listed in this announcement. Please send this information to CDM at the address given above. CDM will forward the information to the appropriate NTP staff scientist.

#### NTP Technical and Toxicity Report Series

The NTP conducts toxicology and carcinogenesis studies of agents of public health concern. Any scientist, organization, or member of the public may nominate a chemical for NTP testing. Details about the nomination process are available on the NTP Web site (<http://ntp-server.niehs.nih.gov>, select How to Nominate Substances). The results of short-term rodent toxicology studies are published in the NTP Toxicity Report series. Longer-term studies, generally, rodent carcinogenicity studies, are published in the NTP Technical Report series. Shorter-term carcinogenicity studies will appear in a new Technical Report Series being unveiled at the upcoming meeting. The studies of aspartame and acesulfame potassium will be the first two studies reported in the new series. Study abstracts for all reports are available at the NTP Web site under NTP Study Information. PDF files of completed reports are available free-of-charge from ehpOnline under Publications and hard copies of published reports can be obtained through subscription to ehpOnline (<http://ehp.niehs.nih.gov/> contact information: T: 919-653-2595 or 866-541-3841, e-mail: [ehponline@ehp.niehs.nih.gov](mailto:ehponline@ehp.niehs.nih.gov)).

#### NTP Board of Scientific Counselors

The NTP Board of Scientific Counselors ("the Board") is a technical advisory body composed of scientists from the public and private sectors who provide primary scientific oversight and

peer review to the NTP. Specifically, the Board advises the NTP on matters of scientific program content, both present and future, and conducts periodic review of the program for the purpose of determining and advising on the scientific merit of its activities and overall scientific quality. The Technical Reports Review Subcommittee of the Board provides scientific peer review of the findings and conclusions of NTP Technical Reports. The Report on

Carcinogens Subcommittee of the Board provides scientific peer review of nominations to the Report on Carcinogens, a Congressionally mandated listing of agents known or reasonably anticipated to be human carcinogens.

The Board's members are selected from recognized authorities knowledgeable in fields such as toxicology, pharmacology, pathology, biochemistry, epidemiology, risk

assessment, carcinogenesis, mutagenesis, molecular biology, behavioral toxicology, neurotoxicology, immunotoxicology, reproductive toxicology or teratology, and biostatistics. The NTP strives for equitable geographic distribution and for minority and female representation on the Board.

Dated: April 8, 2003.

**Kenneth Olden,**  
Director, National Toxicology Program.

**NATIONAL TOXICOLOGY PROGRAM (NTP) TECHNICAL REPORTS TENTATIVELY SCHEDULED FOR REVIEW BY THE NTP BOARD OF SCIENTIFIC COUNSELORS TECHNICAL REPORTS REVIEW SUBCOMMITTEE ON MAY 22, 2003 AT THE NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES, RESEARCH TRIANGLE PARK, NC**

Chemical CAS number	Report number	Primary uses	Route and exposure levels	Review order
Propylene Glycol Mono- <i>t</i> -butyl Ether 57018-52-7.	TR 515	Solvent .....	Two-year study by inhalation 0, 75, 300, or 1,200 ppm in air to F344/N rats and B6C3F1 mice.	1
2-Methylimidazole 693-98-1.	TR 516	Chemical and pharmaceutical intermediate.	Two-year study by feed 0, 300, 1,000, or 3,000 ppm to male F344/N rats 0, 1,000, 2,500 or 5,000 ppm to female F344/N rats 0, 625, 1,250, or 2,500 ppm to male and female B6C3F1 mice.	2
Triethanolamine 102-71-6	TR 518	Large variety of industrial and manufacturing applications.	Two-year dermal study 0, 200, 630, or 2,000 mg/kg to male B6C3F1 mice and 0, 100, 300, or 1,000 mg/kg to female B6C3F1 mice.	3
Stoddard Solvent IIC 64742-88-7.	TR 519	Paint and dry cleaning solvent	Two-year study by inhalation 0, 550, 1,100, or 2,200 mg/cubic meter in air to F344/N rats and B6C3F1 mice.	4
Aspartame 22839-47-0 .....	NEW 01	Artificial sweetener .....	Nine-month study by feed 0, 3,125, 6,250, 12,500, 25,000, or 50,000 ppm to p53 (+/-) haploinsufficient mice.	5
Acesulfame Potassium 55589-62-3.	NEW 02	Artificial sweetener .....	Nine-month study by feed 0, 0.3%, 1%, or 3% to p53 (+/-) haploinsufficient mice.	6

[FR Doc. 03-9283 Filed 4-15-03; 8:45 am]  
BILLING CODE 4140-01-P

**DEPARTMENT OF HOMELAND SECURITY**

**Directorate of Information Analysis and Infrastructure Protection; National Infrastructure Advisory Council; Notice of Open Meeting**

The National Infrastructure Advisory Council (NIAC) will meet on Tuesday, April 22, 2003, from 4:30 p.m. until 6:30 p.m. EDT. The meeting, which will be held telephonically, will be open to the public via a "listen only" telephone bridge line. Members of the public interested in attending by telephone should call (toll free) 1-800-304-8043 or (toll) 1-719-955-1038 and, when prompted, enter pass code 1129948.

The Council advises the President of the United States on the security of information systems for critical infrastructure supporting other sectors of the economy, including banking and finance, transportation, energy, manufacturing, and emergency government services. At this meeting, the Council will discuss potential future

issues to take up for consideration and potential dates for future meetings.

**Agenda:**

- I. Opening of Meeting and Roll Call of Members: Nancy J. Wong, Director, Office of Planning and Partnerships, U.S. Department of Homeland Security (DHS)/Designated Federal Officer, NIAC.
- II. Opening Remarks: Robert P. Liscouski, Assistant Secretary of Infrastructure Protection, DHS; Richard K. Davidson, Chairman, NIAC; and John T. Chambers, Vice Chairman, NIAC.
- III. Introduction of Possible Topics for Future NIAC Study: Chairman Davidson.
  - a. Internet Protocol ver. 6: Vice Chairman Chambers.
  - b. Cyber Vulnerability Disclosure Guidelines: Vice Chairman Chambers and John W. Thompson, Chairman and CEO, Symantec Corporation, Member of the NIAC.
  - c. Other topics: NIAC Members.
- IV. Discussion of Topics: NIAC Members.

V. Discussion of Possible Dates for Future Meetings: Chairman Davidson, NIAC Members.

**VI. Adjournment**

Written comments may be submitted at any time before or after the meeting. However, to facilitate distribution of public presentation materials to Council members, the Council suggests that presenters forward the public presentation materials ten days prior to the meeting date to the following address: Mr. Eric T. Werner, Office of Planning and Partnerships, Directorate of Information Analysis and Infrastructure Protection, U.S. Department of Homeland Security, 14th Street & Constitution Avenue, NW., Room 6073, Washington, DC 20230.

For more information contact Eric Werner on (202) 482-7470.

Dated: April 11, 2003.

**Eric T. Werner,**  
Council Liaison Officer.

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**NATIONAL TOXICOLOGY PROGRAM  
BOARD OF SCIENTIFIC COUNSELORS**

**Technical Reports Review Subcommittee Meeting**

**Agenda**

*May 22, 2003*

*8:30 a.m. – 5:00 p.m.*

National Institute of Environmental Health Sciences  
Rall Building, Rodbell Auditorium  
111 T.W. Alexander Dr.  
Research Triangle Park, NC

8:30 a.m.	Welcome		Dr. Christopher Portier, NIEHS and Dr. Mary Anna Thrall, Board Chair Colorado State University	
<b>Chemical/CAS #</b>	<b>Report Number</b>	<b>Primary Use, Route &amp; Species</b>	<b>Staff Scientist and Pathologist</b>	<b>Principal Reviewers</b>
Propylene Glycol Mono- <i>t</i> -butyl Ether 57018-52-7	TR 515	solvent  inhalation F344/N rats and B6C3F1 mice	Dr. Adriana Doi Dr. Ronald Herbert	Dr. Stephen Roberts Dr. Kim Boekelheide Dr. Cheryl Walker
2-Methylimidazole 693-98-1	TR 516	chemical and pharmaceutical intermediate  feed F344/N rats and B6C3F1 mice	Dr. Po-Chuen Chan Dr. Robert Sills	Dr. Walter Piegorsch Dr. Michael Elwell Dr. Mary Vore
Triethanolamine 102-71-6	TR 518	large variety of industrial and manufacturing applications  dermal B6C3F1 mice	Dr. Fernando Suarez Dr. Gail Pearse	Dr. Cheryl Walker Dr. Stephen Roberts Dr. Hillary Carpenter
Stoddard Solvent IIC 64742-88-7	TR 519	paint and dry cleaning solvent  inhalation F344/N rats and B6C3F1 mice	Dr. Rajendra Chhabra Dr. John Peckham	Dr. Mary Vore Dr. Hillary Carpenter Dr. Kim Boekelheide
Presentation on the p53 (+/-) and the p16 (+/-) haploinsufficient transgenic mouse models for short-term cancer bioassays			Dr. John French	
Aspartame 22839-47-0	GMM 1	artificial sweetener  feed p53 mice	Dr. John Bucher Dr. David Malarkey	Dr. Michael Elwell Dr. Richard Storer Dr. Walter Piegorsch
Acesulfame K 55589-62-3	GMM 2	artificial sweetener  feed p53 mice	Dr. Richard Irwin Dr. David Malarkey	Dr. Richard Storer Dr. Michael Elwell Dr. Walter Piegorsch

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**THE NATIONAL TOXICOLOGY PROGRAM  
BOARD OF SCIENTIFIC COUNSELORS  
TECHNICAL REPORTS REVIEW SUBCOMMITTEE MEETING  
May 22, 2003  
Attending Members**

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Kim Boekelheide, M.D., Ph.D.  
Professor  
Division of Biology and Medicine  
Department of Pathology and Laboratory Medicine  
Brown University, Box G-B5  
171 Meeting Street  
Providence, RI 02912

Hillary M. Carpenter, III, Ph.D.  
Toxicologist, Minnesota Department of Health  
121 East Seventh Place, Suite 220  
P.O. Box 64975  
St. Paul, MN 55101

Michael R. Elwell, D.V.M., Ph.D.  
Research Advisor  
Pathology, Drug Safety Evaluation  
Pfizer Global Research and Development  
Eastern Point Road  
Bldg 274, Rm 1704D, MS 8274-1231  
Groton, CT 06340

Shuk-Mei Ho, Ph.D. \*\*\*  
Professor of Surgery and Cell Biology  
Department of Surgery, Division of Urology  
University of Massachusetts Medical School  
55 Lake Avenue North, Room S4-746A  
Worcester, MA 01655

James E. Klaunig, Ph.D. \*\*\*  
Director and Professor  
Division of Toxicology  
Indiana University School of Medicine  
635 Barnhill Drive, MS-1021  
Indianapolis, IN 46202-5196

Walter W. Piegorsch, Ph.D.  
Professor of Statistics  
Department of Statistics  
University of South Carolina  
LeConte Building  
1523 Greene St.  
Columbia, SC 29208

Stephen M. Roberts, Ph.D.  
Professor  
Center for Environmental & Human Toxicology  
University of Florida, Box 110885  
Bldg 471, Mowry Rd. Rm. 14  
Gainesville, FL 32611

Richard D. Storer, Ph.D., M.P.H.  
Senior Investigator  
Department of Genetic and Cellular Toxicology  
Merck Research Laboratories, WP45-311  
770 Sumneytown Pike  
West Point, PA 19486

Mary Anna Thrall, D.V.M., M.S.  
Diplomate, ACVP  
Department of Microbiology,  
Immunology, and Pathology  
Colorado State University  
1682B Campus Delivery  
Fort Collins, CO 80523

Mary Vore, Ph.D.  
Professor and Director  
Graduate Center for Toxicology  
306 HSRB Chandler Medical Center  
University of Kentucky  
800 Rose Street  
Lexington, KY 40536

Cheryl Lyn Walker, Ph.D.  
Professor  
Department of Carcinogenesis  
The University of Texas  
M.D. Anderson Cancer Center  
Science Park-Research Division  
P.O. Box 389  
Smithville, TX 78957

\*\*\*not in attendance