61789-51-3

NATIONAL TOXICOLOGY PROGRAM

BOARD OF SCIENTIFIC COUNSELORS

November 25, 1986

SUMMARY MINUTES

National Toxicology Program
Board of Scientific Counselors Meeting
November 25, 1986

Summary Minutes

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ATTACHMENT 2

AGENDA
BOARD OF SCIENTIFIC COUNSELORS
NATIONAL TOXICOLOGY PROGRAM

November 25, 1986

CONFERENCE CENTER, BUILDING 101, SOUTH CAMPUS
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
RESEARCH TRIANGLE PARK, NORTH CAROLINA

Morning

8:30 a.m.- 9:00 a.m.	Report of the Director, NTP	Dr. D. P. Rall, NIEHS
9:00 a.m.- 9:30 a.m.	Overview of the NIEHS Intramural Research Program	Dr. M. B. Rodbell, NIEHS
9:30 a.m.-10:00 a.m.	Overview of the NTP	Dr. E. E. McConnell, NIEHS
10:15 a.m.-11:45 a.m.	Review of Chemicals Nominated for NTP Studies	Board Dr. D. A. Canter, NIEHS

Afternoon

12:30 p.m.- 4:45 p.m.	NIEHS Cellular and Genetic Toxicology Branch - Short-term Assay Evaluation		
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	II.	Comparison of *In Vitro* Assay Results with Rodent Carcinogenicity	Dr. E. Zeiger
	III.	Statistical Aspects of the Evaluation Process	Dr. B. Margolin and Dr. J. K. Haseman, Biometry and Risk Assessment Program
	IV.	Comparative Evaluation of Short-Term *In Vivo* Assays	Dr. M. D. Shelby
	V.	Strategies for Testing and Other Implications of the Evaluation	Dr. R. W. Tennant
	VI.	Discussion	Board and Staff

NATIONAL TOXICOLOGY PROGRAM BOARD OF SCIENTIFIC COUNSELORS

November 25, 1986

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NATIONAL TOXICOLOGY PROGRAM

BOARD OF SCIENTIFIC COUNSELORS MEETING

November 25, 1986

SUMMARY MINUTES

The National Toxicology Program (NTP) Board of Scientific Counselors met on November 25, 1986, in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences (NIEHS), Research Triangle Park, North Carolina. (Attachment 1: Federal Register Meeting Announcement; Attachment 2: Agenda and Roster of Members and Expert Consultants). Members of the Board are Drs. Henry Pitot (Chairman), Norman Breslow, Michael Gallo, Donald Mattison, Mortimer Mendelsohn, Frederica Perera, Adrianne Rogers, and Robert Scala. Drs. Mattison, Rogers, and Scala are new members while Dr. Pitot is the new chairman. All members were at the meeting.

I. Report of the Director, NTP: Dr. David Rall reported that: (1) Dr. Robert Goyer, NIEHS Deputy Director, will return to London, Ontario early in 1987 to become Professor and Chairman, Department of Pathology, University of Western Ontario; (2) Dr. Anne Sassaman recently became the new Associate Director, NIEHS Extramural Program; (3) the NIEHS will be celebrating its 20th anniversary December 3, 4 and 5 with a scientific conference - "The Environment and Human Health, Achievements and New Directions" - on December 3 and 4 and a commemorative program on December 5; (4) the NIEHS FY 1987 budget will be increased by 12% over FY 1986; (5) the Superfund Act (Superfund Amendments and Reauthorization Act of 1986 or SARA) was passed by Congress with significant new authorities for NIEHS. The purpose is to support basic research (including epidemiologic and ecologic studies) primarily through grants, contracts and cooperative agreements with institutions of higher education for development of advanced techniques to detect, assess and evaluate health effects of hazardous substances, of risk assessment methods, and of methods and technologies to detect hazardous substances in the environment, and basic biological, chemical and physical methods to reduce the amount of toxicity of hazardous substances. The initial funding in FY 1987 is $3 million which will increase up to $35 million by 1991 with 10% available for training. The NIEHS will work closely with the Agency for Toxic Substances and Disease Registry, CDC, and the Office of Research and Development and Solid Waste Office, EPA, in implementing Superfund. A broadly based advisory committee will assist in developing a research plan and providing for coordination and cooperation. A public meeting will be held at NIEHS on December 15 to describe the proposed research programs. This will be followed by a public meeting in Washington, D.C., in January to outline guidelines for development of service grants concerned with safety training of workers who handle toxic substances. The receipt date for the first research and service grants will be May 1 with review and awards expected in September; (6) there are three inhouse research programs within the NIEHS - the Intramural Research Program which does basic research in biomedical aspects of

toxicology and to be described by Dr. Martin Rodbell; the Toxicology Research and Testing Program, the NIEHS component of the NTP, concerned primarily with applied research and management of the largest toxicology testing program in the world, and to be described by Dr. Ernest McConnell; and the Biometry and Risk Assessment Program headed by Dr. David Hoel which provides computer technology, statistics and biomathematics, epidemiology and biochemical risk analysis. This program may be described at the next Board meeting.

II. Overview of the NTP: Dr. McConnell, Director, Toxicology Research and Testing Program (TRTP), briefly described the historical background and organizational structure of the NTP, and its goals. He spoke in more detail about the NIEHS component of the NTP, and its four branches - the Carcinogenesis and Toxicology Evaluation Branch, the Cellular and Genetic Toxicology Branch, the Chemical Pathology Branch, and the Systemic Toxicology Branch. Dr. McConnell briefly explained the functions of the branches. He discussed the toxicology and carcinogenesis studies process and the impact that the findings can have outside of the NTP. He described planned extensive studies to characterize the toxicology and carcinogenicity of methylene chloride. Dr. McConnell also updated the Board on activities relating to the use of an estimated maximum tolerated dose, (EMTD) as the high dose for long-term rodent studies. He reported that the NTP uses the EMTD as defined and supported in the report of the Board's Ad Hoc Panel on Chemical Carcinogenesis Testing and Evaluation. He noted there was a half day symposium on MTD scheduled during the annual Society of Toxicology meeting in late February. Also, papers related to the MTD and its usefulness were being prepared by the NIEHS's Biometry and Risk Assessment Program and by the EPA.

III. Overview of the NIEHS Intramural Research Program: Dr. Martin Rodbell, NIEHS Scientific Director, said the Intramural Research Program plans and conducts basic biomedical research through six laboratories and a workgroup. One branch, the Comparative Medicine Branch, serves as a central resource for laboratory animal medicine, animal model development, microbiology, experimental surgery, and mammalian reproduction support service. The laboratories and their primary scientific areas are as follows: (1) Laboratory of Behavioral and Neurological Toxicology - studies neurobehavior, peptide neurochemistry, neurotransmitter mechanisms, and membrane physiology; (2) Laboratory of Molecular Biophysics - uses electron spin resonance to study free radical mechanisms, studies prostaglandin biochemistry and co-oxidation mechanisms, and conducts research in analytical mass spectrometry, nuclear magnetic resonance spectroscopy and bio-organic chemistry as well as provides core service to other IRP programs; (3) Laboratory of Genetics - studies population genetics and transposable elements in Drosophila, molecular mechanisms in mutagenesis, structure of lactic dehydrogenase genes in mammals, and DNA synthesis and topoisomerases in eukaryotic cells; (4) Laboratory of Pulmonary Pathobiology - studies mechanisms of cell differentiation of airway epithelium, cellular and molecular mechanisms of neoplastic transformation, mechanisms of particle and fiber toxicity, and biochemical pathology of epithelial secretory cells; (5) Laboratory of Pharmacology - studies role of chemical metabolism, transport, and excretion in mediation of toxicity, and studies membrane physiology and secretory processes in aquatic animals; and (6) Laboratory of Reproductive and Developmental Toxicology - studies developmental endocrinology and pharmacology, experimental teratogenesis, gamete

biology, and reproductive neuroendocrinology. The Membrane Transduction Workgroup studies the molecular basis for actions of hormones and neurotransmitters acting through cell membrane receptors.

IV. Review of Chemicals Nominated for NTP Studies: Dr. Dorothy Canter, NIEHS, briefly described the chemical nomination and selection process. This was followed by an interactive discussion of improvements already made and needed in the Executive Summaries, and requests by Board members for better public access to NTP data bases.

There were 10 chemical nominations to be considered by the Board. All had been reviewed previously by the NTP Chemical Evaluation Committee (CEC). Five of the chemicals were benzodiazepine drugs. Dr. Pitot chaired the review and Dr. Canter, also a member of the CEC, and Dr. Victor Fung, NIEHS, NTP Chemical Selection Coordinator, served as resource persons. Each Board member had been asked to serve as principal reviewer for one or two chemicals. Following oral presentation of each chemical review and discussion, a motion was made and voted on by the members.

The Board's recommendations, priority for testing, and additional remarks and/or caveats for the 10 chemicals reviewed are summarized in Attachment 3.

NIEHS Cellular and Genetic Toxicology Branch - Short-Term Assay Evaluation

V. Introduction: Dr. Raymond Tennant, Chief, Cellular and Genetic Toxicology Branch (CGTB), NIEHS, stated that the short-term assay evaluation was performed in response to a recommendation from the Board of Scientific Counselors in 1984. The initial focus of the effort was to address two major impediments; firstly, lack of data compiled across all test systems and across all chemicals for making systemetic comparisons, and secondly, an inadequate number of non-carcinogens for judging the specificity of the short-term tests for predicting carcinogenicity. The impediments were overcome first by careful selection of 73 chemicals for which adequate data was available from chronic carcinogenicity studies in rodents, and then by completing adequate genetic toxicity testing on these chemicals. Criteria for acceptability of an individual test result and criteria by which results were evaluated were predetermined. Dr. Tennant concluded by defining the two primary parameters; i.e., (1) sensitivity=the proportion of chemicals positive for genetic toxicology among all carcinogens evaluated; and (2) specificity=the proportion of chemicals negative for genetic toxicity among all non carcinogens tested.

VI. Comparison of In Vitro Assay Results with Rodent Carcinogenicity: Dr. Errol Zeiger, CGTB, discussed the relationship between the various assay systems and the biological perspectives. The four in vitro assays in which all 73 chemicals were evaluated were: (1) Salmonella (SAL) typhimurium (Ames) test; (2) mouse lymphoma (ML) L5178Y assay; (3) chromosome aberrations (CAs) in Chinese hamster ovary (CHO) cells; and (4) sister chromatid exchanges (SCEs) in CHO cells. Forty four of the 73 chemicals were evaluated for effects on unscheduled DNA synthesis (UDS) in rat primary hepatocyte while 26 were examined for effects on the sex-linked recessive lethal (SLRL) assay in Drosophila. Besides sensitivity and specificity, other correlative measures applied to the data base were: positive (+) predictivity - defined as - the

proportions of carcinogens among the chemicals giving positive results in short-term tests (STTs); negative (-) predictivity - defined as - the proportion of non-carcinogens among the chemicals giving negative results in STTs; and, accuracy (or concordance) - defined as - the proportion of "correct" results among all chemicals tested.

Dr. Zeiger discussed the findings and correlations in some detail. Among the conclusions to be drawn were:

(1) Among the four STTs, Salmonella showed the lowest sensitivity but the highest specificity and (+) predictivity. SCE and ML were highest in sensitivity (but lowest in specificity and (+) predictivity) while there were no differences among the four in (-) predictivity and concordance.

(2) Comparisons of various batteries of two, three or all four assays for (+) or (-) predictivity or concordance indicated there was no advantage of a battery over an individual STT. When all possible combinations were examined, the predictivity for carcinogens or noncarcinogens does not exceed the predictivity for SAL alone.

(3) Using the assays in a sequential manner does not appear to provide any additional insight into the differentiation of carcinogens from noncarcinogens.

(4) Two measures of potency that were used did not discriminate between "true" carcinogens and "false" carcinogens, i.e., false positives in the in vitro tests.

(5) For the other two assays, the UDS and SLRL, a very low sensitivity precluded further evaluation. Based on this study they are not recommended for routine screening of chemicals for carcinogenicity.

VII. Statistical Aspects of the Evaluation Process: Dr. Joseph Haseman, Biometry and Risk Assessment Program, NIEHS, described how the data base of 73 chemicals was decided upon. Selected were all NCI/NTP two-year studies in both rats and mice with final sacrifice dates of December, 1976 or later, including all studies whose final conclusions were approved by the NCI/NTP External peer review process as of January 1, 1985. Of the original list of 83 chemicals, 10 were excluded for technical reasons such as insolubility or volatility, e.g., four gums.

Dr. Haseman presented statistical evaluations supporting conclusions made by the previous speaker. He also gave an analysis of how often rats and mice produce similar outcomes, showing a 67% correlation between the species for the 73 chemicals. This represented a slightly lower concordance than for all NCI/NTP studies, which show a 75% correlation. He reiterated the conclusion that the strongest association between in vivo carcinogenesis and a short-term test was seen for the Salmonella test.

Dr. Barry Margolin, Biometry and Risk Assessment Program, NIEHS, commented on the study design noting that results were replicated within a given laboratory as a general rule. He observed that all four primary in vitro assays showed some concordance with each other, certainly greater with each other than with the results of the animal studies. He said complementarity among the STTs was

expected because the tests measure different genetic endpoints. However, complementarity was not observed. This observation had an important and immediate consequence for the field of short-term tests. He said that anyone proposing a new assay either in vitro or in vivo for which either improved predictivity or complementarity is claimed will ultimately need to undertake a similar evaluation study. Finally, he said there will be an opportunity to validate the present findings using another group of 30 chemicals.

VIII. Comparative Evaluation of Short-Term In Vivo Assays: Dr. Michael Shelby, CGTB, prefaced his remarks by noting that the biological differences existing between in vitro short-term tests and rodent carcinogenicity studies are largely overcome in the three short-term rodent in vivo assays he would describe.

For the first of these assays, the in vivo - in vitro UDS rodent hepatocyte assay, 14 of the 73 chemicals were tested, with a negative result in every case. Since 13/14 were carcinogens and 10 of these induced liver tumors in two-year studies, it was clear that the UDS assay would not be useful as a primary screen for in vivo carcinogenicity.

Results from the second, the mouse bone marrow cytogenetics assay, were more promising based on CAs and SCEs for 16 chemicals (8 carcinogens and 8 noncarcinogens) studied, as well as for an expanded group of 27 chemicals (15 carcinogens and 12 noncarcinogens). Relative performances of the two endpoints were similar to that for CAs and SCEs in the in vitro cytogenetics assay. Dr. Shelby reported on studies with seven structurally-related carcinogen/non-carcinogen pairs of chemicals. Results showed the in vivo bone marrow CA assay successfully discriminated between five of the seven pairs while the SCE assay discriminated between only one pair. Published results on studies with 17 of the International Agency for Research on Cancer (IARC) Group I Human Carcinogens report 16 positive for in vivo chromosomal tests indicating a strong link between human carcinogens and rodent cytogenetic effects. Thus, the findings to date support further development and evaluation of the rodent bone marrow assay, and its use by the NTP in safety evaluation of chemicals.

Dr. Shelby said plans for further in vivo somatic cell studies include: (1) completing testing of the 73 chemicals; (2) investigating the bone marrow micronucleus assay as a replacement for the CA assay as a primary in vivo test; (3) investigating the association between the rodent liver S-phase endpoint and liver carcinogens; and (4) pursuing the possibility of incorporating in vivo genetic toxicity assays into the prechronic phase of NTP toxicology and carcinogenesis studies.

IX. Strategies for Testing and Other Implications of the Evaluation: Dr. Tennant restated and summarized some of the conclusions:

(1) a clear positive response in the SAL assay is sufficient to indicate a high probability of tumorigenicity in rodents;

(2) the other three assays may confirm the SAL findings but do not generally complement the assay:

(3) chemicals not positive in SAL may be potential carcinogens which may act through nonmutagenic mechanisms although several genotoxic carcinogens are known to be negative in SAL;

(4) the current in vitro systems do not discriminate between nonmutagenic carcinogens and nonmutagenic noncarcinogens. This represents a major blind spot for in vitro assays;

(5) it is anticipated, although there is yet a lack of sufficient evidence to support the presumption, that a positive response to a chemical in the in vivo bone marrow assay substantiates a higher probability while a negative response indicates a lower probability of tumorigenicity in rodents; and

(6) therefore, it is worthwhile exploring the potential complementarity of the in vivo and SAL assays.

Dr. Tennant described the meaning and use of the results in the NTP program: (1) results of STTs should be available for use in design of prechronic studies while in vivo assays should be run in parallel with the prechronic studies so results can be used in decisions about long term studies; (2) no single type of data can be considered predictive of in vivo carcinogenicity; and (3) insights developed about nonmutagenic carcinogens have suggested studies to characterize carcinogenic mechanisms for some of these chemicals, e.g., inclusion of "stop" groups in the chronic study design.

Dr. Tennant concluded by mentioning related upcoming Branch activities which include: (1) completing evaluation of the 73 chemicals in the in vivo cytogenetics assay; (2) consolidating short-term test data input in conjunction with prechronic studies; (3) consolidating efforts to study mechanisms for carcinogenic chemicals that are non-mutagenic; and (4) continuing to develop and evaluate other assays, e.g., mammalian cell transformation, inhibition of metabolic cooperation, and aneuploidy.

General Discussion: There were comments that agreement across the short-term tests (STTs) was quite good. The evaluation provided a good retrospective data base for use in comparisons with new chemicals. Concerns were expressed about overinterpreting the data. There was some discussion about the extent of correlations between mutagenicity and teratogenicity and inclusion of such information in the data base. The staff cautioned that the STTs be not thought of as surrogates for long term rodent studies but rather as being among factors to be taken into consideration in assessing carcinogenic potential.

(4) Very few facilities have extensive design and operational controls and very few facilities have systems to monitor releases; and

(5) State Subtitle D regulations and resources vary by State and Territory.

Dated: October 27, 1986.

J.W. McGraw,

Acting Assistant Administrator, Office of Solid Waste and Emergency Response.

[FR Doc. 86-25101 Filed 11-5-86; 8:45 am]

BILLING CODE 6560-50-M

FEDERAL RESERVE SYSTEM

Change in Bank Control Notice; Acquisition of Banks or Bank Holding Companies

The notificants listed in this notice have applied for the Board's approval under the Change in Bank Control Act (12 U.S.C. 1817(j) and § 225.41 of the Board's Regulation Y (12 CFR 225.41) to acquire a bank or bank holding company. The factors that are considered in acting on the notices are set forth in paragraph 7 of the Act (12 U.S.C. 1817(j)(7).

The notices are available for immediate inspection at the Federal Reserve Bank indicated. Once the notices have been accepted for processing, they will also be available for inspection at the offices of the Board of Governors. Interested persons may express their views in writing to the Reserve Bank indicated for that notice or to the offices of the Board of Governors.

Comments regarding these applications must be received not later than November 21, 1986.

A. **Federal Reserve Bank of St. Louis** (Randall C. Sumner, Vice President) 411 Locust Street, St. Louis, Missouri 63166:

1. *The Citizens National Bank of Bowling Green Employee Stock Ownership Plan and Related Trust,* Bowling Green, Kentucky; to acquire 16.58 percent of the voting shares of Trans Financial Bancorp, Inc., Bowling Green, Kentucky, and thereby indirectly acquire The Citizens National Bank of Bowling Green, Bowling Green, Kentucky.

B. **Federal Reserve Bank of Minneapolis** (James M. Lyon, Vice President) 250 Marquette Avenue, Minneapolis, Minnesota 55480:

1. *Arnold B. Chace, Jr.*, Malcolm G. Chace, III, Malcolm G. Chace III Trust, Malcolm G. Chace, Jr. Trust, Jane Chace Trust, Jonathan Chace Clay Trust, Eliot Chace Trust, Christian Nolen Trust, Arnold B. Chace III Trust, Leigh Fibers, Inc., and William R. Dimeling to acquire 83.2 percent of the voting shares of Escrow Corporation of America, Inc., Pennock, Minnesota, and thereby indirectly acquire State Bank of Pennock, Pennock, Minnesota; and Heritage Bank, National Association, Willmar, Minnesota.

2. *David G. Smith,* to acquire 51.13 percent, and Keith G. Eltreim, to acquire 48.87 percent of the voting shares of Jasper Investment Company, Inc., Jasper, Minnesota, and thereby indirectly acquire Jasper State Bank, Jasper, Minnesota.

Board of Governors of the Federal Reserve System, October 31, 1986.

James McAfee,

Associate Secretary of the Board.

[FR Doc. 86-25084 Filed 11-5-86; 8:45 am]

BILLING CODE 6210-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Toxicology Program, Board of Scientific Counselors, Meeting

Pursuant to Pub. L. 92-463, notice is hereby given of a meeting of the National Toxicology Program (NTP) Board of Scientific Counselors, U.S. Public Health Service, in the Conference Center, Building 101, South Campus, National Institute of Environmental Health Sciences, Research Triangle Park, North Carolina, on November 25, 1986.

The meeting will be open to the public from 8:30 a.m. until adjournment on November 25. The preliminary agenda with *approximate* times are as follows:

8:30 a.m.-9:00 a.m.—Report of the Director

9:00 a.m.-9:30 a.m.—Overview of the NIEHS Intramural Research Program

9:30 a.m.-10:00 a.m.—Overview of the NTP

10:15 a.m.-11:45 a.m.—Review of Chemicals Nominated for NTP Studies.

(Ten chemicals will be reviewed. Of these, five were reviewed by the NTP Chemical Education Committee (CEC) on April 29, 1986, and listed in the **Federal Register**, Volume 51, No. 111, p. 21020, June 10, 1986: (1) Cobalt naphthenate; (2) Di(2-ethylhexyl) sebecate; (3) Methylcyclopentadienyl manganese tricarbonyl; (4) 2-Methylquinoline; and (5) 4-Methylquinoline. The remaining five chemicals, which are benzodiazepine drugs, were reviewed by the CEC on September 16, 1986, and listed in the **Federal Register**, Volume 51, No. 197, pp. 36479-36480, October 10, 1986: (1) Chlordiazepoxide; (2) Clorazepate; (3) Diazepam; (4) Flurazepam; and (5) Oxazepam.)

12:30 p.m.-4:45 p.m.—NIEHS Cellular and Genetic Toxicology Branch—Short-term Assay Evaluation.

I. Introduction.

II. Comparison of *In Vitro* Assay Results with Rodent Carcinogenicity.

III. Comparative Evaluation of Short-term *In Vivo* Assay.

IV. Statistical Aspects.

V. Strategies for Testing and Other Implications of the Evaluation.

The Executive Secretary, Dr. Larry G. Hart, Office of the Director, National Toxicology Program, P.O. Box 12233, Research Triangle Park, North Carolina 27709, telephone (919) 541-3971, FTS 629-3971, will have available a roster of Board members and other program information prior to the meeting and summary minutes subsequent to the meeting.

Dated: October 30, 1986.

David P. Rall,

Director, National Toxicology Program.

[FR Doc. 86-25087 Filed 11-5-86; 8:45 am]

BILLING CODE 4140-01-M

Reestablishments

Pursuant to the Federal Advisory Committee Act, Pub. L. 92-463 (5 U.S.C., Appendix 2), the Office of the Assistant Secretary for Health announces the reestablishment by the Secretary, DHHS, with concurrence by the General Services Administration, of the following advisory committees:

Designation: Health Care Technology Study Section.

Purpose: The Study Section shall advise the Secretary and make recommendations to the Director, National Center for Health Services Research and Health Care Technology Assessment, on research grant applications in medicine, technology assessment, the information sciences, decision sciences (operations research, industrial engineering, health care administration), communications technology, bioengineering, and related fields as applied to hospital-based ambulatory, and community health care. The members of this Study Section shall survey, as scientific leaders, the status of research in their fields.

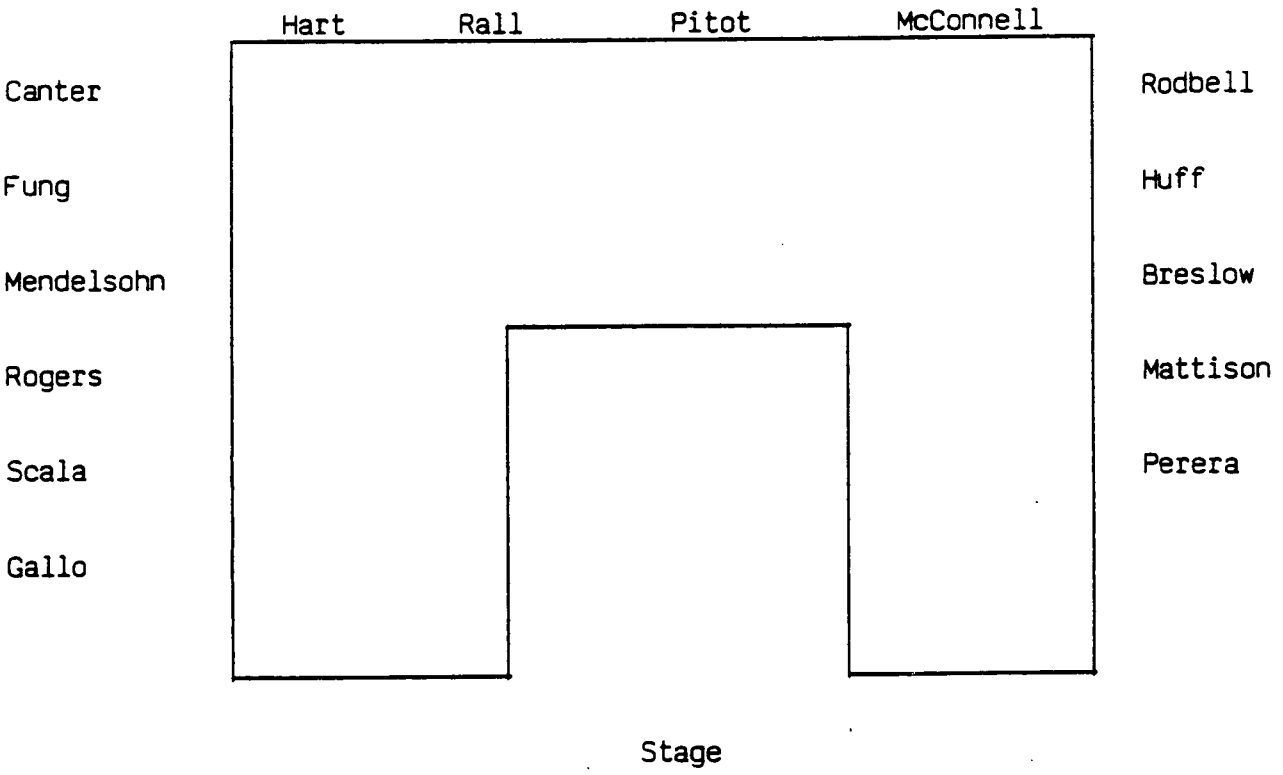
Designation: Health Services Research and Developmental Grants Review Committee.

Purpose: The Committee shall advise the Secretary and make recommendations to the Director, National Center for Health Services Research and Health Care Technology Assessment, on research grant applications of two general types. One

NTP BOARD OF SCIENTIFIC COUNSELORS MEETING

Conference Center, Building 101, South Campus
National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina

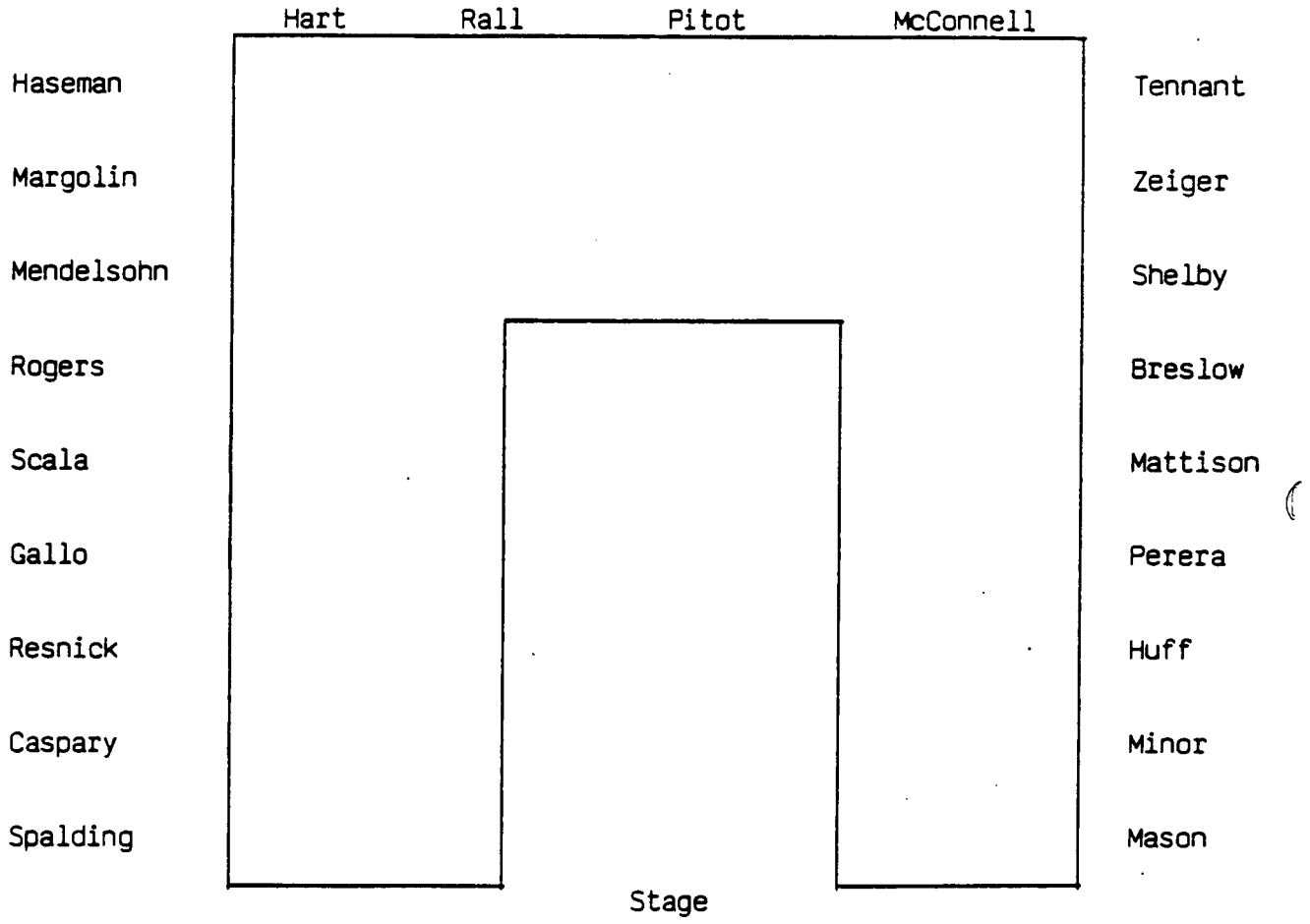
November 25 (a.m.), 1986



NTP BOARD OF SCIENTIFIC COUNSELORS MEETING

Conference Center, Building 101, South Campus
National Institute of Environmental Health Sciences
Research Triangle Park, North Carolina

November 25 (p.m.), 1986



Testing Recommendations for Chemicals Reviewed by Board of Scientific Counselors on November 25, 1986

Chemical (CAS Number)	Nomination Source	Testing Recommended (Priority)	Rationale/Remarks
A. Benzodiazepine (BZD) Drugs			
1. Oxazepam (604-75-1)	1. NIEHS 2. FDA	Class study on all five benzodiazepine drugs for carcinogenicity and reproductive effects testing (High)	-Widespread use -Concern about the toxicological potential of the BZD drugs -Directed NTP staff to perform extensive review of literature, unpublished studies to assess adequacy of previous testing to determine sex/species combination in which to test individual chemicals
2. Flurazepam (17617-23-1)	FDA		
3. Diazepam (439-14-5)	1. NIEHS 2. FDA		
4. Clorazepate (23887-31-2)	1. NIEHS 2. FDA		
5. Chlordiazepoxide (58-25-3)	1. NIEHS 2. FDA		
B. Others			
1. Cobalt naphthenate (61789-51-3)	NCI	-Chemical disposition by oral and dermal routes of administration -Genetic toxicity studies other than Salmonella (Low)	-Potential for exposure -Lack of information on potential toxicity and dermal absorption of naphthenates -Structural interest
2. Di(2-ethylhexyl)-sebacate (DEHS) (122-62-3)	NIEHS	-No testing by NTP	-Recommended study to determine capability of DEHS to migrate from material used in food packaging -Inform Board of results of study by appropriate group

Chemical (CAS Number)	Nomination Source	Testing Recommended (Priority)	Rationale/Remarks
3. Methylcyclopentadienyl manganese tricarbonyl (MMT) (12108-13-3)	EPA	No testing	-Low exposure -Reconsider if new uses developed for MMT
4. 2-Methylquinoline (~~96~~ 91-63-4)	EPA	-Carcinogenicity -Mutagenicity (Low)	-Structural interest even though low production -Suggest testing additional methylquinoline in which methyl group is on the non-heterocyclic ring.
4-Methylquinoline (491-35-0)	EPA		