

NATIONAL TOXICOLOGY PROGRAM

BOARD OF SCIENTIFIC COUNSELORS' MEETING

OCTOBER 22 and 23, 1981

National Toxicology Program
Board of Scientific Counselors' Meeting
October 22 and 23, 1981

SUMMARY MINUTES

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Summary Minutes

The National Toxicology Program (NTP) Board of Scientific Counselors met on October 22 and 23, 1981, in the Auditorium, Robert A. Taft Laboratories, National Institute for Occupational Safety and Health (NIOSH), 4676 Columbia Parkway, Cincinnati, Ohio (Attachment 1: Federal Register Meeting Announcement; Attachment 2: Agenda).

Dr. N. Nelson, Chairman, presided. The minutes of the May 27 and 28, 1981 Board of Scientific Counselors' meeting were approved.

Review of NTP Programs in Inhalation Toxicology at NIOSH and the National Institute of Environmental Health Sciences (NIEHS): (Attachment 3: Review of the Pulmonary Toxicology Program of the National Toxicology Program; Attachment 4: Review of NTP Program in Inhalation Toxicology; Attachment 5: Review of the Program of the Inhalation Toxicology Workgroup, National Toxicology Program, Toxicology Research and Testing Program, Systemic Toxicology Branch, National Institute of Environmental Health Sciences). Ad hoc consultants who supplemented the Board members as peer reviewers were Dr. M. McKenna, Dow Chemical Company and Dr. J. D. MacEwen, University of California - Irvine. Dr. T. R. Lewis, Program Leader, introduced the NIOSH program. Dr. Lewis said that, due to cost and the desire to maximize scientific return from research investment, stress was placed during inhalation toxicology studies on also assessing effects on functional status of other organs. For example, cardiovascular and other major organ system effects often need to be determined. He also commented on the differentiation between primary pulmonary effects (e.g., pneumoconiosis) and systemic effects following inhalation exposure, and emphasized that the program often required development of novel exposure systems to mimic the occupational environment. The latter requires a research capability in the area of inhalation technology. Dr. Lewis then described the objectives and results to date of long-term studies as outlined in Attachment 4, and including I. Chronic Inhalation Toxicity of Organic Oxides (Intramural); II. Chronic Toxicity of Insulation Materials (Fibrous Glass) (Contract); III. Diesel Exhaust/Coal Dust Animal Exposure Studies (Intramural); IV. Carcinogenicity of Short Asbestos Fibers (Chrysotile) (Contract); and V. Chronic Biologic Effects of Dimethylformamide (Contract). Ongoing short-term studies described were: I. Comparative Cardiac Toxicity of Inhaled Amines (Intramural), and II. Pulmonary Hypersensitivity of Industrial Metals (Intramural). Dr. Lewis also described two intramural research efforts just initiated: I. Emergency Toxicological Assessment, and II. Cardiopulmonary Animal Modeling - Rodent. Details of the objectives, methods, findings and proposed course for the long-term and short-term studies and the new initiatives were given in Attachment 3.

Discussion centered on the diesel exhaust/coal dust studies. Dr. Mendelsohn expressed concern about NIOSH committing to just one type of diesel engine since such engines release emissions of variable composition. Dr. Lewis replied that they were using the engine most commonly employed in mine operations.

Mr. W. J. Moorman, NIOSH, discussed two studies, one concerned with chronic effects resulting from inhalation of fibrous glass of varying diameters and lengths, and a second study characterizing differences in methodology for assessing rodent cardiopulmonary function. Mr. R. E. Biagini, NIOSH, discussed the study on pulmonary hypersensitivity of industrial metals. The primary objective was to develop a primate animal model for occupational asthma. He reviewed the types of occupational asthmogens and stated that the first step was to characterize physiologic and immunologic responses with an asthmogen appropriate to modeling occupational asthma in man. Platinum salts were chosen. The monkey was chosen as the animal model due to the similarity to humans of its pulmonary anatomy, physiology and immune system. Marked dermal and pulmonary hypersensitivity and hyperreactivity reactions were demonstrated in monkeys exposed to platinum aerosols by the nose-only route, and by direct nebulization into the trachea. The latter phase also included concomitant exposure to a common industrial irritant, hydrochloric acid, aerosol which acted as a coasthmogen.

Dr. Lewis talked about how NIOSH chooses chemicals for study. Chemicals are chosen primarily to (1) expand the state of knowledge for chemicals encountered in occupational settings; (2) investigate those assigned high priority by NTP; or (3) followup NIOSH health hazard evaluations and objectives of the NIOSH/NTP program in inhalation toxicology (Attachment 4).

Dr. R. T. Drew, Brookhaven National Laboratory (BNL), outlined the status of the interagency agreement between NTP and BNL. The study, titled Evaluation of Respiratory Mechanics and other End Points as Indices of Chemical Toxicity, has the objective of comparing the sensitivity and utility of pulmonary function testing with pathological examination in rodents exposed to typical classes of airborne toxicants. Studies with two chemicals, acrolein and ozone, have been completed and a study with chlorine is ongoing. Besides pulmonary function, endpoints examined include pulmonary biochemistry, histopathology, reproductive potential (females), and cytogenetics. There were no reproductive or cytogenetic (sister chromatid exchange) effects of these chemicals with the exception of alterations in sperm morphology by ozone at the highest dose. He said that studies beginning in FY 1982 would include silica, cadmium chloride and tungsten carbide (alone and with cobalt). Styrene oxide would not be studied because of problems with room contamination.

Dr. D. Costa, BNL, discussed in more detail the comparative findings among pulmonary function tests, biochemical analyses and histopathologic measurements. Preliminary conclusions from these studies are (1) that pulmonary function tests correlate well but are more sensitive than histopathology for detecting damage from exposure to acrolein and ozone; (2) pulmonary function tests pick up significant small airway damage not detected by histopathology; and (3) biochemical changes correlate less well with pulmonary function tests.

Dr. E. W. Van Stee, NIEHS/NTP, described three principal NTP projects supported by the Inhalation Toxicology workgroup at the NIEHS (Attachment 5). The first was the nitrogen dioxide-amines project. This study was based on the postulated interaction of inhaled nitrogen dioxide (NO_2) with orally injected morpholine to form N-nitrosomorpholine. The animal model chosen to examine potential tumorigenic effects of this combination was the formation of lung adenomas in CD-1 mice. There were increases in lung adenomas

in mice treated with both NO_2 and morpholine but of borderline significance. Similar studies in Strain A mice, with or without alpha-tocopherol in the diet, were negative. To determine whether, indeed, N-nitrosomorpholine is formed in vivo, metabolism studies are underway.

The second study described by Dr. Van Stee had to do with the vascular toxicology of carbon disulfide in the rabbit. Objectives are (1) to study the relationship of thyroid function with acceleration of atherogenesis by CS_2 in the hypercholesterolemic rabbit, and (2) to measure the mechanical performance and metabolic activity of hearts isolated from rabbits previously exposed to CS_2 . He elaborated on studies aimed at testing the thyroid hypothesis, i.e., that the acceleration of atherosclerosis by exposure to CS_2 is an indirect result, in part, of a depression of thyroid activity.

Thirdly, Dr. Van Stee outlined a proposed two-year study to validate Strain A mouse lung adenoma formation after inhalation exposure as a useful bioassay system. Of the chemicals chosen, some would be known as pulmonary carcinogens, while some would not be.

Review of NTP Programs in Neurobehavioral Toxicology at NIOSH and NIEHS: (Attachment 6: Neurobehavioral Research NTP/NIOSH; Attachment 7: Neurobehavioral Toxicology Summary Statement (NIEHS)). Ad hoc consultants who supplemented the Board members as peer reviewers were Dr. S. Norton, University of Kansas, and Dr. Repko, University of Arizona. Dr. W. K. Anger, Program Leader, introduced the NIOSH program, and stated that the NIOSH component of NTP focuses on neurobehavioral effects of substances found in the workplace. Emphasis is given to experimental use of inhalation and skin routes of exposure. Chemicals chosen for study are primarily those given priority by NTP for which NIOSH has interest and expertise, and industrial chemicals with neurotoxic potential in workers, including possible causation of a predisposition to on-the-job and off-the-job accidents, and development of preclinical indicators for neurotoxicity. He listed the four major goals of the NIOSH program as: (1) assessment of neurobehavioral effects from workers, chronic industrial exposures studies intended to evaluate the adequacy of permissible exposure levels (PELs) for specific chemical agents; (2) assessment of neurobehavioral effects from acute exposures, using animal and human laboratory studies to verify adequacy of PELs for industrial chemicals when presented alone and in combination with other agents; (3) coupling neurobehavioral testing to standard toxicologic approaches in animal studies to enlarge the toxicity data base; and (4) development of improved neurobehavioral tests of toxicity.

Dr. Anger described the three major research/testing approaches by NIOSH: (1) field testing of worker populations; (2) laboratory testing of volunteer human subjects; and (3) laboratory testing of animal subjects. Past accomplishments, current research, and planned activities for the three areas are described in Attachment 6. He stressed the continuing objective of attempting to correlate animal with human (worksite or laboratory) studies. In the laboratory, human volunteers are exposed to levels at or below those permitted by the OSHA. In human studies using combinations of chemicals, the assumption is made that the effects are additive unless shown to be otherwise. With regard to animal studies, a current effort involves screening a large group of

cellosolves (glycol ethers) for a range of behavioral teratologic effects, and then choosing a few for indepth studies. Paternal (prior to mating) as well as gestational exposures are used. In addition to standard neuro-behavioral tests, neurochemical tests are also performed (acetylcholine, dopamine, 5-hydroxytryptamine, etc).

Dr. Anger commented briefly on coordinative aspects of the NTP neurobehavioral toxicology programs. He noted the involvement and support by NIOSH of the NCTR-led behavioral teratology initiative. He said that NIOSH and NIEHS maintain awareness of each other's projects. Dr. Repko asked what criteria were used in selecting chemicals for human inhalation studies. Dr. Anger replied that a chemical must not have other than acute effects, and classes of chemicals are chosen which have well known but not well-defined neuro-behavioral effects at low levels. Dr. B. Johnson, NIOSH, added that chemicals are also chosen to meet the needs of the Criteria Documents Group. Dr. Norton asked why aluminum was chosen for current animal studies in operant/instrumental behaviors. Dr. Anger replied that aluminum was chosen as a model agent for possible induction of Alzheimer's disease.

Dr. H. Tilson, NIEHS, discussed test developments in the Neurobehavioral Workgroup at NIEHS. The major emphasis has been placed on the development, standardization, and validation of a battery of tests to assess neurotoxicity in laboratory animals. This project, completed at the end of FY 1981, successfully met four objectives set prior to initiation of the study (Attachment 7). The eight compounds chosen to be studied in the battery were known to display various degrees and types of neurotoxicity. The battery of tests was designed to measure neuromotor, reactivity, sensory, and general health parameters. Details of the study protocol and findings are given in Attachment 7a (Test Battery for the Neurobehavioral Assessment of Potential Neurotoxins). Dr. Tilson discussed the method of data transformation across experiments, the neurobehavioral profiles for the chemicals tested, and the relative toxicities based on neurobehavioral effects. His conclusions were that the battery provided a good overall nucleus for routine screening and an index for future studies. However, the battery could be improved with regard to certain tests. For instance, there is still a need to continue development of procedures to assess sensory dysfunction in laboratory animals. He briefly discussed a new study which would determine home cage behaviors as an early measure of toxicant effect, i.e., before marked changes in body weight were seen (Attachment 7).

Concept Review: Three cellular and genetic toxicology proposals were reviewed for concept by the Board (Attachment 8: National Toxicology Program Statement of Concept Review). Two of the proposals are ongoing contract efforts which are due to be recompeted and awarded in FY 1983. The third (Heritable Translocation Test) is a new testing initiative. The concept proposals are as follows:

- 1) Salmonella Mutagenicity Testing: (Attachment 8) The Salmonella test is well established as the NTP's primary initial screen for mutagenic activity of chemicals. Results from Salmonella testing contribute to making decisions regarding further testing. By the end of the present contract period data on over 700 unique chemicals will be in the Salmonella data file, with 100-200 of these chemicals also tested in Drosophila and/or Chinese hamster

ovary cells. The proposal, presented by Dr. R. Tennant, NIEHS, is to award competitively up to four contracts in December 1982 for testing of up to 1600 samples for mutagenicity in Salmonella. Dr. Mendelsohn said this testing system was and remains a valid approach, and the NTP is the best equipped program to do such studies. He stated that the time and resources proposed are reasonable. Dr. Horning moved that the proposal be approved for concept, and the motion was approved unanimously by the Board.

- 2) Mammalian Cell (L5178Y Mouse Lymphoma TK⁺/-) Mutagenesis Assays: (Attachment 8) A dual laboratory evaluation and validation of the mouse lymphoma mutagenesis system is now in the final year of a five-year effort. Dr. W. Caspary, NIEHS, described the background and current protocol in some detail, and commented on the very high (>95%) inter-laboratory reliability and intralaboratory reproducibility of the test. The proposal is to fund two contracts, each having the capacity for testing 50 chemicals per year. Dr. Mendelsohn said there were at least three reasons why this test system is important: (1) it is a mammalian cell test; (2) it may be two dimensional in that it detects both point mutations and chromosome aberrations; and (3) this test may be sensitive to a wider range of chemicals than other tests for mutagenic activity, including the Salmonella test, and has performed the best of any test in measuring the mutagenic activity of chlorinated pesticides. Dr. Nelson questioned whether NTP should place major emphasis on this assay since there are other tests in mammalian systems. Dr. Tennant replied that NTP is evaluating and will be evaluating other mammalian test systems. Dr. Mendelsohn moved for approval of the concept proposal and the motion was approved unanimously by the Board.
- 3) Assay of Chemicals for Induction of Heritable Translocations in Mice: (Attachment 8) Dr. M. Shelby, NIEHS, described the heritable translocation test (HTT) and gave examples of human genetic diseases known to be associated with heritable translocations. The HTT is currently the only practicable method for detecting and quantifying chemically induced heritable chromosome damage in mammals. The proposal is to support a two-year mouse HTT study in which about six chemicals will be tested. In response to a question by Dr. Whittemore, Dr. Shelby said at least three of the chemicals will be the same as those being tested under NTP in mouse specific locus tests. Dr. Mendelsohn commented that the HTT measures important endpoints oriented toward large chromosomal lesions while the specific locus test gives information on smaller lesions. He moved for approval of the concept proposal and the motion was approved unanimously.

- Chemicals Projected for Multiple Tests in FY 1982 and FY 1983:
Dr. Tennant described briefly to the Board, plans by NIH/NTP for multiple cellular and genetic toxicology testing of chemicals including a description of the criteria on which priority for testing would be based

(Attachment 9). Highest priority would be given to the 19 chemicals scheduled to begin prechronic testing in FY 1982 (Attachment 9).

- Toxicology Data Management System (TDMS) Status Report: Dr. J. Moore, NIEHS, said that pilot studies had been completed and field studies were being implemented at selected bioassay laboratories through supplementation of existing contracts. For purposes of cross comparison, there would be some overlap of existing data management systems at these laboratories with TDMS. He said that in about one year there would be further peer review of TDMS.
- Peer Review and Priority Ranking of Chemicals Nominated for NTP Testing: This was the second Board meeting at which review and recommendation of testing priorities were implemented. There were 26 chemical nominations to be considered by the Board. Thirteen of these nominations had been previously reviewed by the NTP Chemical Evaluation Committee at their meeting on April 8, 1981, and the other 13 had been reviewed by the Committee on May 19, 1981. Comments received on five of the chemicals in response to a Federal Register announcement were given to the Board as addenda to the draft Executive Summaries and would be included in the final Executive Summaries. During the review, specific comments and data were presented by persons in the audience on two of the nominated chemicals: turmeric and sodium chromate.

Dr. Horning, Chairperson of the Board Subcommittee on Chemical Nomination and Selection, chaired the review of the individual chemicals. The Chairperson of the NTP Chemical Evaluation Committee, Dr. L. Fishbein, NCTR, and two members of the Committee, Dr. D. Canter, NIEHS, and Dr. B. Johnson, NIOSH, were present in an advisory role to the Board. Each Board member had been asked to review four to six chemicals prior to the meeting. Following oral presentation of the review and testing recommendations for a chemical there was discussion. A motion was then made and voted on by all of the Board members present. The approved recommendations, priority for testing, and additional remarks and/or caveats are summarized (Attachment 10: 26 Chemicals Reviewed by the Board of Scientific Counselors on October 23, 1981).

- Recommendations for Categorizing Bioassay Results as to Strength of Evidence for Carcinogenicity in Animals: Dr. Whittemore led the discussion and said that the Board subgroup studying the issue had recommended a procedure for evaluating bioassay evidence for carcinogenicity. She said the subgroup suggests the use of a decision tree to arrive at one of six mutually exclusive and exhaustive categories for strength of evidence for carcinogenicity in animals. (Attachment 11: A description of the decision tree and definition of the six categories).

Dr. Moore introduced the topic on the difficulty of differentiating between benign and malignant tumors, e.g., with adenomas and carcinomas of the lung. In such instances, tumors are often combined by NTP. Dr. J. Huff, NIEHS, stated that the category titled 'negative evidence' may better be labelled 'no evidence'. Dr. B. Johnson, NIOSH, suggested that the regulatory agencies should have a look at the decision tree approach when finalized. Dr. Nelson replied that NTP and the Board should come to a consensus before this is done. Dr. Moore said that NTP

staff may consider trying to score bioassay reports approved in FY 1981 using this procedure. He proposed that we ask the peer review panel to use the scheme on a trial basis with the six bioassay reports to be reviewed on December 16. The Board agreed with Dr. Moore's proposal. [ED. NOTE - The Technical Reports Review Subcommittee and Panel of Experts applied the decision tree approach on a trial basis with the six draft reports reviewed on December 16. The reviewers were divided as to utility of the approach and it was recommended that the approach be returned to the Board subgroup for further study.]

(4110-08)

Department of Health and Human Services
U.S. Public Health Service
National Toxicology Program

Notice of Meeting
National Toxicology Program Board of Scientific Counselors

Pursuant to Public Law 92-463, notice is hereby given of the meeting of the National Toxicology Program (NTP) Board of Scientific Counselors, U.S. Public Health Service, in the auditorium, Robert A. Taft Laboratories, National Institute for Occupational Safety and Health, 4676 Columbia Parkway, Cincinnati, Ohio, on October 22 and 23, 1981.

The meeting will be open to the public from 8:45 a.m. to 4:00 p.m., October 22. The preliminary agenda is as follows:

8:45 a.m. - 11:30 a.m.	Review of NTP Program in Inhalation Toxicology
11:30 a.m. - 12:00 noon	Other Business
1:00 p.m. - 2:30 p.m.	Review of NTP Program in Neurobehavioral Toxicology
2:30 p.m. - 4:00 p.m.	NTP Cellular and Genetic Toxicology Program - Concept Review and Status Report on Short-Term Test Development Initiatives

In accordance with the provisions set forth in Section 552b(c)(6) Title 5 U.S. Code and Section 10(d) of Public Law 92-463, the meeting will be closed to the public on October 22 from 4:00 p.m. to adjournment for further evaluation of NTP programs in inhalation toxicology, and neuro-behavioral toxicology, including the consideration of personnel qualifications and performance, the competence of individual investigators, and similar items, the disclosure of which would constitute a clearly unwarranted invasion of personal privacy.

The meeting on October 23 will be open to the public from 8:45 a.m. to adjournment. The preliminary agenda is as follows:

8:45 a.m. - 12:00 noon

Peer Review and Priority Ranking of Chemicals Nominated for NTP Testing. (Twenty-six chemical nominations will be reviewed and are listed in the Federal Register, Volume 46, page 35792, July 10, 1981 and Volume 46, page 38143, July 24, 1981.)

1:00 p.m. - 2:00 p.m.

Recommendations for Categorizing Bioassay Results as to Strength of Evidence for Carcinogenicity in Animals

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 furnish summary minutes of the meeting, rosters of Board members, and other program information.

9/15/81

Date

David P. Rall

David P. Rall, M.D., Ph.D.
Director
National Toxicology Program

AGENDA

Board of Scientific Counselors
National Toxicology Program
October 22-23, 1981

Auditorium, Robert A. Taft Laboratories
National Institute for Occupational Safety and Health
4676 Columbia Parkway
Cincinnati, Ohio

October 22, 1981

OPEN

8:45 a.m. - 11:30 a.m.

Review of NTP Program
in Inhalation Toxicology

Dr. T. Lewis and
Staff, NIOSH

Dr. R. Drew, Brookhaven
National Laboratory

Dr. E.W. Van Stee,
NIEHS

11:30 a.m. - 12:00 noon

Other Business

Drs. Rall and Moore

1:00 p.m. - 2:30 p.m.

Review of NTP Program in
Neurobehavioral Toxicology

Dr. K. Anger, NIOSH
Dr. H. Tilson, NIEHS

2:30 p.m. - 4:00 p.m.

Cellular and Genetic
Toxicology Program -
Concept Reviews:
(1) *Salmonella* Mutagenicity
Testing
(2) Assay of Chemicals for
Induction of Heritable
Translocations in Mice
(3) Recombination of Mamma-
lian Cell (L5178Y Mouse
Lymphoma TK⁺/-) Muta-
genesis Assay Contracts

Dr. R. Tennant, NIEHS

Dr. E. Zeiger, NIEHS

Dr. M. Shelby, NIEHS

Dr. W. Caspary, NIEHS

CLOSED

4:00 p.m. - 5:00 p.m.

Evaluation of Programs and
Personnel in Inhalation
Toxicology and Neurobehavioral
Toxicology

Board and Consultants

October 23, 1981

OPEN

8:45 a.m. - 12:00 noon

Peer Review and Priority
Ranking of Chemicals Nominated
for NTP Testing

Board

TABLE 34

CHEMICALS REVIEWED BY THE BOARD OF SCIENTIFIC COUNSELORS

On October 23, 1981

<u>Chemical (CAS No.)</u>	<u>Recommendation (Priority)</u>	<u>Comments</u>
<u>April 8 Chemicals</u>		
1 Benzethonium chloride (121-54-0)	Battery of short term mutagenicity tests (High) Carcinogenicity (Moderate)	Consider utility of skin paint bioassay
2 Benzotrichloride (98-07-7)	No testing	-Reviewed by IARC (10/81): sufficient carcinogenicity in animals (skin paint bioassay in mice), inadequate data in humans -NIOSH should review workplace exposure
3 Benzoyl chloride (98-88-4)	Battery of short term mutagenicity tests Carcinogenicity (skin paint or inhalation) (High)	Reviewed by IARC (10/81): inadequate human data, no good animal studies
4 t-Butyl perbenzoate (614-45-9)	Battery of short term mutagenicity tests 90-day subchronic test (High)	Defer carcinogenicity bioassay pending results other studies
5 Butyric anhydride (106-31-0)	No testing	
6 m-Chloroaniline (108-42-9)	Mutagenicity testing Teratogenicity (Moderate to High)	Defer carcinogenicity bioassay pending results of other testing
7 Methyl trifluoromethane sulfonate (333-27-7)	Salmonella assay (Moderate)	

6	N-Methyl-N-nitroso-p-toluenesulfonamide (80-11-5)	Mouse strain A lung adenoma assay (Low)	
7	Salicylazosulfamidine (599-79-1)	Battery of short term mutagenicity tests Carcinogenicity (High)	
8	Scopolamine (51-34-3)	Battery of short term mutagenicity tests (excluding <u>Salmonella</u> assay) (Moderate)	
9	Sodium Chromate * (7775-11-3)	Carcinogenicity (inhalation) (Very low)	-Study likely to be negative since compound not persistent -Sodium chromate similar to sodium dichromate; monitor rat carcinogenicity study of dichromate
10	Sulfamethizole (144-82-1)	Battery of short term mutagenicity tests (High)	
11	Sulfanilamide (63-74-1)	Battery of short term mutagenicity tests (High)	
12	Sulfathiazole (72-14-0)	Battery of short term mutagenicity tests (High)	
13	Theophylline (58-55-9)	Battery of short term mutagenicity tests Reproductive effects (High)	Reproductive studies should be complementary to those performed on caffeine

* Information submitted in response to notice published in Federal Register requesting data on nominated chemicals and comments on recommended types of testing.

9	O-Phenanthroline (66-71-7)	Battery of short term mutagenicity tests (Low)
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April 8 Chemicals (Con't.)

10	Tetrachlorophthalic anhydride (117-08-8)	In vitro cytogenetics Drosophila testing Carcinogenicity (Moderate)
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11	Triethanolamine (102-71-6)	Battery of short term mutagenicity tests 90-day subchronic test Reproductive effects (High)	Defer carcinogenicity study pending results other testing
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12	2,4,5-Trimethoxybenzal- dehyde (4460-86-0)	Battery of short term mutagenicity tests (High)
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13	Turmeric * (8024-37-1)	Proceed with scheduled testing of turmeric oleo- resin containing 95% curcumin Review as class spices struc- turally related to curcumin
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May 19, 1981 Chemicals

1	Codeine * (76-57-3)	Reproductive effects (Moderate)
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2	Gallium arsenide (1303-00-0)	Metabolism (High)	-NIOSH industry-wide study underway -Defer further studies pending results metabolism, NIOSH studies
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3	Mercuric oxide, yellow (21908-53-2)	No testing
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4	Methiodal sodium (126-31-8)	Salmonella assay Mouse lymphoma study (High)
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5	Nickel oxide * (1313-99-1)	Carcinogenicity (inhalation) (Moderate) Carcinogenicity studies utilizing pellet implant and intratracheal instilla- tion on group of nickel com- pounds including nickel oxide and nickel sulfate (High)	Perform inhalation carcinogenicity study on nickel sulfate also (Moderate Priority)
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