

# Carcinogenesis Bioassay Results from the National Toxicology Program

James Huff\*

This article begins a series of condensations on the National Toxicology Program's (NTP) toxicology and carcinogenesis bioassay results as summarized from the *NTP Technical Report* collection. This first compilation lists those 40 carcinogenesis bioassay studies (Table 1) that have undergone both NTP staff interpretation and evaluation as well as external peer review and critique. The majority of these studies were initiated by the National Cancer Institute's Carcinogenesis Testing Program, now part of the National Institute of Environmental Health Sciences, National Toxicology Program.

Précis on individual *NTP Technical Reports* will be submitted for publication in *Environmental Health Perspectives (EHP)* at the same time that the approved reports are delivered for printing. For instance, information and data condensations on four recently printed carcinogenesis bioassay reports [caprolactam, cytembena, di(2-ethylhexyl) adipate, and FD&C Yellow No. 6] appear as separate inserts following this introductory article. Considerably more abbreviated results are published routinely in the *NTP Technical Bulletins*. More extensively treated manuscripts are being prepared for publication consideration in *EHP* and in other recognized peer-review journals. This allows not only more rapid and wider dissemination of results generated by the NTP, but permits open interchange between scientists/organizations engaged or interested in similar research and testing activities.

For orientation purposes, the following overview highlights the National Toxicology Program, the chemical nomination and selection process, and the toxicology and carcinogenesis bioassay program.

## National Toxicology Program

The NTP completed its fourth year of operation and first year in permanent status in Fiscal Year (FY) 1982. The NTP was established in November 1978 as a Department of Health and Human Services (DHHS) cooperative effort to coordinate and provide information about potentially toxic chemicals to regulatory and research agencies and to strengthen the science base in toxicology. The need for creation of such a program evolved from increasing scientific, regulatory, and congressional concerns about the human health effects of chemical agents in the environment.

A major reorganization occurred within NIH in FY 1981: the transfer of the carcinogenesis bioassay program from the National Cancer Institute (NCI) to the National Institute of Environmental Health Sciences (NIEHS) was approved by the Secretary, DHHS, in the fourth quarter of FY 1981. Further, at the beginning of FY 1982, the Secretary granted permanent status to the National Toxicology Program.

Under the broad objective of providing the necessary scientific information for prevention of human disease related to chemical exposure, the NTP emphasizes four principal goals: (1) broaden the toxicological characterization of chemicals that are tested; (2) increase the rate of chemical testing (as funding will permit); (3) develop protocols appropriate for regulatory needs; and (4) communicate program plans and results to governmental agencies, the medical and scientific communities, and the public.

Although testing chemicals for toxicity, particularly for carcinogenicity and mutagenicity, remains an important program focus, increasing emphasis over the first four years has been placed on short-term test methods development and validation. A second primary emphasis continues to be

---

\*National Toxicology Program, P. O. Box 12233, Research Triangle Park, North Carolina 27709

Table 1. National Toxicology Program toxicology and carcinogenesis bioassay results.

Chemical CAS No. NTP No.	NTP Report No. TR Report No. Peer Review Date	Use	Route/dose	Testing laboratory	NTP chemical manager	Results under the conditions of these tests <sup>a,c</sup>
Agar 9002-18-0 10754-C	NTP-80-084 TR-230 P <sup>a</sup> 02/18/81	Gelling agent in foods and pharmaceuticals	Feed: 25,000 or 50,000 ppm	EG&G Mason Research Institute	Dr. R. L. Melnick	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
Allyl isothiocyanate 57-06-7 10867-A	NTP-81-036 TR-234 06/23/81	Flavor agent, major component in brown mustard seed	Gavage (corn oil): 12 or 25 mg/kg 5 times/week	Southern Research Institute	Dr. J. Dunnick	Carcinogenic to male F344 rats causing transitional cell papilloma in the urinary bladder (0/49, 2/49, 4/49). (Additionally, epithelial hyperplasia of the urinary bladder occurred at 0/49, 1/49, 6/49 in male rats not having papillomas.) Not carcinogenic to female F344 rats or B6C3F <sub>1</sub> mice of either sex.
11-Aminoundecanoic acid 2432-99-7 10788-W	NTP-80-034 TR-216 P 02/18/81	Monomer used in manufacture of polyamide nylon 11	Feed: 7500 or 15,000 ppm	Litton Bionetics Inc.	Dr. J. Dunnick	Carcinogenic for male F344 rats, inducing neoplastic nodules of the liver (1/50, 9/50*, 8/50*) and transitional-cell carcinomas in the urinary bladder (0/48, 0/48, 7/49*); not carcinogenic for female F344 rats. Not carcinogenic for B6C3F <sub>1</sub> mice of either sex, although the increase in male mice with malignant lymphoma (2/50, 9/50*, 4/50) may have been associated with the administration of 11-aminoundecanoic acid.
Arabic gum 9000-01-5 10751-P	NTP-80-081 TR-227 P 02/18/81	GRAS food additive, flavor fixative, foam stabilizer, emulsifier	Feed: 25,000 or 50,000 ppm	EG&G Mason Research Institute	Dr. J. E. Huff	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
Asbestos, amosite 12172-73-5 10761-X	NTP-81-058 TR-249 06/23/81	Asbestos-cement pipe	1% in diet	Illinois Inst. of Technology Research Inst.	Dr. E. E. McConnell	Not carcinogenic for Syrian golden hamsters of either sex.
Asbestos, chrysotile 12001-29-5 10758-S	NTP-81-051 TR-246 06/23/81	Asbestos-cement, textiles, insulation	1% in diet (short-range, SR, intermediate range, IR)	Illinois Inst. of Technology Research Inst.	Dr. E. E. McConnell	Not carcinogenic for Syrian golden hamsters of either sex. [Increased incidence of adrenal cortical adenomas in hamsters exposed to IR chrysotile when compared to pooled controls—males: 31/466 (7%) versus 29/244 (12%)*; females: 19/468 (4%) versus 23/234 (10%)*].
Asbestos, chrysotile and 1,2-dimethylhydrazine (CAS no. 540-78-8) 12001-29-5 10758-S	NTP-81-051 TR-246 06/23/81	Asbestos-cement, textiles, insulation; positive control, intestinal carcinogen	1% in diet, (intermediate range, IR); gavage (4 mg/kg every other week for 5 doses)	Illinois Inst. of Technology Research Inst.	Dr. E. E. McConnell	Combination study in Syrian golden hamsters of either sex was considered inadequate because no increase in DMH-induced intestinal neoplasia (DHM is known to induce gastrointestinal tumors in animals).

CARCINOGENESIS BIOASSAY RESULTS FROM THE NTP

2-Biphenylamine hydrochloride (2-amino-biphenyl) 2185-92-4 10438-K	NTP-81-035 TR-233 06/23/81	Chemical intermediate for C.I. Acid Red 15	Diet: 1000 and 3000 ppm	EG&G Mason Research Institute	Dr. K. M. Abdo	Not carcinogenic for F344 rats of either sex. Equivocal for male B6C3F <sub>1</sub> mice causing hemangiosarcoma of the circulatory system 0/50, 2/50, 3/50 (however, poor survival); carcinogenic for female B6C3F <sub>1</sub> mice causing hemangiosarcomas of the circulatory system (0/49, 1/50, 7/50*).
Bis(2-chloro-1-methyl ethyl) ether (BCMEE) 108-60-1 10523-N	NTP-81-055 TR-239 12/16/81	Paint and varnish removers; intermediate in dyes, resins and pharmaceuticals manufacture; and nematocide in Japan	Gavage (corn oil) 5 times/week: mice, 100 or 200 mg/kg	EG&G Mason Research Institute	Dr. M. Powers	Carcinogenic for B6C3F <sub>1</sub> mice causing alveolar/bronchiolar adenomas in males (5/50, 13/50*, 11/50) and in females (1/50, 4/50, 8/50*) and inducing in males dose-related hepatocellular carcinomas (5/50, 13/50, 17/50*). Rare forestomach tumors were probably associated with the test chemical (low dose: 1 male; high dose: 2 males and 3 females).
Bisphenol A 80-05-7 10034-Y	NTP-80-035 TR-215 P 10/15/80	Intermediate in manufacture of resins, flame retardants, and rubber chemicals	Feed: rats, 1000 or 2000 ppm; mice, 1000 Inc. 5000 or 10,000 ppm (female)	Litton Bionetics, Inc.	Dr. J. E. Huff	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex (increased incidences of leukemia in male rats 13/50, 12/50, 23/50* and lymphoma in male mice 2/49, 8/50*, 3/50 may have been associated with the test chemical).
Butyl benzyl phthalate 85-68-7 10422-E	NTP-80-025 TR-213 06/27/80	Additive to polymers (PVC) for flexibility and softness; plasticizer	Feed: 6000 or 12,000 ppm	EG&G Mason Research Institute	Dr. J. E. Huff	Male F344 rat data inadequate for evaluation (early death caused by hemorrhage); probably carcinogenic for female F344 rats, causing an increased incidence of mononuclear cell leukemia (7/49, 7/49, 18/50*); not carcinogenic for B6C3F <sub>1</sub> mice of either sex.
Caprolactam 105-60-2 10505-F	NTP-80-026 TR-214 P 06/27/80	To produce polycaprolactam (nylon 6); manufacture of polyamide synthetic fibers	Feed: rats, 3750 or 7500 ppm; mice, 7500 or 15,000 ppm	Litton Bionetics, Inc.	Dr. J. Dunnick	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
C.I. Acid Orange 10 1936-15-8 10698-Y	NTP-80-030 TR-211 02/18/81	Monoazo dye, in biological materials; paper, wood, leather, wool, silk, inks; and pencil coatings	Feed: rats, 1000 or 3000 ppm; mice, 3000 or 6000 ppm	Battelle Columbus Laboratories	Dr. J. E. Huff	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
C.I. Acid Red 14 3567-69-9 10723-Y	NTP-80-067 TR-220 P 10/15/80	Dye for nylon, silk, wool, leather, paper, wood	Feed: rats, 6000 or 12,000 ppm (male) and 12,000 or 25,000 ppm (female); mice 3000 or 6000 ppm	Battelle Columbus Laboratories	Dr. R. D. Irwin	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.

Table 1. (continued)

Chemical CAS No. NTP No.	NTP Report No. TR Report No. Peer Review Date	Use	Route/dose	Testing laboratory	NTP chemical manager	Results under the conditions of these tests <sup>b,c</sup>
C.I. Disperse Yellow 3 2832-40-8 10716-D	NTP-81-080 TR-222 P 02/18/81	Monoazo dye in nylon, wool, fur, poly(vinyl chloride), acrylic fibers, polystyrene, other thermoplastics	Feed: rats 5000 or 10,000 ppm; mice, 2500 or 5000 ppm	Battelle Columbus Laboratories	Dr. J. H. Mennear	Carcinogenic for male F344 rats, causing neo- plastic nodules of the liver (1/49, 15/50*, 10/50*); rare stomach tumors may have been associated with the test chemical (0/49, 4/50, 1/50). Not car- cinogenic for female rats or male B6C3F <sub>1</sub> mice. Carcinogenic for female mice causing hepato- cellular adenomas (0/50, 6/50*, 12/50**).
C.I. Solvent Yellow 14 842-07-9 10662-W	NTP-80-081 TR-226 02/18/81	Monoazo dye in hydrocarbon solvents, oils, fats, shoe polish, gasoline, soap	Feed: rats, 250 or 500 ppm; mice, 500 or 1000 ppm	Battelle Columbus Laboratories	Dr. R. D. Irwin	Carcinogenic for F344 rats, inducing neoplastic nodules of the liver in both males (5/50, 10/50, 30/50*) and females (2/50, 3/49, 10/48*); not carcinogenic for B6C3F <sub>1</sub> mice of either sex.
Cytembena 21739-91-3 10778-H	NTP-80-027 TR-207 P 06/27/80	Cytostatic agent	IP, 3 times/ week: rats, 7 or 14 mg/kg; mice, 12 or 24 mg/kg	Southern Research Institute	Dr. C. Grieshaber	Carcinogenic for F344 rats (male: mesotheliomas in the tunica vaginalis 0/50, 11/50*, 10/50* and in multiple organs 3/50, 26/50*, 26/50*; female: fibroadenomas in the mammary gland 13/49, 22/50, 36/50*); not carcinogenic for B6C3F <sub>1</sub> mice of either sex.
D&C Red No. 9 5160-02-1 10729-X	NTP-80-079 TR-225 P 02/18/81	Pigment in topical drugs and cosmetics	Feed: rats, 1000 or 3000 ppm; mice, 1000 or 2000 ppm	Battelle Columbus Laboratories	Dr. C. Grieshaber	Carcinogenic in male F344 rats inducing sarcomas of the spleen (0/50, 0/50, 26/48*) and neoplastic nodules in the liver (0/50, 6/50*, 7/49*); not carcinogenic for female F344 rats, although the increased number of female rats with neoplastic nodules of the liver (1/50, 1/50, 5/50) may have been related to compound administration. not carcinogenic for B6C3F <sub>1</sub> mice of either sex.
1,2-Dibromo-3- chloropropane (DBCP) 96-12-8 10465-X	NTP-81-021 TR-206 P 06/27/80	Soil fumigant for the control of nematodes	Inhalation, 6 hr/day, 5 days/week: 0.6 or 3.0 ppm	Hazleton Laboratories America, Inc.	Dr. J. E. Huff	Carcinogenic for F344 rats (nasal cavity tumors - male: 0/50, 40/50*, 39/49*; female: 1/50, 27/50*, 42/50* and tumors of tongue - male: 0/50, 1/50, 11/49*; female: 0/50, 4/50, 9/50* and cortical adenomas of the adrenal glands in females 0/50, 7/50*, 5/48*). Carcinogenic for B6C3F <sub>1</sub> mice (nasal cavity tumors - male: 0/45, 1/42, 21/48*; female: 0/50, 11/50*, 38/50* and alveolar/bronchiolar adenomas - male: 0/41, 1/40, 6/45*; female: 3/49, 3/49, 10/47**).

CARCINOGENESIS BIOASSAY RESULTS FROM THE NTP

1,2-Dibromoethane (ethylene dibromide) 106-93-4 10513-F	NTP-80-028 TR-210 P 06/27/80	Scavenger for lead in gasoline, soil and grain fumigant, intermediate in dye and drug syntheses	Inhalation, 6 hr/day, 5 days/week: 10 or 40 ppm	Hazleton Laboratories America, Inc.	Dr. M. Powers	Carcinogenic for F344 rats (both sexes - tumors of the nasal cavity and hemangiosarcomas of the circulatory system; male - mesotheliomas in the tunica vaginalis; female - alveolar/ bronchiolar tumors and mammary fibroadenomas). Carcinogenic for B6C3F <sub>1</sub> mice (both sexes - alveolar/bronchiolar adenomas and carcinomas; female - hemangiosarcomas, subcutaneous fibrosarcomas, nasal cavity tumors, and mammary gland adenocarcinomas).
2,6-Dichloro-p-phenylenediamine 609-20-1 10647-A	NTP-80-036 TR-219 P 10/15/80	Intermediate in manufacture of polyamide fiber; a polyurethane curative	Feed: rats, 1000 or 2000 ppm (males) and 2000 or 6000 ppm (females); mice, 1000 or 3000 ppm	Litton Bionetics, Inc.	Dr. C. Whitnire	Not carcinogenic for F344 rats. Carcinogenic for B6C3F <sub>1</sub> mice (male: hepatocellular adenomas 4/50, 7/50, 15/50*, carcinomas not significant 12/50, 13/50, 17/50; female: hepatocellular carcinomas 2/50, 2/50, 7/50 and adenomas 4/50, 4/50, 9/50 combined 6/50, 6/50, 16/50*).
Di(2-ethylhexyl) adipate 103-23-1 10497-E	NTP-80-029 TR-212 P 06/27/80	Plasticizer in vinyl plastics	Feed: 12,000 or 25,000 ppm	EG&G Mason Research Institute	Dr. M. Powers	Not carcinogenic for F344 rats of either sex. Carcinogenic for B6C3F <sub>1</sub> mice (male: hepatocellular adenomas 6/50, 8/49, 15/49*; female: hepatocellular carcinomas 1/50, 14/50*, 12/49*).
Di(2-ethylhexyl) phthalate (DEHP) 117-81-7 10188-J	NTP-80-037 TR-217 P 10/15/80	Plasticizer for PVC polymers	Feed: rats, 6000 or 12,000 ppm; mice, 3000 or 6000 ppm	EG&G Mason Research Institute	Dr. J. Douglas	Carcinogenic for F344 rats (male: hepatocellular carcinomas and neoplastic nodules combined 3/50, 6/49, 12/49*; female: hepatocellular carcinoma 0/50, 2/49, 8/50*). Carcinogenic for B6C3F <sub>1</sub> mice (hepatocellular carcinomas—male: 9/50, 14/48, 19/50*; female: 0/50, 7/50*, 17/50*).
Eugenol 97-53-0 10468-J	NTP-80-068 TR-223 02/18/81	Flavoring agent and fragrance, GRAS food additive	Feed: female rats, 6000 or 12,500 ppm; male rats and mice, 3000 or 6000 ppm	Southern Research Institute	Dr. J. A. Moore	Not carcinogenic for F344 rats of either sex; equivocal for B6C3F <sub>1</sub> mice (male: hepatocellular adenomas 4/50, 13/50*, 10/49 or carcinomas 10/50, 20/50*, 9/49 combined 14/50, 28/50*, 18/49; female: hepatocellular carcinomas 2/50, 3/49, 6/49 or adenomas 0/50, 4/49, 3/49 combined 2/50, 7/49, 9/49*).
FD&C Yellow No. 6 2783-94-0 10714-V	NTP-80-033 TR-208 P 06/27/80	Food and cosmetics coloring agent	Feed: 12,500 or 25,000 ppm	Battelle Columbus Laboratory	Dr. M. P. Dieter	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
Guar gum 9000-30-0 10752-T	NTP-80-083 TR-229 P 02/18/81	GRAS food additive, cosmetic stabilizer, pharmaceutical binder	Feed: 25,000 or 50,000 ppm	EG&G Mason Research Institute	Dr. M. P. Dieter	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.

Table 1. (continued)

Chemical CAS No. NTP No.	NTP Report No. TR Report No. <sup>a</sup> Peer Review Date	Use	Route/dose	Testing laboratory	NTP chemical manager	Results under the conditions of these tests <sup>b,c</sup>
Locust bean gum (carob seed gum) 9000-40-2 10753-X	NTP-80-066 TR-221 P 10/15/80	Stabilizer, thickener, and binder in foods and cosmetics	Feed: 25,000 or 50,000 ppm	EG&G Mason Research Institute	Dr. J. E. Huff	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
D-Mannitol 69-65-8 10868-L	NTP-81-052 TR-236 12/16/81	Chewable tablets, sugar replacement, candies and gums, osmotic diuretic, and fluid replacement	Feed: 25,000 or 50,000 ppm	Southern Research Institute	Dr. K. M. Abdo	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
Pentachloro- ethane 76-01-7 10149-G	NTP-81-084 TR-232 06/23/81	Solvent; intermediate (formerly) for tetrachloro- ethane manufacture	Gavage (corn oil): rats, 75 and 150 mg/kg, 5 times/week; mice, 250 and 500 mg/kg, 5 times/week	Gulf South Research Institute	Dr. J. H. Menear	Not carcinogenic for F344 rats of either sex (nephrotoxic for males: diffuse inflammation - 4/50, 14/49*, 83/50*, mineralization - 4/50, 29/49*, 29/50*); carcinogenic for B6C3F <sub>1</sub> mice (male: hepatocellular carcinoma 4/48, 26/44*, 7/45; female: hepatocellular carcinoma 1/46, 28/42*, 13/45* and hepatocellular adenoma 2/46, 8/42*, 19/45*).
Polybrominated biphenyl mixture (Firemaster FF-1) 67774-32-7 10800-C	NTP-81-082 TR-244 06/23/81	Flame retardant	Gavage (corn oil): 0, 0.1, 0.3, 1.0, 3.0, and 10 mg/kg, 5 times/week for 6 months, held for lifetime observation	NIEHS/NTP	Dr. B. N. Gupta	Carcinogenic for F344 rats (male: hepatocellular carcinoma 0/33, 2/39, 0/40, 1/33, 7/33*, 7/31*, female: neoplastic nodules 0/20, 2/21, 0/21, 2/11, 5/19*, 8/20* and hepatocellular carcinoma 0/20, 0/21, 0/21, 0/11, 3/19, 7/20*); carcinogenic for B6C3F <sub>1</sub> mice causing hepatocellular carcinoma (male: 12/25, 8/27, 8/24, 12/25, 15/23, 21/22*; female: 0/13, 0/19, 2/15, 2/11, 3/17, 7/8*).
Propyl gallate 121-79-9 10564-Y	NTP-81-042 TR-240 12/16/81	Antioxidant in foods containing fats/ oils, in food packaging and in cosmetics	Feed: 6000 or 12,000 ppm	Southern Research Institute	Dr. K. M. Abdo	Not considered carcinogenic for F344 rats, although there was evidence of an increased number of male rats with preputial gland tumors (1/50, 8/50*, 0/50), islet-cell adenomas of the pancreas (0/50, 8/50*, 2/50), and pheochro- mocytes of the adrenal glands (4/50, 13/48*, 8/50); rare tumors of the brain occurred in female rats (0/50, 2/50, 0/49). Not carcinogenic for B6C3F <sub>1</sub> mice of either sex, although the increased number of male mice with malignant lymphoma (1/50, 3/49, 8/50*) may have been associated with the administration of propyl gallate.

Stannous chloride 7772-99-8 10747-F	NTP-81-033 TR-231 06/23/81	Food preservative, reducing agent in tinplating, stabilizer (colors, perfumes, soaps)	Diet: 1000 or 2000 ppm	Southern Research Institute	Dr. M. P. Dieter	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex. (Increase in C-cell tumors of the thyroid gland in male rats may have been associated with the administration of the test chemical: adenomas 2/50, 9/49*; 5/50 or carcinomas 0/50, 4/49, 3/50 combined 2/50, 13/49*, 8/50*.)
Tara gum 39800-88-4 10793-E	NTP-80-078 TR-224 P 02/18/81	Formerly cosmetic stabilizer, no longer imported into U.S.	Feed: 25,000 or 50,000 ppm	EG&G Mason Research Institute	Dr. C. Grieshaber	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex.
2,3,7,8-Tetra-chlorodibenzo-p-dioxin (TCDD) 1746-01-6 10157-G	NTP-80-031 TR-209 P 06/27/80	Chemical contaminant in trichlorophenols; 2,4,5-trichloro-phenoxyacetic acid; hexachlorophene	Gavage, 2 days/week; rats and male mice-0.01, 0.05, or 0.5 mg/kg/wk; female mice-0.04, 0.2, or 2.0 mg/kg/wk	Illinois Inst. of Technology Research Inst.	Dr. J. A. Moore	Carcinogenic for Osborne-Mendel rats (male: follicular cell thyroid adenomas 1/69, 5/48*, 6/50*, 10/50*; female: neoplastic nodules of the liver 5/75, 1/49, 3/50, 12/49*); carcinogenic for B6C3F <sub>1</sub> mice (male: hepatocellular carcinomas 8/73, 9/49, 8/49, 17/50*; female: 1/73, 2/50, 2/48, 6/47*; female: follicular cell adenoma 0/69, 3/50, 1/47, 5/46*).
2,3,7,8-Tetra-chlorodibenzo-p-dioxin (TCDD) 1746-01-6 10157-G	NTP-80-032 TR-201 P 06/27/80	Chemical contaminant in trichlorophenols; 2,4,5-trichloro-phenoxyacetic acid; hexachlorophene	Dermal, 3 days/week; male mice, 0.001 mg; female mice, 0.005 mg	Illinois Inst. of Technology Research Inst.	Dr. J. A. Moore	Not carcinogenic for male Swiss-Webster mice; (increase in fibrosarcomas of the integumentary system—3/42, 7% versus 6/28, 21%—may have been associated with skin application of TCDD); carcinogenic for female Swiss-Webster mice (fibrosarcomas of the integumentary system—2/41, 5% versus 8/27*, 30%).
2,3,7,8-TCDD and dimethyl-benzanthracene (DMBA) 1746-01-6 10157-G	NTP-80-032 TR-201 P 06/27/80	Chemical contaminant in trichlorophenols; 2,4,5-trichloro-phenoxyacetic acid; hexachlorophene	DMBA—50 mg 1 week prior to TCDD dermal	Illinois Inst. of Technology Research Inst.	Dr. J. A. Moore	Initiation-promotion study considered inadequate because DMBA was not tested alone and DMBA-TCDD induced fibrosarcoma incidence not greater than that observed with TCDD alone (Swiss-Webster mice).
1,1,1,2-Tetra-chloroethane 630-20-6 10651-J	NTP-81-053 TR-237 12/16/81	Chemical intermediate for producing tri- and tetra-chloroethylene	Gavage (corn oil) 5 times/week; rats, 125 or 250 mg/kg; mice, 250 or 500 mg/kg	Gulf South Research Institute	Dr. L. Birnbaum	Not demonstrated carcinogenic for F344 rats (increased incidence of combined neoplastic nodules and hepatocellular carcinomas in males 0/49, 1/49, 3/48 and fibroadenomas of mammary gland in females 6/49, 15/49*, 7/46 may have been associated with test chemical). Carcinogenic in B6C3F <sub>1</sub> mice (hepatocellular carcinomas - females: 1/49, 5/46, 6/48*; hepatocellular adenomas - male: 6/48, 14/46*, 21/50*; females 4/49, 8/46, 24/48*).

Table 1. (continued)

Chemical CAS No. NTP No.	NTP Report No. TR Report No. Peer Review Date	Use	Route/dose	Testing laboratory	NTP chemical manager	Results under the conditions of these tests <sup>b,c</sup>
Vinylidene chloride (1,1-dichloroethylene) 75-35-4 10109-A	NTP-80-082 TR-228 02/18/81	Intermediate for 1,1,1-trichloroethane, monomer for vinylidene copolymers	Gavage, 5 times/week; rats, 1 or 5 mg/kg; mice, 2 or 10 mg/kg	Gulf South Research Institute	Dr. R. S. Chhabra	Not carcinogenic for F344 rats or B6C3F <sub>1</sub> mice of either sex (increased incidence of liver necrosis in male mice 1/46, 3/46, 7/49*).
Zearalenone 17924-92-4 10770-C	NTP-81-054 TR-235 12/16/81	Nonsteroid estrogenic mycotoxin (anabolic steroid)	Feed: rats, 25 or 50 ppm; mice, 50 or 100 ppm	Southern Research Institute	Dr. D. Goldman	Not carcinogenic for F344 rats of either sex; should be considered carcinogenic for B6C3F <sub>1</sub> mice (male: pituitary adenoma 0/40, 4/45, 6/44*; female: pituitary adenoma 3/46, 2/43, 13/42*; hepatocellular adenoma 0/50, 2/49, 7/49*).
Ziram (Zinc dimethyldithiocarbamate) 137-3-4 10590-G	NTP-81-057 TR-238 12/16/81	Fungicide and accelerator in rubber vulcanization	Feed: rats, 300 or 600 ppm; mice, 600 or 1200 ppm	Southern Research Institute	Dr. D. Goldman	Carcinogenic for male F344 rats causing C-cell carcinomas of the thyroid 0/50, 2/49, 7/49*; not carcinogenic for female F344 rats or for male B6C3F <sub>1</sub> mice; interpretation of the increased number of female B6C3F <sub>1</sub> mice with alveolar/bronchiolar adenoma (2/50, 5/49, 10/50*) is complicated because of a concomitant Sendai viral infection (in all groups of mice).

<sup>a</sup>P = published.<sup>b</sup>Incidence results are ordered by concurrent controls, low dose, and high dose groups, with the numerator being the number of tumor (or noneoplastic lesion) bearing animals and the denominator the number of animals examined.<sup>c</sup>\* = statistically significant,  $p < 0.05$ .

the broadening of the testing protocols through addition of other specific studies to the prechronic phases (single, 14-day, and 90- or 120-day studies) of the long-term bioassay and, to a lesser extent, to the chronic phase (104 weeks) of the bioassay.

Accomplishments of NTP programs during FY 1981 and program plans for FY 1982 are described in the *NTP Annual Plan for Fiscal Year 1982*.

## NTP Chemical Nomination and Selection

Because more chemicals are nominated for NTP consideration than can be selected for study, the NTP Executive Committee formulated a set of program guidelines. These resultant eight chemical selection criteria motivate an NTP matrix which operates throughout the NTP. All research, testing and test development/validation efforts start here.

The NTP Executive Committee acts under the principle that industry will test chemicals for health and environmental effects as intended and mandated by Congress under legislative authorities. Therefore, the NTP, using these chemical selection principles, will test: (1) chemicals found in the environment that are not closely associated with commercial activities; (2) desirable substitutes for existing chemicals, particularly therapeutic agents, that might not be developed or tested without federal involvement; (3) chemicals that should be tested to improve scientific understanding of structure-activity relationships and thereby assist in defining groups of commercial chemicals that should be tested by industry; (4) certain chemicals tested by industry, or by others, the additional testing of which by the federal government is justified to verify the results; (5) previously tested chemicals for which other testing is desirable to cross-compare testing methods; (6) "old chemicals" with the potential for significant human exposure which are of social importance but which generate too little revenue to support an adequate testing program (some of these may be "grandfathered" under FDA laws); (7) two or more chemicals together, when combined human exposure occurs (such testing probably cannot be required of industry if the products of different companies are involved); and (8) in special situations, as determined by the Executive Committee, marketed chemicals which have potential for large-scale and/or intense human exposure, even if it may be possible to require industry to perform the testing.

Most chemicals are nominated and selected for testing because toxicologic information is lacking and because the potential exists for human exposure. Other important criteria include production

levels, physical and chemical properties, agency interests, and significance to society. The NTP toxicology testing strategy: identify with assurance the major toxic effects for each chemical studied. This includes (in addition to identifying chemical mutagens and carcinogens) damage to critical target organs such as the reproductive system, lungs, liver, and nervous system.

Nominations of chemicals for toxicological testing are submitted by the NTP participating agencies as well as other government agencies, industry, labor, and the public. The nominating source is asked to submit the name of the chemical, the particular toxicological tests desired, the rationale for testing, and to provide the available background data on production, use, exposure, environmental occurrence, and toxic properties in a supporting summary document.

An initial examination determines which proposed chemicals have already been tested, are being tested, are scheduled for test, or have been previously considered and rejected for testing by the NTP or its predecessors.

Literature containing relevant data is assessed and literature summaries are prepared for each chemical. Included in each literature summary are sections on chemical identification and physical properties, surveillance index (production, use, environmental occurrence, and available regulatory status and exposure limits), human exposure and health effects, research hypothesis to be tested, categories of study, and source of and reason(s) for nomination. Chemicals nominated for mutagenicity testing are reviewed only with regard to the available genetic toxicology information.

These summaries are reviewed and evaluated by the Chemical Evaluation Committee (composed of representatives from CPSC, EPA, FDA, OSHA, NCI, NCTR, NIEHS, NIOSH, and NTP)\* who recommend the type(s) of testing to be considered. All suggestions and recommendations for future research and testing activities must satisfy at least one of the eight NTP principles of chemical selection.

Announcements listing the chemicals and the recommended types of testing appear in the *Federal Register* and the *NTP Technical Bulletin*. These notices solicit comments as well as informa-

---

\*CPSC = Consumer Product Safety Commission; EPA = Environmental Protection Agency; OSHA = Occupational Safety & Health Administration; NCI = National Cancer Institute; NCTR = National Center for Toxicological Research; NIEHS = National Institute of Environmental Health Sciences; NIOSH = National Institute for Occupational Safety and Health; and NTP = National Toxicology Program.

tion on completed, ongoing, and planned testing in the private sector. These steps are taken to encourage others outside the immediate program to participate in the NTP evaluation and selection process, as well as to specifically prevent unnecessary duplication. Revised summaries with additional public input are forwarded to the Board of Scientific Counselors for review. The Board evaluates these data and makes recommendations to the Executive Committee.

Final summaries are submitted to the NTP Executive Committee who decide whether to select, defer, or reject the chemicals for testing. Following Executive Committee action, the chemicals are referred by the NTP Steering Committee to one or more participating agencies within the NTP: NIEHS, NIOSH, NCTR. At this stage certain approved chemicals may be identified as being inappropriate candidates for testing as a result of technical or budgetary reasons or in some cases public information describing ongoing testing may only have been submitted following Executive Committee decision. Such chemicals are then returned to the Executive Committee for reconsideration.

All chemicals selected are then tested as time and resources permit.

## Toxicology and Carcinogenesis Bioassay

The "standard" two-year carcinogenesis bioassay remains as the most definitive method for detecting chemical carcinogens in animals. The standard protocol as developed by the NCI (and frequently still used by the NTP) typically uses two rodent species (usually Fischer 344 rats and B6C3F<sub>1</sub> mice), both sexes, and administration of multiple dose levels (concurrent controls, low dose, and high dose) of a chemical to groups of 50 animals, beginning at weaning and ending after two years. These experiments are designed primarily to determine whether selected chemicals produce cancer in animals. Chemicals tested in the NTP Carcinogenesis Bioassay Program are chosen primarily on the bases of human exposure, available (or lack of) toxicology data, level of production, and chemical structure. Selection *per se* is not an indicator of a chemical's carcinogenic potential.

Negative results, in which the test animals do not have a greater incidence of cancer than control animals, do not necessarily mean that a test chemical is not a carcinogen, inasmuch as the experiments are conducted under a limited set of conditions. Positive results demonstrate that a test chemical is carcinogenic for animals under the

conditions of the test and indicate that exposure to the chemical is a potential hazard to humans. The determination of the risk to humans from chemicals found to be carcinogenic in animals often requires a wider analysis which at present extends beyond the purview of these studies.

The results of the bioassay also serve as the reference base for the validation of short-term carcinogenesis assays. Two additional objectives have been identified as priority items: (1) to expand the bioassay experimental protocols to extend and better characterize the toxicologic profile of chemicals; and (2) to investigate, develop, and validate accurate, less costly, and more rapid methods for detecting carcinogenic potential.

Under the NTP, the carcinogenesis bioassay procedure(s) has been and continues to be changed to meet the objective of a broadened toxicologic characterization of chemicals and, further, to lead or stay abreast of advancing scientific developments. Prior to NTP involvement, the prechronic phases of the bioassay—which include single dose (acute), 14-day repeated dose, and 90- to 120-day repeated dose studies—were conducted to determine gross toxicity and general target organ effects at different dose levels as a primary basis for setting appropriate doses for the two-year bioassay studies. Now, the NTP has begun to gather routinely other information related to target organ effect: chemical disposition, fertility and reproduction, urinalysis, and hematology also are obtained from the prechronic studies—especially the 90-day study; certain other specific studies as applicable are included in the chronic two-year studies as well. Once those parameters that may be altered through exposure to the tested chemicals are identified, then suspect chemicals are referred to specific organ system groups for more detailed study of the functional, biochemical, and morphologic effects of the test compounds. Also, wider analysis of the quantitative and comparative absorption, distribution, metabolism, and excretion patterns may be desired. For instance, 28 (70%) of the 40 chemical starts in FY 1980 included specific toxicology studies in the prechronic testing phase. All chemicals started on test in FY 1981 had an expanded design including other select studies. Significantly all chemicals selected for chronic bioassay will be profiled for chemical disposition patterns. The goal is to ensure that all major toxic effects will be identified for each chemical being considered for long-term bioassays.

With this composite information base, the doses for the chronic study are selected. The high dose, termed the estimated maximum tolerated dose (EMTD), represents the highest dose of a chemical

or substance given during a chronic study that can be predicted not to alter the treated animals' normal longevity from toxic effects other than carcinogenicity. The low dose ordinarily equals 1/2 EMTD. Other empirical factors include weight gain/food consumption data; for instance, a decrease in weight gain near 10-15% (not associated with a tumorigenic response) is often used as a general indication that the EMTD was achieved.

Prior to commencing the actual long-term carcinogenesis bioassay, all chemicals undergo genetic toxicology testing in at least five *in vitro* short-term assays: (1) gene mutations in bacteria—*Salmonella typhimurium* microsome; (2) gene mutations in mammalian cells—mouse lymphoma (L5178Y, thymidine kinase); (3) chromosome damage in mammalian cells—cytogenetic damage and sister chromatid exchange (*in vitro*, CHO); (4) a mammalian cell transformation assay—(BALB/c -3T3); and (5) a direct measure of DNA damage/repair (which does not necessarily result in mutation or transformation)—unscheduled DNA synthesis (rat hepatocytes). These data, together with other prechronic bioassay information, are used by the experimental design groups for preparing appropriate study protocols and are used by staff for assisting in establishing priorities for chemicals queued into the long-term carcinogenesis bioassay. A key decision that must be made at this juncture between the completion of the prechronic phase and the beginning of the chronic study centers directly on whether indeed the lifetime bioassay should be done at all.

Thus, while the lifetime animal bioassay remains the best procedure for determining the carcinogenic potential of chemicals, NTP does not ordinarily use a standardized design. Rather the design is adapted to the special testing needs identified for the particular chemical. The NTP tailors its testing protocols to the particular chemicals based on the results from the prechronic testing phases, on available literature, and on structure-activity rela-

tions. These new protocols permit better, more specific information to be generated for the tested compounds, which increases the effectiveness of the tests for potential human risk estimations. Such protocols also will be useful as guidelines for testing undertaken by other agencies and by industry. As examples, the NTP continues to pursue actively other design methodologies—increase the number of dose levels, "unbalanced" distribution of animals among dose groups, interim kills, and reduced essential histopathology.

## Bioassay Results

During FY 1981, 23 long-term carcinogenesis bioassays were completed and the conclusions and data were evaluated and approved by the NTP staff review committee and subsequently by the external NTP peer review panel. Under the conditions of these carcinogenesis bioassays, 12 (52%) were considered negative, 10 (44%) positive, and 1 (4%) equivocal. One, polybrominated biphenyl (PBB) mixture (Firemaster FF-1), was conducted using a broadened experimental protocol aimed at providing a better dose-response determination (through use of six doses) and at giving more data on toxicologic end points other than induction of cancer. Nontumor toxicities of this PBB included porphyrogenic effects, decreases in serum thyroid hormones, hematotoxicity, enzyme alterations, and hepatotoxicity.

Since the NTP became actively involved in the carcinogenesis bioassay technical report review process, 40 experimental studies have been completed (with draft or final reports being issued): 20 (50%) positive, 14 (35%) negative, 4 (10%) equivocal, 2 (5%) inadequate; see Table 1.

As of February 1982: (1) Twenty-five chemicals have been newly assigned to the testing laboratories (Table 2). (2) Seventy-nine chemicals (89 separate studies) were in the prechronic testing

Table 2. Chemicals assigned to testing laboratories (February 1982).

Azodicarbonamide (inhalation)	Glutaraldehyde	Proprantheline bromide
<i>o</i> -Benzyl- <i>p</i> -chlorophenol	<i>N</i> -Isopropyl- <i>N'</i> -phenyl- <i>p</i> -phenylenediamine	Quercetin
C.I. Acid Red 114	Isoproterenol hydrochloride	Riddelliine
C.I. Direct Blue 15	Manganese sulfate	Triamterene
C.I. Direct Blue 218	Methdilazine (gavage)	1,2,3-Trichloropropane
3,3'-Dimethoxybenzidine	Methdilazine (feed)	Tricresyl phosphate
3,3'-Dimethylbenzidine	Methylphenidate	Trimellitic anhydride
<i>N,N</i> -Dimethylformamide	<i>p</i> -Nitroaniline	Turmeric, oleoresin (curcumin)
Ethyl benzene	<i>o</i> -Nitroanisole	

phase (Table 3); most include one or more additional toxicology studies in the prechronic testing phase. (3) Ninety-six chemicals frequent the chronic two-year testing stage (Table 4). There are a number of new or ongoing long-term carcinogenesis studies concerned with chemicals or mixtures of chemicals which humans encounter in occupational settings (benzene, diesel fuel marine, gentian violet, naphthalene, Navy fuels JP-5, as examples). (4) Twenty-nine chemicals (35 separate studies) are in the histopathology phase (Table 5). (5) For 10 chemicals, reports are being written or draft reports are

in program review (Table 6). Including the new chemical starts, there were 185 bioassays in either the prechronic or the chronic bioassay testing phases at the end of FY 1981 (Tables 3 and 4). (6) In FY 1982, the NTP expects to complete (through peer review) 29 long-term bioassays (Tables 6 and 7).

Abstracted from the peer-reviewed approved draft technical reports, Table 1 contains assorted information about the particular chemical carcinogenesis study (CAS Registry Number, peer review date, use, route and dose, contract laboratory, and

Table 3. Chemicals in the prechronic testing phase (February 1982).

Acetonitrile	Furfuryl alcohol
Allyl glycidyl ether	HC Yellow 4
1-Amino-2,4-dibromoanthraquinone	Hexachlorocyclopentadiene
Amphetamine sulfate	Hexachloroethane
Azodicarbonamide (gavage)	Hydroquinone
Benzaldehyde	4-Hydroxyacetanilide
2,2-Bis(bromomethyl)-1,3-propanediol (gavage)	5-Hydroxytryptophan
2,2-Bis(bromomethyl)-1,3-propanediol (dermal)	Isobutyl nitrite
$\gamma$ -Gamma-butyrolactone	Mercuric chloride
$\beta$ -Cadinene	Methapyriline (acidified H <sub>2</sub> O)
Caffeine	Methapyriline (neutral H <sub>2</sub> O)
Carbon disulfide	6-Methylcoumarin
<i>d</i> -Carvone	<i>N</i> -Methylolacrylamide
Catechol	Monochloroacetic acid
Chloramine	Nitrobenzene (gavage)
Chloramphenicol	Nitrobenzene (dermal)
Chloroacetophenone	Ochratoxin A
<i>p</i> -Chloroaniline	Palladium (II) chloride
<i>o</i> -Chlorobenzalmalononitrile	Pentachloroanisole
Chlorpromazine hydrochloride	Pentachlorophenol, Dowicide EC-7
1,8-Cineol (eucalyptol)	Pentachlorophenol, DP-2
Cinnamaldehyde	Pentachlorophenol, purified
C.I. Pigment Red 23	Pentachlorophenol, technical
C.I. Pigment Red 3	Phenolphthalein
Coumarin	Phenytoin
2,4-Diaminophenol hydrochloride	Polybrominated biphenyl (FF-1)
4,4'-Diamino-2,2'-stilbenedisulfonic acid	Polysorbate 80
2,3-Dibromo-1-propanol (gavage)	Probenecid
2,3-Dibromo-1-propanol (dermal)	Promethazine
Diethyl phthalate	Pyrimidine
3,4-Dihydrocoumarin	<i>p</i> -Quinone
Dimethoxane	Resorcinol
Dimethyloldihydroxyethyleneurea (gavage)	Sodium azide
Dimethyloldihydroxyethyleneurea (inhalation)	Tetrahydrofuran
Doxylamine	Tetranitromethane
Epinephrine hydrochloride	Thenyldiamine
1,2-Epoxybutane	Titanocene dichloride
Ethyl bromide	Toluene, commercial (gavage)
Ethyl chloride	Toluene, commercial (inhalation)
Ethylenediamine	Tripeleneamine
Ethylene glycol	Tris(2-chloroethyl) phosphate
Ethylenethiourea	1-Vinyl-3-cyclohexene dioxide (gavage)
Formaldehyde	1-Vinyl-3-cyclohexene dioxide (dermal)
Furan	2,6-Xylidine
Furfural	

Table 4. Chemicals in the chronic testing phase (February 1982).

2-Amino-4-nitrophenol	HC Blue 2
2-Amino-5-nitrophenol	HC Red 3
Ampicillin trihydrate	Hexylresorcinol
Benzene	Hydrochlorothiazide
Benzofuran	Iodinated glycerol
Benzyl alcohol	Isophorone
Benzyl chloride	Lauric acid diethanolamine
Boric acid	D-Limonene
Bromodichloromethane	Malonaldehyde
Bromoform	2-Mercaptobenzothiazole
1,3-Butadiene	8-Methoxypsoralen
2-Butanone peroxide	$\alpha$ 1-Methylbenzyl alcohol
<i>t</i> -Butyl alcohol	Methyl carbamate
<i>n</i> -Butyl chloride	Methyl Dopa
Castor oil	Methylene chloride
Chlorendic acid	Methyl methacrylate
Chlorinated trisodium phosphate	Nalidixic acid
Chlorodibromomethane	Navy fuels JP-5 (petroleum derived)
3-Chloro-2-methylpropene	Nitrofurantoin
Chlorowax 40	Nitrofurazone
Chlorowax 500C	Oleic acid diethanolamine
Chlorpheniramine maleate	Oxytetracycline hydrochloride
C.I. Acid Orange 3	Penicillin V potassium
C.I. Basic Red 9 ( <i>p</i> -rosaniline)	Pentachloronitrobenzene
C.I. Disperse Blue 1	Pentaerythritol tetranitrate
Coconut oil acid diethanolamine	Phenylbutazone
Decabromodiphenyl oxide	Phenylephrine hydrochloride
<i>p</i> -Dichlorobenzene	<i>N</i> -Phenyl-2-naphthylamine
2,4-Dichlorophenol	<i>o</i> -Phenylphenol
Dichlorvos	Pyridine
Diesel fuel marine	Rhodamine 6G
Diethanolamine	Rotenone
Diglycidylresorcinol ether (DGRE)	Roxarsone
<i>N,N</i> -Dimethylaniline	Sodium fluoride
Dimethyl hydrogenphosphite	Styrene oxide
Dimethyl methylphosphonate	Succinic anhydride
Dimethyl morpholinophosphoramidate	Sulfamethazine
Dimethylvinylchloride	Tetrachloroethylene
Diphenhydramine hydrochloride	Tetracycline hydrochloride
Ephedrine sulfate	Tetrakis(hydromethyl)phosphonium chloride (THPC)
1,2-Epoxyhexadecane	Tetrakis(hydroxymethyl)phosphonium sulfate (THPS)
Erythromycin stearate	Trichlorfon
Ethylene chlorohydrin	Tris(2-ethylhexyl) phosphate
Ethylene glycol monoethyl ether	4-Vinylcyclohexene
Ethylene oxide	Vinyl toluene
Furosemide	Witch hazel
Gentian violet	Xylenes
Glutaraldehyde	Xylene sulfonic acid, sodium salt
Glycidol	

the NTP scientist responsible for design, implementation, interpretation, and report preparation) and the abbreviated results. This table includes summary information on the six chemical carcinogenesis bioassays evaluated in December 1981, on the 23 reported in FY 1981, on the nine completed and peer reviewed in June 1980, and on two

considered inadequate (TCDD-DMBA dermal and asbestos-DMH oral studies). The letter "P" following the *Technical Report (TR)* number in column two means that the *NTP Technical Report* has been published; detailed condensations of four carcinogenesis bioassays so designated follow this article. The others settle into various stages of publica-

Table 5. Chemicals in the histopathology phase (February 1982).

Asbestos, amosite	Diglycidylresorcinol ether (DGRE)	Monuron
Asbestos, chrysotile (SR)	Dimethylbenzanthracene (DMBA)/	<i>p</i> -Nitrophenol
Asbestos, chrysotile (IR)	tetradecanoyl phorbol acetate (TPA)	Propylene
Asbestos, crocidolite	Dodecyl alcohol, ethoxylated	Propylene oxide
Chlorobenzene	Ethyl acrylate	Sodium dodecyl sulfate
C.I. Acid Yellow 73	Gilsonite	Sodium (2-ethylhexyl) alcohol sulfate
Diallyl phthalate (rats)	HC Blue 1	Tetrachloroethylene
<i>o</i> -Dichlorobenzene	8-Hydroxyquinoline	Tremolite
1,2-Dichloropropane	Methylene chloride	1,1,1-Trichloroethane
1,3-Dichloropropane	Mirex	Trichloroethylene

Table 6. Chemicals in the draft report—program review process (February 1982).

Allyl isovalerate	Geranyl acetate	2,4-Toluene diisocyanate and
Ascorbic acid	Melamine	2,5-toluene diisocyanate
Benzyl acetate	4,4'-Methylenedianiline dihydrochloride	Trichloroethylene
Diallyl phthalate (mice)	Tetrachloroethylene	

Table 7. Chemicals for which carcinogenesis bioassays will be completed (through peer review) in FY 1982 (February 1982).<sup>a</sup>

Agaritrine <sup>b</sup>	Dimethylbenzanthracene (DMBA)/	Tetrachloroethylene
Asbestos, amosite	12-O-tetradecanoylphorbol-13-acetate (TPA)	Tremolite
Asbestos, chrysotile (short range)	D-Mannitol	Trichloroethylene
Asbestos, chrysotile (intermediate range)	<i>N</i> -Nitrosodiethanolamine <sup>b</sup>	2,6-Xylidine
Asbestos, crocidolite	Propyl gallate	Zearalenone
Bis(2-chloro-1-methylethyl) ether (BCMEE)	Rotenone	Ziram
and 2-chloro-1-methylethyl	Sodium (2-ethylhexyl) alcohol sulfate	
(2-chloropropyl) ether	1,1,1,2-Tetrachloroethane	

<sup>a</sup>Plus those ten chemicals listed in Table 6.

<sup>b</sup>Journal publication (no technical report).

tion; these will be featured in future carcinogenesis bioassay results articles from the National Toxicology Program.

*Document Availability*—To receive copies of the *NTP Annual Plan for Fiscal Year 1982* (and for FY 1981), the *NTP Technical Bulletin*, and the *NTP Technical Reports* on a particular chemical carcinogenesis bioassay study, write: Mr. S. d'Arazién, NTP Public Information Office, National Toxicology Program, P. O. Box 12233, Research Triangle Park, North Carolina 27709 (919-541-3991; FTS 8-629-3991).

*Technical Information*—For more detailed information about completed, ongoing, or planned carcinogenesis bioassay studies, contact: Ms. Joan Chase, National Toxicology Program, 3A06

Landow Building, 7910 Woodmont Avenue, Bethesda, Maryland 20205 (301-496-1152; FTS 8-496-1152).

*Chemical Nominations*—Persons or organizations wishing to nominate other chemicals for testing should send the name of the chemical, testing requested, rationale, and other supporting information to: Dr. D. Canter, Chemical Nominations, National Toxicology Program, Building 31, Room 2B55, Bethesda, Maryland 20205.

I thank Dr. Larry Hart for use of the preprint version of the *NTP Annual Plan for Fiscal Year 1982*; Dr. Joseph Haseman for helping prepare and verify Table 1; Mr. Jeffrey Sensenig and Mr. R. Michael Rowley for developing the BIOTEXT software file (Table 1); Ms. Florence Jordan and Ms. Pamela Lemon for initiating and maintaining the BIOTEXT file; each listed Chemical Manager; and Ms. Gerry Wandrisco for assistance in preparing this manuscript.