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UNITED STATES GOVERNMENT

U.S. CONSUMER PRODUCT
SAFETY COMMISSION

Memorandum

RECEIVED
OFFICE OF THE SECRETARYTO : The Commissioners
THRU : Michael Brown, Executive Director

NOV 3 10 24 PM '78

DATE: Oct. 31, 1978

FROM : Joann H. Langston, Associate Exec. Dir., Hazard Identification & Analysis
Don Clay, Acting Associate Exec. Dir., Engineering and Science

SUBJECT: Staff Chemical Screening Procedures and Transmittal of Information on Certain Chemicals

The purpose of this memo is to transmit information on two lists of carcinogenic chemicals and to inform the Commission about the procedures that are used by the staff to screen information on chemicals for their carcinogenicity and for their presence in consumer products. Reports and other information on chemicals that have been received periodically by the staff are being processed systematically in order to provide the information the Commission needs for its decision making. These procedures are described below; specific reference is made to the lists which are the result of applying these procedures.

On October 5, 1978, the Commission directed the staff to provide information on two lists of chemicals totaling 53, that had come to the Commission's attention. These lists are the International Agency for Research on Cancer (IARC), compilation of 26 known human carcinogens and a current listing of 27 National Cancer Institute (NCI) bioassay reports which show carcinogenic effects in animals. The lists of chemicals and the accompanying information are attached. The lists represent a partial output of the continuing screening process and, as such, they are certain to change as additional information is acquired.

The two lists of 53 chemicals have been separated and recombined into 4 lists in order to show more easily the process status of each chemical.

- List 1. The original two lists: all 26 chemicals from the IARC human carcinogen list and all 27 chemicals that show carcinogenic responses in animals selected by the staff from 102 bioassays received from NCI.
- List 2. Those chemicals from List 1 for which the staff has determined that the Commission has no jurisdiction.
- List 3. Those chemicals from List 1 for which regulatory action has been, or is being, taken by CPSC or another agency.
- List 4. The remaining chemicals that are of interest to CPSC because they may be possible candidates for remedial action. These chemicals need additional investigation or research work to further establish their priority rankings, determine whether they are in consumer products and determine whether they may pose a hazard to consumers.

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The IARC list of 26 is, for the most part, an old list which incorporates many of the well known carcinogens that have long been the target of concern by this agency, other agencies and the IRLG. Several have been regulated by CPSC. Eight of the chemicals are considered by the staff to require some additional investigation to determine their precise status with regard to hazards, the jurisdiction of CPSC and possible remedial alternatives.

The list of 27 chemicals was derived by the staff of Hazard Identification and Analysis (HIA) and Engineering and Science (ES) over the past two months from 102 NCI bioassay reports that had been received by August 1978. The 27 have reached an interim stage in the ongoing screening process of the carcinogen policy. They are chemicals that have the possibility of being in consumer products and that are possible carcinogens. Since screening is incomplete on all these chemicals, no definite answer to the likelihood of their being candidates for remedial action can be made at this time. The 75 other chemicals from the 102 bioassay reports have been dropped from further consideration on the basis of jurisdiction or lack of evidence of carcinogenicity.

List 4 contains the 8 chemicals from the IARC list; on which further information must be developed, and the 27 chemicals selected from the bioassay reports. We emphasize that these chemicals are now in the process of being assessed for their remedial requirements. List 4 arrays these chemicals in a preliminary ordering for further study which will provide the toxicological, use, and exposure data with which the Commission can make decisions on whether to pursue remedial action.

As new bioassay reports and other information are received, additions will be made to the group that List 4 represents. For example, two other groups of bioassay reports, totaling 31, were started through the screening process in October and an additional group of 37 was received last week and are about to start the process. The procedure that the staff is using to handle all candidates for screening is essentially as follows:

- (1) New (NCI) bioassay reports (or reports indicating a carcinogenic concern from any source) are received by ES or HIA and a copy is immediately sent to the National Injury Information Clearinghouse for retention with notice of the transfer sent to other HIA and ES staff and OPM. The report is then handled by each unit according to its assigned function.
- (2) A list of these new bioassay reports is prepared by Epidemiology--Program Analysis and, in consultation with Economic Analysis, each report is given a preliminary priority ranking.
- (3) This initial list (the 102 bioassays was such a list) is forwarded to Health Sciences for a preliminary indication as to whether the substance may be carcinogenic (yes-no) (the list of 27 chemicals from the bioassay reports is the result of this step in the screening process).

The purpose of the first three steps is to organize the chemical data, start them through the formal screening process and eliminate those chemicals which definitely do not warrant further CPSC consideration, thus conserving resources.

(4) Program Analysis processes the "yes" chemicals by searching several computer data bases for toxicological, product and use information, and provides these data to Economics.

(5) On the basis of this and other information, Economics makes a determination of whether each chemical is in a consumer product and prepares a written report to that effect. Lists of those chemicals which are eliminated because of jurisdiction (i.e., drugs, pesticides, etc.) are forwarded to the Office of the General Counsel for its concurrence.

(6) If the chemical is found to be contained in a consumer product, the package of data and the report are forwarded to Health Sciences, which, in turn, makes a definitive determination and prepares a report on the chemical's carcinogenicity on existing information, if possible, or indicates what additional information must be sought or developed.

These searches and assorted analyses are in process for the 35 chemicals on List 4.

(7) These two reports form the basis upon which the Office of Program Management, working with the Chronic Hazards Team, develops a briefing package that informs the Commission about the chemical and provides priority recommendations and regulatory options.

These procedures represent how reports that are received periodically are handled by the staff. The essential guiding principle is immediate communication among all functional units at this early stage in the process of handling carcinogens so that items are dealt with promptly, tracking of items is established, and resource expenditures are conserved.

cc: OPM

No mention of IRLG

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CARCINOGENS FROM IARC LIST OF HUMAN CARCINOGENS
AND BIOASSAYS

A. IARC List (26) of Human Carcinogens

*SUSPECTED,
but GENERALLY
ACCEPTED.*

Aflatoxins	Diethylstilbestrol
Aminobiphenyl	Hematite Mining (Radon)
Arsenic Compounds	Isopropyl Oils
Asbestos	Melphalan
Auramine	Mustard Gas
Benzene	2-Naphtylamine
Benzidine	Nickel (Refining)
Bis (chloromethyl) ether	N-N Bis (2 Chloroethyl) 2 Naphthalamine
Cadmium	Oxymetholone
Chlora Amphenicol	Phenacetin
Chloromethyl Ether	Phenytoin
Chromium	Soot, Tars, Oils
Cyclophosphamide	Vinyl Chloride

B. NCI Bioassay Data

ANIMAL TESTS
*1 or more species, RAT, Mouse
1 or more assays -*

✓ Aniline Hydrochloride	3-Amino-9-Ethylcarbazole (Hydrochloride)
3-Amino-r-Ethoxyacetanilide	Hydrazobenzene
5-Nitroacenaphthene	p-Cresidine
1,5-Napthalene Diamine	2,4-Diaminoanisoie Sulfate
✓ 2,4-Dinitro-Toluene	m-Cresidine
4-Chloro-m Phenylene Diamine	O-Anisidine Hydrochloride
4-Amino-2-Nitrophenol	2-Methyl-1-Nitroanthraquinone
2-Aminoanthraquinone	1,2-Dibromoethane
Trimethylthiourea	Nitrotriactic Acid (NTA) and Nitrilo-
Trimethyl Phosphate	triactic Acid, Trisodium Salt, Monohydrate
5-Chloro-o-Toluidine	1,4-Dioxane
1,1,2-Trichloroethane	Cupferron
Hexachloroethane	N-N'-Diethylthiourea
3,3'-Dimethoxybenzidine-4,4'-	Daminozide
Diisocyanate	1,1,2,2-Tetrachloroethane
Pivalolactone	

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11/1/78

List 2. Carcinogens for Which CPSC Lacks Jurisdiction

IARC List of Human Carcinogens

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
Aflatoxins	Liver carcinogen	Food microorganism toxin	Ingestion and uptake	Not in consumer products.
Bis(chloromethyl) ether	Lung cancer - Occupational exposures	Chemical intermediate	Inhalation	Not in consumer products.
Chloramphenicol	Hemopoietic system	Medicinal	Injection	Not in consumer products.
Chloromethyl ether	Lung cancer - Occupational exposure	Chemical intermediate	Inhalation	Not in consumer products.
Cyclophosphamide	Bladder	Medicinal	Injection	Not in consumer products.
Diethylstilbestrol	Uterus, vagina	Medicinal	Oral	Not in consumer products.
Hematite Mining (Radium?)	Lung - Occupational exposure	Ore production	Inhalation	Not in consumer products. (Rado or Hemalite)
Isopropyl oils	Nasal, larynx	By product	Inhalation	
Melphalan	Hemopoietic system	Medicinal	Injection	Not in consumer products.
Mustard gas	Lung, larynx	War gas	Inhalation	Not in consumer products.
N-N-Bis (2 chloroethyl) 2 naphthal-amine	Bladder	Medicinal	Oral	Not in consumer products.

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List 2. Carcinogens for Which CPSC Lacks Jurisdiction

IARC List of Human Carcinogens

Substance	Carcinogen Data	Use	Availability	Potential Exposure
Oxymetholone	Liver	Medicinal	Oral	Not in consumer products.
Phenacetin	Kidney	Medicinal	Oral	Not in consumer products.
Phenytoin	Lymphoreticular tissues	Medicinal	Oral injection	Not in consumer products.
Soot, tars, and oils	Lung skin (scrotum)	By products	Inhalation, skin	Environmental.

List 3. Carcinogens Being Regulated by CPSC or Other Agencies

IARC List of Human Carcinogens

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
Asbestos	Human epidemiology - Lung cancer	Insulation, fire resistant fabrics, brake linings, etc.	Inhalation, little movement thereafter	Naturally occurring contaminant. Wide consumer exposure.
Benzene	Leukemias by occupational exposures	Petrochemical intermediate and solvent	Skin absorption, inhalation, ingestion	Occurs naturally in petrochemicals.
Vinyl chloride	Liver, lung - Occupational exposure	Chemical intermediate	Inhalation	Previously regulated.

List 4. Ranking of Carcinogens for Further Attention

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1.

IARC List of Human Carcinogens

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
Auramine	Bladder cancer - Occupational exposure	Dyes, paper, cardboard <i>Fluorescent dye</i> <i>Biological stain</i>	Metabolized by mammals Ingestion	Wide.
Benztidine	Bladder cancer - Occupational exposures	<i>the Intermediate for many dyes in current use</i>	Inhalation, ingestion, skin absorption	Fabric, leather, paper dye - very wide.
2-Naphthyl-amine	Bladder cancer - Occupational exposure	Dye intermediate	Inhalation, skin, oral	<i>May be impurity in some dyes - paper + cardboard</i>
Nickel (refining)	Nasal, lung Occupational exposure	Metal plating, alloys chemicals	Inhalation	Widespread as noted in consumer products <i>Hazards to consumers not identified</i>
Arsenic compounds	Lung and skin cancer Occupational exposures	Fungicide		Naturally occurring contaminant.
Cadmium	Prostate cancer - Occupational exposure	Plating, dyes, fungicides <i>Silver solder</i> <i>Paint pigment</i>	Inhalation	Wide exposure
Chromium	Lung, nose cancer - Occupational exposure	Metal plating, alloys chemicals	Inhalation	In consumer products as salts and metal. <i>Not seen as a hazard.</i>
Aminobiphenyl	Bladder cancer - Occupational exposures	Rubber antioxidant <i>Carcinogen in cancer research</i>	Inhalation, skin absorption	<i>Probably not used in rubber mfg since 1955</i>

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Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
1,4-dioxane	(+) In H and F rats (+) In H and F mice	Industrial solvent for paints, varnishes, lacquers, plastics, dyes, oils, waxes, resins, and as an inhibitor in chlorinated solvents. Also, a solvent for tissue processing, liquid scintillation counting, and photochemical reactions.	Highly toxic by inhalation, absorbed by skin. Tolerance, 100 ppm in air.	Primary exposure for industrial workers, laboratory workers, and painters. <i>Effective substitute solvent. Experience last may be used in spot removers and glass cleaners</i>
1,1,2-Trichloroethane	(-) In H and F rats (+) In H and F mice	Chemical intermediate for the production of vinylidene chloride, in adhesives, in teflon tubing, in lacquer, and as a solvent for fats, oil, waxes, and other products.	Primary human exposure through inhalation of vapors released during its manufacture and subsequent use as a chemical intermediate. Readily absorbed through the skin.	
1,1,2,2-Tetrachloroethane	(-) In H and F rats (+) In H and F mice	Industrial solvent for cellulose acetate, fats, waxes, greases, rubber, and sulfur used also as an intermediate in the manufacture of trichloroethylene and tetrachloroethylene.		Major concerns in occupational exposure for causing liver damage as well as gastrointestinal and neurological disturbances.

NCI BIOASSAY DATA

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Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
Nitrotriacetic Acid (NTA) and Nitrilotriacetic Acid, Trisodium Salt, Monohydrate	(+) in M and F rats (+) in M and F mice	Replacement for phosphates in detergents. Major non-detergent uses include water treatment, textile treatment, metal plating and cleaning, and pulp and paper processing. Leather tanning, photographic development, synthetic rubber production, manufacture of pharmaceuticals, agriculture, and separation of rare earth elements.	If present, available for absorption.	Significant. <i>wide potential use in detergents as now used in Canada</i>
Trimethyl Phosphate	(7) in M rats (fibromas of subcutaneous tissue) (-) in F rats (-) in M mice (+) in F mice	Alkylating agent used as a gasoline additive, a methylating agent, an intermediate for the production of polymethyl polyphosphates, flame retardant in polymers.	Known to cause sterility in mice, rats, and rabbits, produces chromosomal abnormalities in the bone marrow cells of rats and dominant lethal effects in mice.	Available commercially, but no longer manufactured in the U.S. Its production and industrial applications could result in the exposure of workers in the chemical industry.
N-N'-Diethylthiourea	(+) in M and F rats (-) in M and F mice	Corrosion inhibitor for ferrous metals and a vulcanization accelerator in the manufacture of elastomers.		Greatest for workers manufacturing this compound, and for others using corrosion inhibitive solutions. Workers in elastomer industry. <i>Potential ingredient in consumer products</i>

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NCI BIOASSAY DATA

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
1,2-Dibromo- ethane	(+) in M and F rats (+) in M and F mice	Used in gasoline as a lead scavenger, also used as a soil and grain fumigant, has been used as a solvent and chemical intermediate.	Probably high. Severe irritant, inducing blisters subsequent to der- mal exposure upon inhalation, it causes pulmonary lesions and mild central nervous system depression.	Extensive potential for human exposure. <i>Probable loss of jurisdiction</i>

NCI BIOASSAY DATA

Substance	Carcinogen Data	Use	Bioavailability*	Potential Exposure
Pivalolactone	(+) in M and F rats (-) in M and F mice	Preparation of co-polymers for sutures, prosthetic devices, etc., and as a plasticizer for cyanoacrylate adhesives.	Probably low because it is used as co-polymers.	Greatest for workers engaged in the preparation of this compound or co-polymers. <u>Does not appear to be produced or sold in the U.S. in large quantities.</u>
3,3'-dimethoxybenzidine-4,4'-Diisocyanate	(+) in M and F rats (-) in M and F mice	Used in the synthesis of railway car couplers, polyurethane gaskets and seals, aerosol mounting cups, lacquers for steel cans, and anti-reflective coating for color photographs.	Toxic by inhalation and ingestion at high temperatures. Skin irritant. <i>Not stable in environment but may convert to hazardous material.</i>	Not currently produced in large commercial quantities. Exposure limited to researchers, particularly those involved in the experimental synthesis of elastomers and polymeric coatings.
Hexachloroethane	(-) in M and F rats (+) in M and F mice	Veterinary anthelmintic, solvent, a camphor substitute in the preparation of Celluloid [®] , a rubber vulcanizing accelerator, a fermentation retarding agent, and used in the production of explosives, pyrotechnics, and smoke devices.	Risk of inhalation minimal because the compound is a solid with a relatively low vapor pressure. Exposure would occur primarily through dermal contact or ingestion.	Risk of exposure greatest for workers in the chemical, rubber, plastics, pharmaceutical and explosives industries, and for those persons using the compound for veterinary purposes.

NCI BIOASSAY DATA

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
Trimethyl- thiourea	(-) In M and (+) In F rats (-) In M and F mice	Chemical inter- mediate in the production of vinyl- thiourea Tannin, various Nucleosides		Not oral among various in a variety of industries, including the clothing, elastomer, textile and dye, and pharmaceutical manu- facturing industries.
O-methylthio hydro- chloride	(+) In M and F rats (+) In M and F mice	Dye precursor.	Not known, but absorbed following ingestion.	Large population, but low concentration out- side of the industrial environment.
2,4-diaminobenzoic Sulfate	(+) In M and F rats (+) In M and F mice	hair dye component and textile dye intermediate	Not known, but absorbed following dermal exposure.	Large population, but low concentration out- side of the industrial environment and hair dye users.
3-Amino-9-Ethylcar- bazole (Hydrochloride)	(+) In M and F rats (+) In M and F mice	Dye intermediate and biological stain.	Not known, but absorbed following ingestion.	Large population, but low concentration out- side of the industrial and laboratory environ- ment.
2-Aminobenzoquinone	(+) In M and (2) In F rats (+) In M and F mice	Dye intermediate.	Not known.	Large population, but low concentration out- side of the industrial environment.
Hydroquinone	(+) In M and F rats (-) In M and (+) In F mice	Dye precursor and dye precursor.	Not known, but absorbed following ingestion or dermal exposure.	Large population, but low concentration out- side of the industrial environment and dye users.

NCI BIOASSAY DATA

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
5-Nitroacenaphthene	(+) in M and F rats (-) in M and (+) in F mice	None in U.S. Dye intermediate in Japan.	Not known, but absorbed following ingestion.	Limited to research users. <i>2 steps removed from dye products.</i>
1,5-Naphthalene Diamine	(-) in M and (+) in F rats (+) in M and F mice	Dye and drug intermediate	Not known.	Large population, but low concentration outside of the industrial environment and drug
4-Chloro-m Phenylene Diamine	(+) in M and (-) in F rats (-) in M and (+) in F mice	Dye intermediate.	Not known.	Large population, but low concentration outside of the industrial environment.
p-Cresidine	(+) in M and F rats (-) in M and F mice	Dye intermediate	Not known, but absorbed following ingestion or dermal exposure.	Large population, but low concentration outside of the industrial environment.
Aniline Hydrochloride	(+) in M and F rats (-) in M and F mice	Dye intermediate and drug precursor.	Not known, but absorbed following ingestion, inhalation, or dermal exposure.	Large population, but low concentration outside of the industrial environment.
5-Chloro-o-Toluidine	(-) in M and F rats (+) in M and F mice	Dye intermediate.		Greatest for workers in the chemical and dye manufacturing and textile industries.
3-Amino-4-Ethoxy-acetanilide	(-) in M and F rats (+) in M and F mice	Dye intermediate for textiles.	Not known, but absorbed following ingestion.	Large population, but low concentration outside of the industrial environment.
m-Cresidine	(+) in M and F rats (?) ^{***} in M and (-) F mice	Dye intermediate.	Not known, but absorbed following ingestion.	Large population, but low concentration outside of the industrial environment.

NCI BIOASSAY DATA

Substance	Carcinogen Data	Use	Bioavailability	Potential Exposure
4-Amino-2-Nitrophenol	(+) in M and (?)*** in F rats (-) in M and F mice	Oxidation base for fur dying and in hair dyes.	Not known, but absorbed following ingestion.	Limited population outside of the industrial environment and hair dye users.
2-Methyl-1-Nitroanthraquinone	(+) in M and (-) in F rats. (Non-malignant tumor M and F)	Dye intermediate.	Not known, but absorbed following ingestion.	Large population, but low concentration outside of the industrial environment. <i>Two steps removed from dye.</i>
2,4-Dinitro-Toluene	(-) in M and F rats (Non-malignant tumors in M and F) (-) in M and F mice	Dye precursor and explosive modifier.	Not known, but absorbed following ingestion.	Large population, but low concentration outside of the industrial environment. <i>Two steps removed from dye.</i>