9.11 Monitoring and Treatment

# World Trade Center Chemicals of Potential Concern and Selected Other Chemical Agents

## Summary of Cancer Classifications by the National Toxicology Program and International Agency for Research on Cancer

**DEPARTMENT OF HEALTH AND HUMAN SERVICES**
Centers for Disease Control and Prevention
National Institute for Occupational Safety and Health

World Trade Center Health Program

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# Contents

# Abbreviations

| | |
|---|---|
| ATSDR | Agency for Toxic Substances and Disease Registry |
| COPC | chemicals of potential concern |
| EPA | Environmental Protection Agency |
| IARC | International Agency for Research on Cancer |
| NL | not listed |
| NTP | National Toxicology Program |
| NYCDOHMH | New York City Department of Health and Mental Hygiene |
| PAH | polycyclic aromatic hydrocarbon |
| RoC | National Toxicology Program Report on Cancer |
| syn | synonym |
| TEQ | dioxin toxic equivalent |
| WTC | World Trade Center |

# I. Introduction

The James Zadroga 9/11 Health and Compensation Act of 2010, Public Law 111-347, Title XXXIII of the Public Health Service Act, 124 Stat. 3623 (codified at 42 United States Code section 300mm–300mm-61), requires the Administrator of the World Trade Center (WTC) Health Program to

> *"periodically conduct a review of all available scientific and medical evidence, including findings and recommendations of Clinical Centers of Excellence, published in peer-reviewed journals to determine if, based on such evidence, cancer or a certain type of cancer should be added to the applicable list of WTC-related health conditions." 42 U.S.C. sec. 300mm-22(a)(5)(A).*

The National Institute for Occupational Safety and Health (NIOSH) presented the first periodic review of cancer for the WTC Health Program in July 2011. This review included findings from the peer-reviewed scientific and medical literature about exposures and cancer resulting from the September 11, 2001, terrorist attacks [NIOSH 2011]. The Exposure section of the first periodic review provided an initial list of agents detected in the area around the World Trade Center (WTC) during the disaster response and recovery periods. The Contaminants of Potential Concern (COPC) Committee of the World Trade Center Indoor Air Task Force Working Group[1] developed the initial list from the chemicals identified in air sample testing results included in four databases [COPC Committee 2003]. The committee used this list to select COPCs and set health-based benchmarks for indoor environments. The four data sources were the

- Environmental Protection Agency (EPA) Region 2 database of environmental sampling results, which contains more than 200,000 records on sampling results for 137 agents[2];
- New York City Department of Health and Mental Hygiene (NYCDOHMH)/ Agency for Toxic Substances and Disease Registry (ATSDR) public health investigation database, which includes results from Lower Manhattan samples of six minerals, 354 air samples from residential buildings, and 32 samples of fibers collected outdoors and analyzed by phase contrast microscopy[3];

[1] http://www.tera.org/peer/WTC/COPC%20-%20Benchmark%20Report%20with%20appendices.pdf. Note that this is a large database assembled by the USEPA and centralizes exposure measurements from many different entities.

[2] Only confirmed compounds were included in this list. Measurements for the dioxin and furan compounds were considered one contaminant in this tally and were screened by means of a TEQ analysis. TEQ is a dioxin toxic equivalent, calculated relative to the most toxic form of dioxin (2,3,7,8-Tetrachlorodibenzodioxin). Measurements for asbestos were not differentiated by the asbestos minerals, although measurements used different analytical methods and counted different subsets of fiber types and sizes. All measurements for polychlorinated biphenyls were considered one contaminant, although the studies reported concentrations under several different groupings of congeners (e.g., total polychlorinated biphenyls, Aroclors).

[3] These data are described in a 2002 report: Agency for Toxic Substances and Disease Registry (ATSDR), New York

- New York City Department of Education findings from sampling in schools, which involved samples collected both indoors and outdoors from six schools between September 2001 and June 2002 and includes more than 30,000 records of air sampling results for more than 70 agents; and
- Chatfield and Kominsky's[4] survey of indoor air quality.

A total of 287 chemicals or chemical groups were identified from the report [COPC Committee 2003], and each of them was checked against (1) the United States National Toxicology Program (NTP) 12th Report on Carcinogens (RoC)[5] [NTP 2011] and (2) the United Nations International Agency on Research on Cancer (IARC) list of agents and documented in the IARC monographs, Volumes 1–102 [IARC 2006]. The list and cancer designations of these chemicals were provided in Appendix E of the First Periodic Review of Scientific and Medical Evidence Related to Cancer for the World Trade Center Health Program [NIOSH 2011].

In addition to the agents identified by the COPC Committee [COPC 2003], several other agents of potential concern have been included because of the potential for widespread exposure. In particular, the fires at the WTC site produced over an extended period of time substantial amounts of combustion products from building materials, including wood and plastics. Also, a large number of trucks, many of which run on diesel fuels, were used at the WTC site. These trucks likely produced large quantities of diesel particulates, which were discharged into the air at and around the WTC site. Because of the potential exposure of rescue and recovery workers, as well as workers and residents in area buildings, to soot, biomass fuel, and diesel particulates, these are included with the COPC agents identified by EPA. Tables 1, 2, and 3 (Section IV) provide the cancer classifications of NTP and IARC and expand upon the information provided in the first periodic report by providing a summary of the basis for the IARC classification. NTP and IARC do not address decomposition products from plastics as a group; they are addressed only as individual compounds. Therefore, the individual compounds from thermal decomposition of plastics that were identified by the COPC Committee are included in the tables.

A summary of the studies cited in the IARC monographs is provided in Section IV. Hyperlinks to the NTP Report on Carcinogens and the IARC monographs are provided as well. The agents identified as COPC and other select agents are grouped according to their IARC designation as Group 1, 2A, or 2B. Agents categorized by IARC as Group 3

City Department of Health and Mental Hygiene (NYCDOHMH) [2002]. Final Technical Report of the Public Health Investigation to Assess Potential Exposures to Airborne and Settled Surface Dust in Residential Areas of Lower Manhattan. September 2002.

[4] These data are described in a 2001 report: Chattfield EJ, Kominsky JR [2001]. Summary Report: Characterization of Particulate Found in Apartments After Destruction of the World Trade Center. Report Requested by "Ground Zero" Elected Officials Task Force.

[5] http://ntp-server.niehs.nih.gov/?objectid=03C9AF75-E1BF-FF40-DBA9EC0928DF8B15

or Group 4 are not summarized because they are not expected to contribute to potential cancer outcomes among the rescue and recovery workers and the survivors. Descriptions of uncategorized agents are not available in the IARC Monographs. A total of 63 agents are included from the original list of 287 COPCs, and the additional three agents (soot, biomass fuel, and diesel) have been added.

# II. National Toxicology Program 12th Report on Carcinogens

The NTP RoC [NTP 2011] considers evidence such as data from traditional cancer epidemiology studies, clinical studies, and studies of tissues or cells (from humans exposed to the substances in question) that can be useful for evaluating whether a relevant cancer mechanism is operating in people. The RoC does not present quantitative assessments of the risks of cancer associated with these substances. Thus, listing of substances in the RoC indicates only a potential hazard and does not establish the exposure conditions that would pose cancer risks to individuals in their daily lives. The criteria for listing an agent, substance, mixture, or exposure circumstance in the RoC are as follows:

***Known to be a human carcinogen (Category A)***

> *There is sufficient evidence of carcinogenicity from studies in humans and indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.*

***Reasonably anticipated to be a human carcinogen (Category B)***

There is limited evidence of carcinogenicity from studies in humans, and indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded; or

> *There is sufficient evidence of carcinogenicity from studies in experimental animals, which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors (1) in multiple species or at multiple tissue sites, (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site, or type of tumor, or age at onset;*

or

> *There is less than sufficient evidence of carcinogenicity in humans or laboratory animals; however, the agent, substance, or mixture belongs to a well-defined, structurally related class of substances whose members are listed in a previous RoC as either known to be a human carcinogen or reasonably anticipated to be a human carcinogen, or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.*

The NTP RoC identifies and discusses agents, substances, mixtures, or exposure circumstances that may pose a hazard to human health by virtue of their carcinogenicity. The RoC serves as a meaningful and useful compilation of data on the following:

- Carcinogenicity, genotoxicity, and biologic mechanisms of the listed substance in humans and/or animals;

- Potential for human exposure to these substances; and
- Federal regulations to limit exposures.

NTP conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes but is not limited to dose–response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive subpopulations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals, but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.

# III. International Agency for Research on Cancer Monographs

The categorization of the carcinogenic potential of an agent is a matter of scientific judgment that reflects the strength of the evidence derived from studies in humans and in experimental animals and from mechanistic and other relevant data. IARC working groups consider the body of evidence as a whole to reach an overall evaluation of the carcinogenicity of the agent to humans. The working groups also strive to achieve a broad consensus evaluation but not necessarily unanimity.

IARC classifies the evidence relevant to carcinogenicity from studies in humans according to the following categories: (1) sufficient evidence of carcinogenicity; (2) limited evidence of carcinogenicity; (3) inadequate evidence of carcinogenicity; and (4) evidence suggesting lack of carcinogenicity. In addition to the results of epidemiological and toxicological studies, the IARC working groups consider mechanistic and other evidence judged to be relevant to an evaluation of carcinogenicity and of sufficient importance to affect the overall evaluation. This may include data on pre-neoplastic lesions, tumor pathology, genetic and related effects, structure–activity relationships, metabolism and toxicokinetics, physicochemical parameters, and analogous biological agents. This information is not summarized in the Tables I, II, and III but can be found in the monographs by means of the hyperlinks provided.

The working groups make scientific judgments to classify agents based on the strength of the evidence as a whole, and they classify them according to the five categories below. Agents that have not been reviewed are not listed by IARC.

### Group 1—Carcinogenic to Humans

*This category is used when there is sufficient evidence of carcinogenicity in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than sufficient, but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that carcinogenicity acts through a relevant mechanism of carcinogenicity.*

### Group 2A—Probably Carcinogenic to Humans

*This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in*

*this category solely on the basis of limited evidence of carcinogenicity in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one of more members have been classified in Group 1 or in Group 2A.*

### Group 2B—Possibly Carcinogenic to Humans

*This category is used for agents for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in experimental animals. In some instances, an agent for which there is inadequate evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals, together with supporting evidence from mechanistic and other relevant data, may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.*

### Group 3—Not Classifiable as to Its Carcinogenicity to Humans

*This category is used most commonly for agents for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals. Exceptionally, agents for which the evidence of carcinogenicity is inadequate in humans but sufficient in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans. Agents that do not fall into any other group are also placed in this category. An evaluation in Group 3 is not a determination of non-carcinogenicity or overall safety. It often means that further research is needed, especially when exposures are widespread or the cancer data are consistent with differing interpretations.*

### Group 4—Probably Not Carcinogenic to Humans

*This category is used for agents for which there is evidence suggesting lack of carcinogenicity in humans and in experimental animals. In some instances, agents for which there is inadequate evidence of carcinogenicity in humans but evidence suggesting lack of carcinogenicity in experimental animals, consistently and strongly supported by a broad range of mechanistic and other relevant data, may be classified in this group.*

# IV. Summary of Cancer Classifications

## Table 1. Summary of Classification Basis for COPC and Select Other Agents as IARC Group 1—Carcinogenic to Humans

This category is used when there is sufficient evidence of carcinogenicity in humans. Exceptionally, an agent may be placed in this category when evidence of carcinogenicity in humans is less than sufficient but there is sufficient evidence of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent acts through a relevant mechanism of carcinogenicity.

Table 1. Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Arsenic** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Arsenic.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol84/mono84-6E.pdf | | | | |
| | | | human | oral | urinary bladder, lung, skin, liver, and kidney cancer |
| | | | human | | lung cancer |
| | | | mouse | oral | dimethylarsinic acid—tumor promoter in the skin and lung |
| | | | mouse | perinatal | arsenic trioxide and calcium arsenate induced lung adenomas |
| | | | mouse | transplacental | sodium arsenite—liver and lung carcinomas, ovarian tumors (benign and malignant) and adrenal cortical adenomas, and promoted skin carcinogenesis in mouse. |
| | | | hamster | intratracheal | negative for carcinogenicity |
| | | | hamsters | intratracheal | lung adenomas |
| | | | rat | oral | dimethylarsinic acid—tumor promoter in the liver, urinary bladder, kidney and thyroid gland |
| **Asbestos** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Asbestos.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/suppl7/Suppl7-20.pdf | | | | |
| | | | human | | chrysotile, amosite and anthophyllite asbestos and to mixtures containing crocidolite results in an increased risk of lung cancer, as does exposure to minerals containing tremolite and actinolite and to tremolitic material mixed with anthophyllite and small amounts of chrysotile |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | human | | mesotheliomas have been observed after occupational exposure to crocidolite, amosite, tremolitic material and chrysotile asbestos. Gastrointestinal cancers occurred at an increased incidence in groups occupationally exposed to crocidolite, amosite, chrysotile or mixed fibers containing crocidolite. An excess of laryngeal cancer. |
| | | | rat | inhalation | chrysotile, crocidolite, amosite, anthophyllite and tremolite produced mesotheliomas and lung carcinomas in rats |
| | | | mouse | intraperitoneal | chrysotile, crocidolite and amosite induced peritoneal tumors, including mesotheliomas |
| | | | rat | intraperitoneal | chrysotile, crocidolite and amosite induced peritoneal tumors, including mesotheliomas |
| | | | hamster | intraperitoneal | crocidolite produced abdominal tumors |
| | | | rat | oral | chrysotile—malignant tumors |
| | | | rat | oral | amosite or tremolite—no increase in tumors |
| | | | hamster | oral | amosite—no increase in tumors |
| | | | hamster | oral | chrysotile—no increase in tumors |
| | | | rat | oral | 2 studies: low incidence of benign adenomatous polyps of the large intestine in males; mesenteric hemangiomas |
| **Benzene** | **1** | **A** | | | |
| NTP hyperlink: | http://monographs.iarc.fr/ENG/Monographs/suppl7/Suppl7-24.pdf | | | | |
| IARC hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Benzene.pdf | | | | |
| | | | human | | leukemia |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | mouse | oral | neoplasms at multiple sites |
| | | | rat | oral | neoplasms at multiple sites |
| | | | mouse | inhalation | tendency towards induction of lymphoid neoplasms |
| | | | rat | inhalation | neoplasms (mainly carcinomas) at various sites |
| | | | mouse | IP injection | Males: lung adenomas |
| **Benzo[a]pyrene (PAHs)** | **1** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolycyclicAromaticHydrocarbons.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol92/mono92-10.pdf | | | | |
| | | | human | | lung cancer |
| | | | human | | urinary bladder cancer |
| | | | human | | laryngeal cancer |
| | | | mouse | skin | benign and malignant skin tumors |
| | | | mouse | skin | active as initiator in initiator studies |
| | | | mouse | IP injection | liver and lung tumors; occasionally forestomach and lymphoreticular tumors |
| | | | mouse | subcutaneous injection | malignant tumors (mainly fibrosarcomas) |
| | | | mouse | Intratracheal instillation | benign and malignant respiratory tumors |
| | | | rat | Intratracheal instillation | benign and malignant respiratory tumors |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | hamster | Intratracheal instillation | benign and malignant respiratory tumors |
| | | | mouse | gavage or diet | lung, forestomach, liver, lymphoreticular tissue, esophagus, and tongue |
| | | | rats | gavage or diet | lung, forestomach, liver, lymphoreticular tissue, esophagus, and tongue |
| | | | mouse | oral | lymphomas |
| | | | mouse (transgenic) | gavage | splenic lymphomas and forestomach |
| | | | mouse (transgenic) | diet | forestomach tumors |
| | | | rat | injection in lung | malignant lung tumors |
| | | | hamsters | inhalation | Males: polyps, papillomas, squamous-cell carcinomas of upper resp. tract and upper digestive tract |
| | | | hamster | application to buccal pouch mucosa | Males: forestomach papillomas |
| | | | rat | subcutaneous tracheal grafts | squamous cell carcinomas |
| | | | rat | intramamillary | benign and malignant mammary gland tumors |
| | | | mouse | intracolonic instillation | benign and malignant in various organs, not colonic tumors |
| **Beryllium** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Beryllium.pdf | | | | |

(Continued)

**Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans**

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol58/mono58-6.pdf | | | | |
| | | | human | | lung cancer |
| | | | rats | inhalation | malignant and benign lung tumors |
| | | | rats | intratracheal instillation | lung tumors - adenomas and adenocarcinomas |
| | | | rats | inhalation | lung tumors - adenocarcinomas |
| | | | rats | inhalation | malignant epithelial lung tumors |
| | | | rat | intratracheal instillation | lung adenocarcinomas and adenomas; malignant lung tumors |
| | | | rabbit | IV injection | osteosarcomas |
| | | | rabbit | implantation or injection into bone | osteosarcomas |
| **1,3-Butadiene** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Butadiene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol97/mono97.pdf | | | | |
| | | | human | | leukemia and non-Hodgkin lymphoma |
| | | | mouse | inhalation | Males: lymphoma and neoplasms of the heart, lung, forestomach, liver, Harderian gland, preputial gland and kidney |
| | | | mouse | inhalation | Females: lymphomas and neoplasms of the heart, lung, forestomach, liver, Harderian gland, ovary and mammary gland |
| | | | rat | inhalation | Males: pancreatic exocrine adenomas and carcinomas and interstitial-cell tumors of the testis |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | inhalation | Females: thyroid follicular-cell tumors, uterine sarcomas, Zymbal gland carcinomas and benign and malignant mammary tumors |
| **Cadmium and compounds** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Cadmium.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol58/mono58-7E.pdf | | | | |
| | | | human | | lung cancer |
| | | | mouse | oral | inadequate for evaluation |
| | | | rat | oral | Males: leukemia, interstitial cell tumors of the testis, proliferative lesions of the prostate |
| *Cd chloride, Cd sulfide/sulfate, Cd sulfate and Cd oxide fume and dust* | | | mouse | inhalation | some groups exposed to cadmium oxide fume or dust had increased incidences of lung tumors |
| | | | hamster | inhalation | no increase in the incidence of lung tumors |
| | | | rat | inhalation | malignant lung tumors |
| *Cd sulfide* | | | rat | intraperitoneal | malignant tumors within the peritoneal cavity. |
| *Cd chloride, Cd sulfide* | | | rat | intratracheal instillation | malignant pulmonary tumors |
| *Cd chloride, Cd sulfide/sulfate, Cd-containing rat liver ferritin* | | | rat | subcutaneous injection | local sarcomas |
| *Cd powder, Cd chloride and Cd sulfide* | | | rat | intramuscular injection | local sarcomas |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| *Cd chloride* | | | rat | subcutaneous | tumors of the prostate |
| *Cd chloride* | | | mouse | subcutaneous | testicular interstitial tumors |
| *Cd powder, Cd chloride, Cd sulfide* | | | rat | subcutaneous injection | local sarcomas; testicular interstitial tumors |
| *Cd chloride* | | | rat | injection into prostate | malignant prostatic tumors |
| **Chromium VI** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/ChromiumHexavalentCompounds.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol49/mono49-6.pdf | | | | |
| | | | human | | lung cancer; sinonasal cancer |
| *Calcium chromate* | | | mouse | inhalation | lung adenomas borderline significant |
| | | | rat | intratracheal instillation | lung tumors |
| | | | hamster | intratracheal instillation | no lung tumors |
| | | | rat | intrabronchial | lung tumors |
| | | | rat | intrapleural | local tumors |
| | | | mouse | intramuscular injection | local tumors |
| | | | rat | intramuscular injection | local tumors |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| *Chromium Trioxide (chromic acid)* | | | mouse | inhalation | low incidence of lung adenomas at higher dose; nasal papillomas at lower dose |
| | | | rat | intrabronchial implantation | few lung tumors |
| *Sodium dichromate* | | | rat | inhalation | lung tumors, benign and malignant |
| | | | rat | intratracheal instillation | lung tumors, benign and malignant |
| | | | rat | intrabronchial | no increase of local tumors |
| | | | rat | intrapleural | no increase of local tumors |
| | | | rat | intramuscular injection | no increase of local tumors |
| *Barium chromate* | | | rat | intrabronchial | no increase of local tumors |
| | | | rat | intrapleural | inadequate for assessment of carcinogenicity |
| | | | rat | intramuscular injection | inadequate for assessment of carcinogenicity |
| *Lead chromate* | | | rat | intrabronchial | no increase of local tumors |
| | | | rat | subcutaneous | malignant tumors at the site of injection |
| | | | rat | intramuscular injection | malignant tumors at the site of injection |
| *Basic lead chromate* | | | rat | subcutaneous | local sarcomas |

(Continued)

## Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| *Zinc chromates* | | | rat | intrabronchial | bronchial carcinomas |
| | | | rat | intraperitoneal | local tumors |
| | | | rat | subcutaneous | local sarcomas |
| | | | rat | intramuscular injection | local sarcomas |
| *Strontium chromate* | | | rat | intrabronchial implantation | high incidence of bronchial carcinomas |
| | | | rat | intrapleural | local sarcomas |
| | | | rat | intramuscular | local sarcomas |
| **Formaldehyde** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Formaldehyde.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol88/mono88-6.pdf | | | | |
| | | | human | | nasopharyngeal |
| | | | human | | strong but not sufficient evidence for leukemia |
| | | | human | | limited evidence for sinonasal cancer |
| | | | rat | inhalation | squamous-cell carcinomas of the nasal cavities |
| | | | rat | drinking water | Males: forestomach papillomas |
| | | | rat | drinking water | Males and Females: gastrointestinal leiomyosarcomas |
| | | | rat | drinking water | negative |
| | | | rat | drinking water | Males: lymphomas and leukemias and testicular interstitial-cell adenomas |
| | | | mouse | skin | concomitant exposure to dimethylbenz[a]anthracene reduced latency of skin tumors |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | drinking water | concomitant exposure to N-methyl-N'-nitro-N-nitrosoguanidine increased incidence of adenocarcinomas of the glandular stomach |
| | | | hamster | inhalation | concomitant subcutaneous injection of N-nitrosodiethylamine increased tracheal tumors |
| **Nickel compounds** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Nickel.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol49/mono49-7.pdf | | | | |
| | | | human | | lung and nasal cancers |
| *Nickel Monoxide* | | | rat | inhalation | inadequate for assessment of carcinogenicity |
| | | | hamster | inhalation | inadequate for assessment of carcinogenicity |
| | | | mouse | intramuscular injection | local sarcomas |
| | | | rat | intramuscular injection | local sarcomas |
| | | | rat | intrapleural | local sarcomas |
| | | | rat | intraperitoneal | local sarcomas |
| | | | rat | intrarenal injection | no renal tumors |
| | | | rat | intratracheal instillation | significant incidence of lung carcinomas |
| *Nickel Trioxide* | | | rat | intramuscular injection | inadequate for assessment of carcinogenicity |
| | | | rat | intracerebral | inadequate for assessment of carcinogenicity |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| *Nickel hydroxide* | | | rat | intramuscular injection | local sarcomas |
| *Nickel subsulfide* | | | rat | inhalation | benign and malignant lung tumor |
| | | | rat | intratracheal instillation | malignant lung tumors (adenocarcinomas, squamous-cell carcinomas and mixed tumors) |
| | | | mouse | subcutaneous injection | sarcomas |
| | | | rat | subcutaneous injection | rhabdomyosarcomas and fibrous histiocytomas |
| | | | mouse | intramuscular injection | local sarcomas |
| | | | rat | intramuscular injection | local sarcomas |
| | | | hamster | intramuscular injection | local sarcomas |
| | | | rabbit | intramuscular injection | local sarcomas |
| | | | rat | intrapleural | local sarcomas |
| | | | rat | intraperitoneal | mesotheliomas |
| | | | rat | intrarenal injection | renal-cell neoplasms |
| | | | rat | intratesticular | high incidence of sarcomas, including rhabdomyosarcomas |
| | | | rat | intraocular | eye neoplasms (including retinoblastomas, melanomas, and gliomas) |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | intra-articular | sarcomas (including rhabdomyosarcomas and fibrous histiocytomas) |
| | | | rat | retroperitoneal fat | fibrous histiocytomas |
| | | | rat | implantation heterotopic tracheal transplant | carcinomas and sarcomas |
| | | | rat | pregnant | inadequate for assessment of carcinogenicity |
| *Nickel disulfide* | | | rat | intramuscular injection | high incidences of local tumors were induced |
| | | | rat | intrarenal injection | high incidences of local tumors were induced |
| *Nickel monosulfide* | | | rat | intramuscular injection | crystalline form induced local tumors, but the amorphous form did not |
| | | | rat | intrarenal injection | crystalline form induced local tumors, but the amorphous form did not |
| *Nickel ferrosulfide* | | | rat | intramuscular injection | local sarcomas |
| *Nickel sulfate* | | | rat | intramuscular injection | did not induce local tumors |
| | | | rat | intraperitoneal | induced malignant tumors in the peritoneal cavity |
| *Nickel chloride* | | | rat | intraperitoneal | malignant tumors in the peritoneal cavity |

(Continued)

**Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans**

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| *Nickel acetate* | | | rat | intraperitoneal | malignant tumors in the peritoneal cavity |
| | | | mouse | intraperitoneal | lung adenocarcinomas were induced in 1 study; increased incidence of pulmonary adenomas in two studies |
| *Nickel carbonyl* | | | rat | inhalation | a few lung carcinomas |
| | | | | intravenous injection | increased incidence of neoplasms in several organs |
| *Nickelocene* | | | rat | intramuscular injection | some local tumors |
| | | | hamster | intramuscular injection | some local tumors |
| **Quartz** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Silica.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol68/mono68-6.pdf | | | | |
| | | | human | inhalation | lung cancer |
| | | | rat | inhalation | adenocarcinomas and squamous-cell carcinomas of the lung |
| | | | rat | intratracheal | adenocarcinomas and squamous-cell carcinomas of the lung |
| | | | rat | intrapleural | thoracic and abdominal malignant lymphomas, primarily of the histiocytic type (MLHT) |
| | | | rat | intraperitoneal | thoracic and abdominal malignant lymphomas, primarily of the histiocytic type (MLHT) |
| | | | hamster | intratracheal | no pulmonary tumor |

(Continued)

Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | hamster | intratracheal | no pulmonary tumor from 1:1 mixture quartz/ferric oxide |
| | | | mouse | lung assay | no increase in lung tumor in a strain A mouse lung adenoma assay |
| | | | mouse | inhalation | no increase in lung tumor in a limited study |
| **Soot**[1] | **1** | **B** | | | |
| NTP hyperlink | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Soots.pdf | | | | |
| IARC hyperlink | http://monographs.iarc.fr/ENG/Monographs/vol35/volume35.pdf | | | | |
| | | | human | | The carcinogenicity of soot is demonstrated by numerous case reports, dating back over 200 years, of skin cancer, particularly of the scrotum, among chimney sweeps. Cohort studies of mortality among chimney-sweeps in Sweden and Denmark have shown a significantly increased risk of lung cancer. Supporting evidence for an association with lung cancer was provided by two earlier epidemiological studies in the German Democratic Republic and the UK. The potentially confounding and interactive effects of smoking could not be evaluated; however, cigarette smoking is not believed to have seriously biased these estimates. In addition to lung cancer, statistically significant excess mortality from esophageal cancer, primary liver cancer and leukemia, was found among chimney sweeps in one study. |
| **Sulfuric Acid** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/StrongInorganicAcidMists.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol54/mono54-6.pdf | | | | |
| | | | human | inhalation | nasal, laryngeal, and lung cancer |

(Continued)

## Table 1 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 1—Carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Vinyl chloride** | **1** | **A** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/VinylHalides.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol97/mono97-8.pdf | | | | |
| | | | human | inhalation | angiosarcomas of the liver and hepatocellular carcinoma |
| | | | rat | inhalation | hepatic angiosarcomas |
| | | | rat | inhalation | mammary, skin, renal, and nasal tumors |
| | | | rat | inhalation | Zymbal gland and hepatocellular carcinomas |
| | | | rat | oral | hepatic and extrahepatic angiosarcomas, hepatocellular carcinoma |
| | | | mouse | inhalation | hepatic angiosarcomas |
| | | | mouse | inhalation | mammary and lung tumors |
| | | | hamsters | inhalation | angiosarcomas |
| | | | human | | no strong epidemiologic link for cancers of the brain, lymphatic tissue, hematopoietic tissue, or melanoma |
| | | | rats | subcutaneous | no hepatic angiosarcomas induced |
| | | | rats | intraperitoneal | no hepatic angiosarcomas induced |
| | | | rats | transplacental | no angiosarcomas or liver-cell tumors developed in the offspring |
| | | | hamsters | inhalation | mammary, glandular stomach, and skin tumors |

[1]As found in occupational exposure of chimney sweeps.

## Table 2. Summary of Classification Basis for COPC and Select Other Agents as IARC Group 2A—Probably Carcinogenic to Humans

This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent may be classified in this category when there is inadequate evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans. An agent may be assigned to this category if it clearly belongs, based on mechanistic considerations, to a class of agents for which one of more members have been classified in Group 1 or in Group 2A.

## Table 2. Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Benzyl Chloride** | **2A** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-19.pdf | | | | |
| | | | mouse | cutaneous | skin tumors |
| | | | mouse | subcutaneous | local skin tumors |
| | | | mouse | gavage | forestomach tumors |
| | | | rat | gavage | Males: few neoplasms of forestomach |
| **Biomass fuel, (primarily wood, indoor emissions from household combustion)** | **2A** | **NL** | | | |
| NTP hyperlink | Not applicable | | | | |
| IARC hyperlink | http://monographs.iarc.fr/ENG/Monographs/vol95/mono95-6A.pdf | | | | |
| | | | human | | Case-control study found significantly increased lung cancer and when expanded found significant threefold increased risk for squamous–cell carcinoma and adenocarcinoma of the lung; in another case control study a significant 20–30% increased risk for lung cancer was found among those who cooked or heated with wood. However, information on the effect of duration and intensity of exposure was lacking. |

(Continued)

Table 2 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | human | | One study of nasopharyngeal carcinoma among Chinese reported a statistically significant fivefold increased risk associated with current use of wood as fuel—no exposure-response relationship presented. |
| | | | mouse | inhalation | Increased incidence of lung adenocarcinomas—not observed in rat |
| | | | mouse | inhalation | No tumor formations |
| | | | mouse | dermal | increased incidence of benign skin papillomas in two tumor initiation–promotion studies by dermal application |
| | | | mouse | dermal | non-statistically significant increase in the incidence of skin carcinomas in female |
| **Dibenz[a,h] anthracene** | **2A** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolycyclicAromaticHydrocarbons.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol92/mono92-10.pdf | | | | |
| | | | mouse | dermal | The majority of these studies exhibited significant carcinogenic activity. |
| | | | mouse | subcutaneous | |
| | | | rat | subcutaneous | |
| | | | mouse | intraperitoneal | |
| | | | mouse | intrapulmonary implantation | |
| | | | rat | intrapulmonary implantation | |
| | | | rat | intramammary | |

(Continued)

Table 2 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | intratracheal | |
| **Engine Exhaust, diesel** | **2A** | **B** | | | |
| NTP hyperlink | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/DieselExhaustParticulates.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol46/volume46.pdf | | | | |
| | | | human | | lung cancer increased significantly with duration of exposure in one study and with increased likelihood of exposure in a second cohort study; in 2 case-control studies modest increases in lung cancer were observed—one significant. |
| | | | human | | Bladder cancer was elevated but not significantly in 3 cohort studies |
| | | | human | | 3 of 4 case-control studies of bladder cancer showed a significantly increased risk of bladder cancer |
| **Ethylene Dibromide** | **2A** | **B** | | | |
| NTP hyperlink | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dibromoethane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-28.pdf | | | | |
| | | | rat | oral | squamous-cell carcinomas of the forestomach; hemangiosarcomas in males |
| | | | mouse | oral | squamous-cell carcinomas of the forestomach; alveolar/bronchiolar lung tumors in females |

(Continued)

Table 2 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | inhalation | adenomas and carcinomas of the nasal cavity, hemangiosarcomas, mammary gland tumors, subcutaneous mesenchymal tumors, alveolar/bronchial lung tumors; peritoneal mesotheliomas in males |
| | | | mouse | inhalation | adenomas and carcinomas of the nasal cavity, hemangiosarcomas, mammary gland tumors, subcutaneous mesenchymal tumors, alveolar/bronchial lung tumors |
| | | | mouse | cutaneous | skin and lung tumors |
| **Lead (Inorganic)** | **2A** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Lead.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol87/index.php | | | | |
| Lead phosphate | | | rat | IP and/or subcutaneous | renal cancers |
| Lead oxide | | | rat | inhalation | did not produce tumors in males |
| Lead acetate | | | rat | oral | adenomas and adenocarcinomas in the kidney |
| | | | mouse | oral | renal tumors exposed during pregnancy and lactation |
| | | | rat | oral | brain gliomas |
| | | | rat | oral | adrenal gland, testes, and prostate in males and adrenal gland in females |
| Lead subacetate | | | mouse | oral | renal cancer |
| | | | rat | oral | 6 studies: renal cancer |
| | | | rat | oral | brain gliomas |
| | | | mouse | IP injection | lung tumor |

(Continued)

Table 2 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | mouse | oral | negative |
| | | | hamster | oral | negative |
| **Nitrate ion (ingested)** | **2A** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol94/mono94-6F.pdf | | | | |
| | | | | | ingested nitrate or nitrite under conditions that result in endogenous nitrosation is probably carcinogenic in humans |
| **Polychlorinated Biphenyls** | **2A** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolychlorinatedBiphenyls.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/suppl7/suppl7.pdf | | | | |
| | | | human | skin | melanoma of the skin |
| | | | human | | Males: cancers of the digestive system and of the lymphatic and hematopoietic tissues |
| | | | human | | Females: cancer of the liver and biliary passages and lymphatic and hematopoietic tissues |
| | | | human | | Males: PCB mixtures containing up to 42% chlorine had been used, no significant excess of cancer deaths was noted |
| | | | rats | oral | Aroclor 1254 - low, statistically nonsignificant incidence of stomach adenocarcinoma |
| | | | human | | Females: hematological neoplasms |

(Continued)

Table 2 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | mouse | oral | benign and malignant liver neoplasms |
| | | | rat | oral | benign and malignant liver neoplasms, hepatocellular adenomas and carcinomas, intestinal metaplasia |
| **Tetrachloro-ethylene** | **2A** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Tetrachloroethylene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol63/volume63.pdf | | | | |
| | | | human | | consistently positive association with esophageal and cervical cancer and non-Hodgkins lymphoma |
| | | | mouse | oral | significant increase in the incidence of hepatocellular carcinomas |
| | | | rat | oral | inadequate for an evaluation of carcinogenicity |
| | | | mouse | inhalation | hepatocellular adenomas and carcinomas was significantly increased |
| | | | rat | inhalation | mononuclear-cell leukemia was significantly increased, and nonsignificant increase in uncommonly occurring renal-cell adenomas and adenocarcinomas was observed in male rats |
| | | | mouse | topical application | did not produce skin tumors |
| **Trichloro-ethylene** | **2A** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Trichloroethylene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol63/mono63-6.pdf | | | | |

(Continued)

Table 2 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2A—Probably carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | human | | liver and biliary tract cancer; non-Hodgkin's lymphoma |
| | | | mouse | oral | benign and malignant liver tumors |
| | | | mouse | inhalation | lymphomas |
| | | | mouse | inhalation | liver and lung tumors |
| | | | human | | cohort studies—occurrence of cancer of the kidney was not elevated |
| | | | hamster | inhalation | no increase in tumor incidence |
| | | | mice | topical application or subcutaneous injection | TCE and proposed metabolite trichloroethylene oxide did not increase incidence of skin tumors or local sarcoma |
| | | | rat | oral | Males: renal-cell tumors |
| | | | rat | oral | interstitial testicular tumors |
| | | | rat | inhalation | interstitial testicular and renal-cell tumors |

[1]NL = not listed

## Table 3. Summary of Classification Basis for COPC and Select Other Agents as IARC Group 2B—Possibly Carcinogenic to Humans

This category is used for agents for which there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when there is inadequate evidence of carcinogenicity in experimental animals. In some instances, an agent for which there is inadequate evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals, together with supporting evidence from mechanistic and other relevant data, may be placed in this group. An agent may be classified in this category solely on the basis of strong evidence from mechanistic and other relevant data.

## Table 3. Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Acrylonitrile** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Acrylonitrile.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-7.pdf | | | | |
| | | | rat | inhalation | glial cell tumors of the central nervous system |
| | | | rat | inhalation | Zymbal gland carcinoma |
| | | | rat | inhalation | malignant mammary tumors |
| | | | rat | inhalation | benign and malignant hepatocellular tumor |
| | | | human | | 4 cohort studies—no significant excess risk for any type of cancer when all exposed workers were compared with unexposed, or with an external comparison population |
| | | | rat | inhalation | extrahepatic angiosarcomas |
| **Antimony trioxide** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol47/volume47.pdf | | | | |
| | | | rat | inhalation | Females: lung tumors (scirrhous and squamous—cell carcinomas and bronchio-loalveolar tumors) |
| **Benzene Hexachloride (syn: lindane)** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Lindane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/suppl7/Suppl7-88.pdf | | | | |
| | | | mouse | oral | liver tumors; lymphoreticular neoplasms |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | oral | a few thyroid tumors |
| **Benz[a]anthracene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolycyclicAromaticHydrocarbons.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol92/mono92-10.pdf | | | | |
| | | | mouse | | positive in initiation-promotion studies on mouse skin. |
| **Benzo[b]fluoranthene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolycyclicAromaticHydrocarbons.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol92/mono92-10.pd | | | | |
| | | | mouse | dermal | significant carcinogenic activity |
| | | | mouse | IP injection | significant carcinogenic activity |
| | | | rat | intrapulmonary implantation | significant carcinogenic activity |
| **Benzo[k]fluoranthene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolycyclicAromaticHydrocarbons.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol92/mono92-10.pdf | | | | |
| | | | mouse | dermal | significant carcinogenic activity |
| | | | mouse | IP injection | significant carcinogenic activity |
| | | | rat | intrapulmonary implantation | significant carcinogenic activity |
| **Bromodichloromethane** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Bromodichloromethane.pdf | | | | |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-73.pdf | | | | |
| | | | rat | oral gavage | increased the incidences of adenomatous polyps and adenocarcinomas of the large intestine and of tubule-cell adenomas and adenocarcinomas of the kidney |
| | | | mouse | oral gavage | Males: tubule-cell adenomas and adenocarcinomas of the kidney; Females: hepatocellular adenomas and carcinomas |
| **Carbon tetrachloride** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/CarbonTetrachloride.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/volume71.pdf | | | | |
| | | | mouse | oral | liver tumors, including hepatocellular carcinomas |
| | | | mouse | intrarectal | liver tumors, including hepatocellular carcinomas |
| | | | rat | oral | benign and malignant liver tumors |
| | | | rat | subcutaneous | benign and malignant liver tumors; mammary adenocarcinomas |
| | | | rat | inhalation | benign and malignant liver tumors |
| **Cobalt sulfate and Soluble Cobalt** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/CobaltSulfate.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol86/mono86-6E.pdf | | | | |
| | | | mouse | inhalation | alveolar/bronchiolar neoplasms |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | inhalation | alveolar/bronchiolar neoplasms; adrenal pheochromocytomas in female rats |
| **Chlordane** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol79/mono79-17.pdf | | | | |
| | | | mouse | oral | increased incidences of hepatocellular neoplasms (including carcinomas) |
| | | | rat | | thyroid follicular-cell adenomas and carcinomas |
| | | | rat | | Males: marginally increased the incidence of liver adenomas |
| | | | mouse | | in initiation–promotion studies increased incidences of hepatocellular tumors |
| **4-Chloroaniline** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol57/mono57-21.pdf | | | | |
| | | | mouse | diet | hemangiosarcomas |
| | | | mouse | gavage | Males: hemangiosarcomas of the spleen and liver |
| | | | mouse | gavage | Males: hepatocellular adenomas and carcinomas |
| | | | rat | diet | Males: sarcomas of the spleen and splenic capsule |
| | | | rat | gavage | sarcomas of the spleen and splenic capsule |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Chloroform** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Chloroform.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-10.pdf | | | | |
| | | | mouse | oral | renal tubular tumors |
| | | | mouse | inhalation | renal tubular tumors |
| | | | rat | oral | renal tubular tumors |
| **Chrysene** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol92/mono92-10.pdf | | | | |
| | | | mouse | newborn | positive response in 2 of 3 studies |
| | | | mouse | initiation-promotion | positive response in 1 of 3 studies |
| | | | rat | pulmonary implantation | positive response |
| **DDT** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dichlorodiphenyltrichloroethane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol53/mono53-9.pdf | | | | |
| | | | mouse | oral | liver-cell tumors including carcinomas; lung carcinomas, malignant lymphomas |
| | | | rat | oral | liver tumors |
| | | | hamster | oral | increased incidence of adrenocortical adenomas |
| | | | mice | subcutaneous injection | liver tumors |
| | | | mouse | oral | Males: hepatoblastomas |

(Continued)

## Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **1,4-Dichlorobenzene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dichlorobenzene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-13.pdf | | | | |
| | | | mouse | oral | adenomas and carcinomas of the liver |
| | | | rats | | did not promote hepatic foci in a two-stage model of carcinogenesis |
| | | | rat | oral | Males: renal tubular carcinomas |
| **3,3'-Dichlorobenzidine** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dichlorobenzidine.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol99/mono99-10.pdf | | | | |
| | | | mouse | oral | lung (alveolar-cell adenomas and adenocarcinomas) |
| | | | rat | oral | Zymbal-gland tumors (adenomas and carcinomas), liver tumors (neoplastic nodules or hepatocellular carcinomas), large intestine tumors (adenomatous polyps or adenocarcinomas), skin tumors (basal cell adenomas and carcinomas), and oral cavity tumors (squamous cell papillomas and carcinomas) |
| | | | rat | oral | Males: preputial gland tumors (carcinomas), small intestine tumors (adenocarcinomas) and lung tumors |
| | | | dog | oral | bladder tumors |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | oral | Females: clitoral gland tumors (adenomas and carcinomas) and mammary gland tumors (adenocarcinomas) |
| | | | rat | subcutaneous | Zymbal-gland tumors |
| | | | rat | subcutaneous | Males: skin, preputial gland and forestomach tumors |
| | | | rat | subcutaneous | Females: mammary gland tumors |
| **p,p'-Dichlorodiphenyldichloroethane (TDE)** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol53/mono53-9.pdf | | | | |
| | | | mouse | oral | liver tumors in males and lung tumors in both M&F |
| | | | rat | oral | Males: thyroid tumors |
| **p,p'-Dichlorodiphenyldichloroethylene (DDE)** | **2B** | **NL** | | | |
| NTP hyperlink: | | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol53/mono53-9.pdf | | | | |
| | | | mouse | oral | high incidence of liver tumors in male and female mice in two studies |
| | | | hamster | oral | increased incidence of neoplastic liver nodules |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **1,2-Dichloroethane (syn: Ethylene dichloride)** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dichloroethane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-21.pdf | | | | |
| | | | human | | lymphatic, hematopoietic, stomach, pancreatic cancers |
| | | | mouse | oral | benign and malignant lung tumors and malignant lymphomas |
| | | | mouse | oral | Males: hepatocellular carcinoma |
| | | | mouse | oral | Females: mammary and uterine adenocarcinomas |
| | | | mouse | inhalation | liver, lung, and mammary gland tumors |
| | | | rat | oral | hemangiosarcomas |
| | | | rat | oral | Males: carcinomas of the forestomach |
| | | | mice | two-stage mouse-skin assay | not active as an initiator of skin carcinogenicity |
| | | | rat | inhalation | liver, lung, and mammary gland tumors |
| | | | rat | oral | Females: benign and malignant mammary tumors |
| **2,4-Dinitrotoluene** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol65/mono65-9.pdf | | | | |
| | | | mouse | oral | Males: renal tubular epithelium |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | mouse | oral | no tumorigenic effect reported |
| | | | rat | oral | Males: integumentary system |
| | | | rat | oral | hepatocellular carcinomas |
| | | | rat | oral | Females: fibroadenomas of the mammary gland |
| **2,6-Dinitrotoluene** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol65/volume65.pdf | | | | |
| | | | rat | oral | Males: hepatocellular neoplastic nodules and carcinomas in 2 studies |
| **1,4-Dioxane** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dioxane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-25.pdf | | | | |
| | | | mouse | oral | hepatocellular adenomas |
| | | | rats | oral | nasal cavity, liver subcutaneous tissues, mammary gland, and peritoneal mesotheliomas |
| | | | guinea pig | oral | liver and gall bladder |
| | | | rat | inhalation | no increase in tumors |
| | | | mouse | IP injection | Males: lung tumors |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | | promoting activity in two-stage liver foci assay |
| **Ethylbenzene** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol77/mono77-10.pdf | | | | |
| | | | mouse | inhalation | lung adenomas in males and liver adenomas in females |
| | | | rat | inhalation | Males: increased incidence of renal tubule adenomas and carcinomas; Females: renal adenomas after step-sectioning |
| | | | rat | oral | could not be evaluated |
| **Heptachlor** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol79/mono79-17.pdf | | | | |
| | | | mouse | oral | increased incidences of hepatocellular neoplasms (including carcinomas) |
| | | | rat | | thyroid follicular-cell adenomas and carcinomas |
| | | | mouse | | In initiation–promotion studies increased incidences of hepatocellular tumors |
| **Hexachlorobenzene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Hexachlorobenzene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol79/mono79-18.pdf | | | | |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | mouse | oral | liver-cell tumors |
| | | | rat | oral | liver-cell tumors |
| | | | rat | oral | renal tubular tumors |
| | | | hamster | oral | liver-cell tumors; liver hemangioendothelio-mas and thyroid follicular-cell adenomas |
| | | | rat | perinatal | parathyroid adenomas in males and adrenal pheochromocytomas in females |
| **Hexachloroethane** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Hexachloroethane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol73/mono73-15.pdf | | | | |
| | | | mouse | oral | liver tumors |
| | | | rat | oral | Males: renal tubular tumors |
| | | | rat | | promoting activity in two-stage liver initia-tion-promotion assay |
| **Indeno[1,2,3-cd] pyrene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/PolycyclicAromaticHydrocarbons.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol32/volume32.pdf | | | | |
| | | | mouse | subcutaneous injection | a complete carcinogen and an initiator for skin carcinogenesis -local sarcomas |
| **Methylene chloride (syn: dichloromethane)** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Dichloromethane.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol32/volume32.pdf | | | | |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | mouse | oral | no increase |
| | | | rat | oral | inconclusive |
| | | | mouse | inhalation | increased incidences of benign and malignant lung and liver tumors |
| | | | rat | inhalation | Females: benign mammary tumors |
| | | | rat | | Males: incidence of mammary gland adenomas and fibroadenomas was increased |
| | | | hamster | inhalation | negative |
| | | | mouse | IP injection | negative lung adenoma |
| **Mirex** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Mirex.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol20/volume20.pdf | | | | |
| | | | mouse | oral | benign and malignant liver tumors |
| | | | rat | oral | benign and malignant liver tumors |
| | | | mouse | subcutaneous injection | liver tumors were also found in males of one of the two strains of mice; suggested that it produced reticulum-cell sarcomas in males of both strains |
| **Naphthalene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Naphthalene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-8.pdf | | | | |
| | | | mouse | inhalation | Females: lung adenomas per tumor-bearing mouse |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | inhalation | neuroblastomas of the olfactory epithelium and adenomas of the nasal respiratory epithelium |
| | | | rat | oral | studies too limited |
| | | | mouse | IP injection | studies too limited |
| | | | rat | subcutaneous injection | studies too limited |
| | | | mouse | inhalation | bronchiolo-alveolar adenomas in female mice; -increase in males but not significant |
| **Nickel metallic** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Nickel.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol49/mono49-7.pdf | | | | |
| | | | mouse | inhalation | inadequate for assessment of carcinogenicity |
| | | | rat | inhalation | inadequate for assessment of carcinogenicity |
| | | | guinea pig | inhalation | inadequate for assessment of carcinogenicity |
| | | | rat | intramuscular injection | sarcomas |
| | | | hamster | intramuscular injection | sarcomas |
| | | | rat | intrapleural | sarcomas |
| | | | rat | subcutaneous | sarcomas |
| | | | rat | intraperitoneal | sarcomas and carcinomas |
| | | | rat | intratracheal instillation | significant numbers of squamous-cell carcinomas and adenocarcinomas of the lung |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | intrarenal injection | no significant increase in local kidney tumors |
| **Nitrobenzene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Nitrobenzene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol65/mono65-11.pdf | | | | |
| | | | mouse | inhalation | alveolar-bronchiolar neoplasms and thyroid follicular-cell adenomas |
| | | | rat | inhalation | Males: hepatocellular neoplasms, thyroid follicular-cell adenomas and adenocarcinomas, renal tubular-cell adenomas |
| | | | rat | inhalation | Females: hepatocellular neoplasms and endometrial stromal polyps were increased |
| | | | rat | | Males: hepatocellular neoplasms were increased. |
| **N-Nitroso-Di-n-propylamine** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Nitrosamines.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol17/volume17.pdf | | | | |
| | | | rat | oral | benign and malignant tumors of the liver, kidney, esophagus, and respiratory tract |
| | | | rat | subcutaneous injection | benign and malignant tumors of the liver, kidney, esophagus, and respiratory tract |
| | | | hamster | subcutaneous injection | benign and malignant tumors of the liver, kidney, esophagus, and respiratory tract |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Pentachlorophenol** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-34.pdf | | | | |
| | | | mouse | oral | Males: hepatocellular adenomas and carcinomas; adrenal pheochromocytomas |
| | | | mouse | oral | Females: hepatocellular adenomas; adrenal pheochromocytomas; malignant vascular tumors of the liver and spleen |
| | | | rat | oral | mesotheliomas of the tunica vaginalis |
| **Styrene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Styrene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol82/mono82-9.pdf | | | | |
| | | | mouse | inhalation | Males: pulmonary adenomas; Females: pulmonary adenomas; carcinomas in the high-dose group |
| | | | mouse | oral gavage | 2 studies negative |
| | | | mouse | oral gavage | 2 studies inadequate for an evaluation of the carcinogenicity of styrene |
| | | | rat | gavage | no reliable evidence for an increase in tumor incidence in 4 studies |
| | | | rat | drinking water | no reliable evidence for an increase in tumor incidence in 1 study |
| | | | rat | inhalation | no reliable evidence for an increase in tumor incidence in 2 studies |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| **Titanium Dioxide** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol93/mono93-7F.pdf | | | | |
| | | | rat | inhalation | in 2 studies: lung tumors in both sexes in one study and another in females only |
| | | | rat | intratracheal instillation | increases in the incidence of lung tumors |
| | | | mouse | intratracheal instillation | no increases |
| **Toxaphene** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Toxaphene.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol79/mono79-19.pdf | | | | |
| | | | mouse | oral | hepatocellular adenomas and carcinomas |
| | | | rat | oral | thyroid follicular-cell adenomas and carcinomas; pituitary adenomas in females |
| **2,4-Toluenediisocyanate** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/TolueneDiisocyanates.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-37.pdf | | | | |
| | | | mouse | gavage | Females: hemangiomas and hemangiosarcomas and hepatocellular adenomas |
| | | | rat | gavage | Males: subcutaneous fibromas and fibrosarcomas; pancreatic acinar-cell adenomas |

(Continued)

Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| | | | rat | gavage | Females: pancreatic isle-cell adenomas, neoplastic nodules of the liver and mammary gland fibroadenomas |
| | | | mouse | inhalation | no treatment-related tumor; study results not fully reported |
| | | | rat | inhalation | no treatment-related tumor; study results not fully reported |
| **2,6-toluene diisocyanate** | **2B** | **B** | | | |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/TolueneDiisocyanates.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-37.pdf | | | | |
| | | | rat | gavage | Males: subcutaneous fibromas and fibrosarcomas |
| | | | rat | gavage | Males: pancreatic acinar-cell adenomas |
| | | | rat | gavage | Females: pancreatic islet-cell adenomas, neoplastic nodules of the liver, and mammary gland fibroadenomas |
| | | | mouse | gavage | Females: hemangiomas and hemangiosarcomas, hepatocellular adenomas; no tumors observed in male mice |
| | | | mouse | inhalation | No treatment-related tumor—study results not fully reported |
| | | | rat | inhalation | No treatment-related tumor—study results not fully reported |
| **2,4,6-Trichlorophenol** | **2B** | **B** | | | |

(Continued)

## Table 3 (Continued). Summary of classification basis for COPC and select other agents as IARC Group 2B—Possibly carcinogenic to humans

| Agent | Category | | Summary of IARC findings on cancer | | |
|---|---|---|---|---|---|
| | IARC | NTP[1] | Species | Route of administration | Type of cancer/Tumor/Promoting activity |
| NTP hyperlink: | http://ntp.niehs.nih.gov/ntp/roc/twelfth/profiles/Trichlorophenol.pdf | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-34.pdf | | | | |
| | | | mouse | oral | benign and malignant liver tumors |
| | | | rat | oral | mononuclear cell leukemia |
| **Vanadium Pentoxide** | **2B** | **NL** | | | |
| NTP hyperlink: | Not applicable | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol86/mono86-10.pdf | | | | |
| | | | mouse | inhalation | alveolar/bronchiolar neoplasms |
| | | | rat | inhalation | Males: alveolar/bronchiolar neoplasms |
| **Vinyl acetate** | **2B** | **NL** | | | |
| NTP hyperlink: | | | | | |
| IARC hyperlink: | http://monographs.iarc.fr/ENG/Monographs/vol63/mono63-19.pdf | | | | |
| | | | mouse | inhalation | no treatment-related increase in tumor incidence |
| | | | rat | inhalation | increased incidence of nasal cavity tumors |
| | | | rat | drinking water | in utero and life: No treatment-related increase in tumor incidence |

[1]NL = not listed

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