Abstract

People are continuously exposed to varying amounts of chemicals that have been shown to have carcinogenic or mutagenic properties in experimental systems. Chemical carcinogens can occur exogenously or endogenously in living organisms (aerobic metabolic processes, hormonal changes, oxygen uptake and distribution, pathophysiologic states such as inflammation, genetic factors, etc.). Exogenous exposure to carcinogens can occur through food consumption, air, occupational exposure and drinking water. It has been estimated that exposure to extrinsic or environmental carcinogens may contribute significantly to the causation of a sizable fraction of human cancers, estimated to the range of 75-80%. Epidemiological studies provide evidence that lifestyle causes of cancer such as diet, tobacco smoking, obesity, alcohol, etc., are the major contributors to human malignant neoplasms. Carcinogenesis is a multistep process that affects to a great extent old age. The carcinogenic risk to chemical carcinogens is a composite of its effects on multiple genetic and epigenetic processes. International and national organizations, such as the International Agency for Research on Cancer (IARC), the National Toxicology Program (NTP) and other health and safety agencies, evaluate the carcinogenic risks of various chemicals, physical and biological agents. The European Commission through the Directive 67/548/EEC and 93/101/EEC on Chemical Carcinogens and Mutagens, has collected experimental data and risk assessment studies on chemical carcinogens. Also, numerous scientific studies evaluated the carcinogenic potential through in vivo studies on experimental animals and in vitro studies in cell lines. These organizations also set the limits of exposure (especially in the working environment) and legislate to restrict the use of chemical carcinogens in other applications.

Keywords: carcinogenic chemicals, classification of risks, IARC, REACH.
Introduction: Chemical Carcinogens, Molecular Mechanisms of Carcinogenesis and Risks to Humans

Chemical carcinogens are substances or mixtures which have the potential to induce cancer to humans under certain conditions and for prolonged or excessive periods of exposure. Chemical carcinogens can be natural chemicals, synthetic compounds or mixtures of both, that are produced or used for industrial, agricultural or commercial purposes. Carcinogens can cause cancer by direct action in the cellular DNA or through mechanisms that generate chemical species (such as free radicals, reactive oxygen species, carcinogenic metabolites) which enter the cell nucleus causing mutations to cellular DNA. Chemically-induced cancer generally develops many years after exposure to a carcinogenic agent. A latency period of as much as thirty years has been observed between exposure to asbestos fibres (a known carcinogenic agent), for example, and incidence of lung cancer.1,2

Carcinogenesis is a multistep process that proceeds through multiple discernible stages, including initiation, promotion, and progression. The transition between these stages is driven by different environmental and endogenous factors and involves different mechanisms and genetic elements. Several types of chemicals initiate the carcinogenic process by yielding highly reactive species that bind covalently to cellular DNA. These carcinogenic agents distort the conformation of DNA and its functions during DNA replication and transcription. These changes have implications with respect to oncogene activation, DNA amplification, gene transposition and chromosome translocation. Carcinogenic chemicals may influence the carcinogenic process by mutational activation of protooncogenes and/or inactivation of tumor suppression genes. In addition, chemical carcinogens may act on non-mutational processes such as the clonal expansion of premalignant cells. The carcinogenic risk of specific chemical carcinogens is a composite of its effects on multiple genetic and epigenetic processes.3,4

Exogenous chemical carcinogenesis is an extremely complex multi-factorial process during which gene-environment interactions involving chronic exposure to chemical carcinogens and polymorphisms of cancer susceptibility genes add further complexity. These exogenous chemical carcinogens could be major contributors to human cancer.5

Chemicals related to environmental pollution appear to be of critical importance in inducing cancer, such as occupational cancers. Scientists have established that outdoor air pollution (suspended particulate matter associated with PAHs and other carcinogenic chemicals), indoor air pollution (environmental tobacco smoke, formaldehyde, VOCs such as benzene and 1,3-butadiene), food pollution (food additives, pesticide residues, dioxins, organochlorines) and other chemical pollutants (such as metals, metalloids, pharmaceutical medicines, cosmetics, etc) may contribute to malignant neoplasms in humans.6

In recent years, epidemiologists and cancer specialists agree that environmental factors play an important part in carcinogenesis. But, it is evident to them that especially lifestyle factors (tobacco smoking, diet, alcohol consumption, obesity, sedentary life and other known lifestyle factors (excessive exposure to sunlight, viruses, sexual life, hormonal changes, etc) are contributing to a major proportion of human cancers.7 Occupational cancers are known to cause, approximately, 4-5% of human cancers, but in recent years new health and safety regulations in the working environment and the substitution and/or restriction of many known chemical carcinogens reduced substantially the risk of exposure to workers.8,9

International Agency for Research on Cancer (IARC): Classification and Evaluation of Carcinogenic Agents

There are many international and national organizations that collect information, scientific studies and toxicological data which help to classify and regulate chemical carcinogens, complex mixtures, occupational exposures, physical agents and lifestyle factors. The most prominent is the International Agency for Research on Cancer (IARC, Lyon, France, http://www.iarc.fr ), an international scientific organization of the World Health Organization (WHO). IARC has
international teams of toxicologists, cancer biologists, epidemiologist of cancer and experts. These teams (Working Groups) since 1971 collected data on more than 900 agents and evaluated the carcinogenicity of approximately 400, especially their carcinogenic potential to humans and the risk to cause cancers under certain environmental conditions.10

IARC established criteria for the classification of carcinogenic agents and evaluated their risks to humans. Until now IARC (2009) has published a series of 97 Monographs on the Evaluation of Carcinogenic Risks to Humans. Also, IARC has published more than 150 related Scientific Publications on cancer, carcinogenic risk and carcinogenesis by well known independent experts and research scientists from all over the world.11

Each monograph consists of a brief description, data on chemical and physical properties, methods of production, use and occurrence, relevant epidemiological studies, evidence of carcinogenicity, toxicity and genetic effects. These monographs are used worldwide by research scientists, public health authorities and international regulatory agencies. IARC classifies carcinogenic agents as follows:

- **Group 1: the agent is carcinogenic to humans** (number 108 agents) (sufficient evidence of carcinogenicity to humans, epidemiologic evidence, occupational exposure, and animal studies. Strong evidence that the agent acts through relevant mechanisms of carcinogenicity to humans).

- **Group 2A: The agent is probably carcinogenic to humans** (number of agents 66) (limited evidence of carcinogenicity to humans. Sufficient evidence of carcinogenicity in experimental animals. Strong evidence that the carcinogenesis is mediated by mechanisms that are also operate in humans)

- **Group 2B: The agent is possibly carcinogenic to humans** (number of agents 248) (limited evidence in humans. Less than sufficient evidence in experimental animals. Inadequate evidence in humans but sufficient or limited in experimental animals).

- **Group 3: The agent is not classifiable as to its carcinogenicity to humans** (number of agents 515) (Inadequate evidence in humans. Inadequate or limited to experimental animals. Mechanisms of carcinogenesis in animals does not operate in humans).

- **Group 4: The agent is probably not carcinogenic to humans** (group 4 is not used, negative evidence of carcinogenicity, contains only one chemical, caprolactam).

**The National Toxicology Program (USA) for Long-term Cancer Studies of Suspected Chemicals**

The National Toxicology Program (NTP) was established in 1978 by the Secretary of Health and Human Services (U.S.A.) to coordinate toxicology research and testing of potential hazardous chemicals. The NTP supports national public health programmes by initiating research designed to understand the physiological, metabolic and genetic basis of chemical toxicity. Among the responsibilities of NTP are in vitro and in vivo toxicity testing of suspected chemical carcinogens, broadening the spectrum of toxicological information on known hazardous chemicals, developing and validating toxicologic assay systems and rapidly communicating test results to government agencies with regulatory responsibilities as well as to medical and scientific communities.12

The concept of testing chemical carcinogens in experimental animals as a surrogate for human risk was formulated in 1960 by the National Cancer Institute (Director Dr. K. Endicott). The NTP tumor bioassay system in rats and mice has become the universally accepted standard for rodent toxicity tests. Also, the NTP has added numerous in vivo non-cancer assays, both chronic and sub-chronic, to the toxicological evaluation including metabolic fate of the chemical, tissue distribution, specific organ toxicity, neurotoxicity, reproductive failure and teratology. The growth of molecular genetics has stimulated the NTP to initiate efforts into development of potentially new assays based upon transgenic technology that will extent understanding of the metabolic mechanisms of chemical toxicity down to the level of the gene.12
The National Toxicology Program started publishing the Reports of Carcinogens in 1980, and the last one is the 11\textsuperscript{th} Report (January 2005). The 11\textsuperscript{th} Report has a total of 246 entries, of which 58 are known to be human carcinogens and 188 reasonably anticipated to be human carcinogens.\textsuperscript{13}

The criteria used by the NTP for listing an agent, substance, mixture, or exposure circumstance in the Reports of Carcinogens (RoC) are as follows:

1. **Known To Be Human Carcinogen:** There is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure to the agent, substance, or mixture, and human cancer.

2. **Reasonably Anticipated To Be Human Carcinogen:** There is limited evidence of carcinogenicity from studies in humans which indicates that causal interpretation is credible, but that alternative explanations, such as chance, bias, or confounding factors, could not adequately be excluded,

   2a. 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, or (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

   2b. 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 Report on Carcinogens 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 considers that its studies, regarding carcinogenicity to 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 sub-populations, 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. This evidence can include traditional cancer epidemiology studies, data from clinical studies, and/or data derived from the study of tissues or cells from humans exposed to the substance in question that can be useful for evaluating whether a relevant cancer mechanism is operating in people.\textsuperscript{13}

**Other Organizations and Systems for Classification and Evaluation of Chemical Carcinogens**

The Globally Harmonized System of Classification and labeling of Chemicals (GHS) is a United Nations (UN) initiative to attempt to harmonize the different systems of assessing chemical risk which currently exist (as of March 2009) around the world. It classifies carcinogens into two categories, of which the first may be divided again into subcategories if so desired by the competent regulatory authority:

- **Category 1:** known or presumed to have carcinogenic potential for humans
- **Category 1A:** the assessment is based primarily on human evidence
- **Category 1B:** the assessment is based primarily on animal evidence
- **Category 2:** suspected human carcinogens
The Revised third edition of Globally Harmonized System of Classification and Labelling of Chemicals (GHS) was published in July 2009. (http://www.unece.org/thans/danger/publi/ghs/ghs_rev03/03files_e.html)

The American Conference of Governmental Industrial Hygienists (ACGIH)

The ACGIH is a private organization in the United States, best known for its publication of threshold limit values (TLVs) for occupational exposure and monographs on workplace chemical hazards. The ACGIH assesses carcinogenicity as part of wider assessment of the occupational hazards of chemicals. The ACGIH has the following classification (http://www.acgih.org).

- **Group A1:** Confirmed human carcinogen
- **Group A2:** Suspected human carcinogen
- **Group A3:** Confirmed animal carcinogen with unknown relevance to humans
- **Group A4:** Not classifiable as a human carcinogen
- **Group A5:** Not suspected as a human carcinogen

The European Union on Classification and Evaluation of Chemical Carcinogens

The European Union has its own classification of carcinogens which is part of the Directive for Dangerous Substances and the Dangerous Preparations Directive. It consists of three categories of carcinogenic agents:


The new regulations about dangerous chemicals in the European Union have changed with the new regulation of REACH (Registration, Evaluation and Authorization of Chemicals, 2006). Hazard assessment of carcinogens for the REACH system can follow various techniques, including QSARs (Quantitative Structure-Activity Relationships), transgenic mouse assays and other alternative methodologies. 20-22

There are recent developments and parallel discussions of how to assess carcinogenicity of chemicals in Europe. The European center for Ecotoxicology and Toxicology of Chemicals (ECETOX) and the European Environmental Mutagen Society (EEMS) discussed new concepts of thresholds in mutagenesis and carcinogenesis within the EUROTOX Congress (Budapest, Sept. 2002) and in other recent conferences.23, 24

The classification of carcinogens, according to the EU, consists of three categories of carcinogenic agents:

- **Category 1:** Substances known to be carcinogenic to humans.
- **Category 2:** Substances which should be regarded as if they are carcinogenic to humans.
- **Category 3:** Substances which cause concern for humans, owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment.

This assessment scheme of the European Union is being phased out in favor of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) of the United Nations, to which it is very close in category definitions.
The Carcinogenic Potency Project (CPDB)

The Carcinogenic Potency Project started in 1980 by Professors Bruce Ames and Lois Swirsku Gold (Berkeley, University of California). The project publishes regular updates of their results. The CPDB has contacted 6540 chronic animal cancer tests on 1547 chemicals for their carcinogenic potency, expressed as TD50, and its statistical significance in rats, mice, hamsters, dogs, and nonhuman primates. (http://potency.berkeley.edu)

Scandinavian Countries and Carcinogen Classification

Scandinavian countries are very active for decades in setting standards for carcinogenic agents in the working environment aiming for the protection of workers. Carcinogen classification approaches and risk assessment methodologies differ between countries.25

In Europe, differences between countries and organizations exist in terms of how chemical carcinogenicity is evaluated, how risk assessments are performed and how occupational exposure limits (OELs) are established.26 Differences in cancer classification exist in part due to differences in the ultimate purpose of classification and to the relative importance of different types of data. For example, there are differences in how some scientists extrapolate carcinogenic data from animal studies to human data, or interpret mechanistic data, or characterize benign and malignant tumour. But the various groups of experts tend to agree on classification of chemicals with good evidence of carcinogenicity in humans, and agree less on classification or limited evidence in humans. Most distinguish between genotoxic and non-genotoicx chemicals when conducting risk assessment. Also, risk assessment approaches include other factors and selection criteria, such as health vs technology-based exposure limits, technology feasibility and socio-economic factors.27-30

The differences on carcinogenic classification of certain chemicals (acrylonitrile, asbestos, benzene, chloroform, cadmium, etc) among IARC, European Union, Germany, Netherlands, Sweden and Norway are presented in the following Table 1.

Table 1. Differences on carcinogenic classification of certain chemicals in various countries, IARC and the European Union.

<table>
<thead>
<tr>
<th>Chemical</th>
<th>IARC</th>
<th>European Union</th>
<th>Germany</th>
<th>Netherlands</th>
<th>Sweden</th>
<th>Norway</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetonitrile</td>
<td>2B</td>
<td>nc</td>
<td>2</td>
<td>1</td>
<td>nc</td>
<td>K2</td>
</tr>
<tr>
<td>Asbestos</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>K2</td>
</tr>
<tr>
<td>Benzene</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>K2</td>
</tr>
<tr>
<td>Benzo[a]pyrene</td>
<td>2A</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>K1</td>
</tr>
<tr>
<td>Cadmium</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>II</td>
</tr>
<tr>
<td>Chloroform</td>
<td>2B</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>K3</td>
</tr>
<tr>
<td>Chromium (VI)</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>K1</td>
</tr>
<tr>
<td>1,2-Dichloroethylene</td>
<td>2B</td>
<td>Nc</td>
<td>2</td>
<td>1</td>
<td>nc</td>
<td>K2</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>K1</td>
</tr>
<tr>
<td>Methylene Chloride</td>
<td>2B</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>K3</td>
</tr>
<tr>
<td>Propylene oxide</td>
<td>2B</td>
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<td>2</td>
<td>2</td>
<td>2</td>
<td>K2</td>
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<tr>
<td>Tetrachloroethylene</td>
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<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>K2</td>
</tr>
<tr>
<td>Trichloroethylene</td>
<td>2A</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>3</td>
<td>K3</td>
</tr>
<tr>
<td>Vinylchloride</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>K2</td>
</tr>
</tbody>
</table>

nc: not classified. Acetonitrile and 1,2-Dichloroethylene are classified as dangerous, but not carcinogenic, by the EU and Sweden.

Conclusions

Identification, classification and risk assessment of carcinogenic chemicals by international organizations and national agencies of health and safety in the working environment, have been advanced in recent years. Despite the differences in interpreting the results of carcinogenic studies, there are general agreements on the classification of most chemicals and preventative actions to restrict or avoid completely the use or exposure to carcinogens in the natural environment and especially under occupational condition in the workplaces.

References

13. Hoenerhoff MJ, Hong HH, Ton TV, Lahouse SA, Sills RC. A review of the molecular mechanisms of chemically induced neoplasia in rat and mouse models in National Toxicology Program Bioassays and their relevance to human cancer. Toxicol Pathol 2009 [Epub ahead of print].
APPENDIX
IARC Overall Evaluations of Carcinogenicity to Humans

Group 1: Carcinogenic to humans
Agents and groups of agents (108 agents up to 2009)

4-Aminobiphenyl [CAS No.: 92-67-1]
Aristolochic acid
(NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant data)
Arsenic [7440-38-2]
(NB: This evaluation applies to the group of compounds as a whole and not necessarily to all individual compounds within the group)
Asbestos [1332-21-4]
Azathioprine [446-86-6]
Benzene [71-43-2]
Benzidine [92-87-5]
Benzo[a]pyrene [50-32-8]
(BNB: Overall evaluation upgraded from 2B to 1 based on mechanistic and other relevant data)
Beryllium [7440-41-7] and beryllium compounds
N,N-Bis(2-chloroethyl)-2-naphthylamine (Chlornaphazine) [494-03-1]
Bis(chloromethyl)ether [542-88-1] and chloromethyl methyl ether [107-30-2] (technical-grade)
1,3-Butadiene [106-99-0]
1,4-Butanediol dimethanesulfonate (Busulphan; Myleran) [55-98-1]
Cadmium [7440-43-9] and cadmium compounds
Chlorambucil [305-03-3]
1-(2-Chloroethyl)-3-(4-methylcyclohexyl)-1-nitrosourea (Methyl-CCNU; Semustine) [13909-09-6]
Chromium[VI]
Cyclophosphamide [50-18-0] [6055-19-2]
Cyclosporine [79217-60-0]
Diethylstilboestrol [56-53-1]
Dyes metabolized to benzidine
(NB: Overall evaluation upgraded to Group 1 based on mechanistic and other relevant data)
Epstein-Barr virus
Erionite [66733-21-9]
Estrogen-progestogen menopausal therapy (combined)
Estrogen-progestogen oral contraceptives (combined)
(NB: There is also convincing evidence in humans that these agents confer a protective effect against cancer in the endometrium and ovary)
Estrogens, nonsteroidal
(NB: This evaluation applies to the group of compounds as a whole and not necessarily to all individual compounds within the group)
Estrogens, steroidal
(NB: This evaluation applies to the group of compounds as a whole and not necessarily to all individual compounds within the group)
Estrogen therapy, postmenopausal
Ethanol [64-17-5] in alcoholic beverages (Vol. 96; in preparation)
Ethylene oxide [75-21-8]
(NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant data)
Etoposide [33419-42-0]
(NB: Overall evaluation upgraded from 2A to 1 based on mechanistic and other relevant data)
Etoposide in combination with cisplatin and bleomycin
Formaldehyde [50-00-0]
Gallium arsenide [1303-00-0]
[Gamma Radiation: see X- and Gamma (g)-Radiation]
Helicobacter pylori (infection with)
Hepatitis B virus (chronic infection with)
Hepatitis C virus (chronic infection with)
Human immunodeficiency virus type 1 (infection with)
Human papillomavirus types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59 an 60
(NB: The HPV types that have been classified as carcinogenic to humans can differ by an order of magnitude in risk for cervical cancer)
Human T-cell lymphotropic virus type 1
Melphalan [148-82-3]
8-Methoxypsoralen (Methoxsalen) [298-81-7] plus ultraviolet A radiation
Methylenebis(chloroaniline) (MOCA) [101-14-4]
(NB: Overall evaluation upgraded to Group 1 based on mechanistic and other relevant data)
MOPP and other combined chemotherapy including alkylating agents
Mustard gas (Sulfur mustard) [505-60-2]
2-Naphthylamine [91-59-8]
Neutrons
(NB: Overall evaluation upgraded from 2B to 1 with supporting evidence from other relevant data)
Nickel compounds
\( N'\)-Nitrosonornicotine (NNN) [16543-55-8] and 4-(\(N\)-Nitrosomethylamino)-1-(3-pyridyl)-1-butane (NNK) [64091-91-4]
(NB: Overall evaluation upgraded from 2B to 1 based on mechanistic and other relevant data)
\[Oestrogen: \text{see} \ \text{Estrogen}\]
Opisthorchis viverrini (infection with)
[Oral contraceptives, combined estrogen-progestogen: see Estrogen-progestogen oral contraceptives (combined)]
Oral contraceptives, sequential
Phenacetin [62-44-2]
(NB: Overall evaluation upgraded from 2A to 1 with supporting evidence from other relevant data)
Phosphorus-32, as phosphate
Plutonium-239 and its decay products (may contain plutonium-240 and other isotopes), as aerosols
Radioiodines, short-lived isotopes, including iodine-131, from atomic reactor accidents and nuclear weapons detonation (exposure during childhood)
Radionuclides, a-particle-emitting, internally deposited
(NB: Specific radionuclides for which there is sufficient evidence for carcinogenicity to humans are also listed individually as Group 1 agents)
Radionuclides, b-particle-emitting, internally deposited
(NB: Specific radionuclides for which there is sufficient evidence for carcinogenicity to humans are also listed individually as Group 1 agents)
Radium-224 and its decay products
Radium-226 and its decay products
Radium-228 and its decay products
Radon-222 [10043-92-2] and its decay products
Schistosoma haematobium (infection with)
Silica [14808-60-7], crystalline (inhaled in the form of quartz or cristobalite from occupational sources)
Solar radiation
Talc containing asbestiform fibres
Tamoxifen [10540-29-1]
(NB: There is also conclusive evidence that tamoxifen reduces the risk of contralateral breast cancer)

2,3,7,8-Tetrachlorodibenzo-para-dioxin [1746-01-6]
(NB: Overall evaluation upgraded from 2A to 1 with supporting evidence from other relevant data)
Thiotepa [52-24-4]
Thorium-232 and its decay products, administered intravenously as a colloidal dispersion of thorium-232 dioxide
Or-tho-Toluidine [95-53-4]
Treosulfan [299-75-2]
Vinyl chloride [75-01-4]
X- and Gamma (γ)-Radiation

Mixtures
Aflatoxins (naturally occurring mixtures of) [1402-68-2]
Alcoholic beverages
Areca nut
(NB: Overall evaluation based on human data, animal data, and mechanistic and other relevant data)
Betel quid with tobacco
Betel quid without tobacco
Coal-tar pitches
Coal-tars [8007-45-2]
Household combustion of coal, indoor emissions from
Mineral oils, untreated and mildly treated
Phenacetin, analgesic mixtures containing
Plants containing aristolochic acid
Salted fish (Chinese-style)
Shale-oils [68308-34-9]
Soots
Tobacco, smokeless
Wood dust

Exposure circumstances
Aluminium production
Arsenic in drinking-water
Auramine production
Boot and shoe manufacture and repair
Chimney sweeping
Coal gasification
Coal-tar distillation
Coke production
Furniture and cabinet making
Haematite mining (underground) with exposure to radon
Involuntary smoking (exposure to secondhand or 'environmental' tobacco smoke)
Iron and steel founding
Isopropyl alcohol manufacture (strong-acid process)
Magenta production
Painter (occupational exposure as a)
Paving and roofing with coal-tar pitch
Rubber industry
Strong-inorganic-acid mists containing sulfuric acid (occupational exposure to)
Tobacco smoking and tobacco smoke

Last updated: 16 January 2009
IARC: Group 2A
(number of agents 66)
(http://monographs.iarc.fr/ENG/Classification/crthgr02a.php)

The agent is probably carcinogenic to humans (limited evidence of carcinogenicity to humans. Sufficient evidence of carcinogenicity in experimental animals. Strong evidence that the carcinogenesis is mediated by mechanisms that are also operate in humans).

Selection of chemicals
Acrylamide[79-06-1]  
(NB: Overall evaluation upgraded from 2B to 2A with supporting evidence from other relevant data)
Adriamycin[23214-92-8]  
(NB: Overall evaluation upgraded from 2B to 2A with supporting evidence from other relevant data)
Azacitidine[320-67-2]  
(NB: Overall evaluation upgraded from 2B to 2A with supporting evidence from other relevant data), etc.

IARC: Group 2B
(number of agents 248)
(http://monographs.iarc.fr/ENG/Classification/crthgr02b.php)

The agent is possibly carcinogenic to humans (limited evidence in humans. Less than sufficient evidence in experimental animals. Inadequate evidence in humans but sufficient or limited in experimental animals).

Selection of the first chemicals (Group 2B)
Acetaldehyde [75-07-0]
Acetamide [60-35-5]
Acrylonitrile [107-13-1]
AF-2 [2-(2-Furyl)-3-(5-nitro-2-furyl)acrylamide] [3688-53-7]
Aflatoxin M1 [6795-23-9]
para-Aminoazobenzene [60-09-3]
ortho-Aminoazotoluene [97-56-3]
2-Amino-5-(5-nitro-2-furyl)-1,3,4-thiadiazole [712-68-5]
Amsacrine [51264-14-3]
ortho-Anisidine [90-04-0]
Antimony trioxide [1309-64-4], etc.

IARC: Group 3
(number of agents 515)
(http://monographs.iarc.fr/ENG/Classification/crthgr03.php)

The agent is not classifiable as to its carcinogenicity to humans (Inadequate evidence in humans. Inadequate or limited to experimental animals. Mechanisms of carcinogenesis in animals does not operate in humans).

Selection of first chemicals (Group 3)
Acenaphthene [83-32-9]
Acepyrene (3,4-dihydrocyclopenta(cd)pyrene) [25732-74-5]
Aciclovir [59277-89-3]
Acridine orange [494-38-2]
Acriflavinium chloride [8018-07-3]
Acrolein [107-02-8]
Acrylic acid [79-10-7]
Acrylic fibres
Actinomycin D [50-76-0], etc.