The occupational environment has been a most fruitful one for investigating the etiology of human cancer. Many recognized human carcinogens are occupational carcinogens. There is a large volume of epidemiologic and experimental data concerning cancer risks in different work environments. It is important to synthesize this information for both scientific and public health purposes. Various organizations and individuals have published lists of occupational carcinogens. However, such lists have been limited by unclear criteria for which recognized carcinogens should be considered occupational carcinogens, and by inconsistent and incomplete information on the occupations and industries in which the carcinogenic substances may be found and on their target sites of cancer. Based largely on the evaluations published by the International Agency for Research on Cancer, and augmented with additional information, the present article represents an attempt to summarize, in tabular form, current knowledge on occupational carcinogens, the occupations and industries in which they are found, and their target organs. We have considered 28 agents as definite occupational carcinogens, 27 agents as probable occupational carcinogens, and 113 agents as possible occupational carcinogens. These tables should be useful for regulatory or preventive purposes and for scientific purposes in research priority setting and in understanding carcinogenesis. Key words: cancer, environment, epidemiology, occupation, review. Environ Health Perspect 112:1447–1459 (2004). doi:10.1289/ehp.7047 available via http://dx.doi.org/ [Online 15 July 2004]

Occupational carcinogens occupy a special place among the different classes of human carcinogens. The occupational environment has been a most fruitful one for investigating the etiology and pathogenesis of human cancer. Up to the 1970s, most recognized human carcinogens were substances or circumstances found primarily in the occupational environment, and although this may no longer be true with the growing list of recognized non-occupational carcinogens, they still represent a large fraction of the total. Although it is important to discover occupational carcinogens for the sake of preventing occupational cancer, the potential benefit of such discoveries goes beyond the factory walls because most occupational exposures find their way into the general environment, sometimes at higher concentrations than in the workplace.

There is a large volume of epidemiologic and experimental data concerning cancer risks in different work environments. It is important to synthesize this information for both scientific and public health purposes. Various national and international bodies have published lists of carcinogens, but available lists of occupational carcinogens have been limited in various ways. Among the issues that are often missing, or treated rather casually, are a coherent assessment of which substances should be considered occupational carcinogens; information on the occupations and industries in which the carcinogenic substances may be found; and the target sites of cancer. The present article represents an attempt to summarize, in tabular form, current knowledge on occupational carcinogens, the occupations and industries in which they are found, and their target organs.

Methods and Results

Difficulties in listing occupational carcinogens. Although it seems like a simple enough task, it is very difficult to draw up an unambiguous list of occupational carcinogens. The first source of ambiguity concerns the definition of an "occupational" carcinogen. Most occupational exposures are also found in the general environment, and/or in consumer products; most general environmental exposures and consumer products, including medications, foods, and others, are found in some occupational environments. The distinctions can be quite arbitrary. For instance, although tobacco smoke, sunlight, and immunosuppressive medications are not primarily considered to be occupational exposures, there certainly are workers whose occupations bring them into contact with these agents. Also, although asbestos, benzene, and radon gas are considered to be occupational carcinogens, they are also found widely among the general population, and indeed, it is likely that many more people are exposed to these substances outside than inside the occupational environment. There is no simple rule to earmark occupational carcinogens as opposed to nonoccupational ones. Further, some carcinogens are chemicals that are used for research purposes and to which few people would ever be exposed, whether occupationally or nonoccupationally. Our operational criterion for designating occupational carcinogens is outlined below.

A second source of ambiguity derives from the rather idiosyncratic nature of the evidence. In some instances, we know that an occupational or industrial group is at excess risk of cancer, and we have a good idea of the causative agent; for example, scrotal cancer among chimney sweeps and polyaromatic hydrocarbons (PAHs) in soot (Waldron 1983), and lung cancer among asbestos miners and asbestos fibers [International Agency for Research on Cancer (IARC) 1977]. In some instances, we know that a group experienced excess risk but the causative agent is unknown or at least unproven [e.g., lung cancer among painters (IARC 1989c), bladder cancer among workers in the aluminum industry (IARC 1987)]. The strength of the evidence for an association can vary. For some associations, the evidence of excess risk seems incontrovertible [e.g., liver angiosarcoma and vinyl chloride monomer (IARC 1979b), bladder cancer and benzidine (IARC 1982b)]. For some associations, the evidence is suggestive [e.g., lung cancer and diesel engine exhaust (IARC 1989a), bladder cancer and employment as a painter (IARC 1989c)]. Among the many substances in the industrial environment for which there are no human data concerning carcinogenicity, there are hundreds that have been shown to be carcinogenic in some animal species and thousands that have been shown to have some effect in assays of mutagenicity or genotoxicity. These considerations complicate the attempt to devise a list of occupational carcinogens.

IARC Monographs. For this task we drew on the authoritative IARC Monograph Program and its evaluation of carcinogenic risks to humans (IARC 1987). The objective of the IARC Monograph Program, which has
been operating since 1971, is to publish critical reviews of epidemiologic and experimental data on carcinogenicity for chemicals, groups of chemicals, industrial processes, other complex mixtures, physical agents, and biologic agents to which humans are known to be exposed, to evaluate the data in terms of human risk, and to indicate where additional research efforts are needed.

Substances are selected by IARC for evaluation on the basis of two main criteria: a) humans are exposed, and b) there is reason to suspect that the substance may be carcinogenic. Direct evidence concerning carcinogenicity of a substance can come from epidemiologic studies among humans or from experimental studies of animals (usually rodents). Additional evidence comes from the results of studies of chemical structure–activity analysis, absorption and metabolism, physiology, mutagenicity, cytotoxicology, and other aspects of toxicity. In the IARC Monographs, all types of data contribute to the evaluation.

In this article, we outline the IARC process because it is important to understand how decisions are made in order to properly interpret these decisions. IARC evaluations are carried out during specially convened meetings that typically last a week. The meetings may evaluate only one agent, such as silica, or they may address a set of related agents or even exposure circumstances such as an occupation or an industry. For each such meeting, and there have typically been three per year, IARC convenes an international working group, usually involving from 15 to 30 experts on the topic(s) being evaluated, from four perspectives, a) exposure and occurrence of the substances being evaluated, b) human evidence of cancer risk (i.e., epidemiology), c) animal carcinogenesis, and d) other data relevant to the evaluation of carcinogenicity and its mechanisms. The working group is asked to review all of the literature relevant to an assessment of carcinogenicity. In the first part of the meeting, four subgroups (based on the four perspectives mentioned above) review and revise drafts prepared by members of the subgroup, and each subgroup develops a joint review and evaluation of the evidence on which they have focused. Subsequently, the entire working group convenes in plenary and proceeds to derive a joint text. They determine whether the epidemiologic evidence supports the hypothesis that the substance causes cancer, and, separately, whether the animal evidence supports the hypothesis that the substance causes cancer. The judgments are not simply dichotomous (yes/no), but rather they allow the working group to express a range of opinions on each of the dimensions evaluated. Table 1 shows the categories into which the working groups are asked to classify each substance, when examining only the epidemiologic evidence and when examining only the animal experimental evidence. The operational criteria for making these decisions leave room for interpretation, and the scientific evidence itself is open to interpretation. It is not surprising, then, that the evaluations are sometimes difficult and contentious.

The overall evaluation of human carcinogenicity is based on the epidemiologic and animal evidence of carcinogenicity, plus any other relevant evidence on genotoxicity, mutagenicity, metabolism, or mechanisms. Epidemiologic evidence, where it exists, is given greatest weight. Direct animal evidence of carcinogenicity is next in importance, with increasing attention paid to mechanistic evidence that can inform the relevance of the animal evidence for human risk assessment.

Table 2 shows the categories for the overall evaluation and how they are derived from human, animal, and other evidence. Each substance is classified into one of the following groups: carcinogenic (group 1), probably carcinogenic (group 2A), possibly carcinogenic (group 2B), not classifiable (group 3), probably not carcinogenic (group 4). However, the algorithm implied by Table 2 is only indicative, and the working group may derive an overall evaluation that departs from the strict interpretation of the algorithm. For example, neutrons have been classified as human carcinogens (group 1) despite the absence of epidemiologic data, because of overwhelming experimental evidence and mechanistic considerations (IARC 2000a). The IARC process relies on consensus, and this is usually achieved, but sometimes differing opinions among experts lead to split decisions. In the end, the published evaluations reflect the views of at least a majority of participating experts. The results of IARC evaluations are published in readily available and user-friendly volumes, and summaries are published on the IARC website (IARC 2003).

For our purpose, there are several limitations to bear in mind. First, IARC does not provide any explicit indication as to whether the substance evaluated should be considered an occupational exposure. Second, although the working groups certainly study the evidence in relation to cancer sites, until recently the formal evaluations did not identify which sites of cancer may be at risk. Site-specific information needs to be gleaned from the working group’s report and other literature. Third, the evaluations are anchored in the

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**Table 1. Classifications used in the IARC Monographs to characterize evidence of carcinogenicity.**

| Category of evidence | In humans | In animals |
|----------------------|-----------|-----------|
| Sufficient evidence of carcinogenicity | A causal relationship has been established between exposure to the agent, mixture, or exposure circumstances and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. | A causal relationship has been established between the agent or mixture and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in a) two or more species of animals or b) in two or more independent studies in one species carried out at different times or in different laboratories or under different protocols. |
| Limited evidence of carcinogenicity | A positive association has been observed between exposure to the agent, mixture, or exposure circumstance and cancer for which a causal interpretation is considered to be credible, but chance, bias, or confounding could not be ruled out with reasonable confidence. | The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, for example, a) the evidence of carcinogenicity is restricted to a single experiment; b) there are unresolved questions regarding the adequacy of the design, conduct, or interpretation of the study; or c) the agent or mixture increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential, or of certain neoplasms that may occur spontaneously in high incidences in certain strains. |
| Insufficient evidence of carcinogenicity | The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of a causal association between exposure and cancer, or no data on cancer in humans are available. | The studies cannot be interpreted showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available. |
| Evidence suggesting lack of carcinogenicity | There are several adequate studies covering the full range of levels of exposure that human beings are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent, mixture, or exposure circumstance and any studied cancer at any observed level of exposure. | Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent or mixture is not carcinogenic. |
time that the working group met and reviewed the evidence; it is possible that evidence appearing after the IARC review could change the evaluation.

Current knowledge on occupational carcinogens. From 1972 through 2003, the IARC Monograph Program published 83 volumes, representing evaluations of more than 880 substances, complex mixtures, and industrial processes. Of these, 89 have been classified as definite human carcinogens, 64 as probable, and 264 as possible human carcinogens (IARC 2003). We reviewed each one and earmarked those that we consider to be “occupational exposures.”

In developing a decision rule, we considered the following dimensions: whether the evidence of an effect drew on studies in exposed workers, whether the agent was found more often in the occupational or nonoccupational environments, and the numbers of workers exposed. In the end, the first two dimensions became redundant when we applied the third. Thus, a substance was considered an occupational exposure if there are, or have been, significant numbers of workers exposed to the substance at significant levels. The fact that some workers were exposed to a substance was not enough to label it as an occupational carcinogen. There are many carcinogens to which few workers are exposed, and we did not want to dilute the lists with such obscure agents.

Unfortunately, the knowledge base for determining how many workers are or have been exposed, and at what levels, is very fragmentary. We relied on available documentation such as the IARC Monographs, surveys by the National Institute for Occupational Safety and Health (NIOSH 1990), the National Toxicology Program (NTP) Report on Carcinogens, Tenth Edition (NTP 2002), and informed guesses on the part of expert industrial hygienists. Where we could come up with approximate numbers of workers exposed, we had to have some type of operational threshold for what should be considered a significant number. As a rule of thumb, we used > 10,000 workers exposed worldwide or > 1,000 in any country, presently or at any time in the past. These were the guidelines against which we measured our imprecise and semisubjective estimates. We also had to operationalize the notion of a level of exposure that was significant. This was even less explicit than the criteria used for numbers of workers exposed; it depended, inter alia, on the known range of exposure levels to the agent.

Despite the fact that they may be found in occupational environments, some classes of agents were summarily excluded from consideration on the grounds that the exposures are rare or very infrequent or at very low doses. These included hormones, pharmaceuticals, microbiologic agents, and dietary constituents. Pharmaceuticals represent a special case. Many have been evaluated, and many are considered to be carcinogenic. Although the main population exposed consists of patients undergoing therapy, there can also be exposure of workers who produce the drugs and of health care workers who administer them. But because the exposure doses are orders of magnitude higher among patients than among workers, we have not listed these as occupational carcinogens. Analogously, we have not listed carcinogenic viruses, notably, human immunodeficiency virus (HIV) and hepatitis B and C viruses, although health care workers may be at risk.

With these criteria, we derived the following lists of occupational carcinogens:
- 28 definite human occupational carcinogens (IARC group 1; Table 3)
- 27 probable human occupational carcinogens (IARC group 2A; Table 4)
- 113 possible human occupational carcinogens (IARC group 2B; Table 5)
- 18 occupations and industries that possibly, probably, or definitely entail excess risk of cancer (IARC groups 1, 2A, and 2B; Table 6).

Tables 3–6 only include agents and circumstances that were reviewed and published by the IARC Monograph Program as of 2003. As discussed above, the evaluations are rooted in the information base that was available at the time of the IARC evaluation. As evidence accumulates, the evaluation of an agent can change, as has already occurred in some cases (e.g., cadmium, acrylonitrile). This is why we have included in the tables a reference to the IARC volume in which the substance was evaluated and its date. Evaluations with early dates are more vulnerable to being out of date.

In a special review published in 1987 (Supplement 7), all substances and occupations covered in the first 15 years of the program were reevaluated (IARC 1987). Thus, every substance for which the Supplement 7 reference is cited had an earlier monograph. For many of the substances, there was little, if any, new information, and consequently, we have quoted the original monograph for those without any new data in 1987. For those substances referenced as Supplement 7, new data were available for the reevaluation.

Table 2. Guidelines used by the IARC Monographs Program in evaluating human carcinogenicity based on the synthesis of epidemiologic, animal, and other evidence.*

| Group | Description of group | Epidemiologic evidence | Animal evidence | Other evidence |
|-------|----------------------|------------------------|----------------|---------------|
| 1     | The agent, mixture, or exposure circumstance is carcinogenic to humans | Sufficient | Any | Any |
|       |                      | Less than sufficient | Sufficient | Strongly positive |
|       |                      | Limited               | Sufficient | Less than strongly positive |
| 2A    | The agent, mixture, or exposure circumstance is probably carcinogenic to humans | Inadequate or not available | Sufficient | Strongly positive |
| 2B    | The agent, mixture, or exposure circumstance is possibly carcinogenic to humans | Limited | Less than sufficient | Any |
|       |                      | Inadequate or not available | Sufficient | Less than strongly positive |
|       |                      | Inadequate or not available | Limited | Strongly positive |
| 3     | The agent, mixture, or exposure circumstance is not classifiable as to its carcinogenicity to humans | Inadequate or not available | Limited | Less than strongly positive |
| 4     | The agent, mixture, or exposure circumstance is probably not carcinogenic to humans | Suggesting lack of carcinogenicity | Suggesting lack of carcinogenicity | Any |
|       |                      | Inadequate or not available | Suggesting lack of carcinogenicity | Strongly negative |

*This table shows our interpretation of the IARC Monographs Program guidelines to derive the overall evaluation from the combined epidemiologic, animal, and other evidence. However, the IARC working groups can, under exceptional circumstances, depart from these guidelines in deriving the overall evaluation (IARC 2003). For example, the overall evaluation can be downgraded if there is less than sufficient evidence in humans and strong evidence that the mechanism operating in animals is not relevant to humans.
For the agents in Tables 3–5, we devised a set of subheadings to help the reader digest the long lists of often obscure chemical names: physical agents, respirable dusts and fibers, metals and metal compounds, PAHs, wood and fossil fuels and their by-products, monomers, intermediates in plastics and rubber manufacturing, chlorinated hydrocarbons, aromatic amine dyes, azo dyes, intermediates in the production of dyes, pesticides, nitro compounds, and others. Tables 3–5 indicate some of the main occupations or industries in which each listed substance is found, and the strength of evidence from human and animal studies. In Tables 3 and 4, we show the type(s) of cancer affected, with an indication of the strength of evidence for each type listed. Information on target organ is not shown in Table 5 because, for agents listed as possible carcinogens, evidence concerning humans is either conflicting or not available at all.

For many of the agents listed, but not all, there has been some epidemiologic evidence of carcinogenicity among exposed workers. For most of the agents listed, but not all, the occupational environment represents the most common locale of exposure. The most prominent exceptions to this rule are aflatoxins, sunlight, involuntary tobacco smoking, and radon. Whether these cause more cases of cancer as a result of occupational or nonoccupational exposure depends on numbers exposed and exposure levels in the two types of milieu. It is plausible that there may be more cases resulting from nonoccupational exposure.

The IARC Monograph Program has occasionally addressed cancer risk in various occupations and industries, as well as agents. However, although the monograph program

| Substance or mixture | Occupation or industry in which the substance is found | IARC Monograph volume (year) | Human evidence | Animal evidence | Site(s) |
|----------------------|--------------------------------------------------------|-----------------------------|----------------|----------------|---------|
| Physical agents      |                                                        |                             |                |                |         |
| Ionizing radiation and sources thereof, including, notably, X rays, γ rays, neutrons, and radon gas | Radiologists; technologists; nuclear workers; radium-dial painters; underground miners; plutonium workers; cleanup workers following nuclear accidents; aircraft crew | Vol. 75 (2000a) | Sufficient | Sufficient | Bone<sup>a</sup> Leukemia<sup>a</sup> Lung<sup>a</sup> Liver<sup>a</sup> Thyroid<sup>a</sup> Others<sup>a</sup> |
| Solar radiation      | Outdoor workers                                        | Vol. 55 (1992b)            | Sufficient     | Sufficient     | Melanoma<sup>a</sup> Skin<sup>a</sup> |
| Respirable dusts and fibers | Mining and milling; by-product manufacture; insulating; shipyard workers; sheet-metal workers; asbestos cement industry | Suppl. 7 (1987)          | Sufficient     | Sufficient     | Lung<sup>a</sup> Mesothelioma<sup>a</sup> |
| Asbestos             | Erionite                                               | Suppl. 7 (1987)            | Sufficient     | Sufficient     | Lung<sup>a</sup> Gl tract<sup>a</sup> Mesothelioma<sup>a</sup> |
| Silica, crystalline  | Waste treatment; sewage; agricultural waste; air pollution control systems; cement aggregates; building materials | Vol. 68 (1997b)           | Sufficient     | Sufficient     | Lung<sup>a</sup> |
| Talc containing asbestos fibers | Manufacture of pottery, paper, paint, and cosmetics | Suppl. 7 (1987)            | Sufficient     | Sufficient     | Lung<sup>a</sup> Mesothelioma<sup>a</sup> Nasal cavities and paranasal sinuses<sup>a</sup> |
| Wood dust            | Logging and sawmill workers; pulp and paper and paperboard industry; woodworking trades (e.g., furniture industries, cabinetmaking, carpentry and construction); used as filler in plastic and linoleum production | Vol. 62 (1995b)           | Sufficient     | Sufficient     | Lung<sup>a</sup> |
| Metals and metal compounds | Nonferrous metal smelting; production, packaging, and use of arsenic-containing pesticides; sheep dip manufacture; wool fiber production; mining of ores containing arsenic | Suppl. 7 (1987)            | Sufficient     | Limited        | Skin<sup>a</sup> Lung<sup>a</sup> Liver (angiosarcoma)<sup>a</sup> Lung<sup>a</sup> |
| Arsenic and arsenic compounds | Beryllium extraction and processing; aircraft and aerospace industries; electronics and nuclear industries; jewelers | Vol. 58 (1993a)           | Sufficient     | Sufficient     | Lung<sup>a</sup> |
| Beryllium            | Cadmium-smelter workers; battery production workers; cadmium-copper alloy workers; dyes and pigments production; electroplating processes | Vol. 58 (1993a)           | Sufficient     | Sufficient     | Lung<sup>a</sup> |
| Cadmium and cadmium compounds | Chromium compounds, hexavalent | Vol. 49 (1990a)            | Sufficient     | Sufficient     | Lung<sup>a</sup> Nasal sinuses<sup>a</sup> |
| Chromium compounds, hexavalent | Nickel refining and smelting; welding | Vol. 49 (1990a)            | Sufficient     | Sufficient     | Lung<sup>a</sup> Nasal cavity and sinuses<sup>a</sup> |
| Selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry | Production; solvents in the shoe production industry; chemical, pharmaceutical, and rubber industries; printing industry (rotogravure plants, bindery departments); gasoline additive | Suppl. 7 (1987)            | Sufficient     | Limited        | Leukemia<sup>a</sup> |
| Wood and fossil fuels and their by-products | Production of refined chemicals and coal tar products (patent-fuel); coke production; coal gasification; aluminum production; foundries; road paving and construction (roofers and slaters) | Suppl. 7 (1987)            | Sufficient     | Sufficient     | Skin<sup>a</sup> Lung<sup>a</sup> Bladder<sup>a</sup> |

Continued next page
Table 3. Continued

| Substance or mixture | Occupation or industry in which the substance is founda | IARC Monograph volume (year)b | Human evidencec | Animal evidencec | Site(s) |
|----------------------|--------------------------------------------------------|-------------------------------|-----------------|-----------------|---------|
| Mineral oils, untreated and mildly treated | Production; used as lubricant by metal workers, machinists, engineers; printing industry (ink formulation); used in cosmetics, medicinal and pharmaceutical preparations | Suppl. 7 (1987) | Sufficient | Inadequate | Skin,b Bladder,b Lung,e |
| Shale oils or shale-derived lubricants | Mining and processing; used as fuels or chemical-plant feedstocks; lubricant in cotton textile industry | Suppl. 7 (1987) | Sufficient | Sufficient | Skin,b Lung,e |
| Soots | Chimney sweeps; heating-unit service personnel; brick masons and helpers; building demolition workers; insulators; firefighters; metallurgical workers; work involving burning of organic materials | Vol. 35 (1985) | Sufficient | Inadequate | Skin,b Lung,e Esophagus,b |
| Monomers | Vinyl chloride | Production; production of polyvinyl chloride and co-polymers; refrigerant before 1974; extraction solvent; in aerosol propellants | Suppl. 7 (1987) | Sufficient | Sufficient | Liver (angiosarcoma), Liver (hepato-cellular) |
| Intermediates in plastics and rubber manufacturing | Bis(chloromethyl) ether and chloromethyl methyl ether (technical grade) | Production; chemical intermediate; alkylating agent; laboratory reagent; plastic manufacturing; ion-exchange resins and polymers | Suppl. 7 (1987) | Sufficient | Sufficient | Lung (oat cell) |
| Aromatic amine dyes | 4-Aminobiphenyl | Production; dyestuffs and pigment manufacture | Suppl. 7 (1987) | Sufficient | Sufficient | Bladder,b |
| | Benzidine | Production; dyestuffs and pigment manufacture | Suppl. 7 (1987) | Sufficient | Sufficient | Bladder,b |
| | 2-Naphthylamine | Production; dyestuffs and pigment manufacture | Suppl. 7 (1987) | Sufficient | Sufficient | Bladder,b |
| | Pesticides | Ethylene oxide | Production; chemical industry; sterilizing agent (hospitals, spice fumigation) | Vol. 60 (1994) | Limited | Sufficient | Leukemia,b |
| | | 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) | Production; use of chlorophenols and chlorophen oxy herbicides; waste incineration; PCB production; pulp and paper bleaching | Vol. 69 (1997a) | Limited | Sufficient | All sites combined,b Lung,f Non-Hodgkin lymphoma,b Sarcoma,b |
| Others | Aflatoxin | Feed production industry; workers loading and unloading cargo; rice and maize processing | Vol. 82 (2002b) | Sufficient | Sufficient | Liver,b |
| | Involuntary (passive) smoking | Workers in bars and restaurants; office workers | Vol. 83 (2004) | Sufficient | Sufficient | Lung,f |
| | Mustard gas | Production; used in research laboratories; military personnel | Suppl. 7 (1987) | Sufficient | Limited | Larynx,b Lung,f Pharynx,e Larynx,b Lung,f |
| | Strong inorganic-acid mists containing sulfuric acid | Pickling operations; steel industry; petrochemical industry; phosphate acid fertilizer manufacturing | Vol. 54 (1992a) | Sufficient | Not available | |

*aNot necessarily an exhaustive list of occupations/industries in which this agent is found; not all workers in these occupations/industries are exposed. The term “production” is used to indicate that this substance is man-made and that workers may be exposed in the production process. Most recent IARC evaluation; for those referenced to Supplement 7 (IARC 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date. bAs judged by the IARC working group; we added the notation “not available” to signify those substances for which there was no evidence at all. cWe judged that evidence for an association with this site was strong. dWe judged that evidence was suggestive.
Newly identified monomers that contain a substance on the list (e.g., nitro-PAHs) that may be responsible for the carcinogenicity of the mixture.

The listing of affected cancer sites in Tables 3 and 4 does not come explicitly from the IARC Monographs. Sometimes the affected target organ(s) was rather evident, but sometimes it required that we evaluate the evidence, including evidence published more recently than the IARC evaluation in question. Table 7 shows the same agents listed in Tables 3 and 4 but organized by site of cancer. Again, we indicate clearly which associations are strong and which are only suggestive. The lung is the target organ that has most often been linked to occupational carcinogens.

The evolution of knowledge. In order to appreciate how knowledge has evolved, we searched for information on the current occupational carcinogens at two earlier time periods. As mentioned above, IARC carried out a comprehensive cumulative synthesis in 1987 (IARC 1987). In that report, the results were presented with the same rating system (group 1, 2A, 2B, 3) as is used today, rendering the lists comparable. In 1964, even before the establishment of IARC, the World Health Organization (WHO) commissioned an expert panel to survey available knowledge on human carcinogens (WHO 1964). In the WHO report, there was no explicit rating system. It was a discursive presentation of knowledge and opinions that we attempted, with some license, to translate into a simple system corresponding to definite, probable/possible, or not mentioned. From these two reports, we searched for references to the 168 substances presented in Tables 3–5 and that are currently considered to be definite, probable, or possible occupational carcinogens.

| Substance or mixture | Occupation or industry in which the substance is found | IARC Monograph volume (year) | Human evidence | Animal evidence | Site(s) |
|----------------------|--------------------------------------------------------|-----------------------------|----------------|----------------|--------|
| Physical agents      |                                                        |                             |                |                |        |
| Ultraviolet radiation (A, B, and C) from artificial sources | Arc welding; industrial photoprocesses; sterilization and disinfection; phototherapy; operating theaters; research laboratories; ultraviolet fluorescence in food industry; insect traps | Vol. 55 (1992b) | Inadequate | Sufficient | Melanoma |
| Polyaromatic hydrocarbons | Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics | Vol. 32 (1983b) | Not available | Sufficient | Lung |
| Benz[a]anthracene     | Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics | Vol. 32 (1983b) | Not available | Sufficient | Bladder |
| Benz[a]pyrene         | Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics | Vol. 32 (1983b) | Not available | Sufficient | Skin |
| Diben[a,h]anthracene  | Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics | Vol. 32 (1983b) | Not available | Sufficient | Skin |
| Wood and fossil fuels and their by-products | Brickmaking; wood preserving | Vol. 35 (1985) | Limited | Sufficient | Skin |
| Diesel engine exhaust | Railroad workers; professional drivers; dock workers; mechanics | Vol. 46 (1989a) | Limited | Sufficient | Lung |
| Intermediates in plastics and rubber manufacturing | Production; curing agent for roofing and wood sealing | Vol. 57 (1993b) | Inadequate | Sufficient | Bladder |
| 4,4’-Methylene bis(2-chloroaniline) | Production; styrene glycol production; perfume preparation; reactive diluent in epoxy resin formulations; as chemical intermediate for cosmetics, surface coating, and agricultural and biological chemicals; used for treatment of fibers and textiles; in fabricated rubber products | Vol. 60 (1994) | Inadequate | Sufficient | Bladder |
| Chlorinated hydrocarbons | Production; dye and pesticide manufacture | Vol. 71 (1999a) | Limited | Sufficient | Lung |
| α-Chlorinated toluenes | Production; electrical capacitor manufacturing | Suppl. 7 (1987) | Limited | Sufficient | Liver and biliary tract |
| Polychlorinated biphenyls | Production; dry cleaning; metal degreasing | Vol. 63 (1995a) | Limited | Sufficient | Esophageal |
| Tetrachloroethylene   | Production; dry cleaning; metal degreasing | Vol. 63 (1995a) | Limited | Sufficient | Non-Hodgkin lymphoma |
| Trichloroethylene     | Production; dry cleaning; metal degreasing | Vol. 63 (1995a) | Limited | Sufficient | Liver and biliary tract |
| Monomers              |                                                        |                             |                |                |        |
| Acrylamide            | Chemical industry; water and wastewater treatment; textile, steel, and lumber industries; petroleum refining, mineral processing; sugar production; hospitals | Vol. 60 (1994) | Inadequate | Sufficient | Pancreas |
| 1,3-Butadiene         | Chemical and rubber industries | Vol. 71 (1999a) | Limited | Sufficient | Lymphohematopoietic |
| Epichlorohydrin       | Production and use of resins, glycerine, and propylene-based rubbers; used as a solvent | Vol. 71 (1999a) | Inadequate | Sufficient | Lung |
| Vinyl bromide         | Production; production of vinyl bromide polymers and monoacrylic fibers for carpet backing material; rubber and plastic production | Vol. 71 (1999a) | Not available | Sufficient | CNS |
| Vinyl fluoride        | Production; polyvinyl fluoride and fluoropolymer production | Vol. 63 (1995a) | Not available | Sufficient | Continued next page |
Table 8 shows how the current occupational carcinogens were considered in two earlier times. Half of today’s recognized definite occupational carcinogens were already recognized as such by 1964, in the early period of cancer epidemiology. Nearly 90% were considered to be definite or probable as of 15 years ago. In contrast, > 95% of today’s probable and possible occupational carcinogens had not even been mentioned as of 1964, and about one-third were not mentioned as of 1987. Although it is possible for the classification of agents to change over time in either direction, in practice there have been rather few instances of agents being “downgraded” between successive periods. Notable counter-examples include the following:

- 3,3-Dichlorobenzene, which was considered a definite carcinogen in 1964 but was only considered as a possible carcinogen as of 1987 and 2002
- Acrylonitrile and propylene oxide, which were considered probable carcinogens in 1987, but only as possible carcinogens in 2002
- Glass wool was considered a possible carcinogen in 1988 but was downgraded to unclassifiable in 2002
- Ionizing radiation, a special case, was considered a definite carcinogen in 1964 and is so considered today, but it had not been reviewed by IARC before the 1990s; therefore, we had to classify it as “unrated” in 1987.

### Discussion

Many of the recognized definite occupational carcinogens were first suspected before the era of modern epidemiology (i.e., before 1950). The significance of this observation is unclear. It may be that there were only a limited number of strong occupation–cancer associations, and these were sufficiently obvious that they could produce observable clusters of cases for astute clinicians to notice. It may be that levels of exposure to occupational chemicals were so high before the 1950s as to produce high cancer risks and cancer clusters, but that improvements in industrial hygiene in industrialized countries have indeed decreased risks to levels that are difficult to detect. The number of occupational agents rated by IARC as group 1 carcinogens has tapered off since 1987, whereas the proportion of group 2B evaluations has increased. This reflects the fact that, when the monograph program began, there was a “backlog” of agents for which strong evidence of carcinogenicity had accumulated, and, naturally, these were the agents that IARC initially selected for review. Once the agents with strong evidence had been dealt with, IARC started dealing with others. It would be wrong to infer that the historic trend in IARC designations signals that we are approaching the end of the period of potential to discover occupational carcinogens. There are many thousands of chemicals in workplaces, and new ones are continuously being introduced. Most recognized occupational carcinogens were first suspected on the basis of case reports by clinicians or pathologists (Doll 1975). These discoveries were usually coincidental (Siemiatycki et al. 1981). It is thus reasonable to suspect that there may be some, perhaps many, as yet undiscovered

### Table 4. Continued

| Substance or mixture | Occupation or industry in which the substance is founda | IARC Monograph volume (year)b | Human evidencec | Animal evidencec | Site(s) |
|----------------------|-------------------------------------------------------|-----------------------------|----------------|-----------------|--------|
| Aromatic amine dyes  | Production; used in textile, paper, leather, rubber, plastics, printing, paint, and lacquer industries | Suppl. (1987) | Inadequate | Sufficient | Bladderd |
| Benzidine-based dyes | Production; used in textile, paper, leather, rubber, plastics, printing, paint, and lacquer industries | Vol. 77 (2000b) | Limited | Sufficient | Bladderd |
| 4-Chloro-ortho-toluidine | Dye and pigment manufacture; textile industry | Vol. 77 (2000b) | Limited | Sufficient | Bladderd |
| ortho-Toluidine | Production; manufacture of dyestuffs, pigments, optical brightener, pharmaceuticals, and pesticides; rubber vulcanizing; clinical laboratory reagent; cleaners and janitors | Vol. 77 (2000b) | Limited | Sufficient | Bladderd |
| Intermediates in the production of dyes | Production; manufacture of pharmaceuticals, pesticides, and dyes | Vol. 71 (1999a) | Inadequate | Sufficient | |
| Dimethylcarbamoyl chloride | Production; manufacture of pharmaceuticals, pesticides, and dyes | Vol. 71 (1999a) | Inadequate | Sufficient | |
| Pesticides | | | | | |
| Captofol | Production; fungicide | Vol. 52 (1991b) | Not available | Sufficient | |
| Ethylene dibromide | Production; pest control; petroleum refining and waterproofing; leaded gasoline additive; chemical intermediate and solvent in gums, waxes, resins, dyes, and pharmaceutical preparations | Vol. 52 (1991b) | Not available | Sufficient | |
| Nonarsenical insecticides | Production; pest control and agricultural workers; flour and grain mill workers | Vol. 53 (1991b) | Limited | Not available | |
| Others | | | | | |
| Diethyl sulfate | Ethanol production | Vol. 71 (1999a) | Not available | Sufficient | |
| Formaldehyde | Production; pathologists; medical laboratory technicians; plastics; textile industry | Vol. 71 (1999a) | Not available | Sufficient | |
| Tris(2,3-dibromopropyl)| Production; used in the textile phosphate industry; in phenolic resins (for electronics industry), paints, paper coatings, and rubber | Vol. 71 (1999a) | Inadequate | Sufficient | |

CNS, central nervous system.

*Not necessarily an exhaustive list of occupations/industries in which this agent is found; not all workers in these occupations/industries are exposed. The term “production” is used to indicate that this substance is man-made and that workers may be exposed in the production process. *Most recent IARC evaluation; for those referenced as Supplement 7 (IARC 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date. *As judged by the IARC working group; we added the notation “not available” to signify those substances for which there was no epidemiologic evidence at all. *We judged that the evidence was suggestive.
| Substance or mixture | Occupation or industry in which the substance is found | IARC Monograph volume (year) | Human evidence | Animal evidence |
|----------------------|--------------------------------------------------------|----------------------------|----------------|----------------|
| Respirable dusts and fibers | Production; construction and insulation | Vol. 81 (2002a) | Inadequate | Sufficient |
| Polyethylene (long fibers > 5 µm) | Miners and millers; production of waste absorbents, fertilizers, and pesticides | Vol. 68 (1997b) | Inadequate | Sufficient |
| Refractory ceramic fibers | Production; furnace insulators; ship builders; heat-resistant fabric manufacture | Vol. 81 (2002a) | Inadequate | Sufficient |
| Rock wool | Production; thermal or acoustical insulation | Vol. 81 (2002a) | Inadequate | Limited |
| Special-purpose glass fibers | Reinforced plastic industry | Vol. 81 (2002a) | Not available | Sufficient |
| Polyaromatic hydrocarbons | Ore processing; glass and ceramic production | Vol. 47 (1989c) | Inadequate | Sufficient |
| Antimony trioxide | Miners; processing of copper and nickel ore; glass and ceramic production | Vol. 52 (1991a) | Inadequate | Sufficient |
| Cobalt and cobalt compounds | Lead smelters; plumbers; solderers; occupations in battery recycling smelters | Suppl. 7 (1987) | Inadequate | Sufficient |
| Methyl mercury compounds | Pesticide and fungicide production; paint industry | Vol. 58 (1983a) | Inadequate | Sufficient |
| Nickel: metallic and alloys | Nickel miners; metal fabrication, grinding, electroplating, and welding | Vol. 49 (1990a) | Inadequate | Sufficient |
| Wood and fossil fuels and their by-products | Production; intermediate in coumarone-indene resin polymerization; coke production; coal gasification and combustion | Vol. 63 (1995a) | Not available | Sufficient |
| Benzofuran | Production/refining; road construction; roofing and flooring | Suppl. 7 (1987) | Inadequate | Sufficient |
| Bitumens, extracts of steam-refined and air-refined | Production; paint, ink, plastic and rubber industries | Vol. 65 (1996) | Inadequate | Sufficient |
| Carbon black | Production; petroleum refineries; marine fuel; distribution | Vol. 45 (1989b) | Inadequate | Limited |
| Diesel fuel, marine | Petroleum refineries; distribution; marine fleets; most large diesel engines operated on land; industrial heating systems | Vol. 45 (1989b) | Inadequate | Limited |
| Fuel oils, residual (heavy) | Petroleum refineries; transportation; mechanics and service station attendants | Vol. 45 (1989b) | Inadequate | Limited |
| Gasoline | Transportation and vehicle maintenance workers; drivers; toll attendants; traffic controllers | Vol. 46 (1989a) | Inadequate | Limited |
| Naphthalene | Production; insecticide, resin, and pharmaceutical production | Vol. 82 (2002b) | Inadequate | Sufficient |
| Polyaromatic hydrocarbons | Work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Benzo[a]fluoranthene | Work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Benzo[b]fluoranthene | Work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Dibenz(a,h)acridine | Production; used in dye synthesis; biochemical laboratory workers; work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Dibenz(a,h)acridine | Production; dye synthesis; work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Dibenz(a,h)pyrene | Production; biochemical laboratory workers; work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Dibenz(a,h)pyrene | Production; biochemical laboratory workers; work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Dibenz(a,h)pyrene | Work involving combustion of organic matter | Vol. 32 (1983b) | Not available | Sufficient |
| Monomers | Production; acrylic textile fiber and plastic production (synthetic rubber) | Vol. 71 (1999a) | Inadequate | Sufficient |
| Acrylonitrile | Production; manufacture of polychloroprene | Vol. 71 (1999a) | Inadequate | Sufficient |
| Chloroprene | Production; plastic molding occupations using acrylate resins | Vol. 39 (1986a) | Inadequate | Sufficient |
| Ethyl acrylate | Production; synthetic rubber and plastics industries | Vol. 71 (1999a) | Inadequate | Sufficient |
| Styrene | Polyester resin manufacture; production of packaging materials and fiberglass-reinforced polyester | Vol. 82 (2002b) | Limited | Limited |
| Toluene diisocyanates | Production; production of polyurethane foams and wire coating; insulation workers; ship builders | Vol. 71 (1999a) | Inadequate | Sufficient |
| Urethane | Production; amino-resin production | Vol. 7 (1974a) | Not available | Sufficient |
| Vinyl acetate | Production; plastics, paint, and adhesive industries | Vol. 63 (1995a) | Not available | Limited |
| Intermediates in plastics and rubber manufacturing | Acrylic acid production workers; dyestuff, plastic and synthetic rubber industries | Vol. 71 (1999a) | Inadequate | Sufficient |
| Acetaldehyde | Production; plastics and chemical industries | Vol. 71 (1999a) | Not available | Sufficient |
| Substance or mixture | Occupation or industry in which the substance is found | IARC Monograph volume (year) | Human evidence | Animal evidence |
|----------------------|------------------------------------------------------|-----------------------------|----------------|----------------|
| 2,4-Diaminotoluene   | Production; chemical intermediate in TDI production; dyes for textiles; leather; furs; wood; biologic stain; photo developer | Vol. 16 (1978) | Not available | Sufficient |
| 1,2-Epoxybutane      | Production; metal degreasing; plastics industry | Vol. 71 (1999a) | Not available | Limited |
| Ethylbenzene         | Production; ink, paint, and plastic production | Vol. 77 (2000b) | Inadequate | Sufficient |
| Ethylene thiourea    | Production; vulcanization in the rubber industry; manufacture of ethylenebisdithiocarbamate pesticides; electropolishing baths; dyes; pharmaceuticals; synthetic resins | Vol. 79 (2001b) | Inadequate | Sufficient |
| Phenyl glycidyl ether| Production; epoxy resins, casting and molding | Vol. 71 (1999a) | Not available | Sufficient |
| Propylene oxide      | Production; polyurethane foam and glycol production, fungimant | Vol. 60 (1994) | Inadequate | Sufficient |
| Chlorinated hydrocarbons | 2-Nitroanisole Production; manufacture of the dye intermediates | Vol. 16 (1978) | Not available | Sufficient |
| Carbon tetrachloride | Production; industrial degreasing occupations; dry cleaners; refrigerant production | Vol. 71 (1999a) | Inadequate | Sufficient |
| Chlorinated paraffin of average carbon-chain length C12 | Production; polyvinyl chloride processing industry | Vol. 48 (1990b) | Not available | Sufficient |
| Chloroform           | Refrigerant production; dyes, solvents, and pesticides | Vol. 73 (1999b) | Inadequate | Sufficient |
| 1,2-Dichloroethane   | Vinyl chloride production workers | Vol. 71 (1999a) | Inadequate | Sufficient |
| Dichloromethane      | Production; painters and furniture restorers; pharmaceutical and electronic production | Vol. 71 (1999a) | Inadequate | Sufficient |
| Hexachloroethane     | Production; aluminum refinery; industrial firefighters | Vol. 73 (1999b) | Inadequate | Sufficient |
| Aromatic amine dyes  | 2,4-Diminoanisole Production; dye or intermediate in dyes and pigments | Vol. 79 (2001b) | Not available | Sufficient |
|                      | 3,3’-Dimethylbenzidine (o-tolidine) Production; polyurethane elastomers; coating; plastics; clinical laboratories | Vol. 1 (1972) | Not available | Sufficient |
|                      | 2,6-Dimethylaminiline (2,6-xylidine) Production; dyestuffs and pharmaceutical manufacturing | Vol. 57 (1993b) | Not available | Sufficient |
|                      | 3,3’-Dichlorobenzidine Production; dyestuff manufacturing | Vol. 57 (1993b) | Not available | Sufficient |
|                      | 4,4’-Diaminodiphenyl ether Production; polyamide-type resin manufacturing | Vol. 29 (1982b) | Not available | Sufficient |
|                      | Disperse Blue 1 Production; hair coloring, textiles and plastics | Vol. 48 (1990b) | Not available | Sufficient |
|                      | HC Blue No. 1 Production; hair dye | Vol. 57 (1993b) | Not available | Sufficient |
|                      | 4,4’-Methylenedianiline Production; production of disocyanates, polyisocyanates, and epoxy resins | Vol. 39 (1986a) | Not available | Sufficient |
|                      | Magenta containing Production; textiles and printing; biologic stains in laboratories; photography | Vol. 57 (1993b) | Not available | Sufficient |
|                      | CI Basic Red 9 | | | |
| Azo dyes             | ortho-Aminoazotoluene Production; textiles and leather | Vol. 8 (1975) | Not available | Sufficient |
|                      | para-Aminoazobenzene Production; textiles and leather | Suppl. 7 (1987) | Not available | Sufficient |
|                      | CI Acid Red 114 Production; textiles and leather | Vol. 57 (1993b) | Not available | Sufficient |
|                      | CI Direct Blue 15 Production; textiles and paper | Vol. 57 (1993b) | Not available | Sufficient |
|                      | Citrus Red No. 2 Production; used for food coloring | Vol. 8 (1975) | Not available | Sufficient |
|                      | para-Dimethylanilinazozonebenzene Production; textiles; laboratories | Vol. 8 (1975) | Not available | Sufficient |
|                      | Oil orange SS Production; dyes/pigments for varnishes, oils, fats, and waxes | Vol. 8 (1975) | Not available | Sufficient |
|                      | Ponceau 3R Production; textiles | Vol. 8 (1975) | Not available | Sufficient |
|                      | Ponceau MX Production; textiles; leather; inks; paper; wood stains; food; biology laboratories | Vol. 8 (1975) | Not available | Sufficient |
|                      | Trypan blue Production; textiles and printing; biologic stains in laboratories; photography | Vol. 8 (1975) | Not available | Sufficient |
|                      | Intermediates for the manufacture of dyes | | | |
|                      | para-Cresidine Production; manufacture of dyes, pigments, and perfumes | Vol. 27 (1982a) | Not available | Sufficient |
|                      | 3,3’-Dimethoxybenzidine (ortho-dianisidine) Production; manufacture of dyes and pigments; dye for leather, paper, plastics, rubber, textiles, and laboratories | Suppl. 7 (1987) | Inadequate | Sufficient |
|                      | 2-Methyl-1-nitro antraquinone (of uncertain purity/impurity) Production; synthesis of antraquinone dyes | Vol. 27 (1982a) | Not available | Sufficient |
|                      | 4,4’-Methylene bis (2-methyldiaziline) Production; manufacture of dyes and pigments | Suppl. 7 (1987) | Inadequate | Sufficient |
|                      | 2-Nitroanisole Production; manufacture of the dye intermediates ortho-ansidine and ortho-dianisidine | Vol. 65 (1996) | Not available | Sufficient |
|                      | 4,4’-Thiodianiline Production; manufacture of dyes | Vol. 27 (1982a) | Not available | Sufficient |
|                      | Nitro compounds | | | |
|                      | 2,4-Dinitrotoluene Production; manufacture of disocyanates and munitions | Vol. 65 (1996) | Inadequate | Sufficient |
|                      | 2,6-Dinitrotoluene Production; manufacture of disocyanates and munitions | Vol. 65 (1996) | Inadequate | Sufficient |
|                      | Nitrobenzene Production; manufacture of dyestuffs, detersgents, and cosmetics | Vol. 65 (1996) | Inadequate | Sufficient |
|                      | 2-Nitrofluorene Underground miners using diesel-powered machinery | Vol. 46 (1989a) | Not available | Sufficient |
Others

It is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

A

Pesticides

Table 5. Continued

| Substance or mixture | Occupation or industry in which the substance is found | IARC Monograph volume (year) | Human evidence | Animal evidence |
|----------------------|------------------------------------------------------|-----------------------------|----------------|----------------|
| 2-Nitropropane | Production; ink, paint, explosives industries | Vol. 71 (1999a) | Not available | Sufficient |
| 1-Nitropropane | Production; manufacture of azidothymine, particulate emissions | Vol. 46 (1989a) | Not available | Sufficient |
| 4-Nitropropane | Production; used only as a laboratory chemical; probably present before 1980 in carbon black used in photography machines | Vol. 46 (1989a) | Not available | Sufficient |
| Tetratinemethane | Production; diesel fuel additive, TNT manufacturing | Vol. 85 (1996) | Not available | Sufficient |

Pesticides

Aramite

Production; in miticides in greenhouses, nurseries, and orchards

Chlordane

Production; termite control

Chlordecone

Production; insecticide

Chlorophenoxy herbicides

Production; defoliant

Chlorothalonil

Production; fungicide, bactericide, and nematocide

DDT (p,p'-DDT)

Production; nontoxic insecticide

1,2-Dibromo-3-chloropropane

Production; pesticide, nematocide, and soil fumigant

Dichlorvos

Production; insecticide and nematicide

Heptachlor

Production; termite control

Hexachlorobenzene

Production; in chlorinated pesticides and fungicides; dye manufacture and synthesis of organic chemicals and rubber; plasticizer for polyvinyl chloride; wood preservative; by-product of the production of a number of chlorinated solvents

Hexachlorocyclohexanes (most common form is Lindane)

Production; woodworkers; farm workers

Mirex

Production; fire retardant additive; insecticide; workers at hazardous waste sites

Nitrofen

Production; herbicide

Sodium ortho-phenylphenate

Production; fungicide; chemical intermediate

Toxaphene (polychloronated camphenes)

Production; insecticide

Butylated hydroxyanisole (BHA)

Production; food and pharmaceutical industries

Catechol

Production; insecticide and pharmaceutical production; tanneries

Diglycidyl resorcinol ether

Production; liquid spray epoxy resin in electrical, tooling, adhesive, and laminating applications; production of epoxy resins and rubber; aerospace industry

1,4-Dioxane

Production; chlorinated solvents; textile processing; mixed with pesticides

Hydrazine

Production; manufacture of agricultural chemicals and chemical blowing agents; water treatment; spandex fibers; rocket fuel; oxygen scavenger in water boilers and heating systems; scavenger for gases; plating metals on glass and plastics; solder fluxes; photographic developers; reactant in fuel cells in the military; reducing agent in electrode-less nickel plating; chain extender in urethane; textile dyes; explosives

Nitrotriacetic acid and its salts

Production; textiles; electroplaters; tanners

Polychlorophenols and their sodium salts (mixed exposure)

Herbicide production; wood, textile and leather manufacturing

Potassium bromate

Production; bakeries

Thiourea

Production; photo processing, dyes; rubber industry

Welding fumes

Metal fabricating industry

TDI, toluene disiocyanate.

*Not necessarily an exhaustive list of occupations/industries in which this agent is found; not all workers in these occupations/industries are exposed. The term “production” is used to indicate that this substance is man-made and that workers may be exposed in the production process. Most recent IARC evaluation; for those referenced as Supplement 7 (IARC 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date. As judged by the IARC working group; we added the notation “not available” to signify those substances for which there was no epidemiologic evidence at all.
NTP has been mandated under the Public Health Service Act (1978) to maintain a list of human carcinogens and to provide data on each one concerning exposure circumstances and regulatory policies (NTP 2002). This list uses a two-category scale: “known to be a human carcinogen” and “reasonably anticipated to be a human carcinogen.” Currently, there are 52 agents listed in the first category and 176 in the second. Information concerning each agent is described in a brief report that includes some exposure data as well as health effects data and regulatory data (NTP 2002). The substances on these lists are not limited to occupational agents, and there is no tabular summary of occupational agents, the occupations in which these may occur, or the target organs. It is beyond the scope of this article to carry out a comparison of the procedures and lists of the various national bodies. Suffice it to say that most of them draw heavily on the IARC program and adapt it to their purposes.

There is sometimes a tendency to interpret tables of carcinogens in too categorical a fashion. Although it may be convenient for lobbyists and regulators to divide the world of chemicals and occupational circumstances into “good guys” and “bad guys,” such a dichotomy is simplistic. The determination that a substance or circumstance is carcinogenic depends on the strength of evidence at a given point in time. The evidence is sometimes clear-cut (which would correspond to evaluations of group 1 or group 4), but more often it is not. The balance of evidence can change in either direction as new data emerge.

The characterization of an occupation or industry group as a “high-risk group” is strongly rooted in time and place. For instance, the fact that some groups of nickel refinery workers experienced excess risks of nasal cancer does not imply that all workers in all nickel refineries will be subject to such risks. The particular circumstances of the industrial process, raw materials, impurities, and control measures may produce risk in one nickel refinery but not in another or in one historic era but not in another. The same can be said of rubber production facilities, aluminum refineries, and other industries and occupations. Labeling a chemical substance as a carcinogen in humans is a more timeless statement than labeling an occupation or industry as a high-risk group. However, even such a statement requires qualification. Different carcinogens produce different levels of risk, and for a given carcinogen there may be vast differences in the risks incurred by different people exposed under different circumstances. Indeed, there may be threshold effects or interactions with other factors, environmental or genetic, that produce no risk for some exposed workers and high risk for others.

This raises the issue of quantitative risk assessment, which is an important tool in prevention of occupational cancer. Unfortunately, our tables provide no basis for gauging the strength of the effect of each carcinogen, either in relative risk terms or in absolute risk terms, or in terms of dose–response relationships. The IARC evaluations provide no such indications, and although it would be most desirable to have such information, for most agents the information base to support such quantification is fragmentary.

In summary, the listing of occupational carcinogens is important. It provides a yardstick of our knowledge base, it provides guidance in setting research priorities, and it provides an important tool for prevention of cancer. Regulatory procedures and other aspects of cancer prevention depend on the listing of carcinogens. The IARC Monograph Program has been an indispensable component of this process. The tables presented herein, based on *IARC Monographs* but augmented in various ways, will be useful to researchers in setting research priorities and in furthering our understanding of carcinogenesis, and to those interested in preventing occupational cancer.

Table 6. Occupations or industries that have been evaluated by IARC as definitely (group 1), probably (group 2A), or possibly (group 2B) entailing excess risk of cancer among workers.

| Occupation or industry | Suspected substance | IARC Monograph volume (year) | Group | Site(s) |
|------------------------|---------------------|-----------------------------|-------|---------|
| Aluminum production    | Pitch volatiles; aromatic amines | Suppl. 7 (1987) | 1 | Lung<sup>b</sup>, bladder<sup>b</sup> |
| Auramine manufacture   | 2-Naphthylamine; auramine; other chemicals; pigments | Suppl. 7 (1987) | 1 | Bladder<sup>b</sup> |
| Boot and shoe manufact | Leather dust; benzene and other solvents | Suppl. 7 (1987) | 1 | Leukemia<sup>a</sup>, nose<sup>b</sup>, paranasal sinuses<sup>a</sup>, bladder<sup>c</sup> |
| Carpentry and joinery  | Wood dust           | Suppl. 7 (1987) | 2B | Skin (including scrotum),b, bladder<sup>b</sup>, lung<sup>c</sup>, kidney<sup>c</sup> |
| Coke production        | Coal-tar fumes      | Suppl. 7 (1987) | 1 | Skin (scrotum)<sup>c</sup>, lung<sup>c</sup>, bladder<sup>c</sup>, kidney<sup>c</sup> |
| Dry cleaning           | Solvents and chemicals used in “spotting” | Vol. 63 (1995a) | 2B | |
| Furniture and cabinet  | Wood dust           | Suppl. 7 (1987) | 1 | Nose and sinonasal cavities<sup>b</sup> |
| Hairdressers and barbers| Dyes (aromatic amines, amino-phenols with hydrogen peroxide); solvents; propellants; aerosols | Vol. 57 (1993b) | 2A | Bladder<sup>b</sup>, lung<sup>c</sup>, non-Hodgkin lymphoma<sup>c</sup>, ovary<sup>c</sup> |
| Hematite mining, underground, with radon exposure | Radon daughters; silica | Suppl. 7 (1987) | 1 | Lung<sup>b</sup> |
| Iron and steel foundi | PAHs; silica; metal fumes; formaldehyde | Suppl. 7 (1987) | 1 | Lung<sup>b</sup> |
| Magnesia manufacture   | Magnesi dioxide; 4,4’-methylene bis(2-methylyaniline); ortho-nitrotoluene | Vol. 57 (1993b) | 1 | Bladder<sup>b</sup> |
| Painters               |                    | Vol. 47 (1989c) | 1 | Lung<sup>b</sup>, bladder<sup>c</sup>, stomach<sup>c</sup> |
| Petroleum refining     | PAHs                | Vol. 45 (1989b) | 2A | Bladder<sup>b</sup>, brain<sup>c</sup>, leukemia<sup>a</sup> |
| Printing processes     | Solvents; inks      | Vol. 65 (1998) | 2B | |
| Production of art glass, glass containers, and pressed ware | Lead; arsenic; antimony oxides; silica; asbestos; other metal oxides; PAHs | Vol. 58 (1993a) | 2A | Lung<sup>c</sup> |
| Rubber industry        | Aromatic amines; solvents | Suppl. 7 (1987) | 1 | Bladder<sup>b</sup>, stomach<sup>c</sup>, larynx<sup>c</sup>, leukemia<sup>c</sup>, lung<sup>c</sup> |
| Textile manufacturing  | Textile dust in manufacturing process; dyes and solvents in dyeing and printing operations | Vol. 48 (1990b) | 2B | |

*Most recent IARC evaluation; for those referenced as Supplement 7 (IARC 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date. *We judged that the evidence for an association with this site was strong. **We judged that the evidence was suggestive.*
Table 7. Definite or probable occupational carcinogens and carcinogenic circumstances, by site.

| Site                        | Strength of evidence | High-risk substance or circumstance                                                                 |
|-----------------------------|----------------------|------------------------------------------------------------------------------------------------------|
| Pharynx and nasopharynx     | Suggestive           | Mustard gas; formaldehyde                                                                            |
| Nasal cavities and paranasal sinuses | Strong               | Boot and shoe manufacture and repair; furniture and cabinet making; isopropanol manufacture, strong acid process; selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel-refining industry; wood dust |
| Esophagus                   | Suggestive           | Soots; tetrachloroethylene                                                                           |
| Stomach                     | Suggestive           | Painters; rubber industry                                                                            |
| Gastrointestinal tract      | Suggestive           | Asbestos; ionizing radiation                                                                          |
| Liver and biliary tract     | Strong               | Aflatoxin; ionizing radiation                                                                          |
| Liver (angiosarcoma)        | Strong               | Vinyl chloride                                                                                        |
| Liver (hepatocellular)      | Suggestive           | Arsenic and arsenic compounds                                                                          |
| Pancreas                    | Suggestive           | Acrylamide                                                                                            |
| Larynx                      | Suggestive           | Isopropanol manufacture; strong acid process; inorganic acid mists containing sulfuric acid; mustard gas |
| Lung                        | Strong               | Aluminum production; arsenic and arsenic compounds; asbestos; beryllium; cadmium and cadmium compounds; chromium compounds, hexavalent; coal gasification; coke production; hematite mining, underground, with radon exposure; involuntary (passive) smoking; ionizing radiation; iron and steel founding; selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel-refining industry; painters; silica, crystalline; soots; talc containing asbestos fibers |
| Lung (oat cell)             | Strong               | Bis(chloromethyl) ether and chloromethyl methyl ether (technical grade)                                |
| Bone                        | Strong               | Ionizing radiation                                                                                    |
| Melanoma                    | Strong               | Solar radiation                                                                                       |
| Skin                        | Strong               | Ultraviolet radiation (A, B and C) from artificial sources                                            |
| Mesothelioma                | Suggestive           | Asbestos; erionite; talc containing asbestos fibers                                                    |
| CNS                         | Suggestive           | Epichlorohydrin                                                                                       |
| Sarcoma                     | Strong               | TCDD                                                                                                  |
| Cervix                      | Suggestive           | Tetrachloroethylene                                                                                   |
| Ovary                       | Suggestive           | Hairdressers and barbers                                                                              |
| Kidney                      | Suggestive           | Coke production                                                                                       |
| Kidney (renal cell)         | Suggestive           | Trichloroethylene                                                                                     |
| Bladder                     | Strong               | Aluminum production; 4-aminobiphenyl; auramine manufacture; benzo[a]pyrene; coal gasification; magenta manufacture; 2-naphthylamine; rubber industry |
| Brain                       | Suggestive           | Nonarsonical insecticides; petroleum refining                                                          |
| Thyroid                     | Strong               | Ionizing radiation                                                                                     |
| Non-Hodgkin lymphoma        | Suggestive           | Hairdressers and barbers; nonarsonical insecticides; TCDD; tetrachloroethylene; trichloroethylene     |
| Lympho-hematopoietic system | Suggestive           | 1,3-Butadiene                                                                                         |
| Multiple myeloma            | Suggestive           | Nonarsonical insecticides                                                                             |
| Leukemia                    | Strong               | Benzene; boot and shoe manufacture and repair; ethylene oxide; ionizing radiation                      |
| Other sites                 | Suggestive           | Formaldehyde; nonarsonical insecticides; petroleum refining; rubber industry                          |
| All sites combined          | Strong               | TCDD                                                                                                  |

CNS, central nervous system; TCDD, 2,3,7,8-tetrachlorodibenzo-p-dioxin.

*Our judgment of strength of evidence regarding each site. There is suggestive evidence of an effect of ionizing radiation on several sites in addition to those shown here. *The evidence for an association with TCDD only becomes strong when data are combined for all cancer sites.

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Table 8. Evolution in knowledge regarding current (2003) IARC occupational carcinogens.

| Current rating | Past rating | IARC 1987 | WHO 1964 |
|----------------|-------------|-----------|-----------|
| 1 (n = 28)     | 1           | 19        | 13        |
| 2A             | 4           |           |           |
| 2B             | 1           |           |           |
| 3              | 0           | NA        |           |
| Unrated        | 4           | 11        |           |
| Total          | 28          | 28        |           |
| 2A (n = 27)    | 1           | 0         | 0         |
| 2A             | 16          |           |           |
| 2B             | 6           |           |           |
| 3              | 2           | NA        |           |
| Unrated        | 3           | 27        |           |
| Total          | 27          | 27        |           |
| 2B (n = 113)   | 1           | 0         | 1         |
| 2A             | 2           |           |           |
| 2B             | 63          |           |           |
| 3              | 9           | NA        |           |
| Unrated        | 39          | 107       |           |
| Total          | 113         | 113       |           |

NA, not applicable.