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Jack Siemiatycki, Lesley Richardson, Kurt Straif, Benoit Latreille, Ramzan Lakhani, Sally Campbell, Marie-Claude Rousseau, and Paolo Boffetta

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Jack Siemiatycki[1,2]

Lesley Richardson[3]

Kurt Straif[3]

Benoit Latreille[4]

Ramzan Lakhani[4]

Sally Campbell[4]

Marie-Claude Rousseau[1]

Paolo Boffetta[3, 5]

1 Département de médecine sociale et préventive
Université de Montréal
P.O. Box 6128, stn Centre-Ville
Montreal (QC), H3C 3J7, Canada

2. Department of Epidemiology and Biostatistics
McGill University
1020 Pine Ave West
Montreal, Quebec, H1A 1A0, Canada

3 International Agency for Research on Cancer
150 cours Albert Thomas
69008 Lyon, France

4 INRS-Institut Armand-Frappier
531 boul des Prairies
Laval, Quebec, H7B 1V7, Canada

5 Division of Clinical Epidemiology
German Cancer Research Center (DKFZ)
Im Neuenheimer Feld 280
69120 Heidelberg, Germany

Corresponding author: Jack Siemiatycki, Département de médecine sociale et préventive, Université de Montréal, P.O. Box 6128, stn Centre-Ville, Montreal (Qc). Canada, H3C 3J7

Tel: (450) 686-5676; Fax: (450) 686-5599; j.siemiatycki@umontreal.ca

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Keywords: occupation, environment, cancer, epidemiology, review
Abbreviations:
IARC – International Agency for Research on Cancer
PAHs – poly-aromatic hydrocarbons
HIV – Human immunodeficiency virus
HBV – Hepatitis B virus
HBC – Hepatitis C virus
MOCA - 4,4'-methylene bis(2-chloroaniline)
NIOSH – National Institute for Occupational Safety and Health
NTP – National Toxicology Program
WHO – World Health Organization

OUTLINE

ABSTRACT

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 epidemiological 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 paper 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.

INTRODUCTION

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 while 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 since most occupational exposures find their way into the general environment, sometimes at higher concentrations than in the workplace.

There is a large volume of epidemiological 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 paper 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, while 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, while 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 "non-occupational" ones. Further, some carcinogens are chemicals that are used for research purposes and to which few people would ever be exposed, whether occupationally or non-occupationally. 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 (e.g., scrotal cancer among chimney sweeps and PAHs in soot (Waldron 1983); lung cancer among asbestos miners and asbestos fibres (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 aluminium industry (IARC 1987a)). 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 1982c)). 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 Monograph Programme of the International Agency for Research on Cancer (IARC) - Evaluation of the Carcinogenic Risk of Chemicals to Humans (IARC

1987a). The objective of the IARC Programme, which has been operating since 1971, is to publish critical reviews of epidemiological and experimental data on carcinogenicity for chemicals, groups of chemicals, industrial processes, other complex mixtures, physical agents, and biological 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 for evaluation on the basis of two main criteria: (i) humans are exposed, and (ii) there is reason to suspect that the substance may be carcinogenic. Direct evidence concerning carcinogenicity of a substance can come from epidemiological 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.

We will outline the IARC process, because it is important to understand how decisions are made in order to properly interpret its output. IARC evaluations are carried out during specially convened meetings that typically last a week. The meetings may evaluate only one agent, such as silica, they may address a set of related agents, or they may even address 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, (i) exposure and occurrence of the substances being evaluated, (ii) human evidence of cancer risk (i.e. epidemiology), (iii) animal carcinogenesis, and (iv) 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 ofthe 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 epidemiological 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 epidemiological 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 epidemiological and animal evidence of carcinogenicity, plus any other relevant evidence on genotoxicity, mutagenicity, metabolism, mechanisms, or other. Epidemiological 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 classes (which IARC refers to as "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 epidemiological 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 leads 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 a web site (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 as an occupational exposure. Second, while 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 time that the working group met and reviewed the evidence; it is possible that evidence that appeared after the IARC review could change the evaluation.

Current knowledge on occupational carcinogens

From 1972 to 2003, the IARC Monograph Programme published 83 volumes, representing evaluations of more than 880 substances, complex mixtures and industrial processes. Of these, 89 have been classed 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 /non-occupational 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, NIOSH surveys (NIOSH 1990), the 10th Report on Carcinogens of the National Toxicology Program (US Department of Health and Human Services 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 semi-subjective 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, microbiological agents and dietary constituents. Pharmaceuticals represent a special case. Many have been evaluated and many are considered to be carcinogenic. While the main population exposed consists of patients undergoing therapy, there can also be exposure to workers who produce the drugs, and to 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 HIV, HBV and HCV, though 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 which possibly, probably, or definitely entail excess risk of cancer (IARC Groups 1, 2A and 2B) - Table 6;

These tables only include agents and circumstances which were reviewed and published by the IARC Monograph Programme 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, all substances and occupations covered in the first 15 years of the Programme were re-evaluated (IARC 1987a). 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 was available for the re-evaluation.

For the agents in Tables 3 to 5, we devised a set of subheadings to help the reader digest the long lists of often obscure chemical names. The subheadings are: physical agents; respirable dusts & fibers;

metals & metal compounds; polyaromatic hydrocarbons; wood & fossil fuels and their by-products; monomers; intermediates in plastics & rubber manufacturing; chlorinated hydrocarbons; aromatic amine dyes; azo dyes; intermediates in the production of dyes; pesticides; nitro compounds; others. Tables 3 to 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 non-occupational 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 non-occupational exposure.

The Monograph Programme has occasionally addressed cancer risk in various occupations and industries, as well as agents. However, whereas the Monograph programme aims at a systematic evaluation of agents and complex mixtures, it is not intended to provide a systematic review of cancer risk by industries and occupations. That is, those reviews were conducted where there were particular concerns or anticipated insights regarding specific potential carcinogens. Sometimes this was done when there appeared to be strong evidence of risk in an occupation, but little indication of what the responsible agent might be (e.g.. rubber industry; painter). Sometimes the impetus for an occupation or industry review came from the attempt to evaluate some agent, but it was realized that the evidence regarding that agent was rooted in epidemiological evidence regarding some occupation or industry (e.g., glass industry; hairdresser). Table 6 shows those that IARC has evaluated as definitely, probably or possibly entailing a carcinogenic risk. Because there has been no pretense of exhaustiveness in evaluating occupations and industries, the absence of an occupation or industry in Table 6 does not carry the same significance as the

absence of an agent in Tables 3 to 5. That is, it does not signify that there is no known risk for that occupation or industry.

Since our inclusion criteria admitted substances to which workers were exposed in the past, we included some substances which have been banned or virtually eliminated in some countries, such as mustard gas, bis(chloromethyl)ether, tris(2,3-dibromopropyl) phosphate, and 4,4'-methylene bis(2-chloroaniline) (MOCA), as well as some industries which no longer exist (viz. production of auramine and magenta). These are mentioned partly for historic interest, and partly because it is possible that these might yet be used in some places at some time.

It is important to note that the substances, occupations and industries listed in Tables 3 to 6 are not mutually exclusive. Certainly, some of the occupations and industries listed in Table 6 may be there because of some of the substances that are listed in Tables 3 to 5. But further, the substances relate to each other in complicated ways. There are some families of substances which include some specific substances which are also listed (e.g. non-arsenical insecticides which includes DDT; benzidine-based dyes which includes benzidine). Also there are some complex mixtures (e.g. diesel exhaust) which contain some substance on the list (e.g. nitro-PAHs) and which may be responsible for the carcinogenicity of the mixture.

The listing of affected cancer sites in Tables 3 and 4 does not come explicitly out of 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. As we did in the previous tables, we indicate clearly which associations are strong and which are only suggestive. Lung cancer 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 1987a). In that report, the results were presented with the same rating system (1, 2A, 2B, 3) as is used today, rendering the lists comparable. In 1964, even before

the establishment of IARC, the World Health Organization 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 to 5, and that are currently considered to be definite, probable, or possible occupational carcinogens.

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, over 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. While 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 are :

- 3,3 dichlorobenzene, which was considered a definite carcinogen in 1964 and was only considered as possible as of 1987 and as of 2002;
- acrylonitrile and propylene oxide, which were considered probable carcinogens in 1987, and only as possible in 2002;
- glass wool was considered a possible carcinogen in 1988, and was downgraded to unclassifiable in 2002;
- ionizing radiation, which is 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, so 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 1950's 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, while the proportion of Group 2B evaluations increased. This reflects the fact that, when the Monograph Programme 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 occupational carcinogens. Only a small fraction of occupational agents have been adequately investigated with epidemiological data. There are many reasons for this including, *inter alia*, the magnitude of the numbers of agents to be investigated, a shift away from occupational cancer research in the epidemiologic community and into new areas of epidemiologic interest, the difficulty and challenge of exposure assessment, and increasing barriers to accessing human subjects for occupational studies. These are problems that deserve attention, or we will fail in our responsibilities.

Many countries have agencies that list carcinogens. In the U.S. the two primary sources of information on occupational carcinogens, at least in the form of lists, are the National Institute for Occupational Safety and Health (NIOSH) and the National Toxicology Program (NTP). NIOSH publishes a list of agents which it considers to be occupational carcinogens (NIOSH 2004). Currently there are 133 agents on this list. There is no further information in the NIOSH list regarding: the degree of evidence for different agents; the occupations where these may occur or on the target organs; or the criteria and methods used to establish and update this list. The NTP has been mandated under the Public Health Service Act to maintain a list of human carcinogens and to provide data on each one concerning

exposure circumstances and regulatory policies (US Department of Health and Human Services 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. The substances on these lists are not limited to occupational agents, and there is no tabular summary of occupational agents, of the occupations in which these may occur, or the target organs. It is beyond the scope of this paper to carry out a comparison of the procedures and lists of the various national bodies. Suffice 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 or in absolute risk terms or in terms of dose-response relationships. The IARC evaluations provide no such indications, and while it would be most precious 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 hopefully be useful to researchers in setting research priorities and in furthering our understanding of carcinogenesis, and to those interested in preventing occupational cancer.

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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, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; or (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 which 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.

Table 2. Guidelines used by IARC Monographs Programme in evaluating human carcinogenicity based on the synthesis of epidemiological, animal and other evidence[a]

Group	Description of group	Combinations which fit in this group		
		Epidemiological 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
2A	The agent, mixture, or exposure circumstance is probably carcinogenic to humans	Limited	Sufficient	Less than strongly positive
		Inadequate or not available	Sufficient	Strongly positive
2B	The agent, mixture, or exposure circumstance is prossibly 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
		Not elsewhere classified		
4	The agent, mixture, or exposure circumstance is probably not	Suggesting lack of carcinogenicity	Suggesting lack of carcinogenicity	Any
		Inadequate or not available	Suggesting lack of carcinogenicity	Strongly negative

a This table shows our interpretation of the IARC Monographs Programme guidelines to derive the overall evaluation from the combined epidemiological, animal and other evidence. However, the Working Group can, under exceptional circumstances, depart from these guidelines in deriving the overall evaluation. 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 details of the guidelines refer to the Preamble of the IARC Monographs (IARC 2003).

Table 3. Substances and mixtures which have been evaluated by IARC as definite (Group 1) human carcinogens, and which are occupational exposures

Substance or mixture	Occupation or industry in which substance found[a]	IARC volume & year[b]	Human evidence[c]	Animal evidence[c]	Site(s)[d]
Physical agents					
Ionizing radiation and sources thereof, including notably, X-rays, gamma rays, neutrons and radon gas	Radiologists, technologists, nuclear workers, radium-dial painters, underground miners, plutonium workers, clean-up workers following nuclear accidents, aircraft crew	Vol. 75 (2000a) Vol. 78 (2001a)	Sufficient	Sufficient	Bone Leukemia Lung Liver Thyroid Others
Solar radiation	Outdoor workers	Vol. 55 (1992b)	Sufficient	Sufficient	Melanoma Skin
Respirable dusts and fibers					
Asbestos	Mining & milling; by-product manufacture; insulating; shipyard workers; sheet-metal workers; asbestos cement industry;	Suppl. 7 (1987a)	Sufficient	Sufficient	Lung Mesothelioma *Larynx* *GI tract*
Erionite	Used in waste treatment, sewage and agricultural waste; in air pollution control systems, cement aggregates, building materials	Suppl. 7 (1987a)	Sufficient	Sufficient	Mesothelioma
Silica, crystalline	Granite & stone industries; ceramics, glass, & related industries; foundries & metallurgical industries; abrasives; construction; farming	Vol. 68 (1997b)	Sufficient	Sufficient	Lung
Talc containing asbestiform fibres	Manufacture of pottery, paper, paint & cosmetics	Suppl. 7 (1987a)	Sufficient	Inadequate	Lung Mesothelioma

Wood dust	Logging & sawmill workers; pulp & paper & paperboard industry; woodworking trades (e.g. furniture industries, cabinetmaking, carpentry & construction); used as filler in plastic & linoleum production	Vol. 62 (1995b)	Sufficient	Inadequate	Nasal cavities & paranasal sinuses
Metals & metal compounds					
Arsenic & arsenic compounds	Non-ferrous metal smelting; production, packaging, & use of arsenic-containing pesticides; sheep dip manufacture; wool fibre production; mining of ores containing arsenic	Suppl. 7 (1987a)	Sufficient	Limited	Skin Lung *Liver (angiosarcoma)*
Beryllium	Beryllium extraction & processing; aircraft & aerospace industries, electronics & nuclear industries; jewellers	Vol. 58 (1993a)	Sufficient	Sufficient	Lung
Cadmium & cadmium compounds	Cadmium-smelter workers; battery production workers; cadmium-copper alloy workers; dyes & pigments production; electroplating process	Vol. 58 (1993a)	Sufficient	Sufficient	Lung
Chromium compounds, hexavalent	Chromate production plants; dyes & pigments; plating & engraving; chromium ferro-alloy production; stainless-steel welding; in wood preservatives, leather tanning, water treatment, inks, photography, lithography, drilling muds, synthetic perfumes, pyrotechnics, corrosion–resistance	Vol. 49 (1990a)	Sufficient	Sufficient	Lung *Nasal sinuses*
Selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry	Nickel refining & smelting; welding	Vol. 49 (1990a)	Sufficient	Sufficient	Lung Nasal cavity and sinuses

Wood & fossil fuels and their by-products					
Benzene	Production; solvents in the shoe production industry; chemical, pharmaceutical & rubber industries; printing industry (rotogravure plants, bindery departments); gasoline additive	Suppl. 7 (1987a)	Sufficient	Limited	Leukemia
Coal tars & pitches	Production of refined chemicals & coal tar products (patent-fuel); coke production; coal gasification; aluminum production; foundries; road paving & construction (roofers & slaters	Suppl. 7 (1987a)	Sufficient	Sufficient	Skin *Lung* *Bladder*
Mineral oils, untreated & mildly treated	Production; used as lubricant by metal workers, machinists, engineers; printing industry (ink formulation); used in cosmetics, medicinal & pharmaceutical preparations	Suppl. 7 (1987a)	Sufficient	Inadequate	Skin *Bladder* *Lung* *Nasal sinuses*
Shale oils or shale-derived lubricants	Mining & processing; used as fuels or chemical-plant feedstocks; lubricant in cotton textile industry	Suppl. 7 (1987a)	Sufficient	Sufficient	Skin
Soots	Chimney sweeps; heating-unit service personnel; brick masons & helpers; building demolition workers; insulators; firefighters; metallurgical workers; work involving burning of organic materials	Vol. 35 (1985)	Sufficient	Inadequate	Skin Lung *Esophagus*
Monomers					
Vinyl chloride	Production; production of polyvinyl chloride & co-polymers; refrigerant before 1974; extraction solvent; in aerosol propellants	Suppl. 7 (1987a)	Sufficient	Sufficient	Liver (angiosarcoma) *Liver (hepato-cellular)*
Intermediates in plastics & rubber manufacturing					
Bis(chloromethyl)ether & chloromethyl methyl	Production; chemical intermediate; alkylating agent; laboratory reagent;	Suppl. 7 (1987a)	Sufficient	Sufficient	Lung (oat cell)

ether (technical grade)	plastic manufacturing; ion-exchange resins & polymers				
Aromatic amine dyes					
4-Aminobiphenyl	Production; dyestuffs & pigment manufacture	Suppl. 7 (1987a)	Sufficient	Sufficient	Bladder
Benzidine	Production; dyestuffs & pigment manufacture	Suppl. 7 (1987a)	Sufficient	Sufficient	Bladder
2-Napththylamine	Production; dyestuffs & pigment manufacture	Suppl. 7 (1987a)	Sufficient	Sufficient	Bladder
Pesticides					
Ethylene oxide	Production; chemical industry; sterilising agent (hospitals, spice fumigation)	Vol. 60 (1994b)	Limited	Sufficient	Leukemia
2,3,7,8-Tetrachloro-dibenzo-para-dioxin (TCDD)	Production; use of chlorophenols & chlorophenoxy herbicides; waste incineration; PCB production; pulp & paper bleaching	Vol. 69 (1997a)	Limited	Sufficient	All sites combined *Lung* *non-Hodgkin's lymphoma* *Sarcoma*
Others					
Aflatoxin	Feed production industry, workers loading & unloading cargo; rice & maize processing	Vol. 82 (2002c)	Sufficient	Sufficient	Liver
Involuntary (passive) smoking	Workers in bars & restaurants, office workers	Vol. 83 (in preparation)	Sufficient	Sufficient	Lung
Mustard gas	Production; used in research laboratories, military personnel	Suppl. 7 (1987a)	Sufficient	Limited	Larynx *Lung* *Pharynx*
Strong inorganic-acid mists containing sulfuric	Pickling operations; steel industry; petrochemical industry; phosphate acid fertilizer manufacturing	Vol. 54 (1992a)	Sufficient	Not available	Larynx *Lung*

a 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.

b This is the most recent IARC evaluation. For those referenced to as Supplement 7, it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

c As judged by the IARC Working Group. The notation "Not available" was added by the authors to signify those substances for which there was no epidemiological evidence at all.

d As judged by us. Regular script indicates that the evidence for an association with this site was strong. Italics indicates that the evidence was suggestive.

Table 4. Substances and mixtures which have been evaluated by IARC as probable (Group 2A) human carcinogens, and which are occupational exposures

Substance or mixture	Occupation or industry in which substance found[a]	IARC volume & year[b]	Human evidence[c]	Animal evidence[c]	Site(s)[d]
Physical agents					
Ultraviolet radiation (A, B & C) from artificial sources	Arc welding; industrial photoprocesses; sterilization & disinfection; phototherapy; operating theatres; research laboratories; UV Fluorescence in food industry; insect traps	Vol. 55 (1992b)	Inadequate	Sufficient	*Melanoma*
Polyaromatic hydrocarbons					
Benz[a]anthracene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Vol. 32 (1983b)	Not available	Sufficient	*Lung* *Bladder* *Skin*
Benzo[a]pyrene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Vol. 32 (1983b)	Not available	Sufficient	*Lung* *Bladder* *Skin*
Dibenz[a,h]anthracene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Vol. 32 (1983b)	Not available	Sufficient	*Lung* *Bladder* *Skin*
Wood & fossil fuels and their by-products					
Creosotes	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* *Bladder*
Intermediates in plastics & rubber manufacturing					
4,4'-Methylene bis (2-chloroaniline) (MOCA)	Production; curing agent for roofing & wood sealing	Vol. 57 (1993b)	Inadequate	Sufficient	*Bladder*
Styrene-7,8-oxide	Production; styrene glycol production; perfume preparation; reactive diluent in	Vol. 60 (1994b)	Inadequate	Sufficient	

	epoxy resin formulations; as chemical intermediate for cosmetics, surface coating, & agricultural & biological chemicals, used for treatment of fibers & textiles, in fabricated rubber products				
Chlorinated hydrocarbons					
a-Chlorinated toluenes	Production; dye & pesticide manufacture	Vol. 71 (1999a)	Limited	Sufficient	*Lung*
Polychlorinated biphenyls	Production; electrical capacitor manufacturing	Suppl. 7 (1987a)	Limited	Sufficient	*Liver & biliary tract*
Tetrachloroethylene	Production; dry cleaning; metal degreasing	Vol. 63 (1995a)	Limited	Sufficient	*Cervix* *Esophagus* *Non-Hodgkin's lymphoma*
Trichloroethylene	Production; dry cleaning; metal degreasing	Vol. 63 (1995a)	Limited	Sufficient	*Liver& biliary tract* *Non-Hodgkin's lymphoma* *Renal cell*
Monomers					
Acrylamide	Chemical industry; water & wastewater treatment; textile, steel, & lumber, industries; petroleum refining; mineral processing; sugar production; hospitals	Vol. 60 (1994b)	Inadequate	Sufficient	*Pancreas*
1,3-Butadiene	Chemical & rubber industries	Vol. 71 (1999a)	Limited	Sufficient	*Lympho-haematopoietic*
Epichlorohydrin	Production & use of resins, glycerine, & propylene based rubbers; used as a solvent	Vol. 71 (1999a)	Inadequate	Sufficient	*Lung* *CNS*
Vinyl bromide	Production; production of vinyl bromide polymers & monoacrylic fibers for carpet backing material; rubber & plastic production	Vol. 71 (1999a)	Not available	Sufficient	

Vinyl fluoride	Production; polyvinylfluoride & fluoropolymers production	Vol. 63 (1995a)	Not available	Sufficient	
Aromatic amine dyes					
Benzidine-based dyes	Production; used in textile, paper, leather, rubber, plastics, printing, paint & lacquer industries	Suppl. 7 (1987a)	Inadequate	Sufficient	*Bladder*
4-Chloro-ortho-toluidine	Dye & pigment manufacture; textile industry	Vol. 77 (2000b)	Limited	Sufficient	*Bladder*
ortho-Toluidine	Production; manufacture of dyestuffs, pigments, optical brightener, pharmaceuticals & pesticides; rubber vulcanizing; clinical laboratory reagent; cleaners & janitors	Vol. 77 (2000b)	Limited	Sufficient	*Bladder*
Intermediates in the production of dyes					
Dimethylcarbamoyl chloride	Production; manufacture of pharmaceuticals; pesticides & dyes	Vol. 71 (1999a)	Inadequate	Sufficient	
Pesticides					
Captafol	Production; fungicide	Vol. 53 (1991c)	Not available	Sufficient	
Ethylene dibromide	Production; pest control; petroleum refining & waterproofing, in leaded gasoline; chemical intermediate & solvent in gums, waxes, resins, dyes & pharmaceutical preparations	Vol. 71 (1999a)	Inadequate	Sufficient	
Non-arsenical insecticides	Production; pest control & agriculture workers; flour & grain mill workers	Vol. 53 (1991c)	Limited	Not available	*Brain* *Leukemia* *Lung* *Multiple myeloma* *Non-Hodgkin's lymphoma*
Others					
Diethyl sulfate	Ethanol production	Vol. 71 (1999a)	Not available	Sufficient	

Formaldehyde	Production; pathologists; medical laboratory technicians; plastics; textile industry	Vol. 62 (1995b)	Limited	Sufficient	*Leukemia* *Nasal sinuses* *Nasopharynx*
Tris(2,3-dibromopropyl) phosphate	Production; used in the textile industry; in phenolic resins (for electronics industry), paints, paper coatings & rubber.	Vol. 71 (1999a)	Inadequate	Sufficient	

a 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.

b This is the most recent IARC evaluation. For those referenced as Supplement 7, it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

c As judged by the IARC Working Group. The notation "Not available" was added by the authors to signify those substances for which there was no epidemiological evidence at all.

d As judged by us. Regular script indicates that the evidence for an association with this site was strong. Italics indicates that the evidence was suggestive.

Table 5. Substances and mixtures which have been evaluated by IARC as possible (Group 2B) human carcinogens, and which are occupational exposures

Substance or mixture	Occupation or industry in which substance found[a]	IARC volume & year[b]	Human evidence[c]	Animal evidence[c]
Respirable dusts & fibers				
Glasswool	Production; construction & insulation	Vol. 81 (2002a)	Inadequate	Sufficient
Palygorskite (long fibers > 5 micrometers)	Miners & millers; production of waste absorbents, fertilizers & pesticides	Vol. 68 (1997b)	Inadequate	Sufficient
Refractory ceramic fibers	Production; furnace insulators; ship builders; heat resistant fabric manufacture	Vol. 81 (2002a)	Inadequate	Sufficient
Rockwool	Production; thermal or acoustical insulation	Vol. 81 (2002a)	Inadequate	Limited
Slagwool	Production; thermal or acoustical insulation; fireproofing	Vol. 81 (2002a)	Inadequate	Limited
Special-purpose glass fibres such as E-glass & '475' glass fibres	Reinforced plastic industry	Vol. 81 (2002a)	Not available	Sufficient
Metals & metal compounds				
Antimony trioxide	Ore processing; glass & ceramic production	Vol. 47 (1989c)	Inadequate	Sufficient
Cobalt & cobalt compounds	Miners; processing of copper & nickel ore; glass & ceramic production	Vol. 52 (1991a)	Inadequate	Sufficient
Lead & inorganic lead compounds	Lead smelters; plumbers, solderers & occupations in battery recycling smelters	Suppl. 7 (1987a)	Inadequate	Sufficient
Methylmercury compounds	Pesticide & fungicide production; paint industry	Vol. 58 (1993a)	Inadequate	Sufficient
Nickel - metallic & alloys	Nickel miners; metal fabrication, grinding, electroplating, & welding	Vol. 49 (1990a)	Inadequate	Sufficient
Wood & fossil fuels and their by-products				

Benzofuran	Production; intermediate in the coumarone-indene resin polymerization; coke production, coal gasification & combustion	Vol. 63 (1995a)	Not available	Sufficient
Bitumens, extracts of steam-refined & air-refined	Production/refining; road construction, roofing & flooring	Suppl. 7 (1987a)	Inadequate	Sufficient
Carbon black	Production; paint, ink, plastic & rubber industries	Vol. 65 (1996)	Inadequate	Sufficient
Diesel fuel, marine	Petroleum refineries; marine fuel; distribution	Vol. 45 (1989b)	Inadequate	Limited
Fuel oils residual (heavy)	Petroleum refineries; distribution, marine fleet, majority of large diesel engines operated on land, industrial heating systems	Vol. 45 (1989b)	Inadequate	Sufficient
Gasoline	Petroleum refineries; transportation; mechanics & service station attendants	Vol. 45 (1989b)	Inadequate	Limited
Gasoline engine exhaust	Transportation & vehicle maintenance workers; drivers; toll attendants; traffic controllers	Vol. 46 (1989a)	Inadequate	Limited
Naphthalene	Production; insecticide, resin & pharmaceutical production	Vol. 82 (2002c)	Inadequate	Sufficient
Polyaromatic hydrocarbons				
Benzo(b)fluoranthene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Benzo(j)fluoranthene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Benzo(k)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,j)acridine	Production; used in dye synthesis; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo(a,e)pyrene	Production; biochemical laboratory workers; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo(a,h)pyrene	Production; biochemical laboratory workers ; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo(a,i)pyrene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient

Dibenzo(a,l)pyrene	Production; biochemical laboratory workers; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Monomers				
Acrylonitrile	Production; acrylic textile fiber & plastic production	Vol. 71 (1999a)	Inadequate	Sufficient
Chloroprene	Production; manufacture of polychloroprene (synthetic rubber)	Vol. 71 (1999a)	Inadequate	Sufficient
Ethyl acrylate	Production; plastic molding occupations using acrylate resins	Vol. 39 (1986a)	Not available	Sufficient
Isoprene	Production; synthetic rubber & plastics industries	Vol. 71 (1999a)	Not available	Sufficient
Styrene	Polyester resin manufacture, production of packaging materials & fiberglass-reinforced polyester	Vol. 82 (2002c)	Limited	Limited
Toluene diisocyanates	Production; production of polyurethane foams & 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 & adhesive industries	Vol. 63 (1995a)	Not available	Limited
Intermediates in plastics & rubber manufacturing				
Acetaldehyde	Acetic acid production workers; dyestuff, plastic & synthetic rubber industries	Vol. 71 (1999a)	Inadequate	Sufficient
Acetamide	Production; plastics & chemical industries	Vol. 71 (1999a)	Not available	Sufficient
2,4-Diaminotoluene	Production;chemical intermediate in TDI production, dyes for textiles; leather; furs; wood; biological stain; photo developper	Vol. 16 (1978)	Not available	Sufficient
1,2-Epoxybutane	Production; metal degreasing; plastics industry	Vol. 71 (1999a)	Not available	Limited
Ethylbenzene	Production; ink, paint & plastic production	Vol. 77 (2000b)	Inadequate	Sufficient
Ethylene thiourea	Production; vulcanization in the rubber industry, manufacture of ethylenebisdithiocarbamate pesticides; electroplating baths; dyes, pharmaceuticals & synthetic resins.	Vol. 79 (2001b)	Inadequate	Sufficient
Phenyl glycidyl ether	Production; epoxy resins; casting & molding	Vol. 71 (1999a)	Not available	Sufficient

Propylene oxide	Production; polyurethane foam & glycol production; fumigant	Vol. 60 (1994b)	Inadequate	Sufficient
Chlorinated hydrocarbons				
Carbon tetrachloride	Production; industrial degreasing occupations; dry cleaners; refrigerant production	Vol. 71 (1999a)	Inadequate	Sufficient
Chlorinated paraffin of average carbon-chain length C12	Production; PVC processing industry	Vol. 48 (1990b)	Not available	Sufficient
Chloroform	Refrigerant production; dyes, solvents & pesticides	Vol. 73 (1999b)	Inadequate	Sufficient
1,2-Dichloroethane	Vinyl chloride production workers	Vol. 71 (1999a)	Inadequate	Sufficient
Dichloromethane	Production; painters & furniture restorers; pharmaceutical & electronic production	Vol. 71 (1999a)	Inadequate	Sufficient
Hexachloroethane	Production; aluminum refinery; industrial firefighters	Vol. 73 (1999b)	Inadequate	Sufficient
Aromatic amine dyes				
Auramine (technical grade)	Production; textile, plastic & printing	Suppl. 7 (1987a)	Inadequate	Sufficient
Benzyl violet 4B	Production; food, drugs, cosmetics, textiles	Vol. 16 (1978)	Not available	Sufficient
CI Basic Red 9	Production; textiles & printing; biological stains (basic fushin dye in laboratories)	Vol. 57 (1993b)	Inadequate	Sufficient
2,4-Diaminoanisole	Dyestuff industry; barbers & cosmetologists; furriers	Vol. 79 (2001b)	Not available	Sufficient
3,3'-Dimethylbenzidine (o-tolidine)	Production; dye or intermediate in dyes & pigments production, polyurethane elastomers, coating, plastics, clinical laboratories	Vol. 1 (1972)	Not available	Sufficient
2,6-Dimethylaniline (2,6-xylidine)	Production; dyestuffs & pharmaceutical manufacturing	Vol. 57 (1993b)	Not available	Sufficient
3,3'-Dichlorobenzidine	Production; dyestuff manufacturing	Vol. 29 (1982c)	Inadequate	Sufficient
4,4'-Diaminodiphenyl ether	Production; polyamide-type resin manufacturing	Vol. 29 (1982c)	Not available	Sufficient
Disperse Blue 1	Production; hair colouring; textiles & 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 diisocyanates, polyisocyanates & epoxy resins	Vol. 39 (1986a)	Not available	Sufficient
Magenta containing CI Basic Red 9	Production; textiles & printing; biological stains in laboratories; photography	Vol. 57 (1993b)	Not available	Sufficient
Azo dyes				
ortho-Aminoazotoluene	Production; textiles & leather	Vol. 8 (1975)	Not available	Sufficient
para-Aminoazobenzene	Production; textiles & leather	Suppl. 7 (1987a)	Not available	Sufficient
CI Acid Red 114	Production; textiles & leather	Vol. 57 (1993b)	Not available	Sufficient
CI Direct Blue 15	Production; textiles & paper	Vol. 57 (1993b)	Not available	Sufficient
Citrus red No. 2	Production; used for food coloring	Vol. 8 (1975)	Not available	Sufficient
para-Dimethylaminoazo-benzene	Production; textiles; laboratories	Vol. 8 (1975)	Not available	Sufficient
Oil orange SS	Production; dyes / pigments for varnishes, oils, fats & 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 & printing; biological stains in life science laboratories; used by ophthalmologists	Vol. 8 (1975)	Not available	Sufficient
Intermediates for the manufacture of dyes				
para-Cresidine	Production; manufacture of dyes, pigments & perfumes;	Vol. 27 (1982b)	Not available	Sufficient
3,3'-Dimethoxybenzidine (ortho - dianisidine)	Production; manufacture of dyes & pigments; dye for leather, paper, plastics, rubber, textiles, & laboratories	Suppl. 7 (1987a)	Inadequate	Sufficient
2-Methyl-1-nitro anthraquinone (of uncertain purity/impurity)	Production; synthesis of anthraquinone dyes	Vol. 27 (1982b)	Not available	Sufficient
4,4'-Methylene bis (2-methylaniline)	Production; manufacture of dyes & pigments	Suppl. 7 (1987a)	Inadequate	Sufficient

2-Nitroanisole	Production; manufacture of the dye intermediates ortho-anisidine & ortho-dianisidine	Vol. 65 (1996)	Not available	Sufficient
4,4'-Thiodianiline	Production; manufacture of dyes	Vol. 27 (1982b)	Not available	Sufficient
Nitro compounds				
2,4-Dinitrotoluene	Production; manufacture of diisocyanates & munitions	Vol. 65 (1996)	Inadequate	Sufficient
2,6-Dinitrotoluene	Production; manufacture of diisocyanates,& munitions	Vol. 65 (1996)	Inadequate	Sufficient
Nitrobenzene	Production; manufacture of dyestuffs, detergents & cosmetics	Vol. 65 (1996)	Not available	Sufficient
2-Nitrofluorene	Underground miners using diesel powered machinery	Vol. 46 (1989a)	Not available	Sufficient
2-Nitropropane	Production; ink, paint & explosives industries	Vol. 71 (1999a)	Not available	Sufficient
1-Nitropyrene	Production; manufacture of azidopyrene; particulate emissions	Vol. 46 (1989a)	Not available	Sufficient
4-Nitropyrene	Production; used only as a laboratory chemical; probably present before 1980 in carbon black used in photocopy machines	Vol. 46 (1989a)	Not available	Sufficient
Tetranitromethane	Production; diesel fuel additive; TNT manufacturing	Vol. 65 (1996)	Not available	Sufficient
Pesticides				
Aramite	Production; in miticides in greenhouses, nurseries, & orchards	Vol. 5 (1974b)	Not available	Sufficient
Chlordane	Production; termite control	Vol. 79 (2001b)	Inadequate	Sufficient
Chlordecone	Production; insecticide	Vol. 20 (1979a)	Not available	Sufficient
Chlorophenoxy herbicides	Production; defoliant	Suppl. 7 (1987a)	Limited	Inadequate
Chlorothalonil	Production; fungicide, bactericide & nematocide	Vol. 73 (1999b)	Not available	Sufficient
DDT (p,p'-DDT)	Production; nonsystemic insecticide	Vol. 53 (1991c)	Inadequate	Sufficient
1,2-Dibromo-3-chloropropane	Production; pesticide, nematocide & soil fumigant	Vol. 71 (1999a)	Inadequate	Sufficient
para-Dichlorobenzene	Production; pesticide	Vol. 73 (1999b)	Inadequate	Sufficient
Dichlorvos	Production; insecticide & miticide	Vol. 53 (1991c)	Inadequate	Sufficient
Heptachlor	Production; termite control	Vol. 79 (2001b)	Inadequate	Sufficient

Hexachlorobenzene	Production; in chlorinated pesticides & fungicides; dye manufacture & synthesis of organic chemicals & rubber; plasticizer for PVC; wood preservative, by-product of the production of a number of chlorinated solvents	Vol. 79 (2001b)	Inadequate	Sufficient
Hexachlorocyclohexanes (most common form is Lindane)	Production; woodworkers; farm workers	Suppl. 7 (1987a)	Inadequate	Sufficient
Mirex	Production; fire-retardant additive; insecticide; workers at hazardous waste sites	Vol. 20 (1979a)	Not available	Sufficient
Nitrofen	Production; herbicide	Vol. 30 (1983a)	Not available	Sufficient
Sodium ortho-phenylphenate	Production; fungicide; chemical intermediate	Vol. 73 (1999b)	Not available	Sufficient
Toxaphene (polychloronated camphenes)	Production; insecticide	Vol. 79 (2001b)	Inadequate	Sufficient
Others				
Butylated hydroxyanisole (BHA)	Production; food & pharmaceutical industries	Vol. 40 (1986c)	Not available	Sufficient
Catechol	Production; insecticide & pharmaceutical production; tanneries	Vol. 71 (1999a)	Not available	Sufficient
Diglycidyl resorcinol ether	Production; liquid spray epoxy resin in electrical, tooling, adhesive, laminating applications; production of epoxy resins, rubber; aerospace industry	Vol. 71 (1999a)	Not available	Sufficient
1,4-Dioxane	Production; chlorinated solvents; textile processing; mixed with pesticides	Vol. 71 (1999a)	Inadequate	Sufficient
Hydrazine	Production; manufacture of agricultural chemicals & chemical blowing agents; water treatment, spandex fibers; rocket fuel, oxygen scavenger in water boilers & heating systems; scavenger for gases; plating metals on glass & plastics; solder fluxes; photographic developers; reactant in fuel cells in the military; reducing agent in electrodeless nickel plating; chain extender in urethane; textile dyes; explosives	Vol. 71 (1999a)	Inadequate	Sufficient

Nitrilotriacetic acid & its salts	Production; textiles; electroplaters; tanners	Vol. 73 (1999b)	Not available	Sufficient
Polychlorophenols & their sodium salts (mixed exposure)	Herbicide production, wood, textile & leather manufacturing	Vol. 71 (1999a)	Limited	Inadequate
Potassium bromate	Production; bakeries	Vol. 73 (1999b)	Not available	Sufficient
Thiourea	Production; photoprocessing; dyes; rubber industry	Vol. 79 (2001b)	Not available	Sufficient
Welding fumes	Metal fabricating industry	Vol. 49 (1990a)	Limited	Inadequate

a 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.

b This is the most recent IARC evaluation. For those referenced as Supplement 7, it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

c As judged by the IARC Working Group. The notation "Not available" was added by the authors to signify those substances for which there was no epidemiological evidence at all.

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

Occupation or industry	Suspected substance	IARC volume & year[a]	Group	Site(s)[b]
Aluminium production	Pitch volatiles; aromatic amines	Suppl. 7 (1987a)	1	Lung Bladder
Auramine manufacture	2-naphthylamine; auramine; other chemicals; pigments	Suppl. 7 (1987a)	1	Bladder
Boot and shoe manufacture and repair	Leather dust; benzene and other solvents	Suppl. 7 (1987a)	1	Leukemia Nose and paranasal sinuses *Bladder*
Carpentry and joinery	Wood dust	Suppl. 7 (1987a)	2B	
Coal gasification	Coal tar; coal-tar fumes; PAHs	Vol. 34 (1984b)	1	Skin (including scrotum) Bladder Lung
Coke production	Coal-tar fumes	Suppl. 7 (1987a)	1	Skin (scrotum) Lung *Bladder* *Kidney*
Dry cleaning	Solvents and chemicals used in 'spotting'	Vol. 63 (1995a)	2B	
Furniture and cabinet making	Wood dust	Suppl. 7 (1987a)	1	Nose and sinonasal cavities
Hairdressers and barbers	Dyes (aromatic amines, amino-phenols with hydrogen peroxide); solvents; propellants; aerosols	Vol. 57 (1993b)	2A	*Bladder* *Lung* *non-Hodgkin's lymphoma* *Ovarian*

Hematite mining, underground, with radon exposure	Radon daughters; silica	Suppl. 7 (1987a)	1	Lung
Iron and steel founding	PAHs, silica, metal fumes; formaldehyde	Suppl. 7 (1987a)	1	Lung
Isopropanol manufacture, strong-acid process	Diisopropyl sulfate; isopropyl oils; sulfuric acid	Suppl. 7 (1987a)	1	Paranasal sinuses Larynx *Lung*
Magenta manufacture	Magenta; ortho-toluidine; 4,4'-methylene bis(2-methylaniline); ortho-nitrotoluene	Vol. 57 (1993b)	1	Bladder
Painters		Vol. 47 (1989c)	1	Lung *Bladder* *Stomach*
Petroleum refining	PAHs	Vol. 45 (1989b)	2A	*Bladder* *Brain* *Leukemia*
Printing processes	Solvents, inks	Vol. 65 (1996)	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*
Rubber industry	Aromatic amines; solvents	Suppl. 7 (1987a)	1	Bladder *Stomach* *Larynx* *Leukemia* *Lung*
Textile manufacturing industry	Textile dust in manufacturing process, dyes and solvents in dyeing and printing operations	Vol. 48 (1990b)	2B	

a This is the most recent IARC evaluation. For those referenced as Supplement 7, it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

b As judged by us. Regular script indicates that the evidence for an association with this site was strong. Italics indicates that the evidence was suggestive.

Table 7. Definite or probable occupational carcinogens and carcinogenic circumstances, ordered by site

Site	Strength of evidence[a]	High risk substance or circumstance[b]
Pharynx and nasopharynx	Suggestive	*Mustard gas; formaldehyde*
Nasal cavities and paranasal sinuses	Strong	Boot and choe 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
	Suggestive	*Chromium compounds, hexavalent; Formaldehyde; Mineral oils, untreated and mildly treated*
Esophagus	Suggestive	*Soots; Tetrachloroethylene*
Stomach	Suggestive	*Painters; Rubber industry*
Gastro-intestinal tract	Suggestive	*Asbestos*
Liver and biliary tract	Strong	Aflatoxin; Ionizing radiation
	Suggestive	*Polychlorinated biphenyls; Trichloroethylene*
Liver (angiosarcoma)	Strong	Vinyl chloride
	Suggestive	*Arsenic and arsenic compounds*
Liver (hepatocellular)	Suggestive	*Vinyl chloride*
Pancreas	Suggestive	*Acrylamide*
Larynx	Strong	Isopropanol manufacture, strong acid process; Inorganic acid mists containing sulfuric acid; Mustard gas
	Suggestive	*Asbestos; Rubber industry*
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 asbestiform fibres
	Suggestive	*Benz[a]anthracene; Benzo[a]pyrene; α-Chlorinated toluenes; Coal tars and pitches; Di-benz[a,h]anthracene; Diesel engine exhaust; Epichlorohydrin; Hairdressers and barbers; Inorganic acid mists containing sulfuric acid; Isopropanol manufacture, strong acid process; Mineral oils, untreated and mildly treated; Non-arsenical insecticides;Mustard gas; Production of art glass, glass containers and pressed ware; Rubber industry; 2,3,7,8 Tetrachlorodibenzo-para-dioxin (TCDD)*
Lung (oat cell)	Strong	Bis(chloromethyl)ether and chloromethyl methyl ether (technical grade)
Bone	Strong	Ionizing radiation
Melanoma	Strong	Solar radiation
	Suggestive	*Ultraviolet radiation (A, B & C) from artificial sources*
Skin	Strong	Arsenic and arsenic compounds; Coal tars and pitches; Coal gasification; coke production; Di-benz[a,h]anthracene; Mineral oils, untreated and mildly treated; Shale oils or shale-derived lubricants; Solar radiation; Soots
	Suggestive	*Benz[a]anthracene; Benzo[a]pyrene; Creosotes*
Mesothelioma asbestiform fibres	Strong	Asbestos; Erionite; Talc containing
CNS	Suggestive	*Epichlorohydrin*
Sarcoma *(TCDD)*	Suggestive	*2,3,7,8-Tetrachlorodibenzo-para-dioxin*
Cervix	Suggestive	*Tetrachloroethylene*
Ovary	Suggestive	*Hairdressers and barbers*
Kidney	Suggestive	*Coke production*
Kidney (renal cell)	Suggestive	*Trichlorethylene*
Bladder	Strong	Aluminum production; 4-Aminobiphenyl; Auramine

		manufacture; Benzidine; Coal gasification; Magenta manufacture; 2-Napththylamine; Rubber industry
	Suggestive	*Benz[a]anthracene; Benzidine-based dyes; Benzo[a]pyrene; Boot and shoe manufacture and repair; 4-Chloro-ortho-toluidine; Coal tars and pitches; Coke production; Dibenz[a,h] anthracene; Diesel engine exhaust; Hairdressers and barbers; 4,4'-Methylene bis(2-chloroaniline) (MOCA); Mineral oils, untreated and mildly treated; ortho-Toluidine; Painters; Petroleum refining*
Brain	Suggestive	*Non-arsenical insecticides; Petroleum refining*
Thyroid	Strong	Ionizing radiation
Non-Hodgkin's lymphoma	Suggestive	*Hairdressers and barbers; Non-arsenical insecticides; 2,3,7,8 Tetrachlorodibenzo-para-dioxin (TCDD), Tetrachloroethylene; Trichloroethylene*
Lympho-hematopoietic system	Suggestive	*1,3-Butadiene*
Multiple myeloma	Suggestive	*Non-arsenical insecticides*
Leukemia	Strong	Benzene; Boot and shoe manufacture and repair; Ethylene oxide; Ionizing radiation
	Suggestive	*Formaldehyde; Non-arsenical insecticides; Petroleum refining; Rubber industry*
Other sites	Suggestive	*Ionizing radiation*[c]
All sites combined	Strong	2,3,7,8-Tetrachlorodibenzo-para-dioxin (TCDD)[d]

a This designation refers to the strength of evidence regarding each site, as judged by us.

b Regular script indicates that the evidence for an association with this substance or circumstance was strong. Italics indicates that the evidence was suggestive.

c There is suggestive evidence of an effect of ionizing radiation on several sites in addition to those with which it is associated in this table.

d The evidence for an association with TCDD only becomes strong when data is combined for all cancer sites.

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

		Earlier evaluation	
Curent rating	**Past rating**	**IARC 1987**	**WHO 1964**
1	1	19	13
(n=28)	2A	4	4
	2B	1	
	3	0	n.a.
	Unrated	4	11
	Total	28	28
2A	1	0	0
(n=27)	2A	16	0
	2B	6	
	3	2	n.a.
	Unrated	3	27
	Total	27	27
2B	1	0	1
(n=113)	2A	2	5
	2B	63	
	3	9	n.a.
	Unrated	39	107
	Total	113	113