

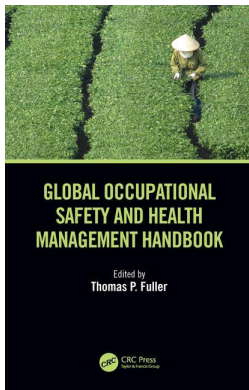
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Access details: *subscription number*

Publisher: *CRC Press*

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Global Occupational Safety and Health Management Handbook

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Global Burden and Aspects of Occupational Cancer

Publication details

<https://test.routledgehandbooks.com/doi/10.1201/9780429056475-13>

Thomas P. Fuller

Published online on: 01 Mar 2019

How to cite :- Thomas P. Fuller. 01 Mar 2019, *Global Burden and Aspects of Occupational Cancer* from: *Global Occupational Safety and Health Management Handbook* CRC Press

Accessed on: 02 Jun 2023

<https://test.routledgehandbooks.com/doi/10.1201/9780429056475-13>

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13 Global Burden and Aspects of Occupational Cancer

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13.1 INTRODUCTION

The global burden of cancer is a major source of morbidity and mortality. In 2012, there were 14 million new cases of cancer and 8 million cancer-related deaths globally (IARC, 2014). By the year 2030, the incidence of cancer cases is globally

expected to increase to 22 million (Bray, 2015). In general, the highest cancer incidence rates occur in the high-income countries of North America and Western Europe, in addition to Japan, Korea, and Australia (IARC, 2018a). The percentage of cancer cases attributable to workplace exposures in these developed nations is expected to decline in the coming years due to occupational exposure restrictions that have been in place now for several decades (Boffetta, 1999; IARC, 2018b). Overall age-adjusted death rates have been falling dramatically in the United States for lung, bronchus, colon, prostate (men), and breast (women) cancers for the past 20 years (ACS, 2018). According to International Agency for Research on Cancer (IARC), based on population sizes, more than 60% of all cancer cases occur in Africa, Asia, and Central and South America. These regions also account for 70% of all cancer fatalities (IARC, 2014). In addition, the burden of disease is expected to increase greatly in these lower economic countries in the next two decades due to aging populations, industrial growth, and other environmental and social risk factors (Stewart, 2016; Torre, 2015).

The broad differences in types of cancers in various world regions lend information about the causes and preventions that could be taken to lower the number of cases. Many of the cancers in the industrialized countries are associated with diet and lifestyle. In these regions, cancers of the breast, colorectum, and prostate are common. However, cancers of the liver, stomach, and esophagus are more common in low-income countries. Decreased survival rates in developing countries are likely to be the result of reduced availability of advanced clinical care or early diagnosis.

In economically advanced countries, efforts have been taken to prevent occupational cancer by reducing the workplace exposure to carcinogens (Blair, 2011). Workers in developed countries tend to be more educated and aware of the hazards and health consequences of exposure to carcinogens, and they are more reluctant to be exposed. Workers in economically developing countries (EDCs) that are becoming more industrialized will likely be at increasingly greater risk of exposure to carcinogens in the workplace. As industrialized countries move towards service-oriented businesses, there are fewer workers exposed to hazardous working conditions, and there are fewer workers exposed to carcinogens overall.

Many of the “dirty” industries (manufacturing, mining, chemical, and petroleum production) that have left the advanced countries are moving rapidly to the less developed nations, and as a result, more workers in the developing countries will be exposed to carcinogens in the future. Sixty-three percent of all cancers occur in low- and middle-income countries (Espina, 2013). Dirty industries are also less likely to be adequately regulated in these less developed nations. Workers in EDCs are less aware and often less concerned about the risks associated with the exposure to carcinogens. These workers also have fewer options for employment and may be willing to accept risks for that reason. Workers in these underdeveloped countries may also be more susceptible to harmful effects of carcinogens due to their poor nutritional levels and other physiological and environmental factors (Hashim, 2014). Technologies that might be used in advanced countries to protect workers from hazardous exposures are often not available in EDCs. And neither companies nor countries are fully aware of the long-term economic benefits of keeping the workforce healthy.

Cancer comes with high socioeconomic costs. Cancer costs the U.S. economy more than \$243 billion in 2009. Ninety-nine billion was due to medical costs, and more than \$144 billion was from lost productivity due to illness or death (Reuben, 2010). If occupational cancers were assumed to make up only 8% of the total number of cancers, this would imply that occupational cancer costs the U.S. \$243 billion \times 0.08 = \$19.44 billion (Nurminen, 2001; Steenland, 2003; Rushton, 2012).

Studies have shown that more than one-third of all cancers are preventable, including those that arise from occupational exposures (Danaei, 2005). Occupational studies of nasal cancer in furniture workers exposed to wood dust as early as 1940 showed a diminution of the disease after exposure was reduced (Hayes, 1986). Numerous opportunities for occupational prevention of exposure to carcinogenic agents or conditions continue to exist today. Collaborative strategies for research and intervention policies and education are needed to fully reduce the incidence of occupational cancer worldwide (Espina, 2013).

13.2 OCCUPATIONAL CANCER DEFINED

Ramazzini was an Italian physician who associated several diseases with various occupational exposures in the 17th century. He related exposures to irritating chemicals, dusts, and metals to health effects in his treatise “Diseases of Workers” (Ramazzini, 1718). Ramazzini related diseases to various workplace exposures in 54 different occupations. He noticed that nuns had a lower incidence of cervical cancer and higher-than-expected incidence of breast cancer. In the 18th century, Percival Pott found links between prolonged exposure to soot, and scrotal cancer among chimney sweeps in London (Pott, 1775).

Since those early years, cancer has been associated with numerous other occupations including paraffin workers, shale oil workers, and in the textile industry. In addition, lung cancer cases were noted in miners and bladder cancer in dye makers. In the first part of the 20th century, cancer clusters were found in varied but discrete occupational settings such as nickel refineries and the manufacture of asbestos products, among others (Siemiatycki, 2006). In most of these discoveries, cancer was related solely to the associated occupation, rather than particular causative agents, through primitive retrospective cohort studies. Cancer itself was not related to a particular known agent until the 1950s, when cigarette smoking was associated with lung cancer.

Today, much of what is known about cancer still comes from occupational exposures. Research on occupational exposures to carcinogens forms the basis of much of the understanding about relative risks, prioritization of controls, and the development of the means for cancer prevention. And as understanding of occupational cancer increases, the consequences of public exposures to the same carcinogens become evident. For example, the awareness that occupational exposures to diesel engine emissions are associated with cancer provided useful information about the relative risks of general public exposures to diesel exhaust, and the need to reduce environmental exposures from vehicle emissions.

As many agents can cause cancer in both environmental and occupational settings, and individuals can be exposed to carcinogens in both the workplace and other public

settings, or the home, it can be difficult to define an “occupational exposure.” There is no simple definition; however, we can consider an occupational carcinogen to be one where the primary exposure to the agent occurs in the workplace and the primary epidemiological evidence comes from increased cancer risks associated with occupational settings at discrete times and places. Some agents are particularly difficult to define as “occupational” as they are commonly encountered in the everyday environment; sunlight, tobacco smoke, and diesel exhaust may be considered to be in this category. However, outdoor workers exposed to sunlight for extended periods, bartenders or waiters exposed to secondhand smoke, or traffic patrol personnel standing in heavy levels of exhaust all day may be considered occupational exposures.

Originally, carcinogens were loosely identified when cancer clusters occurred in a particular industry work group. As epidemiological studies increased in sophistication, they could more closely relate specific worker exposures to cancer. In addition, over time, direct evidence of carcinogenicity was derived from experimental animal studies. Today, toxicological studies of carcinogenesis can include complex analyses of chemical and metabolic interactions of agents with cells and tissues within living organisms. Absorption and metabolism of toxic agents within the body can be followed and analyzed to observe the changes in the organism including toxic, mutagenic, and carcinogenic effects. In the near future, it may be possible to determine carcinogenicity by comparing a chemical molecule with those of other chemicals to identify similar characteristics or traits that equate the likeliness that the new agent is also cancer causing in the absence of time-consuming and expensive epidemiologic or animal studies.

Despite what we have learned about the cancer-causing properties of numerous chemicals and hazardous agents, occupational exposures to them are still widespread. Tens of thousands of workers are still routinely exposed to well-recognized carcinogens such as heavy metals, diesel engine emissions, asbestos, polycyclic aromatic hydrocarbons, and silica. And although there have been increasing controls over occupational carcinogens in developed countries, there is growing evidence that the use of hazardous processes and materials is shifting to EDCs at an increasing pace (Hashim, 2014; Pearce, 1994). The use of carcinogenic agents is expanding in countries where workers tend to be less educated about, and less aware of, the hazardous or carcinogenic properties of chemicals, where there are fewer government regulations for the handling and training on toxic chemicals, and many of the workers are children. Along with this shift in the use of carcinogenic agents in the workplace, a surge in occupational cancers can be expected to occur in developing countries in the decades to come.

Studies have estimated that between 4% and 8% of all cancers in developed countries are caused by occupational exposures (Nurminen, 2001; Steenland, 2003; Rushton, 2012). Attributable fractions for different cancers vary by agent and by regions. In U.S. studies, workplace exposures accounted for 6%–17% of all lung cancers in men (Driscoll, 2005; Steenland, 2003). A similar study conducted in Finland showed that 29% of male lung cancer cases were due to occupational factors (Nurminen, 2001). In Europe, up to 10% of all bladder cancers were attributable to occupational exposures (Boffetta, 1999). In a recent report of a large occupational cancer study in France, it was shown that 42% of occupational cancers were caused by exposure to asbestos (ANSES, 2018). In the United States, cancer of the trachea, bronchus, and lungs made up 12% of all workplace fatalities (Nelson, 2005).

In one global study, cancer was identified as the top killer of workers, surpassing both workplace diseases and accidents in the number of deaths worldwide (Hamalainen, 2007). In a recent analysis of work-related illnesses, cancer was attributed to 26% of all occupationally related fatalities (Hamalainen, 2017).

13.3 GENERAL METHODS USED TO EVALUATE CARCINOGENICITY

In recent years, advances in molecular biology and cancer research have demonstrated that cancer develops from a complex multifactorial web of causes. The most relatable evidence for establishing a relationship between an agent and a carcinogenic outcome in humans historically, however, has been through epidemiological studies. Diseases are identified in a human population, and then the factors associated with its occurrence are identified (Hill, 1971). Some of the first formal epidemiological studies that identified carcinogenic effects were in workers exposed to asbestos, benzene, and vinyl chloride (Fontham, 2009). As it remains today, most agents identified to be carcinogenic to the larger population have first been identified in occupational populations. Other useful epidemiological information comes from studies of human lifestyle (e.g., tobacco and alcohol consumption) and patients receiving various medical therapies or treatments.

Limitations in epidemiological evaluations include the existence of confounders that hide or confuse the understanding of relationships, inaccurate estimates or measures of true exposure or dose, and other study biases that hide the true effects of the agent. Scrupulous study design and mathematical manipulation aid in assuring validity and accuracy of cancer studies. Often, an agent is evaluated by more than one study before a conclusion is drawn. And studies included in the evaluation pass the strict guidelines for the strengths of cancer association between exposure duration and level, consistency with other studies, and the timing of exposure to the development of disease.

In developed countries, the studies of occupational exposures to carcinogens are expensive and time consuming, but they are performed when possible and especially when there are explicit concerns regarding the agent or exposure. These types of exposure studies are grossly lacking in workers exposed in developing countries, and the resulting epidemiological analyses are not possible.

The second most useful method for determining potential carcinogenicity of an agent is the long-term bioassay in experimental animals. Animal testing for toxic effects of chemicals began as early as 1900. Since that time, animal studies have been used to identify approximately 30% of carcinogens known to humans (Huff, 1993, 1999; Fung, 1995; Maronpot, 2004). Due to anatomical, metabolic, genetic, and physiological differences between animals, they are not the perfect means of predicting carcinogenicity of humans to all agents. However, the usefulness of the information they provide has been demonstrated for numerous agents. In recent years, however, the use of animals for toxicity evaluation for humans has been curtailed for ethical reasons.

In order to replace the use of animal studies, new toxicokinetic and mechanistic studies are expanding drastically. These methods use what is already known about the mutational signatures that comprise tumors and cancer cells and compare them

with other similar chemicals that would be expected or likely to result in similar outcomes. It becomes a systematic method to evaluate mechanistic data and identify likely toxicological outcomes for various chemicals by comparing them to the biological outcomes of other known carcinogens. Some of the mechanistic signals of carcinogenesis have included such characteristics as transformation of metabolites that can damage DNA, alteration of gene expression, disruption of the immune system, and interference with molecular communication. Results of these types of studies, combined with sophisticated mathematical and computational manipulations, can lead to the evaluation of significantly more potential carcinogens in much less time than previously possible. Future advances in these types of studies will continually expand to include toxicological predictions based on physical and chemical properties of molecules, genomic responses of biological samples, cancer pathway and network analyses, and even clinical studies of molecular changes in tissues of exposed humans (Cote, 2016; NTP, 1999; EPA, 2017).

13.4 CANCER RESEARCH ORGANIZATIONS

Several internationally respected organizations conduct research and publish reports on cancer-causing agents and environmental conditions. Each organization identifies the methods used to study and evaluate carcinogens. Some of the methods and assumptions used between agencies overlap, whereas some do not. Each organization identifies different levels or types of cancers and creates a rating scale of severity where different chemicals or agents can be categorized. Although some calls for greater harmonization in cancer research methodology and classification, differences between organizations' methods and levels remain for a variety of complex reasons. In most cases, it is useful to evaluate the results from two or more of the cancer research organizations to obtain a more valid and useful perspective of the occupational applicability to the cancer research information available. Some of the more important and significant organizations that provide current information on carcinogens are described in the following sections.

13.4.1 U.S. NATIONAL TOXICOLOGY PROGRAM

In the United States, the National Toxicology Program (NTP) prepares a Report on Carcinogens (RoC) for the Secretary of Health and Human Services through a series of review mechanisms, and publishes reports periodically. Monographs on carcinogens are prepared according to the strict review mechanisms and processes (NTP 2016a, b). The NTP makes two carcinogen classifications: agents are classified as “known to be human carcinogens” when there is sufficient evidence of carcinogenicity from studies in humans, which indicates a causal relationship between exposure and disease, and agents classified as “reasonably anticipated to be human carcinogen” are those that are indicated by limited evidence of carcinogenicity in humans where a causal link is credible but alternative explanations such as bias and confounders cannot be excluded. Evidence of possible human carcinogenicity from animal studies or from convincing information about mechanistic processes that indicate an agent may be carcinogenic to humans can also be used to classify an agent in this category.

In the 14th NTP ROC published in 2016, there are 62 agents listed as known human carcinogens and 186 listed as reasonably anticipated to be human carcinogen. In the latest listing, there are six new agents known to be human carcinogens:

- Epstein–Barr virus
- Human immunodeficiency virus type 1 (HIV-1)
- Human T-cell lymphotropic virus type 1
- Kaposi sarcoma-associated herpesvirus
- Merkel cell polyomavirus
- Trichloroethylene

Five of the six new listings are linked to viruses for which there are no vaccines available. In total, the viruses are linked to more than 20 different types of cancers. These viruses and subsequent cancers are more likely to develop in people with weakened immune systems. These new biological agents, in addition to other infectious diseases previously identified to cause cancer, such as hepatitis B virus (HBV) and hepatitis C virus (HCV), are especially alarming since it is estimated that 16,000 HCV, 66,000 HBV, and 1,000 HIV health-care worker infections occur globally each year due to sharps injuries. The fraction of infections of HCV, HBV, and HIV attributable to occupational exposures represents up to 39%, 37%, and 4.4%, respectively, of all transmissions identified globally (Pruss-Ustun, 2005). In addition, these numbers are most likely underestimated due to the lack of sharps exposure reporting.

In addition to the six new carcinogens listed in the 2016 NTP report, cobalt and cobalt compounds that release cobalt ions *in vivo* were added to the list as reasonably anticipated to be a human carcinogen in an additional report published by the Department of Health and Human Services in 2016 (NTP, 2016c).

13.4.2 INTERNATIONAL LABOR ORGANIZATION

The International Labor Organization (ILO) established the first list of occupational diseases in 1925 (Kim, 2013). It was an important tool for the harmonization of international policies and regulations to protect workers from occupational diseases. In 1934, the list was updated with Convention number 42 to include primary epitheliomatous cancer of the skin. In 1980, the list was updated again to include lung cancer and mesothelioma caused by asbestos.

Today, the ILO recognizes cancer as a leading cause of worker illness and fatality. The ILO Convention C139 was created in 1974 to curtail worker exposures to carcinogens in the workplace. It requires each ratifying member country to work to prohibit or reduce the use of carcinogens, and to take action to minimize worker exposures to carcinogenic substances and agents in the workplace. It also requires the establishment of medical surveillance for workers exposed to carcinogens during and after employment, and the establishment of appropriate associated record-keeping systems (ILO, 1974a). At the same period, the ILO created a recommendation number 147 on how to prevent occupational hazards from carcinogens, (ILO, 1974b).

In 1977, the ILO created a comprehensive guideline on the control and prevention of occupational cancer. Topics discussed in this document included suggested

methods for the determination of safe exposure levels for workers exposed to carcinogens through the use of epidemiologic and animal studies. It also proposed various preventive measures to be taken to minimize worker exposures. Other subjects in the manual included workplace and biological monitoring, administrative controls, and medical surveillance of workers (ILO, 1977).

The ILO document Occupational Safety and Health Series 74 published in 2010 by the ILO provides a list of 21 agents currently believed to cause cancer (ILO, 2010). Occupational carcinogens listed in this report included the following:

- Asbestos
- Benzidine and its salts
- Bis(chloromethyl) ether
- Chromium VI and chromium VI compounds
- Coal tars, coal tar pitches, or soots
- Beta-naphthylamine
- Vinyl chloride
- Benzene
- Toxic nitro- and amino-derivatives of benzene or its homologues
- Ionizing radiations
- Tar, pitch, bitumen, mineral oil, anthracene, or the compounds, products, or residues of these substances
- Coke oven emissions
- Compounds of nickel
- Wood dust
- Arsenic and its compounds
- Beryllium and its compounds
- Cadmium and its compounds
- Erionite
- Ethylene oxide
- Formaldehyde
- HBV and HCV

13.4.3 INTERNATIONAL AGENCY FOR RESEARCH ON CANCER

Over the past several decades, IARC has been evaluating and identifying workplace carcinogens. The IARC is an international agency within the World Health Organization that performs and publishes critical reviews of epidemiological studies and experimental data on the carcinogenicity of chemicals, agents, mixtures, processes, and biological materials to which humans are exposed. Collective bodies of experts review the available information about human exposures and potential carcinogenic outcomes and provide a cancer rating for each subject. The IARC ratings are provided in Table 13.1 (IARC, 2014).

The IARC has identified 32 carcinogenic occupational agents. In addition, they have identified 11 exposure circumstances that are carcinogenic to humans. They have also identified 27 agents and 6 exposure circumstances that are probably carcinogenic to humans. A partial listing of the IARC carcinogenic ratings for occupational agents, occupations, and industries is provided in Table 13.2 (IARC, 2014).

TABLE 13.1
Current IARC Cancer Groups

Group 1: Carcinogenic to humans
Group 2A: Probably carcinogenic to humans
Group 2B: Possibly carcinogenic to humans
Group 3: Unclassifiable as to carcinogenicity in humans
Group 4: Probably not carcinogenic to humans

TABLE 13.2
Partial Listing of IARC Group 1 and 2A

Group 1: Carcinogenic to Humans		
Agent, Occupation, or Industry	Cancer Site/Cancer	Main Industry or Use
Acid mists, strong inorganic	Larynx	Chemical
Arsenic	Lung, skin, bladder	Glass, metals, pesticides
Benzidine	Bladder	Pigments
Leather dust	Nasal cavity	Shoe manufacture and repair
Mineral oils	Skin	Lubricant
Nickel compounds	Nasal cavity, lung	Metal alloy
Silica dust	Lung	Construction, mining
Trichloroethylene	Kidney	Solvent, dry cleaning
Vinyl chloride	Liver	Plastics
Wood dust	Nasal cavity	Wood
Aluminum production	Lung, bladder	
Coal-tar distillation	Skin	
Coke production	Lung	
Painter	Bladder, lung, mesothelioma	
Rubber manufacture	Stomach, lung, bladder, leukemia	
Group 2A Carcinogens		
Acrylamide	—	Plastics
Bitumens	Lung	Roofing
Indium phosphide	—	Semiconductor
Polychlorinated biphenyls	—	Electrical components
Vinyl bromide	—	Plastics, textiles
Art glass workers	Lung, stomach	
High temperature food frying	—	
Hairdressers and barbers	Bladder, lung	
Shiftwork with circadian disruption	Breast	Nursing and others

Source: Adapted from IARC (2014).
Carcinogens with Cancer Site and Industry.

13.4.4 EUROPEAN UNION

International classifications for carcinogens have been harmonized at the community level by the European Union in Regulation (EC) No 1272/2008. Cancer-causing agents were originally established by the Commission on Cancer in 1963 and identified in a Cancer Liaison Program (CLP) (ACS, 2018). The classifications are as follows:

- CLP class 1A: known carcinogenic potential for humans
- CLP class 1B: presumed carcinogenic potential for humans
- CLP class 2: suspected human carcinogens

13.5 OCCUPATIONAL EXPOSURE LIMITS FOR CARCINOGENIC AGENTS

Occupational exposure limits (OELs) have been identified for thousands of chemicals and toxic agents by numerous regulatory and standards development organizations globally. Typically, OELs represent the maximum allowed concentration of a given substance in the air in the workplace. They are generally based on a time-weighted average over an 8-h period. Levels can be set when risks can be reasonably established and safe levels of exposure can be set. Similarly, for non-genotoxic agents (substances that do not directly damage DNA), safe levels of occupational exposure can also be determined. However, for most genotoxic carcinogenic agents, a threshold effect cannot be identified and it becomes extremely difficult to derive a safe level of occupational exposure. Infectious disease carcinogens are considered not to have thresholds.

At this time, there are no international OELs that are consistently recognized or agreed upon. Many occupational carcinogens do not have OELs in many countries. In many countries, OELs have not been established because safe levels of occupational exposure have not been agreed upon. Some governments have characterized risk quantitatively and compared exposures to commonly accepted social and economic criteria in order to set OELs. Even where OELs for carcinogens have been established at the national level, broad scientific and policy differences lead to greatly differing OELs between different countries in many instances (Ding, 2014). In some countries, the as low as reasonably achievable approach used to minimize worker exposure to ionizing radiation has been applied to no-threshold carcinogens.

13.5.1 THE EUROPEAN UNION

In the European Union (EU), indicative OEL values (IOELVs) for carcinogenic substances are determined by a commission of independent scientific experts, called the European Scientific Committee on Occupational Exposure Limits (SCOEL). Determinations are based on the types of carcinogenic effects, mechanisms of action, and whether the substance is genotoxic. Carcinogenic substances are categorized into the following groups:

Group A: Non-threshold genotoxic carcinogens identified by linear non-threshold (LNT) models of extrapolation test results from high-dose animal studies and low-dose human studies

Group B: Genotoxic carcinogens where studies are not sufficient to demonstrate the LNT model and a dose threshold is not identified

Group C: Genotoxic carcinogens where a practical threshold can be determined from available data

Group D: Non-genotoxic carcinogens and non-DNA-reactive carcinogens where a threshold can be set based on a no observable adverse effect level

OELs have been set by SCOEL for carcinogens in groups C and D.

In 2004, the EU promulgated Directive 2004/37/EC for the protection of workers from the risks related to exposure to carcinogens or mutagens. These regulations require employers to assess worker risks of exposure to carcinogens. Specific hygienic workplace practices such as contamination control and personal protective equipment (PPE) are mandated. These laws also delineated requirements for worker information and training (EU, 2004).

13.5.2.1 Registration, Evaluation, Authorisation and Restriction of Chemicals

Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) is the European Community intergovernmental body responsible for registration, evaluation, authorization, and restriction of chemical substances. REACH limits on carcinogenic substances are based on two different effect levels. Derived no-effect levels (DNELs) are set for carcinogens that have a threshold (REACH Regulation Article 119). For carcinogens without a threshold, REACH sets a derived minimal effect level (DMEL) of cancer risk levels of either 10^{-5} or 10^{-6} as indicative tolerable risk levels for workers. Methodologies for DNEL and DMEL are determined by REACH and followed by registrants that manufacture/import/or use over 10 tons per year (ECHA, 2010, 2011).

13.5.2.2 The Netherlands

In the Netherlands, OELs are recommended by the Dutch Health Council. OELs for carcinogenic and mutagenic substances are based on one of the two substance risk levels. A prohibitive risk level limits the additional risk of cancer to less than 10^{-4} per year (4×10^{-3} for a 40-year working lifetime). An additional target risk level allows an additional risk of up to 10^{-6} per year (4×10^{-5} during a 40-year working lifetime).

13.5.2.3 France

In France, OELs are derived for chemicals with and without a threshold. For carcinogens without a threshold, low-risk occupational exposure levels are set at three different levels to control excess risk of developing cancer (10^{-4} , 10^{-5} , or 10^{-6}) INRS (2008). Methods to be used to measure and assess pollutants in the workplace are developed by the OEL committee of the National Agency for Safety and Hygiene in Food, the Environment and work (ANSES, 2017).

13.5.2.4 Germany

Germany sets OELs for carcinogenic substances for which there is evidence of a threshold. For carcinogens without a threshold, risk-based target values are used to limit worker exposures. An acceptable risk target level is currently set at 4×10^{-4} , but moves to 4×10^{-5} in 2018. An additional tolerable risk target level is 4×10^{-3} if certain specified safety and control measures are in place BAuA (2011).

13.6 CONTROLS AVAILABLE TO REDUCE OCCUPATIONAL EXPOSURES TO CARCINOGENS

Despite what is known about the industries and agents that cause cancer, workers continue to be exposed to carcinogenic agents. In a French study from 2005, it was shown that more than 13% of workers are still being exposed to substances known to cause cancer (DARES, 2005). Numerous and significant opportunities to reduce workplace exposures remain untapped. The costs to implement controls and reduce worker exposures remain to be misunderstood in terms of the payback in worker health and other direct and indirect costs. The effectiveness of the most sophisticated means of control is not understood and is not fully used even in the most developed countries. Further yet, undeveloped nations may not only fully understand the consequences of worker exposures to carcinogens but also not be aware of the means to curtail exposures to workers. The most relevant methods to reduce occupational exposure to carcinogenic agents involve four main approaches: (1) elimination or substitution, (2) engineering controls, (3) administrative controls, and (4) PPE.

13.6.1 ELIMINATION AND SUBSTITUTION

Attributable risks to workers from carcinogens can be reduced either by reducing the number of carcinogens to which workers are exposed or by reducing the exposure levels to the carcinogens. The first method that can be used to reduce exposures to carcinogens is often via elimination of the agent in the workplace. In some cases, it is as simple as excluding the material from the production or fabrication process. An example here is the use of alternative fixatives in pathology and histology to replace carcinogenic formaldehyde mixtures. In the 1970s, Sweden was one of the first countries to ban the use of asbestos in products and by the 1990s had seen a reduction in the incidence of pleural mesothelioma in workers (Hemminki, 2008). In other cases, the carcinogenic process can be altered in some way to reduce worker contact or proximity to carcinogens. Substitution of one type of carcinogenic raw material used to produce a product with one that is less toxic and not carcinogenic can be a useful means to reduce occupational exposures (IARC, 2014). Engineering controls such as ventilation or enclosures can be used to reduce worker exposures too. Examples here could be as simple as using lids to keep carcinogenic vapors from escaping into the workers' breathing zone. A process change such as implementing wet hygienic methods to keep dust levels from grinding processes down and prevent the spread of contaminants could also be used to reduce airborne levels of dust. Wet spray methods could also be implemented to control the generation of airborne dust

in stone-cutting operations where silica is a significant component. These alternative production methods can reduce the amounts of silica dust workers who would inhale considerably.

13.6.2 ENGINEERING CONTROLS

The next method to minimize worker exposures to carcinogens is the use of engineering controls. Engineering controls are defined as any system or device that separates the worker from the hazardous agent. This could include a safer needle device to keep nurses from being stuck with a contaminated patient needle to reduce the transmission of bloodborne pathogens such as HIV or HBV. Engineering controls can also include ventilation systems that draw carcinogenic aerosols away from the workers' breathing zones. Ventilation engineering controls can include sophisticated fume hoods and withdrawal systems, or simple designs such as natural airflow or wind patterns in a factory or hospital to carry carcinogenic aerosols away from the workers.

13.6.3 ADMINISTRATIVE CONTROLS

Administrative controls to reduce exposure to carcinogens can include written programs, policies, and procedures that help workers understand carcinogenic hazards and actions needed to be taken to reduce exposures. Worker education, training, and record keeping are all considered forms of administrative controls.

13.6.4 PERSONAL PROTECTIVE EQUIPMENT

Lastly, the use of adequate and effective PPE can lead to significant reductions in worker exposure to carcinogens. Impermeable gloves, aprons, goggles, and face shields are a last line of defense to protect the skin or eyes from coming in direct contact with carcinogens. Respirators can be an effective means to reduce worker exposure to carcinogens through the airborne pathway. In order for any PPE method to be effective, however, workers need adequate levels of training on PPE use, including donning and doffing.

Unfortunately, many of the engineering controls and even PPE used, and even taken for granted, in developed countries are not always available in economically challenged countries. Informal sector workers exposed to airborne carcinogenic dust or vapors may not have access to local exhaust ventilation not only due to the cost of such systems but also because there is no electricity. Appropriate PPE for many jobs is often unavailable in developing countries. Even adequate gloves or simple respiratory protection devices such as an N95 respirator may not be available in sufficient quantities.

With the greater understanding about the relationships between infectious agents and cancer, new opportunities for primary prevention arise. The need to protect health-care and other workers at risk from infectious agents including HIV, herpes virus, Epstein–Barr virus, and HBV becomes even more urgent when the additional risk of cancer is added to the already-inherent biological risks. Many EDCs already

burdened with catastrophic numbers of HIV are now also at an elevated risk of cancer in addition. Health worker training in the effective use of PPE to protect from bloodborne pathogens, the use of impervious gloves, safe needle devices, immediate prophylactic treatment of workers exposed to known infectious agents, the diligent use of medical surveillance of workers, and the use of available vaccines will not only be expected to reduce the transmission of infectious agents to workers but also reduce the subsequent development of infectious agent-related cancers in the population (Vineis, 2014). It is essential that these protective devices and systems be made broadly and consistently available to workers in these developing countries in order to curtail occupational cancer rates.

13.6.5 REGULATION

Another strategy that can be used to mitigate occupational cancer is the development of regulation governing the potential for worker exposures to carcinogens. Regulations on the use of carcinogens and limits on the levels and durations of worker exposures can have significant effects on global outcomes and prevalence of disease (Landrigan, 2011). National development and expansion of existing cancer and infectious disease reporting mechanisms would also aid in reducing cancer rates. Development of vaccines for infectious diseases can also be a tool to reduce the associated subsequent occupational cancers. These societal benefits should be included in decisions regarding funding for research and vaccine development.

13.6.6 COMMUNICATIONS AND EDUCATION

Communications and public health education programs that are expanded to reach greater populations and provide more information regarding hazardous agents, pathways of exposure, and the relations between infectious diseases and cancer will also benefit in the reduction of occupational cancer burden (Landrigan, 2011). Professional organizations can contribute to the awareness and understanding of occupational carcinogens and how they can be controlled to reduce worker exposures and negative outcomes. Conferences, seminars, and workshops can be held on specific occupational carcinogen topics with specific work groups. Health-care workers can be targeted for training on the recent findings regarding carcinogenicity related to infectious agents and the importance for improved worker protections.

13.7 OCCUPATIONAL CANCER RESEARCH

Despite the growing shift in occupational cancers to developing countries, associated research is lagging behind. Most research on occupational cancer has been in the formal sector of developed countries. Very little research on carcinogens in the informal and precarious workforce sector and in developing countries has been completed (Santana, 2009). These informal workers typically work outside of formal industry, in homes or informal settings. They do not have occupational safety and health training or support. They are particularly precarious in that they typically do not fall under any social support system and workers do not typically

have any health-care benefits, including emergency medical care if they get hurt while they are working.

A 2009 report produced by the U.S. Department of Health and Human Services on reducing environmental cancer risks included a section on occupational cancers. It highlighted four general areas where research on occupational cancers should be enhanced: identification of occupational carcinogens, epidemiologic research, risk assessment, and prevention (Reuben, 2010).

Identification of occupational carcinogens can be improved through advanced employee surveillance systems and more accurate workplace exposure assessments. Better strategies for predicting adverse effects of working conditions and mixtures of hazardous agents in combination with advanced computational analyses will also improve the understanding of carcinogens.

Epidemiological studies must be better designed to identify exposed populations and routes of exposure. Cancers in women and minority workers need to be evaluated more broadly. And the relationships between maternal and paternal exposures and genetic effects in offspring need to be evaluated (Ward, 2003).

Increased use of biomarkers associated with occupational carcinogens is seen as a way to improve knowledge about risk. With better understanding of occupational cancer and risks, better primary and secondary prevention and communication strategies can be developed and implemented.

Improved research on the control and prevention of occupational cancer includes greater emphasis on the front end of industrial process design to minimize the potential for worker exposure to carcinogens. Means to identify and protect workers at particularly high risk should be prioritized and implemented (Reuben, 2010).

13.8 CONCLUSIONS/RECOMMENDATIONS

Occupational exposure to carcinogenic agents and working conditions accounts for a significant portion of the global burden of disease and death. And the impacts of these exposures reach far beyond the injured worker to affect families, organizations, and nations.

Due to the lack of reporting, the true occupational contribution to the rates of certain cancers remains unknown. New evidence of the relations between infectious diseases and cancer is particularly alarming. In addition, many occupational illnesses, injuries, and fatalities go unreported for large segments of the informal and contingent workforces. In low-income countries, the lack of efficient health and statistical data collection makes it difficult to accurately assess the burden of cancer on the population (IARC, 2017). Informal workers such as people working from home, children, and migrants are often not included in health statistics databases (Nelson, 2005). Therefore, the true risk of occupational cancer is expected to be higher than what has been reported.

It is estimated that 30%–50% of all cancers could be prevented if public health strategies were put in place to counter known risk factors (Stewart, 2016). This includes a reduction in the contribution from occupational cancers through the use of elimination, substitution, engineering controls, administrative controls, and PPE.

In a 2014 review of occupational cancer epidemiology research, it was determined that there has been a substantial decrease in the number of studies published between 1991 and 2001 (Raj, 2014). This same study demonstrated a lack of data from industrializing countries such as Russia, China, and India, and there are nearly no studies from the Middle East or most countries in Africa. In addition, few studies include female workers.

In not knowing what the true nature of the cancer hazard is or what exposure levels are, many workers go unprotected from toxic or fatal exposures. Much remains to be done in terms of worker protections, ranging from accurate exposure assessment and risk characterization, exposure evaluation, and development and implementation of controls to minimize exposures. Workers exposed to carcinogens in developing countries where sophisticated controls such as ventilation or respiratory protection may not be available are in need of research for alternative methods of protection such as the use of natural ventilation or readymade PPE, and the use of housekeeping and hygienic methods. As the numbers of exposures and illnesses are expected to increase in the next decades, even small changes and improvements can have major impacts globally.

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