Workplace Hazardous Materials Bureau – Confidential Business Information Protection Provisions on Carcinogens and Mutagens: Implications for Canadian Workers

Occupational Cancer Research Centre

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Executive Summary

The Workplace Hazardous Materials Information System (WHMIS) includes a mechanism for ruling on claims for exemption from disclosure of confidential business information (CBI), as well as appeals to these rulings. The objective of this report is to evaluate when the withholding of the identity and/or concentration of carcinogens and mutagens could potentially lead to adverse impacts on the health or well-being of workers.

Cancer is an important disease and the Canadian Cancer Society currently estimates that almost half of us will develop cancer in our lifetime and approximately one quarter of us will die from it. Occupational cancer is not rare and the Canadian Burden of Occupational Cancer Project estimates that there are an estimated 9,700 to 10,400 newly diagnosed occupational cancers per year in Canada. Cancer typically has a long latency period between exposure and diagnosis and exposure to multiple carcinogens may result in synergistic effects. As our understanding of this complex, multifactorial disease evolves, we are continuously updating our recognition of cancer risk factors. In recent years, the International Agency for Research on Cancer's (IARC) classification of the carcinogenicity of many chemicals has been upgraded, often based on our increasing knowledge of the mechanisms by which chemicals cause cancer. As of 2018, IARC had evaluated 1,013 agents, over half of which are encountered in workplaces. The number of established and suspected workplace carcinogens continues to grow. In addition, occupational exposure limits and guidelines are also evolving, and almost always the direction is to lower regulated or recommended exposure levels.

There are many potential adverse impacts on the health or well-being of workers from withholding CBI. In the short term, workers may be put at higher risk, employers and health and safety committees may not have the information they need to ensure the safety of the workplace, and regulatory agencies may be prevented from assessing compliance. In the long term, offering the exemption may prevent early detection of cancer and be a barrier to workers' receiving the compensation for which they are eligible and to which they are entitled.

It is important to point out that the potential harms discussed above are not limited to cancer. De-identified mutagens on safety data sheets (SDSs) puts pregnant workers and those considering starting a family at risk of exposure to developmental and reproductive hazards. Similarly, a lack of knowledge about the presence of sensitizers, which can cause harm at extremely low levels of exposure, could put an exposed, sensitized worker at extreme risk. Interaction between chemicals are possible for all health outcomes. Lastly, our knowledge of the health effects of all categories of hazards is constantly evolving and withholding CBI could impact early detection and compensation for other exposures causing chronic disease.

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Background

The Workplace Hazardous Materials Information System (WHMIS) includes a mechanism for ruling on claims for exemption from disclosure of confidential business information (CBI), as well as appeals to these rulings. The goal is to balance workers' right to know with industry's right to protect CBI. Details of the CBI provisions for WHMIS are reported in a publicly available Government of Canada gazette[1]. Briefly, under current CBI provisions, suppliers can withhold the identity of chemical agents within materials or products if an exemption is granted by Health Canada for trade secret reasons. In addition, the concentration of a chemical agent can be reported as a range rather than an absolute value if a CBI exemption is granted. For example, a Safety Data Sheet (SDS) lists "aromatic hydrocarbon" as one the ingredients in a product. No CAS# is provided, nor is a concentration range given for this or any other ingredient.

The CBI provision includes carcinogens, mutagens, reproductive toxicants and respiratory sensitizers (CMRRs). In relation to the example above, "aromatic hydrocarbon" could include different chemicals, one of which is benzene, an International Agency for Research on Cancer (IARC) Group 1 carcinogen. Other aromatic hydrocarbons include toluene, xylene, ethylbenzene, and styrene, which was recently upgraded to a Group 2A carcinogen by IARC. The underlying assumption appears to be that if the hazards are correctly stated on the SDS (i.e. carcinogenicity), then the listing of the actual constituents and their concentration in the product can be safely withheld. However, over the years, there have been many concerns raised by stakeholders such as unions over the current CBI practices – including interfering with the ability to protect worker health, the need for chemical identity for compensation purposes, and equity with other jurisdictions (Australia and countries within the European Union do not allow for CBI exemptions).

The Workplace Hazardous Materials Bureau (WHMB) has requested that the Occupational Cancer Research Centre (OCRC) examine the potential impact on the health and safety of workers if the protection of CBI provisions allowed in the *Hazardous Materials Information Review Act* (HMIRA) is disallowed for workplace carcinogens and mutagens[2]. The objective of this report is to evaluate when the withholding of the identity and/or concentration of carcinogens and mutagens could potentially lead to adverse impacts on the health or well-being of workers.

Carcinogens and Mutagens

Why focus on carcinogens and mutagens?

Cancer is an important disease with a growing burden. The Canadian Cancer Society currently estimates that almost half of us will develop cancer in our lifetime and approximately one quarter of us will die from it[3]. Cancer is now the leading cause of death in Canada[4]. Recently, researchers from the International Agency for Research on Cancer (IARC) published an analysis of Group 1 (carcinogenic) agents and found that almost half should be considered occupational[5]. The OCRC extended this study

with broader criteria based on potential exposure in workplaces[6]. Our preliminary results are that 57% (n=68) of Group 1 (known human carcinogen), 65% (n=53) of Group 2A (probable human carcinogen), 62% (n=188) of group 2B (possible human carcinogen), and 65% (n=328) of Group 3 (not classifiable as to human carcinogenicity) agents are, or have been in the past, encountered in workplaces[6]. Mutagenicity is one of the mechanisms by which chemicals or other agents cause cancer, although mutagens also have the ability to cause other health effects such as adverse reproductive outcomes.

Occupational cancer is not rare. The Canadian Burden of Occupational Cancer Project estimates that 3.9-4.2% of all cancers in Canada are due to work[7]. While this may not be an overwhelming percentage of all cancers, it adds up to an estimated 9,700 to 10,400 newly diagnosed occupational cancers per year in Canada. The proportion of cancers attributable to work is higher for some specific cancer sites, including lung cancer (14.9%), mesothelioma (81%, the remainder being environmental in origin), and non-melanoma skin cancer (6.5%). Given historic employment patterns, the proportions are even higher for men, with 24.4% of lung cancer, 85% of mesothelioma, and 10.8% of non-melanoma skin cancer due to workplace exposures. Based on the CAREX Canada project[8], exposure to workplace carcinogens is also not rare. Although some of the most common workplace carcinogens are not on SDSs (e.g. solar UV, diesel engine exhaust, night shift work), there are still millions of Canadians exposed to agents found in SDSs. For example, benzene, polycyclic aromatic hydrocarbons, lead and lead compounds, ethylbenzene and formaldehyde all have over 100,000 workers exposed[8].

There are particular characteristics of carcinogens that make them challenging. First and foremost, there is typically a long latency period between exposure and cancer diagnosis, so there is no way to know whether harm has been done for many years, usually decades. In addition, very low levels of exposure can be harmful and often there are no perceptual clues that harm is being done. Almost all carcinogens cause cancer in specific organs or tissues. Since Monograph 100 (which involved the re-evaluation of all known carcinogens at a series of six meetings in 2008 and 2009), IARC has made their evaluations cancer-site specific. For example, nickel is a carcinogen based on sufficient evidence of an increased risk of lung and sino-nasal cancers. In some settings, it is possible for workers to be exposed to multiple carcinogens that target the same site, such as multiple metals that are lung carcinogens, leading to the potential for synergistic effects. Because of these challenges and the large ramifications of developing cancer, many regulations have specific rules or designations for carcinogens. For example, WHMIS requires that a substance be listed as a carcinogen if it is classified by IARC as a Group 1 (carcinogenic), 2A (probable) or 2B (possible) carcinogen or if it is classified by the U.S. National Toxicology Program as a known or reasonably anticipated carcinogen. However, while WHMIS mandates that a substance be listed as a carcinogen on a product SDS if it is classified by IARC, the identity and concentration of the carcinogen can be withheld under CBI provisions.

Our Changing Knowledge of What Causes Cancer

The list of occupational carcinogens is far from static. As our understanding of this complex, multifactorial disease evolves, we are continuously updating our recognition of cancer risk factors. As of Monograph 123 (2018), IARC had evaluated 1,013 agents, but that number continues to grow. Just

considering the occupational agents evaluated since Monograph 100, there were 10 new Group 1, 23 new Group 2A, 45 new Group 2B, and 3 new Group 3 agents. Many of these new evaluations were upgrades from previous evaluations, including 7 Group 1, 19 Group 2A and 9 Group 2B. Thus, within 6 years, 35 agents were upgraded to higher carcinogenic groups, predominantly in the two highest hazard groups, Groups 1 and 2A, while only 15 re-evaluations did not change.

In the last 20 years, more mechanistic evidence of carcinogenicity has emerged and is increasingly being considered in the evaluation of agents. Mechanism of carcinogenicity is now an essential pillar in the IARC classification process and IARC has outlined a basic framework for understanding mechanistic evidence for carcinogenesis[9]. This framework considers that human carcinogens may act through multiple pathways in a multistage carcinogenic process, which can be mediated through genetic alterations and gene expressions. For an agent to have convincing mechanistic evidence of carcinogenesis, the agent under review must exhibit at least one of the ten criteria within the framework. As an example, genotoxicity is a key component of IARC's carcinogenic mechanistic framework[9]. An agent is classified as genotoxic if it induces either DNA damage or mutation or both. Chemically induced damage can manifest in DNA alkylation, adducts, or strand breaks where DNA bonds are directly or indirectly broken by a genotoxic agent. Mutagenic agents are a subset of genotoxic agents wherein the agent induces a genetic mutation in the target cell, which is passed on to progeny cells. Genetic mutations can result in altered cell processes, which can lead to the proliferation of mutated cells and the subsequent induction of malignancies.

Many of the upgraded classifications were supported by the consideration of mechanistic data. The first to be upgraded based on mechanistic data was 2,3,7,8-tetrachlorodibenzo-*para*-dioxin (TCDD), which was upgraded from Group 2B to Group 1 by IARC in 1997 in large part based on strong evidence of binding to the aryl hydrocarbon receptor, suggesting changes in gene expression, cell replication, and apoptosis[10]. It was only at the revaluation of TCDD in 2009 that the evaluation was tied to epidemiologic evidence[11]. A more recent example is styrene, which was classified in 2002 as a 2B carcinogen[12]. However, IARC recently upgraded its classification of styrene to Group 2A, denoting it a probable carcinogen[13]. Although there was some epidemiologic evidence, the presence of strong mechanistic evidence supported its carcinogenicity and upgrade from Group 2B to Group 2A.

Regulating Exposure to Carcinogens and Mutagens

In general, regulation of workplace carcinogens relies on the use of occupational exposure limits (OELs). Most OELs in Canada (which are adopted and enforced provincially) are based on the Threshold Limit Values (TLVs) recommended by the American Conference of Governmental Industrial Hygienists (ACGIH). In addition to the TLVs (which are health-based exposure limits), the ACGIH TLV committee also independently evaluates carcinogenicity using a five-category scale, which is similar to the IARC classification system. However, most jurisdictions rely on IARC's classification, which is more widely recognized.

Exposure to multiple carcinogens in the workplace creates a challenge for regulation. At many workplaces, workers may be exposed concurrently to multiple chemical agents, either in a single

product or through multiple products. When these agents have the same target organ and health effects, their combined effects could be synergistic, additive, or antagonistic. While many studies have focused on the potential synergistic effects of smoking and occupational agents, few have looked at interactions between occupational agents. In the absence of epidemiologic data on the true relationship, ACGIH recommends that an additive relationship be assumed and that exceedance of the TLVs be calculated accordingly[14]. Unfortunately, the ACGIH formula is only for additive relationships. It does not work in the case of a synergistic effect, where the risk conveyed by exposure to two agents is greater than the cumulative additive risk of the agents considered separately (i.e., the effects are *greater* than additive). In this situation, individual OELs are no longer valid. Because Québec regulations also recognize these principles, the Institut de recherche Robert-Sauvé en santé et en sécurité du travail created a tool to apply this approach, which also considers possible greater than or lesser than additive effects[15].

Our Changing Knowledge of Safe Levels of Exposure

Many carcinogens have effects at very low levels of exposure. For example, the current ACGIH TLVs for benzene (an aromatic hydrocarbon), hexavalent chromium, formaldehyde, and β-naphthylamine (an aromatic amine) are 0.5 ppm, 0.2 µg/m^3, 0.1 ppm, and 'as low as possible', respectively. TLVs are set on the basis of respiratory exposure alone and do not take into account absorption through the skin, which can happen readily for some carcinogens[14]. With very low levels of exposure, it may be possible to generate hazardous levels of exposure even if a component represents a small percentage of a product.

Occupational exposure limits and guidelines are evolving and almost always the direction is to lower regulated or recommended exposure levels. This is driven by new research changing our knowledge of safe levels of exposure. For example, the TLV for benzene was 10 ppm until 1997, but is now set at 0.5 ppm (8-hour time-weighted average), with a short-term (15 minute) exposure limit of 2.5 ppm. Similarly, the TLV for formaldehyde was 1 ppm (8-hour time weighted average (TWA)) until 1992, but is now 0.1 ppm (8-hour TWA), with a ceiling set at 0.3 ppm. Sometimes these changes are in response to new carcinogenic classification. For example, 1-bromopropane dropped from 10 ppm to 0.1 ppm on the basis of animal carcinogenicity. The consequence of these changes to the TLVs is that OELs in Canada are regularly updated. A recent example of this occurred in March 2018, when the Ontario Ministry of Labour proposed updated OELs for 38 workplace agents, including diesel engine exhaust and formaldehyde, among others, based on ACGIH recommendations from 2016 and 2017[16]. These efforts were taken to protect worker health and limit the hazardous occupational exposures in Ontario workplaces and the full OCRC commentary can be found elsewhere[17].

The old paradigm of classifying carcinogens as having a safe threshold or not based on mutagenicity is questionable. A threshold effect implies that under a certain exposure level, an agent will not have harmful health effects. Above that exposure threshold, however, the agent can pose a risk. In some jurisdictions, genotoxicity plays a role in the setting of occupational exposure limits, under the

assumption that genotoxicity has no threshold. The European Agency for Safety and Health at Work (EU-OSHA) reflects this approach[18]. The EU-OSHA defines carcinogens into the following four groups: non-threshold genotoxic carcinogens (Group A); genotoxic carcinogens where the existence of a threshold cannot be sufficiently supported (Group B); genotoxic carcinogens with enough information to establish a threshold (Group C); and non-genotoxic and non-DNA reactive carcinogens where a threshold can be implemented (Group D). While some carcinogens have defined threshold levels below which no adverse effects are expected to occur, our understanding of carcinogenesis is constantly evolving as more studies are conducted. Current evidence for many carcinogens does not have the data to support the presence or absence of a threshold.

Potential Harm from Non-disclosure

Immediate impact

Workers may be over-exposed. As discussed above, hazardous exposures can occur at very low levels of exposure. When health effects can occur at levels measured in ppm or µg/m^3, even low concentrations in a product can present a hazard unless strict precautions are taken. Exposure to the same agent in other products or to other agents that impact the risk at the same target organ may compound risk. An example is a product SDS for a rechargeable battery where the identity of all ingredients, including one Group 1 carcinogen and three Group 2B carcinogens, is withheld and all are known or suspected lung carcinogens. If a worker is handling multiple products with CBI provisions, the worker could be repeatedly exposed unknowingly to the same carcinogen, resulting in a higher dose of exposure. Better knowledge of current exposures can provide people with the information they need to raise health and safety issues with their employers, unions, and other workers and better protect themselves. General safety recommendations and listing that a carcinogen is present within a product is not sufficient to protect worker health and safety.

Workers, employers and health and safety committees may not have the information they need to take appropriate preventative actions. Knowledge of a carcinogen's identity is necessary to understand possible routes of exposure (based on properties such as volatility and skin permeability) and other essential information that may be key to taking proper preventative actions, even if that information is listed on the SDS. For example, an SDS of a CBI-protected product may warn against dermal exposure, but the reader may not know whether that property is tied to the least or most toxic constituents. Without the chemical name, the reader is prevented from doing their own research. Even with knowledge of identity, proper risk assessment cannot be performed without knowing the concentration of the chemical. If the identity is not known, the potential for further interactions among chemicals remains unknown and the necessary precautions for chemical handling cannot be executed accordingly. Workers, employers, and health and safety committees are often mandated by regulation to prevent exposure and they may be unable to comply with their legally mandated roles if they are not provided with sufficient information to do so.

Employers and regulatory agencies will not have the information necessary to assess whether exposure levels are in compliance. Without knowing the identity of the hazardous components, employers and regulatory agencies are fundamentally unable to measure exposure and compare the levels to legally mandated occupational exposure limits or guidelines. Additional requirements or guidelines, such as biomonitoring, may also be subverted.

All of these threats are exacerbated when knowledge of effects is changing.

Long-term impact

A characteristic of carcinogens and mutagens is that the most serious health impacts generally occur a long time after exposure. As discussed above, classification of carcinogens by agencies such as IARC and NTP are far from static, with both new evaluations and upgrading of previously evaluated agents occurring on a regular basis. In addition, our knowledge of safe levels of exposure continually changes over time. Thus, what is known when CBI protection is granted may be completely out-dated when the health effect occurs and an exposed worker could be at increased risk without their knowledge.

Without knowledge of the details of exposure, there is no ability to inform health care providers to assist with early detection. Without knowledge of prior exposure, health care providers may not be sensitive to early signs and symptoms of cancer or other health effects. Many workplace carcinogens target the lungs and lung cancer screening is now being piloted in several provinces. While the current referral guidelines are restricted to age and smoking history, discussions are currently underway to include exposure to occupational carcinogens, especially in combination with smoking. Knowledge about what is in the products workers are exposed to is needed for early detection through screening or other diagnostic tests.

Without knowledge of the identity, there is an inability to document exposure for workers' compensation or insurance purposes. Workers may encounter significant barriers in getting workers' compensation if they do not know the details of the substances to which they were exposed. For example, a 2003 SDS provided by UNIFOR (the union representing the workers at General Electric Peterborough) for an amine polymer mixture listed 5-10% of the mixture as "Aromatic Amines" – a generalization of a complex family of organic chemicals, which includes some potent bladder carcinogens. A name as broad as "Aromatic Amine" is not enough to communicate the risk of the substance to workers. There are too many possibilities for the identity of a chemical when only a broad class is named. The presence of a CAS number and the ingredient percent by weight range may not be appropriate to communicate the risk of the chemical. A worker who develops bladder cancer 20 years after working with this chemical would not know they had been exposed and consequently may not think they are eligible to submit a claim.

Conclusions

This report presents information on the characteristics of workplace carcinogens and mutagens and discusses the potential impact of these on the health of workers. In the short term, if CBI protection continues to be granted, workers may be put at higher risk, employers and health and safety committees may not have the information they need to ensure the safety of the workplace, and regulatory agencies may be prevented from assessing compliance. In the long term, offering the exemption may prevent early detection of cancer and be a barrier to workers' receiving the compensation for which they are eligible and to which they are entitled.

The potential harms discussed above are not limited to cancer. De-identified mutagens on SDSs put pregnant workers and those considering starting a family at risk of exposure to developmental and reproductive hazards. Similarly, a lack of knowledge about the presence of sensitizers, which can cause harm at extremely low levels of exposure, could put an exposed, sensitized worker at extreme risk. Interaction between chemicals is possible for all health outcomes. Lastly, our knowledge of the health effects of all categories of hazards is constantly evolving and withholding CBI could impact early detection and compensation for other exposures causing chronic disease.

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