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Priority Setting for Occupational Cancer Prevention

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ABSTRACT

Background: Selecting priority occupational carcinogens is important for cancer prevention efforts; however, standardized selection methods are not available. The objective of this paper was to describe the methods used by CAREX Canada in 2015 to establish priorities for preventing occupational cancer, with a focus on exposure estimation and descriptive profiles.

Methods: Four criteria were used in an expert assessment process to guide carcinogen prioritization: (1) the likelihood of presence and/or use in Canadian workplaces; (2) toxicity of the substance (strength of evidence for carcinogenicity and other health effects); (3) feasibility of producing a carcinogen profile and/or an occupational estimate; and (4) special interest from the public/scientific community. Carcinogens were ranked as high, medium or low priority based on specific conditions regarding these criteria, and stakeholder input was incorporated. Priorities were set separately for the creation of new carcinogen profiles and for new occupational exposure estimates.

Results: Overall, 246 agents were reviewed for inclusion in the occupational priorities list. For carcinogen profile generation, 103 were prioritized (11 high, 33 medium, and 59 low priority), and 36 carcinogens were deemed priorities for occupational exposure estimation (13 high, 17 medium, and 6 low priority).

Conclusion: Prioritizing and ranking occupational carcinogens is required for a variety of purposes, including research, resource allocation at different jurisdictional levels, calculations of occupational cancer burden, and planning of CAREX-type projects in different countries. This paper outlines how this process was achieved in Canada; this may provide a model for other countries and jurisdictions as a part of occupational cancer prevention efforts.

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1. Introduction

The workplace has long been recognized as a useful environment to identify carcinogens because large numbers of people may be exposed to relatively high concentrations of hazardous substances, records of exposures are likely to be better than in the general public, and because the nature of work is ideal for the creation of cohorts that can be traced to establish the link between exposure and disease [1]. A great deal of research has investigated occupationally-related cancers at least partly because they are almost entirely preventable through appropriate control measures.

From this foundation, extensive codification and review of occupational carcinogen exposure situations has been accomplished; for example, Siemiatycki et al [2] used expert judgment and other evaluations to identify occupational carcinogens and summarize evidence. The work of the Monographs program of the International Agency for Research on Cancer (IARC) is a prime example of this effort, and the 2011 article by Coglianò et al [3] summarized this body of work, outlining (by cancer site) the strength of evidence linking a wide variety of exposures to cancer outcomes.

The IARC Monographs program has reviewed over 900 substances or exposure situations to date and hundreds of these are

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known or assumed to be present in workplaces. Priorities for research activities and methodologies have been proposed, for example by Ward et al [4] as part of the National Occupational Research Agenda (NORA) in the United States. With so many potential exposures to consider for control activities, it becomes challenging for those who work in the prevention sector (such as various levels of government, researchers, occupational hygienists, labor organizations, and advocacy groups) to decide which exposures should be prioritized for preventive action. In addition, these priorities may differ depending on the type of organization as well as the country (due to differences in major economic activities and feasibility of enacting prevention and control measures).

The setting of priorities is an important exercise in any situation where there are more claims on resources than there are resources available. In this context, resources could be data related but also include funding caps or available personnel. Priority setting that uses risk assessments and quantitative modeling is a useful approach when sufficient and reliable data is available, and this is often used for environmental exposures. For example, Jayjock et al [5] designed a model that uses publically available information, expert judgment, and stakeholder input to quantitatively estimate exposure and human health risk. In the United Arab Emirates, a quantitative assessment approach was used in combination with stakeholder engagement to rank environmental health risks (including exposure to carcinogens) and inform investments in interventions that would lead to the greatest reductions in environmental disease burden [6]. In the United Kingdom, a prioritization effort was undertaken to select priority carcinogens, in preparation of calculation of large-scale occupational cancer burden estimates [7].

Quantifying the risks associated with exposure to occupational carcinogens is challenging primarily because of a severe lack of relevant and current exposure data [8,9]. Furthermore, since exposures in workplaces are typically many times higher than those in environmental situations, emerging hazards may be more likely to be first noticed in occupational settings. Since they are new hazards, data on which to base a risk assessment will also be limited to non-existent. This is certainly the case in Canada, where, like many other countries, the lack of high-quality, pertinent occupational carcinogen exposure information has been repeatedly identified as a barrier in risk assessment as well as cancer epidemiology, surveillance, and burden research.

To address this deficit, in 2007, CAREX Canada was established as a national occupational and environmental exposure surveillance project [10]. CAREX Canada's mandate at that time was to estimate the prevalence and level of exposure to important occupational carcinogens in Canada and to translate research findings to the scientific community, policy makers, regulators, and the general public. In order to fulfill these mandates, CAREX Canada conducted a preliminary prioritization of occupational carcinogens in 2007 for exposure estimation purposes, and then a second one in 2015 to set an agenda for future workplace cancer prevention efforts in Canada. The three aims for the 2015 prioritization exercise were:

1. To add to the list of occupational carcinogens that should be considered for future cancer prevention work for CAREX Canada;
2. To recommend updates to substances and exposure circumstances where CAREX Canada occupational exposure estimates and/or carcinogen profiles could be improved; and
3. To provide a framework that could be used by people in other countries or jurisdictions to conduct their own prioritization exercise.

The objective of this paper is to describe the methods used by CAREX Canada to establish priorities for preventing occupational cancer through the production of exposure estimates and descriptive profiles.

2. Materials and methods

2.1. Initial prioritization exercise (2007)

In the initial stages of the CAREX Canada project, a prioritization of occupational carcinogens was conducted in 2007 to select the carcinogens that would be profiled as potentially occurring in Canadian workplaces and environments and to generate estimates of the number of people exposed (and levels of exposure if possible). Since a widely accepted set of criteria for undertaking such a process was not available, one was devised that used the following three criteria [11]:

1. Was the substance likely to be present and/or used in Canadian workplaces?
2. How toxic was the substance (both with respect to strength of evidence for carcinogenicity and other health effects)?
3. Was it feasible to produce a profile and/or an occupational estimate (mainly based on data availability)?

The 2007 prioritization process is described in detail in an on-line report [11]; in brief, the list of substances ever reviewed by the IARC Monographs program up until 2007 was used as a starting point, including substances classified as IARC Groups 1 (carcinogenic to humans), 2A (probably carcinogenic to humans), and 2B (possibly carcinogenic to humans). Substances were excluded if they were unlikely to be encountered in Canadian workplaces in 2007 (e.g., long-banned chemicals, biological carcinogens, and personal choice exposures, such as chewing tobacco). Based on a detailed review of resources in Table 1 and the criteria above, an occupational hygienist (CP) classified the remaining substances as immediate high priority (Group A), possible high priority (Group B), moderate priority (Group C), and lowest priority (Group D) for inclusion in CAREX Canada's efforts beginning in 2007 [11].

2.2. Updated prioritization exercise (2015)

For the 2015 updated prioritization exercise, similar resources and the aforementioned three criteria were also used, with the addition of a fourth as follows:

4. Was there special interest in the substance from the public or scientific community (based on evaluations of CAREX materials and public and scientific inquiries received by CAREX Canada)?

This was an important addition that emerged from experiences with stakeholders over the earlier years of the project. A list of substances and exposure circumstances to be considered for the 2015 prioritization of occupational carcinogens was populated from a number of resources in addition to the IARC monographs (Table 1). First, the original list selected by CAREX Canada in 2007 was included to evaluate those substances for current relevance [11]. IARC monographs published (or in press) between 2007 and 2015 were reviewed for new additions. IARC's upcoming priorities for the years 2015–2019 [19] were consulted, and substances with the potential for occupational exposure were included. The 2015 prioritization was also completed by CP and subsequently reviewed by the co-authors. Adjustments were made based on consensus of the team. High priorities included substances that could/should be addressed immediately and had already been reviewed by IARC;

Table 1
Information resources used by CAREX Canada in 2007 and 2015 for prioritizing carcinogens for occupational cancer prevention

Name of resource	Description	Nationality (Type)	Criterion addressed ^a
Canadian Workplace Exposure Database [12]	Repository of exposure data collected in Canadian workplaces	Canadian (government/research: ministries of labor, and academics)	1, 3
CAREX Canada evaluations and communications	CAREX collects data on what practitioners and policy makers are interested in, in addition to the general public	Canadian (researchers: university-based)	4
Chem Sources [13]	Database of chemical suppliers, notes country of origin (collected # of suppliers and # from the USA and Canada)	International (business, with Canadian information extracted)	1
Drug Products Database, Health Canada [14]	Searchable labels database for active registrations on pharmaceutical products	Canadian (government: federal health ministry)	1, 3
Hazardous Substances Data Bank (HSDB) [15]	Toxicology database	USA (government: health ministry)	1, 2
Health Canada/Environment Canada screening assessments [16]	Summaries of a risk assessment program for hazardous substances	Canadian (government: federal health and environment ministries)	1, 2, 3
Household Products Database [17]	Health and safety information on household products (lists chemical ingredients from labels)	USA (government: health ministry)	1
International Agency for Research on Cancer's Monographs program [18]	Summary of meetings to assign carcinogenicity rankings to substances	International (World Health Organization)	1, 2
IARC prioritization document [19] [†]	Report from expert advisory group, recommending what should be reviewed in the monographs program between 2015-2019	International (World Health Organization)	1, 3, 4
National Toxicology Program's Report on Carcinogens [20]	Summary of meetings to assign carcinogenicity rankings to substances	USA (government: health ministry)	1, 2
National Pollutant Release Inventory [21]	National program to track environmental releases of hazardous substances from industrial sources	Canadian (government, environment ministry)	1
Pesticide Management Regulatory Agency [22]	Searchable labels database for active registrations on pesticides	Canadian (government: federal health ministry)	1, 3
TradeMap [23]	International trade database, used as evidence of Canadian import/export	International, with Canada-specific information (business)	1

^a Criteria definitions (also see methods): 1, is the substance likely to be present and/or used in Canadian workplaces?; 2, how toxic is the substance (both with respect to strength of evidence for carcinogenicity and other health effects)?; 3, is it feasible to produce a profile or an occupational estimate?; and 4, is there special interest in the substance from the public or scientific community (based on evaluations of CAREX materials and public and scientific inquiries received)?.

[†] Resource used in 2015 prioritization exercise only.

Table 2
Results of the CAREX Canada 2015 prioritization exercise for new profile preparation ($n = 103$)

High priority exposures, $n = 11$		
Pesticides 2,4-DP Diazinon DDT	Industrial chemicals 1-Bromopropane 1,2-Dichloropropane Acrolein Dimethylformamide Furan	Metals Welding fume Other Gasoline engine exhaust
Fibers/dusts Carbon nanotubes		
Medium priority exposures, $n = 33$		
Pesticides Atrazine Carbaryl Chlorpyrifos EPTC Pendimethalin Permethrin Polychlorophenols Tetrachlorvinphos	Industrial chemicals 1,3-Dichloro-2-propanol 2- and 4-Methylimidazole 2-Mercaptobenzothiazole Anthracene Bisphenol A Cumene Ethyl acrylate Hydrazine Metalworking fluids Methanol Methyl isobutyl ketone Methyl tert-butyl ether Molybdenum trioxide Perfluoro-octanoic acid Phenyl and octyl tin compounds Tetrabromobisphenol A	Fibres/dusts Coal dust Erionite Silicon carbide fibers Silicon carbide whiskers Metals Tungsten Pharmaceuticals Cyclosporine Metronidazole
Exposure circumstances Job stress Sedentary work		
Low priority exposures, $n = 59$		
Pesticides 1,3-Dichloropropene 2,4,5-T Aldrin and dieldrin Biphenyl Hexachlorobenzene Parathion Sodium o-phenylphenate	Fibres/dusts Palygorskite	Hormones Diethylstilbestrol Estrogens Oral contraceptives
Industrial chemicals 1,3-Propane sultone 1,4-Dichloro-2-nitrobenzene 1-Amino-2,4-dibromoanthraquinone 2,4-Diaminotoluene 2,4-Dichloro-1-nitrobenzene 2,4-Dinitrotoluene 2,4-Hexadienal 2,6-Dinitrotoluene 2-Amino-4-chlorophenol 2-Chloronitrobenzene 2-Nitropropane 2-Nitrotoluene 3-Chloro-2-methylpropene 3-Monochloro-1,2-propanediol 4-Chloronitrobenzene 5-hydroxymethyl-2-furfural Allyl chloride	Industrial chemicals Anthraquinone Aspartame and sucralose Benzophenone Beta-myrcene Beta-picoline Bromochloroacetic acid Butyl benzyl phthalate Catechol Chloral and chloral hydrate Diethanolamine Ethyl tertiary butyl ether (ETBE) Indium tin oxide Isoprene Methyleugenol N,N-Dimethylacetamide N,N-Dimethyl-p-toluidine Nitritotriacetic acid	Industrial chemicals N-Nitrosodiethanolamine* N-Nitrosodiethylamine* N-Nitrosodimethylamine* N-Nitrosodi-n-butylamine* N-Nitrosodi-n-propylamine* N-Nitrosomethylethylamine* N-Nitrosomorpholine* N-Nitrosopiperidine* N-Nitrosopyrrolidine* p-Chloroaniline Tert-butyl alcohol (TBA) Trimethylolpropane triacrylate Vinyl acetate Vinyl chloride

2,4-DP: 2-(2,4-Dichlorophenoxy)propionic acid (or Dichlorprop); DDT: Dichlorodiphenyltrichloroethane; EPTC: S-Ethyl dipropylthiocarbamate (or Eptam).

* Consider together in one profile, due to overlapping exposure situations (nitrosamines are not often encountered in isolation). The total number of $n = 59$ exposures, however, includes all of these substances individually.

medium priorities included substances where evidence for Canadian exposure circumstances was limited and/or for which IARC monograph meetings had not yet been scheduled; and low priorities included substances with known declining use, unknown but plausible (based on industrial process) Canadian use, and for which IARC monograph meetings had not yet been scheduled. When possible, an emphasis was placed on Canadian sources of information used to support prioritization; otherwise American and international resources were used.

Recommendations for action were developed separately for CAREX Canada carcinogen profiles and estimates of the number of workers exposed and/or levels of expected exposures in Canadian workplaces. For substances that had already been addressed following the 2007 priority setting exercise (i.e., CAREX Canada had already produced a carcinogen profile and in many cases, an occupational exposure estimate), no further action was recommended unless there was evidence for changes in use in Canadian

workplaces, or new data was available. Recommendations for “no further action” for a given substance were applied in 2015 when a profile and/or occupational exposure estimate had been completed by CAREX Canada already, and no changes to exposure were anticipated based on the resource review, or where all four of the criteria were not met (e.g., evidence for use in Canadian workplaces was lacking). Ethics approval for CAREX Canada was provided by the Research Ethics Board at Simon Fraser University.

3. Results

Overall, 246 substances or exposure circumstances were reviewed for inclusion in the 2015 CAREX Canada occupational priorities list. Of these, 161 were on the original 2007 CAREX priorities list, 54 were identified by IARC as priorities for review for 2015–2019, 25 were reviewed by IARC since 2007, 4 were topics of special public and scientific interest, and 2 were added to the list

during the first 5 years of the project (shiftwork and solar radiation). Shiftwork was added during the first funding cycle of CAREX Canada because it was a topic of public and scientific interest after being classified as a probable carcinogen by IARC in 2010. Solar radiation was added as an occupational exposure only and not as a lifestyle factor, the reason why it was initially excluded.

The results of this priority setting exercise for the creation of new profiles and occupational exposure estimates are summarized in Tables 2 and 3. The substances are categorized into functional groups that can be helpful for addressing several exposures at a time. This may occur where similar data sources can be consulted all at one time, for example, pesticide registration data. These groups include pesticides, industrial chemicals, fibers/dusts, metals, radiation, pharmaceuticals, hormones, exposure circumstances, and "other". Please also see Tables S1 and S2 in the supplementary materials available online for a detailed summary of all data used in this prioritization exercise.

Overall, 103 substances and exposure circumstances were recommended for new profile production; 11 substances were recommended as high priorities, 33 as medium, and 59 as low. Many of the substances in the medium and low categories are yet to be reviewed and categorized by IARC, but have been prioritized for inclusion in IARC meetings before 2019; therefore, it was thought prudent to consider them.

Overall, 36 substances and exposure circumstances were recommended for occupational exposure estimation or updates; 27 of these were new priorities, and an additional 9 were selected for updates to existing CAREX Canada estimates (Table 3). Of these substances, 13 were classified as high priority (6 of which were new

substances and 7 of which were recommended updates to existing estimates), 17 substances fell in the medium priority category (where all but one exposure, shiftwork, were priorities for new estimate generation), and 6 were in the low category of exposure (of which 5 were priorities for new estimate generation).

After prioritization was complete, 126 of the original 246 substances identified in 2007 (51%) required no further action in 2015. Information collected from each resource listed in Table 1 is summarized in the online supplementary Table S1. No further action was recommended for substances where none of the four criteria for prioritization were met ($n = 73$) or when a profile and/or occupational estimate already existed and no new information or data sources were located in the resource review ($n = 53$).

4. Discussion

The results of this priority setting exercise served to highlight where further progress could be made in the generation of new carcinogen exposure information for preventing occupational cancer in Canada. By identifying the resources that were consulted (and the origin of the types of information used), this exercise can also serve as a guide for other countries or jurisdictions who wish to conduct their own regionally-relevant priority setting. Through CAREX Canada's knowledge translation and stakeholder engagement work, we know that agencies and organizations within Canada used our priorities to plan their own prevention programs and outreach including workers' compensation programs, ministries of labor, cancer advocacy organizations, and labor/union groups [24].

The list of CAREX Canada priorities for profile generation is inherently much longer than the list for occupational exposure estimate generation or update (103 profiles vs. 36 occupational exposure estimates) because more data is required to estimate the number of people exposed to a specific substance than to produce a descriptive profile of a carcinogen. Profiles can be produced using a broader set of resources and need not rely on country-specific data (in particular for describing how a substance is used and its health effects, for example).

Many of the substances prioritized for both profile production and occupational exposure estimates were pesticides; this reflects the IARC monograph program's choice in recent years to conduct a first evaluation or re-evaluation of many pesticides. So far, most of the pesticides reviewed have been classified by IARC as at least 2B carcinogens (possibly carcinogenic to humans) and many have been upgraded to 2A (probably carcinogenic to humans). CAREX Canada is currently preparing a broad strategy to address estimating occupational exposure to pesticides.

The substances that were selected for updates to their occupational estimates included several antineoplastic substances, asbestos, crystalline silica, shiftwork, and ionizing radiation. In the first 5 years/stage of the CAREX Canada project (2007–2012), preliminary estimates of exposure to antineoplastic substances were prepared using limited evidence for exposure and numerous expert assumptions. Since then, new data sources have evolved which identify additional jobs at risk of exposure and more thoroughly characterize exposures across occupations and work environments. Updated estimates have recently been published [25].

Quantitative estimates of the level of asbestos exposure were not produced in the initial phases of CAREX Canada because the ability of older exposure data to capture current exposure situations in Canadian workplaces was unknown. The bulk of exposure monitoring for asbestos available in the Canadian Workplace Exposure Database is from the mid-1980s, and asbestos exposure patterns have changed dramatically since then. However, this data could be supplemented with data from other countries, or

Table 3
Results of the CAREX Canada 2015 prioritization exercise for recommending new or updated occupational exposure estimates ($n = 36$)

High priority exposures for estimates production/update, $n = 13$		
Pesticides	Pharmaceuticals	Fibers/dusts
2,4-D Chlorothalonil Glyphosate Malathion MCPA MCP	Adriamycin* Chlorambucil* Cisplatin* Cyclophosphamide* Melphalan*	Asbestos* Crystalline silica*
Medium priority exposures for estimates production/update, $n = 17$		
Pesticides	Industrial chemicals	
2,4-DP Diazinon Atrazine Dichlorvos EPTC Pendimethalin Pentachlorophenol Chlorpyrifos	Acrolein Dimethylformamide Metalworking fluids MOCA	
	Exposure circumstances	
	Shiftwork*	
	Pharmaceuticals	
Other	Metronidazole	
Secondhand smoke Strong acid mists	Fibres/dusts	
	Coal dust	
Low priority exposures for estimates production/update, $n = 6$		
Industrial chemicals	Hormones	
Tert-butyl alcohol (TBA) Ethylbenzene	Diethylstilbestrol Estrogens Oral contraceptives	
Radiation		
Ionizing radiation*		

CAREX: CARcinogen EXposure; EPTC: S-Ethyl dipropylthiocarbamate (or Eptam); MCPA: 2-methyl-4-chlorophenoxyacetic acid; MCP: methylchlorophenoxypropionic acid (or Mecoprop); MOCA: 4,4'-Methylenebis(2-chloroaniline).

* Update recommended: occupational estimate already exists but could be changed based on new evidence.

modeling approaches that capture the changing face of asbestos exposure levels could be used to address this gap.

The original approach for crystalline silica underestimated the exposure levels, mostly due to lack of data on exposures in the construction industry where workers are often over-exposed to silica. This was realized during the process of producing exposure level estimates for silica exposure and via informal confirmation of industrial hygienists and regulators in Canada. As with asbestos, approaches to supplementing the data or adding in other estimation procedures are warranted for silica.

For ionizing radiation, our original exposure estimates relied on data available from Canada's National Dose Registry (NDR) program, a particularly rich data source with ongoing updates. Given the time elapsed since CAREX's preliminary phase, an update in collaboration with the NDR program will be investigated.

For profile selection, country-specific data availability is less vital, particularly when other countries can be assumed to have similar use patterns (e.g., the USA and Canada). A large number of industrial chemicals were recommended for profile production during CAREX's 2015 prioritization exercise, in part because chemicals constitute the largest group of substances reviewed by IARC, and also because many of these were noted as lower priority in the CAREX Canada 2007 prioritization exercise [11]. In establishing a new surveillance program for occupational carcinogens at that time, a greater degree of selectiveness was required. Now that an established system has been created for profile generation, additional substances that were previously low or moderate priorities can be assessed. In this way, the prioritization exercise can incorporate considerations of the resources available to carry out the work.

The general types of resources used to carry out this prioritization exercise are identified in Table 1. Experts in other countries or jurisdictions could seek out similar resources that are relevant to their own contexts. The methodology has been presented as a flexible process that could be adapted to many physical and political locales, such as in Latin America and the Caribbean (where CAREX Canada researchers have collaborated in just such an exercise). In general, we relied mostly on Canadian government sources of data (in particular, from Health Canada, the federal ministry of health). More specific sources (such as a provincial Ministry of Labor) could be used to tailor the prioritization for particular jurisdictions.

Despite a general lack of consensus or gold standard method to undertake prioritization exercises in occupational cancer prevention, some exercises have been applied to identify and estimate exposure to occupational carcinogens. Estimates of occupational exposure to carcinogens were calculated in Quebec, Canada to inform provincial research and intervention priorities (these estimates were partly based on CAREX Canada data and methods) [26]. The selection of carcinogens for these intervention priorities was based on provincial occupational health regulations and IARC classifications and was largely dictated by the availability of data. In Great Britain, priority carcinogens were identified to help assess the burden of occupational cancer and inform exposure reduction planning [7]. Their criteria were: (1) sufficient and good-quality evidence of carcinogenicity based on IARC evaluations; (2) that the majority of exposed people in Great Britain would be included in the prioritization; and (3) the possibility of occupational exposure existed.

A common theme in prioritization exercises for occupational health (including the one presented here) is the reliance on IARC monographs. This approach seems well justified as the monographs program brings together scientists from all over the world to transparently and rigorously evaluate the scientific evidence for carcinogenicity of a huge array of chemicals, dusts, physical

substances, and exposure circumstances [27]. Given limited resources in any given group attempting to prioritize occupational exposures, it makes sense to rely on IARC as a gold standard for selecting carcinogens to consider.

Prioritization exercises for other goals in occupational health have also been completed. For example, the National Institute for Occupational Safety and Health in the United States developed a prioritization framework that uses stakeholder input to guide occupational health and safety research agendas (the NORA) [28]. Written and oral feedback is collected from researchers, health professionals, and other stakeholders at public meetings and working groups. In Ontario, Canada, the Occupational Cancer Research Centre also undertook a similar stakeholder consultation using input from an online survey and targeted follow-up interviews to formulate priorities for their research agenda [29]. In Australia, a carcinogen prioritization strategy for prevention and control of occupational cancer was modeled after CAREX Canada's original criteria, as described above [30]. Their criteria included evidence of carcinogenicity based on IARC evaluations, evidence of use in occupational settings, and use in Australia.

This prioritization exercise had the explicit goal of setting an agenda for creating carcinogen profiles and occupational exposure estimates. In this sense, high priority exposures from the current exercise should not be interpreted as the only exposures meriting focus for other prevention efforts, including knowledge translation activities (e.g., examining where exposure reduction strategies could be most useful and engaging with stakeholders to use our products to inform practice and policy changes). Indeed, several prevalent and important occupational carcinogen exposures (e.g., diesel engine exhaust, benzene, many metals) were recommended as "no further action" in the current priority setting, but only because CAREX Canada carcinogen profiles and occupational exposure estimates were already generated for these substances during the initial phase of the CAREX Canada project.

A potential limitation of this prioritization exercise is that it partially relied on expert judgment for the priority setting. However, 13 different resources were drawn on to collect substance-specific data that allowed for clear criteria to be set and adhered to during the process. A key feature of the appropriate use of expert judgment is that a group consensus is reached. The team process used to evaluate the final priorities may increase confidence in the utility of priorities identified for future CAREX Canada carcinogen profile and occupational exposure estimate generation. In addition, it is very difficult to conceptualize a prioritization exercise that is specific to any one context (i.e., occupational carcinogen exposures) without relying on some kind of expert judgment. Indeed, in all of the previous occupational health priority setting exercises that were located, some degree of reliance on expert judgment (sometimes in combination with input from other groups and stakeholders) was used [2,5–7,26,28–30]. Priorities are not always numbers that can simply be looked up, nor should they be; including a qualitative assessment allows for a better understanding of local contexts and exposure circumstances that impact priority setting and the feasibility of future preventative actions.

As stated at the outset of this paper, "the setting of priorities is an important exercise in any situation where there are more claims on resources than there are resources available"; the 2007 CAREX Canada prioritization exercise successfully generated nearly 100 carcinogen profiles and 44 occupational exposure estimates within a strict funding cap. The second prioritization exercise in 2015 identified additional occupational carcinogens to profile, and opportunities to generate or revise occupational exposure estimates. This increases confidence that we are focusing on the substances of most importance to the Canadian work environment, given limited resources. These developments reflect the changing nature of the

cancer risks associated with occupation as well as emergent issues of importance to pertinent scientific and stakeholder communities in Canada. The process undertaken has been outlined and expanded here so that other countries and jurisdictions can flexibly adapt it for their own purposes and create a framework for effectively selecting occupational carcinogens for research or other purposes, with the ultimate goal of reducing the occupational burden of cancer worldwide.

Conflicts of interest

Funding for this project was provided by the Canadian Partnership Against Cancer. The authors declare no conflicts of interest relating to the material presented in this Article. Its contents, including any opinions and/or conclusions expressed, are solely those of the authors. No disclaimers to report.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.shaw.2017.07.005>.

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