Aspects to consider for selection of chemical risk assessment methodology: the case of formaldehyde occupational exposure

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Abstract

There are several risk assessment methodologies available that can be applied in contexts where occupational exposure to chemical agents occur. However, there are some aspects that should be considered for selecting a more suitable and accurate risk assessment methodology.

A study was carried out where two different risk assessment methodologies in ten anatomy and pathology laboratories were applied. One of the methodologies is propose by the Environmental Protection Agency (EPA) and the other methodology was based on the risk assessment methodology of Queensland University and defined by the authors to study this specific occupational setting.

The two risk assessment methodologies obtained different results. Application of EPA methodology for risk assessment provides data that classifies this occupational setting similar to others where occupational exposure to formaldehyde occurs. However, differences and particular characteristics of this occupational setting are not possible to know due to the fact of relying only on TWA_{8h} values. The proposal methodology ranks with high risk 30% of the activities studied in the ten laboratories and, 70% of the laboratories had at least one activity classified as high risk. The activities that were classified with very high risk and high risk were macroscopic exams developed always by the pathologist.

WIT Transactions on Ecology and the Environment, Vol 132, © 2010 WIT Press
www.witpress.com, ISSN 1743-3541 (on-line)
doi:10.2495/ETOX100031

Despite EPA methodology allowing applications in occupational settings, it only provides information about the risk for work location, not allowing a risk assessment by activity.

Keywords: risk assessment methodology, exposure assessment, occupational exposure, formaldehyde, anatomy and pathology laboratories.

1 Introduction

Nowadays people are exposed in several ways (e.g. food, drinking water, ambient air, indoor air, occupational setting) to chemical substances which are responsible for enhanced cancer risk. Often, substances previously thought to be inert or harmless to humans have been found to be carcinogenic (e.g., asbestos and vinyl chloride monomer) or toxic to the reproductive process (e.g., methylmercury and thalidomide). Moreover, an increasing number of substances have been shown to be mutagenic or carcinogenic in animal studies [1].

There are several risk assessment methodologies available and possible to apply in contexts where occupational exposure to chemical agents occur. However, there are some aspects that should be considered for a select risk assessment methodology that is more suitable and accurate because it might be followed by decisions with wide-ranging and significant consequences for workers' health and for industrial processes. All these modifications involve, usually, immense investments.

Formaldehyde, with the chemical formula CH_2O, is the most simple yet most reactive of all aldehydes. It exists as a colorless gas at room temperature and has a strong pungent smell [2, 3].

Formaldehyde is an economically important chemical with an annual production of approximately 46 billion pounds worldwide. According to the Report on Carcinogens (11th Edition, National Toxicology Program), formaldehyde ranks 25th in overall U.S. chemical production with more than 11 billion pounds produced each year [4].

Commercially, formaldehyde is manufactured as an aqueous solution called formalin, usually containing 37% by weight of dissolved formaldehyde. It is commonly used as a tissue preservative or as a bactericide in embalming procedures and in anatomy and pathology laboratories.

Given its economic importance and widespread use, many people are exposed to formaldehyde environmentally and/or occupationally. Occupational exposure involves not only individuals employed in the direct manufacture of formaldehyde and products containing it, but also those in industries utilizing these products, such as construction.

The exposed workers, commonly found in resin production, textiles or other industrial settings, inhale formaldehyde as a gas or absorb the liquid through their skin. Other exposed workers include health-care professionals, medical-lab specialists, morticians and embalmers, all of whom routinely handle bodies or biological specimens preserved with formaldehyde [5–7].

Concerning exposure limits in occupational settings, OSHA has established the following standards that have remained the same since 1992: the permissible

exposure limit (PEL) is 0,75 ppm (parts per million) in air as an 8-h time-weighted average (TWA_{8h}) and the short-term (15 min) exposure limit (STEL) is 2 ppm. American Conference of Governmental Industrial Hygienists (ACGIH) recommended threshold limit value (TLV) is 0,3 ppm as a ceiling value. The National Institute of Occupational Safety and Health (NIOSH) recommends much lower exposure limits of 0,016 ppm (TWA_{8h}) and 0,1 ppm (STEL), above which individuals are advised to use respirators if working under such conditions. In Portugal, the Portuguese Norm (NP 1796 - 2007) points also 0,3 ppm as a ceiling value.

Human studies have shown that chronic exposure to formaldehyde by inhalation is associated with respiratory symptoms, and eye, nose and throat irritation [7].

Regarding the carcinogenic effects, formaldehyde was long considered as a probable human carcinogen (Group 2A chemical) based on experimental animal studies and limited evidence of human carcinogenicity [8]. However, the International Agency for Research on Cancer (IARC) reclassified formaldehyde as a human carcinogen (Group 1) in June 2004 based on ''sufficient epidemiological evidence that formaldehyde causes nasopharyngeal cancer in humans'' [5].

IARC also concluded that there was ''strong but not sufficient evidence for a causal association between leukemia and occupational exposure to formaldehyde'' [5, 7].

In relation to risk assessment, there are some articles that describe the application in occupational settings of a methodology define by Environmental Protection Agency [9]. In this case cancer risk due to the formaldehyde exposure has been assessed by estimating the excess individual lifetime cancer probability (LCP). LCP is the increase in the probability of cancer occurring.

The estimated excess LCP for formaldehyde exposure can be calculated by the equation: $R_f = C_f \times IUR_f \times L_{w,}$ where *Rf* is the excess LCP for formaldehyde; *Cf* is the formaldehyde exposure concentration, $\mu g/m^3$; *IURf* is the IUR factor for formaldehyde, $(\mu g/m^3)^{-1}$,which would be taken as $1{,}3\times10^{-5}$ $(\mu g/m^3)^{-1}$ [10]; and *Lw* is the adjustment factor for the ratio of the working time (40 years) to entire lifetime (70 years) with the value of 0,113 [11]. This methodology permits to assess cancer risk in different work locations in a specific occupational setting.

The goal of this article is to demonstrate that selection of risk assessment methodology, in the case of occupational exposure to chemical, it's necessary to consider some aspects from the chemical and also the assessment objectives.

2 Materials and methods

A study was carried out applying two different risk assessment methodologies in 10 anatomy and pathology laboratories in Portugal. One of the methodologies was already describe [9] and uses data from formaldehyde exposure assessment obtained from environmental monitoring, namely TWA_{8h} results (averages concentrations obtain in the sampling period) through an NIOSH method application (NIOSH 2541). Three exposure groups were defined, specifically

pathologists, technicians and assistants and one sample for each exposure group was obtained in each laboratory (3 samples per laboratory).

The other methodology was based on a Queensland University proposal [12] that permits to perform risk assessment for each activity developed in a work station. This methodology was applied in 83 different activities developed in the 10 laboratories studied. It also used the results from environmental monitoring but, in this case, ceiling concentrations were used measured by Photo Ionisation Detection (PID) equipment (with 11.7 eV lamp), obtained in the same day of TWA_{8h} measures. Additionally, data was used from research articles about biologic adverse events associated with different formaldehyde exposure values. This data was used to categorize the health effects severity (Table 1).

Prior to methodology application, ergonomic work conditions analysis was performed to identify the different tasks developed in each work location and their execution frequency and then give the exposure probability. With these data it was possible to achieve the exposure probability (Table 2).

In order to assess the risk we multiply the likelihood of exposure by the severity categorization. The higher score gives the higher risk and define priority for applying control measures (Table 3).

Table 1: Health effects severity categorization.

Severity Categorization	Maximum concentration / effect on health associated
1. Negligible	$\leq$ 1 ppm (does not cause damage to the epithelial tissue)
2. Medium	1 $\leq$ 2 ppm (Non-neoplastic lesions of different severities and incidences)
3. Considerable	> 2 < 4 ppm (cell proliferation, metaplasia, cytotoxicity)
4. Serious	$\geq$ 4 ppm < 5 ppm (2x increase in the likelihood of nasopharyngeal cancer)
5.Very Serious	$\geq$ 5,5 ppm (4x increase in the likelihood of nasopharyngeal cancer)

Table 2: Categorization of exposure probability.

Categorization Probability	**Likelihood of Exposure**
1	Never place
2	Annually
3	Monthly
4	Weekly
5	Daily

Table 3: Scoring risk.

Score	Risk Assessment/Action
> 16	Very high risk - emerging acting
> 12 ≤ 16	High risk - Immediate response
> 6 ≤ 12	Medium risk - acting as soon as possible
> 2 ≤ 6	Low risk - No need for action, but surveillance

3 Results

Different results were obtained with the two different methodologies. With the EPA methodology all the results were above 9,2 x 10^{-3} (LCD) (Table 4).

Table 4: Results of EPA methodology.

Laboratories	Exposure Groups	Formaldehyde exposure (TWA) (ppm)	EPA methodology LCD $R_f = C_f \times IUR_f \times L_w$
A	Assistants	0,27	4,8 x 10^{-4}
	Pathologists	ND	
	Technicians	0,16	2,9 x 10^{-4}
B	Assistants	0,15	2,7 x 10^{-4}
	Pathologists	0,24	4,3 x 10^{-4}
	Technician	0,16	2,9 x 10^{-4}
C	Assistants	0,12	2,2 x 10^{-4}
	Pathologists	0,47	8,5 x 10^{-4}
	Technician	0,51	9,2 x 10^{-3}
D	Assistants	ND	
	Pathologists	0,07	1,3 x 10^{-4}
	Technician	0,11	1,9 x 10^{-4}
E	Assistants	ND	
	Pathologists	0,06	1,1 x 10^{-4}
	Technician	0,07	1,2 x 10^{-4}
F	Assistants	0,09	1,6 x 10^{-4}
	Pathologists	0,23	4,1 x 10^{-4}
	Technician	0,12	2,2 x 10^{-4}
G	Assistants	0,16	2,9 x 10^{-4}
	Pathologists	0,05	8,9 x 10^{-5}
	Technician	0,04	7,2 x 10^{-5}
H	Assistants	0,25	4,5 x 10^{-4}
	Pathologists	0,11	1,9 x 10^{-4}
	Technician	0,25	4,5 x 10^{-4}

Table 4: Continued.

Laboratories	Exposure Groups	Formaldehyde exposure (TWA) (ppm)	EPA methodology LCD $R_f = C_f \times IUR_f \times L_w$
I	Assistants	0,05	$8,9 \times 10^{-5}$
	Pathologists	ND	
	Technician	0,06	$1,1 \times 10^{-4}$
J *	Assistants	0,13	$2,3 \times 10^{-4}$
	Pathologists	0,08	$1,4 \times 10^{-4}$

* Do not have assistants working in the laboratory.
ND – Not detectable.

Concerning the proposal methodology results, they have different distribution between the laboratories studied (Figure 1).

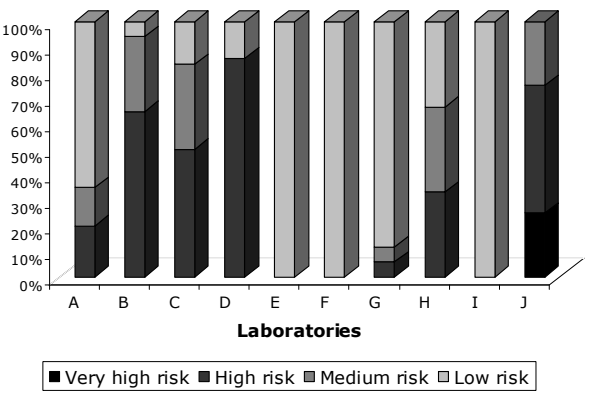

Figure 1: Results of proposal methodology.

Laboratories E, F and I have all the activities classified with low risk. Laboratory D have 86% of the activities classified with high risk.

Concerning the risk classification distribution per activity, 2,41% have very high risk classification, 32,53% obtained the high risk classification, 13,25% were classified with medium risk and, finally, 51,81% have low risk classification.

We could also conclude that 30% of the laboratories have all activities classified with low risk and 70% of the laboratories have at least one activity classified with high risk. The activities that were classified with very high risk and high risk were macroscopic exams developed always by the pathologist.

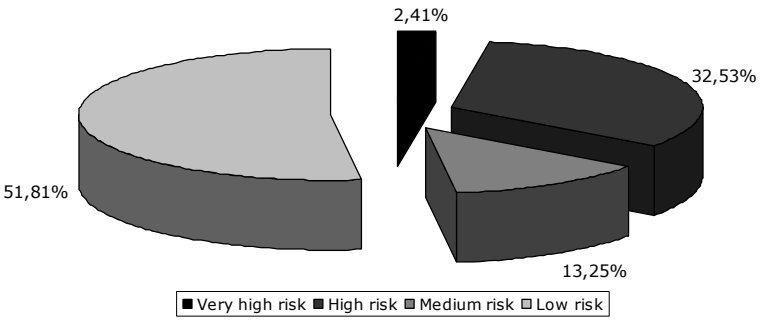

Figure 2: Results of risk classification distribution per activity.

4 Discussion

For some genotoxic carcinogens the existence of a "practical" threshold is supported by studies on mechanisms and/or toxicokinetics. Formaldehyde is one of the chemicals and, therefore, a NOAEL (No Observed Adverse Effects Level) may be established from which to derive a health-based exposure limit [13-16]. Considering these characteristics it was possible to propose this new risk assessment methodology, based on Queensland University proposal and make an association between occupational exposure to formaldehyde air concentrations and health effects.

Recent studies [17, 18] showed EPA methodology application in occupational settings with FA exposure but, as suggested by the methodology described, making use of the TWA_{8h} values obtained in the situations studied. Thus, applying this equation to ours results we obtain values that are lower and equal to 9,3 $x10^{-3}$ (LCP) when, the cancer risk from formaldehyde exposure in general population is $1x10^{-6}$ LCP, and in occupational settings, will be greater than $1x10^{-4}$ LCP [11,19].

We conclude that application of EPA methodology for risk assessment provides data that classifies this occupational setting similar to others where occupational exposure to formaldehyde occurs. However, differences and particular characteristics of this occupational setting are not possible to know due to the fact of relying only on TWA_{8h} values, appointed as less appropriate with regard to assess formaldehyde occupational exposure [5,20].

Despite EPA methodology also allow application in occupational settings, provides only information about the risk for work location, as performed in the study of He and Zhang (2009), not allowing a risk assessment by activity.

Occupational health interventions highlight the importance of knowing the most critical activities because permits intervention prioritization and identification of technical and/or organizational measures aiming to minimize and/or eliminate exposure (to know which activity has a greater contribution to exposure and the constraints of activity, allow knowing the variables that influence the exposure).

Moreover, this kind of information provides important information for raising awareness for exposure prevention (which activity requires protective measures to be strengthened and/or employed by workers) and, last but not least, a risk assessment more detailed, allowing also identifying professional group with the most critical exposure "anticipating" potential effects on health through the adequacy of health vigilance activities. The proposal methodology gives this information allowing more complete and meticulous interventions. In this case the macroscopic exam was the task with higher risk and the pathologist group with the higher exposure.

Finally, many environmental and occupational chemicals, toxicants and carcinogens require metabolic activation to exert their action. However, metabolic polymorphisms can modulate individual response [21]. Also, a consistent, positive association of DNA repair deficiency and increased risk was recently shown by an extended review of inter-individual variability in DNA repair systems and cancer risk [22].

Taking into account these aspects we have to mention that despite the important and useful information that both methodologies gives, there is no consideration about individual variability concerning with the capacity of dealing with a specific chemical exposure.

5 Conclusions

For occupational health interventions it's important to know the activities that increment exposure and the workers group with the higher exposure to define more adequate and successful preventive and protective measures. So, when selecting a risk assessment methodology aiming at occupational health interventions we have to consider these aspects.

In the case of formaldehyde occupational exposure in anatomy and pathology laboratories it seems that "macroscopic exams" is the worst activity concerning exposure and the "pathologists" the workers group with the higher exposure.

In conclusion, all risk assessment methodologies have limitations that have to be considered and known permitting a better methodology selection. Also, obtained data showed that occupational exposure to formaldehyde in anatomy and pathology laboratories in Portugal is still a matter of great concern.

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