



Review

Beyond the Clock: Revisiting Occupational Exposure Limits (OELs) for unusual work schedules in the South African Mining Industry

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ABSTRACT

Workers are exposed to various stressors in their workplace and in many industries, exposure is prolonged due to unusual work schedules. Unfortunately, current Occupational Exposure Limits (OELs) are derived from calculations based on a conventional work schedule of five consecutive, eight-hour days (40 h per week) and do not compensate for prolonged exposure and shortened recovery time. Therefore, standard OELs must be adjusted to ensure worker protection. The aim of this paper was to review different mathematical models available in the literature to adjust OELs for unusual work schedules. Based on the advantages, disadvantages and practical feasibility of the different models, the Brief and Scala, Occupational Safety and Health Administration (OSHA) and Québec models were selected to calculate reduction factors (RFs, i.e., adjustment factors) for three unusual work schedules encountered in the South African Mining Industry (SAMI). Subsequently, the calculated RFs were used to establish adjusted OELs (OEL_A) for 15 chemical substances of interest. The Brief and Scala model yielded the most conservative RFs for all work schedule examples. However, this model may overestimate the degree to which the OELs should be lowered. The OSHA and Québec models incorporate pharmacokinetic parameters (i.e., primary health effects) and generated more realistic RFs compared to the Brief and Scala model. Although pharmacokinetic-based models are more accurate from a toxicological viewpoint, the anatomical, physiological, biochemical, and physiochemical parameters required to apply these models are not available for many chemical substances and therefore the use of such pharmacokinetic-based models is not practically feasible in South Africa. Based on the findings of this study, the authors recommend using the OSHA or Québec models for OEL adjustments in the SAMI. OELs adjusted in this manner will provide an equivalent degree of worker protection during unusual work schedules compared to conventional work shifts.

1. Introduction

Workers in various industries are exposed to different airborne contaminants during their shifts (Mellemsæther & Eide, 2016). In toxicology, it is accepted that an equilibrium occurs between the accumulation of a contaminant in the body during exposure in the workplace and the elimination of the contaminant when away from the workplace (i.e., the period of recovery) until a maximum body burden or an accumulation plateau is reached in the body (Brodeur et al., 2001). However, prolonged exposure can result in the body burden exceeding a threshold which can cause adverse health effects (Mellemsæther & Eide, 2016). It is, therefore, necessary to develop hazard indices to protect exposed workers (Mason & Derishin, 1976).

This premise led to the development of health-based Occupational

Exposure Limits (OELs)—airborne concentrations of chemical substances in a worker's breathing zone that do not cause any discomfort or adverse health effects such as irritation or narcosis (Nielsen et al., 2008; AIOH, 2016). The first OELs were established in 1946 by the American Conference of Governmental Industrial Hygienists (ACGIH) (Schenk et al., 2008a; Mellemsæther & Eide, 2016). The ACGIH published a list with 150 threshold limit values (TLVs®)—then called maximum allowable concentrations—that describes the level of admissible exposure, for a length of time, to a chemical hazard that is not likely to affect the health of a worker. (Weisburger, 2001; Schenk et al., 2008a). In the years following the ACGIH's publication, the TLVs® were adopted by many regulatory agencies around the globe (Schenk et al., 2008a). These ACGIH OELs not only guard against health effects but are also used to assess the quality of the working environment and indicate where

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control measures are required (AIOH, 2016).

Occupational Exposure Limits are based on the chemical properties of a substance and are derived from epidemiological and toxicological data from experimental studies on animals and/or humans (AIOH, 2016). However, even though there is a general agreement that OELs are necessary to protect worker health, there is no harmonised approach for the derivation of OEL concentrations amongst different organisations (Haber & Maier, 2002). There are also national differences in the risk assessment and management of OELs (Schenk et al., 2008a). A general framework is followed where epidemiological and toxicological data is reviewed to identify potential hazards and select critical effects—the main adverse health effects that the OEL should protect against (Haber & Maier, 2002; Schenk, 2010). This is followed by dose–response estimations to derive the suitable concentrations workers can be exposed to (Haber & Maier, 2002). Nonetheless, technical and socio-economic factors, such as the number of workers potentially exposed, also influence the justification and feasibility of the level of precaution (Schenk, 2010). Consequently, OELs still vary amongst countries as evidenced by Schenk et al., (2008a) and Schenk et al., (2008b) who investigated the OELs established by different national regulatory agencies.

The term “OEL” is sometimes synonymously used with “TLV®” (Brief & Scala, 1975; Roach, 1978) or “Permissible Exposure Limit” (Brodeur et al., 2001). In Germany, for example, maximum concentrations at the workplace or MAK values are used to ensure worker protection (Hartwig & MAK Commission, 2023). These MAK values describe the maximum air concentration of a chemical gas, vapour or aerosol which are generally not known to cause adverse health effects and are valid for conventional work shifts of 8 h per day and 40 h per week (German Research Foundation, 2023). However, for this paper and to prevent any confusion, the collective term “OEL” will be used. Overall, there are three main types of OELs used for airborne exposures: ceiling value (C), short-term exposure limit (STEL), and time-weighted average (TWA) (AIOH, 2016). The ceiling value is the concentration that should not be exceeded during any part of the workday (i.e., a concentration that should not be exceeded even instantaneously) (AIOH, 2016). The STEL describes the concentration to which workers can be exposed continuously for a short period without suffering irritation, chronic or irreversible tissue damage, narcosis of sufficient degree to increase the likelihood of accidental injury, impaired self-rescue, or materially reduced work efficiency. It is essentially an average over a 15-minute period (Schenk et al., 2008a). The TWA exposure is the concentration of a chemical substance in the air averaged over a period that it is believed that workers may be repeatedly exposed, day after day, for a working lifetime without adverse health effects. TWAs are usually averaged over an 8-hour workday for a 5-day working week (i.e., a 40-hour workweek) (Schenk et al., 2008b). Time-weighted average concentrations are measured by taking one or more measurements of concentration over a work shift. Since TWAs apply to long-term exposure to a chemical substance over an 8-hour work shift there is a consequent 16-hour break between successive shifts. Occupational exposure limits are expressed in ppm, mg/m³ or f/mL depending on whether the chemical substance of interest is a gas, vapour, aerosol or fiber.

In South Africa, there are currently two sets of OELs used namely those listed in the Regulations for Hazardous Chemical Agents (RHCA) of 2021 (Department of Employment and Labour, 2021) and Schedule 22.9 of the Mine Health and Safety Act (MHSA) (Act No. 29 of 1996) (Department of Mineral Resources, 1996). Although the RHCA 2021 repealed the Hazardous Chemical Substances Regulations (HCSR) of 1995 published under the Occupational Health and Safety Act (Act No. 85 of 1993), the revised OELs are still only for general industries and are not applicable to hazardous chemical agents in the mining industry, or to lead and asbestos (Department of Employment and Labour, 2021). Therefore, in the SAMI, the MHSA of 1996 is applied (Department of Mineral Resources, 1996). The OELs for Airborne Pollutants were published in 2002 and is a guideline to enable employers to protect and improve worker health. These regulations were amended by the

Table 1
Examples of unusual work schedules in the mining industry of different countries.

Country	Industry	Work shift	Reference
Chile	Mining	• 12-hour shift in a 24-hour period (cycle of two day shifts, two night shifts, and four rest days)	Bacaloni et al., 2018
Iran	Mining	• 8-hour shift per day (cycle of 23 day shifts and seven rest days)	Kooshki et al., 2021
South Africa	Mining	• 10-hour shift in a 24-hour period (cycle of five day shifts, five night shifts, and five rest days) • 10-hour shift in a 24-hour period (cycle of four day shifts, four rest days, four night shifts, and four rest days) • 11.5-hour shift in a 24-hour period (cycle of four day shifts, four rest days, four night shifts, and four rest days)	Pelders et al., 2021

Department of Minerals and Energy in 2006 and the OELs for some chemicals were revised and lowered (Department of Minerals and Energy, 2006). Later, the MHSA of 1996 was amended under the Mine Health and Safety Amendment Act 74 of 2008 to strengthen enforcement provisions, simplify the administrative system for issuing fines and ensure consistency with the Mineral and Petroleum Resources Development Act of 2002 (Department of Minerals and Energy, 2009).

As previously mentioned, standard OELs are based on TWAs of occupational exposure during conventional work shifts comprised of 5 consecutive, 8-hour workdays (40 h per week and 2 000 h per year) (Armstrong et al., 2005). However, deviations from convention occur in some industries where workers work shorter or longer shifts or weeks (Armstrong et al., 2005). Work schedules that deviate from conventional work shifts are often called ‘novel work schedules’, ‘compressed work weeks’ or ‘extended work shifts’. However, the term ‘unusual work schedule’ is most often used in literature to describe shifts that exceed the standard 8 h per day, or 40 h per week (Drolet, 2015). Although unusual work schedules were considered ‘novel’ by Brief and Scala (1975), nowadays shifts that exceed 8 h per day or 40 h per week which are implemented to maintain continuous operations are not unusual but, in many cases, the norm (Government of Western Australia, 2019; Hartwig & MAK Commission, 2023). This is especially true for mining, healthcare, military, oil and gas, pharmaceutical, petroleum, petrochemical, processing, rubber, and manufacturing industries. Table 1 lists examples of common unusual work schedules in the mining industry of different countries.

Deviations from conventional work schedules may cause effects in workers and generally these effects are determined by the mechanism of action of the chemical substance, as well as the duration and concentration of exposure to this substance (Laparé et al., 2003; Hartwig & MAK Commission, 2023). It is, therefore, important to adjust standard OELs to compensate for prolonged exposure during a longer work shift and shortened recovery time between shifts (Firth & Drolet, 2014). These modifications are made using a reduction factor (RF, i.e., adjustment factor) (Drolet, 2015). Adjusted OELs (OEL_A) ensure an equivalent degree of protection for workers with unusual work schedules as for workers who have a conventional schedule of 8 h per day, 5 days a week (Armstrong et al., 2005; Brodeur et al., 2001). It ensures that the maximum body burden for workers of unusual shifts does not exceed that of a worker who has a conventional schedule (Brodeur et al., 2001).

Therefore, several mathematical models (‘equations’) have been developed to calculate RFs used to modify OELs. Adjusted OELs are determined by multiplying the standard 8-hour exposure limit with the RF (Hartwig & MAK Commission, 2023). The RF predicts the highest allowable concentration in an unusual exposure situation which will not

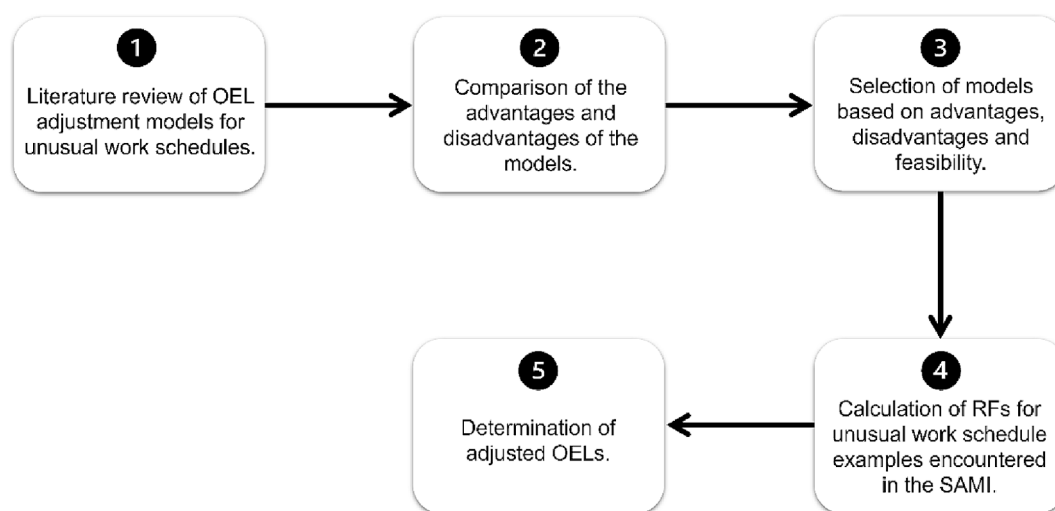


Fig. 1. Methodology followed. OELs: Occupational Exposure Limits; RF: reduction factor; SAMI: South African Mining Industry.

result in a higher-than-normal body accumulation of the inhaled chemical substance (Hickey & Reist, 1977). However, it is important to note that only TWAs are subject to the adjustment principle (Drolet, 2015). STELs and ceiling concentrations are not adjusted (Drolet, 2015; AIOH, 2016). Adjustments to TWA concentrations also only apply to nominal work schedules—a work schedule based on the agreement between the employer and worker without including overtime and occasional replacement work (Firth & Drolet, 2014; Drolet, 2015). Moreover, workers cannot be exposed to higher concentrations compared to standard OELs. Therefore, adjusted average exposure concentrations can never be higher than the TWAs (Drolet, 2015).

Despite the availability of different adjustment models, there is currently no clear legislation on how OELs should be adjusted for unusual work schedules in South Africa. This is concerning since standard OELs used in the SAMI do not necessarily provide adequate worker protection. The aim of this paper was therefore to revisit different mathematical models that are available to adjust OELs for unusual work schedules. Based on this, the authors propose RFs that can be implemented for unusual work schedules and priority chemicals encountered in the South African Mining Industry (SAMI). The objectives of this study included (i) identifying and reviewing available mathematical models to adjust OELs for unusual work schedules, (ii) providing a summary of the advantages and disadvantages of each model, (iii) applying the selected models to examples of unusual work schedules in the SAMI to obtain RFs, and (iv) calculating the OEL_A for 15 chemical substances of interest. Therefore, this work is novel since it applied for the first time OEL adjustment models to examples of real-life unusual work schedules and priority chemicals encountered in the SAMI. The resulting OEL_A were evaluated, and recommendations made on the most suitable methods to use in the SAMI to ensure worker protection.

2. Methods

Fig. 1 provides an overview of the approach followed in this study. A comprehensive literature review was conducted between July and October of 2023 by searching for relevant publications in several scientific databases including EBSCOhost; Google Scholar; JSTOR; ResearchGate; ScienceDirect; Scopus; and WorldCat Discovery. A combination of the following search terms was used: “adjustment factor”, “compressed”, “extended”, “reduction factor”, “unique”, “unusual”, “work schedule”, “work shift” and “work week”. These terms were used to search within the title, abstract, keywords, and main text of articles. Book chapters, mini-reviews, review articles, research articles (journal articles and conference proceedings), and short communications were

all included in the search. Only publications in English were included, while there was no exclusion criterion regarding publication year.

The selected publications were reviewed, and the advantages and disadvantages of the different adjustment models were compared. Based on this, as well as the practicality and ease of use of the mathematical equations, models were selected to be applied to examples of unusual work schedules and 15 priority chemicals encountered in the SAMI.

Verma (2000) used a similar approach, but the OEL adjustment models were applied to unusual work schedules encountered in three different industries namely, mining, smelting and forestry. Here the focus is on the mining industry within the South African context and the work schedule examples used in the current paper differ from those of Verma (2000). Furthermore, although Verma (2000) used adjustment models to calculate the RFs of 34 chemical substances, more than a third of the chemicals in the current study were not reported on by Verma (2000) including coal dust, hydrogen sulphide (H_2S), particles not otherwise classified (PNOC, total dust), titanium dioxide (TiO_2), vanadium pentoxide (V_2O_5) and wood dust (hard-and softwood). Lastly, this article also considers the Mason and Dershin, Iuliucci, Maximum Adjustment Half-Life (MAHL) and physiologically based pharmacokinetic (PBPK) models which were not reported on by Verma (2000).

In this study, the three unusual work schedule examples within the SAMI were as follows:

Work schedule 1 (WS1):

A work schedule during which miners work an 8-hour shift in a 24-hour period. During this schedule, the mine workers work 7 consecutive day shifts followed by 7 rest days for a 4-week cycle.

Week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1	D	D	D	D	D	D	D
2	R	R	R	R	R	R	R
3	D	D	D	D	D	D	D
4	R	R	R	R	R	R	R

D: day shift; R: rest day.

Work schedule 2 (WS2):

A work schedule during which miners work an 11.5-hour shift in a 24-hour period. During this schedule, the mine workers follow a cycle consisting of 4 day shifts, 4 rest days, 4 night shifts and 4 rest days.

Week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1	D	D	D	D	R	R	R
2	R	N	N	N	N	R	R
3	R	R	D	D	D	D	R
4	R	R	R				

Table 2
Priority chemical substances identified in the South African Mining Industry.

Nr	Chemical substance	Chemical formula	CAS number	OEL _{8-hour}	Unit
1	Arsenic (metal, organic and inorganic compounds)	As	7440-38-2	0.01	mg/m ³
2	Benzene	C ₆ H ₆	71-43-2	1.00	ppm
3	Cobalt (elemental and inorganic compounds)	Co	7440-48-4	0.05	mg/m ³
4	Carbon monoxide	CO	630-08-0	30.00	ppm
5	Coal dust*	—	—	2.00	mg/m ³
6	Hexavalent chromium compounds	Cr(VI)	7440-47-3	0.05	mg/m ³
7	Iron oxide (dust and fumes; as Fe)	Fe ₂ O ₃	1309-37-1	5.00	mg/m ³
8	Hydrogen sulphide	H ₂ S	7783-06-4	10.00	mg/m ³
9	Ammonia	NH ₃	7664-41-7	25.00	ppm
10	Lead (elemental and inorganic compounds)	Pb	7439-92-1	0.10	mg/m ³
11	PNOC (total dust)	—	—	10.00	mg/m ³
	Inhalable			3.00	
	Respirable				
12	Silicon dioxide (crystalline silica)*	SiO ₂ *		0.10	mg/m ³
	Cristobalite		14464-46-1		
	Quartz		14808-60-7		
	Tridymite		15468-32-3		
	Tripoli		1317-95-9		
13	Titanium dioxide	TiO ₂	13463-67-7	10.00	mg/m ³
	Inhalable			5.00	
	Respirable				
14	Vanadium pentoxide	V ₂ O ₅	1314-62-1	0.50	mg/m ³
	Inhalable particulate			0.05	
	Fumes and respirable particulate				
15	Wood dust	—	—		mg/m ³
	Softwood			5.00	
	Hardwood			1.00	

Reported Occupational Exposure Limits (OELs) are for inhalable particulates unless indicated otherwise. *respirable; OEL_{8-hour}: 8-hour OEL concentration; CAS: Chemical Abstracts Service; PNOC: particles not otherwise classified.

D: day shift; N: night shift; R: rest day.

Work schedule 3 (WS3):

A work schedule during which miners work a 12-hour shift in a 24-hour period. During this schedule, the mine workers follow a cycle

consisting of 4 day shifts, 3 rest days, 3 day shifts, and 4 rest days for 4 weeks.

Week	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
1	D	D	D	D	R	R	R
2	D	D	D	R	R	R	R
3	D	D	D	D	R	R	R
4	D	D	D	R	R	R	R

D: day shift; R: rest day.

Based on a report by the [Mine Health and Safety Council \(MHSC\) \(2021\)](#), 15 priority chemical substances commonly encountered in the SAMI were identified. [Table 2](#) lists these chemical substances, as well as their chemical formulas, CAS numbers and 8-hour OEL concentrations (OEL_{8-hour}) according to the Occupational Exposure Limits for Airborne Pollutants ([Department of Minerals and Energy, 2006](#)) in Schedule 22.9 of the MHSA (Act No. 29 of 1996) ([Department of Mineral Resources, 1996](#)).

After the RFs were calculated, the OEL_A were determined according to Eq. (1):

$$OEL_A = OEL_{8-hour} \times RF \quad (1)$$

Where OEL_A = adjusted OEL; OEL_{8-hour} = standard 8-hour OEL; and RF = reduction factor.

3. Results and discussion

3.1. Models for OEL adjustments

Since the early 1970s, there have been concerns regarding the protection of workers exposed to chemical substances during work shifts. This has led to several efforts to develop mathematical models that can be used to adjust OELs for unusual work schedules. The aim of these adjustment models is to protect workers with unusual work schedules to an equivalent degree compared to workers with conventional schedules of 8 h per day for 5 days a week ([Armstrong et al., 2005](#); [Brodeur et al., 2001](#)). Based on an extensive literature review, a total of nine adjustment models were identified ([Fig. 2](#)). Although these models apply different approaches such as accounting for extended work hours and increased periods of exposure, the inclusion of uptake and excretion rates, biological half-lives, and current toxicological knowledge ([AIOH, 2016](#)), the models can be classified into two categories: (i) general formula models and (ii) pharmacokinetic-based models ([Verma, 2000](#)). General formula models include the Brief and Scala, Iuliucci, Occupational Safety and Health Administration (OSHA) and Québec models, while the Mason and Dershin, Hickey and Reist, Roach, MAHL and

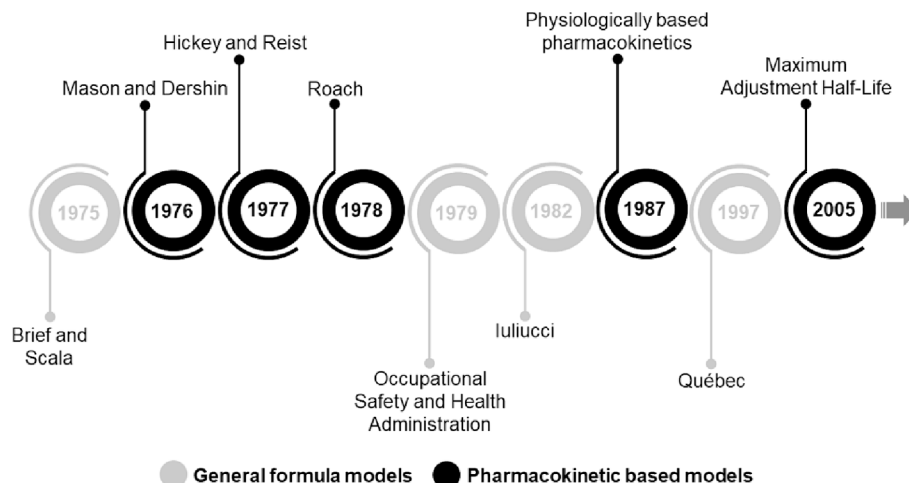


Fig. 2. A timeline indicating the development of Occupational Exposure Limit adjustment models for unusual work schedules.

Table 3

Mathematical equations to calculate the reduction factor (RF) for the different Occupational Exposure Limit adjustment models.

Nr	Model	Equation
<i>General formula models</i>		
1	Brief and Scala	$RF_d = \frac{8}{h_d} x \frac{24 - h_d}{16}$ $RF_w = \frac{40}{h_w} x \frac{168 - h_w}{128}$
2	Iuliucci	$RF = \frac{8h_{worked}}{12h_{worked}} x \frac{12h_{recovery}}{16h_{recovery}} x \frac{4dayworkweek}{5dayworkweek}$
3	OSHA	$RF_d = \frac{8}{h_d}$
4	Québec	$RF_w = \frac{40}{h_w}$
<i>Pharmacokinetic-based models</i>		
5	Mason and Dershin	—
6	Hickey and Reist	$k = \frac{(\ln 2)}{T_1}$ $RF = \frac{(1 - e^{-kt_{1s}})(1 - e^{-k(t_{1s}+t_{2s})^n})(1 - e^{-kT_s})(1 - e^{-k(t_{1s}+t_{2s})})}{(1 - e^{-kt_{1s}})(1 - e^{-k(t_{1s}+t_{2s})^m})(1 - e^{-kT_s})(1 - e^{-k(t_{1s}+t_{2s})})}$
7	Roach	$a = \frac{\log_e 2}{T_1}$ $RF = \frac{(1 - e^{-8a})(1 - e^{-120a})(1 - e^{-la})}{(1 - e^{-24a})(1 - e^{-168a})(1 - e^{-Ma}) \sum e^{-Na}}$
8	MAHL	No general equation is available since mathematical calculation software developed by the McMaster University Occupational & Environmental Health Laboratory (OEHL) in Ontario, Canada is used to calculate the RF.
9	PBPK	No general equation, since PBPK models are specifically developed for individual substances.

—:not available; e: Euler's Number (i.e., mathematical constant, 2.718); h_d : hours worked per day (shift); h_w : hours worked per week (full roster cycle/consecutive workdays); k: biological elimination rate; l: total number of hours for a complete work cycle; m: number of “work” days per “work” week in the extended work schedule; N: number of hours' duration of the work shift; MAHL: Maximum Adjustment Half-Life; n: number of workdays in a standard workweek (i.e., 5 days); N : number of hours from a prior work shift end to the shift end in question; OSHA: Occupational Safety and Health Administration; PBPK: physiologically based pharmacokinetic. RF: reduction factor; RF_d : daily reduction factor; RF_w : weekly reduction factor; $T_{1/2}$: biological half-life; t_{1s} : length of a standard workday (i.e., 8 h); t_{2s} : length of the standard recovery period (i.e., 16 h); $t_{1n} + t_{2n}$: length of a standard day (i.e., 24 h); t_n : length of a standard week (i.e., 168 h); t_{1s} : length of the extended shift workday (in hours); t_{2s} : length of the recovery period between extended shift workdays (in hours); $t_{1s} + t_{2s}$: length of the extended shift “day” (usually, but not always 24 h); t_s : total length of the periodic work cycle (number of days worked and number of recovery days; in hours).

physiologically based pharmacokinetic models (PBPK) are pharmacokinetic-based models (Verma, 2000). Based on the literature reviewed, a detailed description of the different OEL adjustment models can be found in Appendix A. The mathematical equations to calculate the RF for the different adjustment models are shown in Table 3. In addition, the assumptions, advantages, and disadvantages of the models are summarised in Table 4.

3.2. Consideration of models

Although some countries have adopted the Québec model for the adjustment of OELs for unusual work schedules there is no global consensus on which model to use. This is due to several contributing factors. Exposure limits differ between countries and consequently,

there is no universal consensus on adjustment models for unusual work shifts. Most adjustment models are developed for individual chemical substances and cannot be applied to mixtures (AIOH, 2016). The adjustment formulae are generally based on American experiences where annual leave is two or three weeks in duration compared to Australia and some European countries where annual leave is much longer—particularly for shift workers. In addition, the number of public holidays and periods of long service leave is also not the same between countries. There are also differences in how monitoring results are communicated to workers (AIOH, 2016). However, despite this certain “rules of thumb” for adjusting OELs for unusual work schedules were proposed by Paustenbach (2011) which should always be considered regardless of the type of model used:

Table 4

A summary of the advantages and disadvantages of the nine OEL adjustment models identified.

Nr	Model	Year	Type	Assumptions	Advantages	Disadvantages
1	Brief and Scala	1975	General formula	Haber's law – Toxicity is a function of concentration and time. A toxic effect produced by a chemical substance is proportional to the duration and concentration of exposure to this substance.	Takes prolonged exposure time (increased uptake due to longer work exposure) and shortened recovery time (decreased clearance during the shorter time away from work and exposure) into account. Does not require knowledge of a chemical substance's biological half-life and mechanism of action. The most conservative model since it recommends using the most stringent RF. Easy to use.	Does not consider the toxicological action of a chemical substance within the body. Since the model does not consider pharmacokinetics (e.g., biological uptake and excretion rate of a chemical substance) the results are not comparable to PBPK models. The RF for a certain number of worked hours is the same for all chemical substances regardless of their biological half-lives. Identical RFs may lead to an overestimation of the degree to which the OEL should be lowered. Not applicable for work schedules with less than 7–8 h per day or less than 40 h per week; work schedules that exceed 7 consecutive workdays; or those that involve 24-hour continuous exposure (e.g., in submarines and space shuttles). Off-duty periods are not taken into consideration.
2	Iuliucci	1982			The number of hours worked each day and number of days worked each week are accounted for.	Only applicable to a specific work schedule of 12 h per day for 4 days per week.
3	OSHA	1979			The increased uptake due to increased work shift hours is accounted for. Incorporates some pharmacokinetic components (e.g., primary health effects). Describes adjustment categories for specific chemical substances. Available for almost all chemical substances for which there are OELs. Easy to use.	Does not acknowledge the shorter recovery period. Does not consider the biological uptake and excretion of chemical substances, or pharmacokinetics (e.g., biological half-life). Restricts the daily dose or weekly dose, during an unusual work shift or week to the same dose as that obtained during a standard 8-hour shift or 40-hour week. Daily or weekly off-periods are not accounted for. Not as conservative compared to the Brief and Scala model.
4	Québec	1997			Reflects current toxicological data. Incorporates some pharmacokinetic components (e.g., primary health effects). Describes adjustment categories for specific chemical substances. Available for almost all chemical substances for which there are OELs. Results are closer to that of PBPK models. Computer-based and easy to use. Supported by a comprehensive technical guide with a downloadable selection tool for determining the most appropriate adjustment categories.	Does not consider the biological uptake and excretion of chemical substances, or pharmacokinetics (e.g., biological half-life). Governed by a Regulation in Québec, therefore, caution must be exercised when it is used in countries outside of Canada.
5	Mason and Dershin	1976	Pharmacokinetic-based (one-compartment)	The intensity of a toxic effect is a function of the concentration of a toxic agent at the site of action.	Considers the pharmacokinetics of a chemical substance (e.g., biological half-life).	Requires many parameters to be known including absorption rate, distribution volume, and biological half-life of a chemical substance in the human body. However, this information is not always available for all chemical substances of concern.
6	Hickey and Reist	1977		The maximum body burden arising from a particular work schedule is a function of the biological half-life of the chemical substance.	Considers the characteristics of the exposed subject (e.g., alveolar ventilation). Ensures that the maximum body burden accrued for the "unusual" work routine does not exceed that accrued for a normal work shift.	Assumes that the effect of exposure is isolated to a single site within the body and that the body consequently acts as one homogenous compartment.
7	Roach	1978		The body is viewed as a single homogeneous box with a fixed volume. The effect of exposure is isolated to a single site within the body.	Can identify those exposure schedules where a reduction in the OEL is not necessary. From a toxicological point of view, the RFs are more realistic. More accurate compared to other models.	Involves complicated calculations that can be difficult to apply. Limited to simple and repetitive scenarios. Not applicable to chemical substances that exert their principal effect

(continued on next page)

Table 4 (continued)

Nr	Model	Year	Type	Assumptions	Advantages	Disadvantages
8	MAHL	2005			- Not substance-specific. - Only requires knowledge of the general mode of action and the work shift schedule. - Applies to work schedules longer than 7 days since it accounts for daily exposure, daily off periods, and off-duty periods between work schedules. - Can be applied using numeric optimisation tools.	- by sensitisation or irritation due to differences in kinetics. - Yields less conservative RFs. - Too cumbersome for hand calculation.
9	PBPK	1987	Pharmacokinetic-based (multi-compartment)	- Individual organs or tissue groups are arranged as compartments in precise anatomical configurations connected by the cardiovascular system. - The transfer of chemical substances between the different compartments is governed by actual blood flow rates and tissue:blood partition coefficients.	- Has a rigorous biological basis. - Takes physiological differences into account (e.g., body build and metabolic activity) - Can be used to propose OELs not only in blood but also in target tissues and other biological media, for example, fat and urine. - Allows greater flexibility for adjusting OELs for unusual work schedules. - Represents a tool for simulating and predicting the outcome of various exposure scenarios.	- Data-intensive since it requires many anatomical, physiological, biochemical, and physiochemical parameters to be known (e.g., blood-to-air and blood-to-tissue partition coefficients, rate of metabolism of the chemical substance, the biological half-life of the chemical substance or its metabolites, organ volumes, organ blood flow and ventilation in humans). This type of information is seldom known for humans and therefore the data is usually scaled from animal data. - Very specialized since these models are usually specifically developed for one chemical substance. - Not suitable for generalised adjustment applications of OELs for unusual work schedules. - Difficult to apply on a large scale.

MAHL: Maximum Adjustment Half-Life; OSHA: Occupational Safety and Health Administration; PBPK: physiologically based pharmacokinetic.

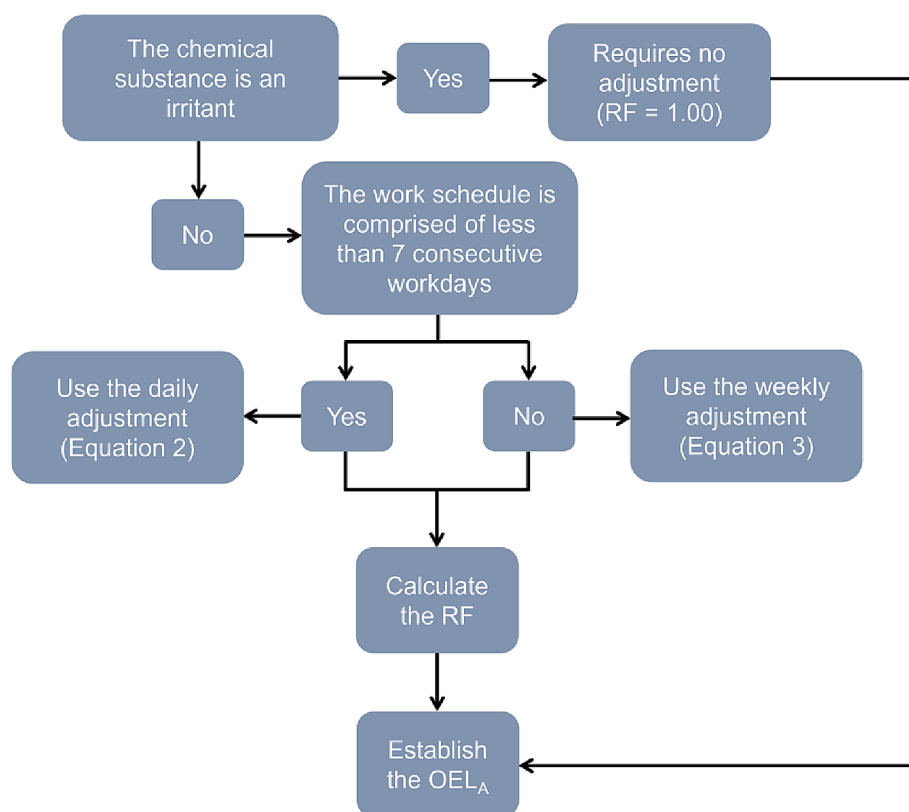


Fig. 3. Approach followed for the adjustment of Occupational Exposure Limits (OELs) according to the Brief and Scala model. RF: reduction factor; OEL_A: adjusted OEL.

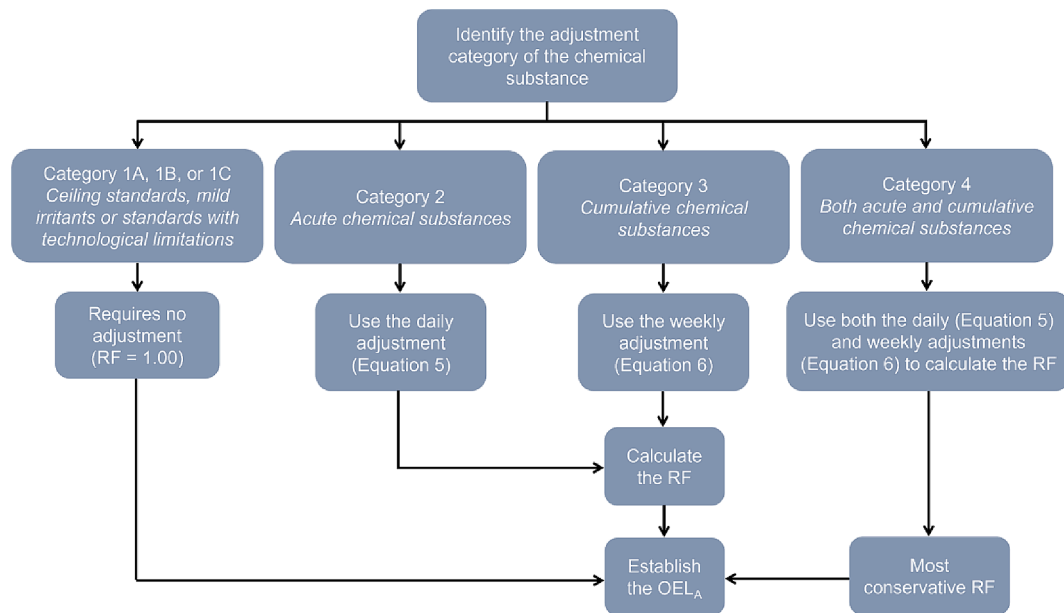


Fig. 4. Approach followed for the adjustment of Occupational Exposure Limits (OELs) according to the Occupational Safety and Health Administration (OSHA) and Québec models. RF: reduction factor; OEL_A: adjusted OEL.

Table 5

Reduction factors and adjusted Occupational Exposure Limits calculated for work schedule 1 (WS1) that consisted of 8 h per day for 7 consecutive workdays, followed by 7 rest days (a 4-week cycle).

Nr	Chemical substance	Chemical formula	OEL _g hour	Units	Brief and Scala model		OSHA model			Québec model		
					RF _{B&S}	OEL _A	Adjustment category	RF _{OSHA}	OEL _A	Adjustment category	RF _Q	OEL _A
1	Arsenic (metal, organic and inorganic compounds)	As	0.01	mg/m ³	0.63	0.006	3	0.71	0.007	3	0.71	0.007
2	Benzene	C ₆ H ₆	1.00	ppm	0.63	0.63	3	0.71	0.71	3	0.71	0.71
3	Cobalt (elemental and inorganic compounds)	Co	0.05	mg/m ³	0.63	0.03	3	0.71	0.04	3	0.71	0.04
4	Carbon monoxide	CO	30.00	ppm	0.63	18.75	4	0.71	21.43	4	0.71	21.43
5	Coal dust*	—	2.00	mg/m ³	0.63	1.25	3	0.71	1.43	3	0.71	1.43
6	Hexavalent chromium compounds	Cr(VI)	0.05	mg/m ³	0.63	0.03	3	0.71	0.04	3	0.71	0.04
7	Iron oxide (dust and fumes; as Fe)	Fe ₂ O ₃	5.00	mg/m ³	0.63	3.13	3	0.71	3.57	3	0.71	3.57
8	Hydrogen sulphide	H ₂ S	10.00	ppm	0.63	6.25	1C	1.00	10.00	1C	1.00	10.00
9	Ammonia	NH ₃	25.00	ppm	1.00	25.00	1B	1.00	25.00	1B	1.00	25.00
10	Lead (elemental and inorganic compounds)	Pb	0.10	mg/m ³	0.63	0.06	3	0.71	0.07	3	0.71	0.07
11	PNOC	—		mg/m ³	0.63		1C	1.00		1C	1.00	
	Inhalable		10.00			6.25			10.00			10.00
	Respirable		3.00			1.88			3.00			3.00
12	Silicon dioxide (crystalline silica)*	SiO ₂ *	0.10	mg/m ³	0.63	0.06	3	0.71	0.07	3	0.71	0.07
	Cristobalite											
	Quartz											
	Tridymite											
	Tripoli											
13	Titanium dioxide	TiO ₂		mg/m ³	0.63		1C	1.00		1C	1.00	
	Inhalable		10.00			6.25			10.00			10.00
	Respirable		5.00			3.13			5.00			5.00
14	Vanadium pentoxide	V ₂ O ₅		mg/m ³	0.63		1B	1.00		1B	1.00	
	Inhalable		0.50			0.31			0.50			0.50
	Fumes and respirable particulate		0.05			0.03			0.05			0.05
15	Wood dust	—		mg/m ³	0.63		3	0.71		3	0.71	
	Softwood		5.00			3.13			3.57			3.57
	Hardwood		1.00			0.63			0.71			0.71

Reported OELs are for inhalable particulates unless indicated otherwise. *respirable; OEL: Occupational Exposure Limit; OEL_A: adjusted OEL; OSHA: the Occupational Safety and Health Administration; PNOC: particles not otherwise classified (total dust); RF_{B&S}: reduction factor according to the Brief and Scala model; RF_{OSHA}: reduction factor according to the OSHA model; RF_Q: reduction factor according to the Québec model.

Table 6

Reduction factors and adjusted Occupational Exposure Limits calculated for work schedule 2 (WS2) that consisted of 11.5 h per day for a cycle of 4D 4R 4 N 4R.

Nr	Chemical substance	Chemical formula	OEL _g hour	Units	Brief and Scala model		OSHA model			Québec model		
					RF _{B&S}	OEL _A	Adjustment category	RF _{OSHA}	OEL _A	Adjustment category	RF _Q	OEL _A
1	Arsenic (metal, organic and inorganic compounds)	As	0.01	mg/m ³	0.54	0.005	3	0.87	0.009	3	0.87	0.009
2	Benzene	C ₆ H ₆	1.00	ppm	0.54	0.54	3	0.87	0.87	3	0.87	0.87
3	Cobalt (elemental and inorganic compounds)	Co	0.05	mg/m ³	0.54	0.03	3	0.87	0.04	3	0.87	0.04
4	Carbon monoxide	CO	30.00	ppm	0.54	16.30	4	0.70	20.87	4	0.70	20.87
5	Coal dust*	—	2.00	mg/m ³	0.54	1.09	3	0.87	1.74	3	0.87	1.74
6	Hexavalent chromium compounds	Cr(VI)	0.05	mg/m ³	0.54	0.03	3	0.87	0.04	3	0.87	0.04
7	Iron oxide (dust and fumes; as Fe)	Fe ₂ O ₃	5.00	mg/m ³	0.54	2.72	3	0.87	4.35	3	0.87	4.35
8	Hydrogen sulphide	H ₂ S	10.00	ppm	0.54	5.43	1C	1.00	10.00	1C	1.00	10.00
9	Ammonia	NH ₃	25.00	ppm	1.00	25.00	1B	1.00	25.00	1B	1.00	25.00
10	Lead (elemental and inorganic compounds)	Pb	0.10	mg/m ³	0.54	0.05	3	0.87	0.09	3	0.87	0.09
11	PNOC	—	10.00	mg/m ³	0.54	5.43	1C	1.00	10.00	1C	1.00	10.00
	Inhalable		3.00			1.63			3.00			3.00
12	Respirable											
	Silicon dioxide (crystalline silica)*	SiO ₂ *	0.10	mg/m ³	0.54	0.05	3	0.87	0.09	3	0.87	0.09
	Cristobalite											
	Quartz											
	Tridymite											
	Tripoli											
13	Titanium dioxide	TiO ₂	10.00	mg/m ³	0.54	5.43	1C	1.00	10.00	1C	1.00	10.00
	Inhalable		5.00			2.72			5.00			5.00
	Respirable											
14	Vanadium pentoxide	V ₂ O ₅	0.50	mg/m ³	0.54	0.27	1B	1.00	0.50	1B	1.00	0.50
	Fumes and respirable particulate		0.05			0.03			0.05			0.05
15	Wood dust	—	5.00	mg/m ³	0.54	2.72	3	0.87	4.35	3	0.87	4.35
	Softwood		1.00			0.54			0.87			0.87
	Hardwood											

Reported OELs are for inhalable particulates unless indicated otherwise. *respirable; D: day shift; N: night shift; OEL: Occupational Exposure Limit; OEL_A: adjusted OEL; OSHA: the Occupational Safety and Health Administration; PNOC: particles not otherwise classified (total dust); R: rest day; RF_{B&S}: reduction factor according to the Brief and Scala model; RF_{OSHA}: reduction factor according to the OSHA model; RF_Q: reduction factor according to the Québec model.

- Where the goal of the OEL is to minimise the likelihood of a systemic effect, the concentration of the chemical substance to which persons can be exposed should be less than the OEL if they work more than 8 h per day or more than 40 h per week, and the substance has a half-life between 4 and 400 h.
- Where the goal of the OEL is to avoid excessive irritation or odour, there is no modification required to protect persons working unusual shifts.
- Adjustments to OELs are not generally necessary for unusual work shifts if the biological half-life of the chemical substance is less than 3 h or greater than 400 h.
- The biological half-life of a chemical in humans can often be estimated by extrapolation from animal data.
- The four most widely accepted approaches to modifying exposure limits will recommend RFs that will vary. In order of conservatism, the Brief and Scala (1977) model will recommend the lowest limit and the pharmacokinetic models the highest.
- Whenever the biological half-life is unknown, a “safe” level can be estimated by assuming that the chemical has a biological half-life of about 20 h. This will generally yield the most conservative RF for typical 8-, 10-, 12- and 14-hour workdays.
- Where shorter exposure periods or shifts exist, exposure adjustment models should not be used to justify higher exposures or exposure limits.

3.3. Application of models to unusual work schedules in the South African Mining Industry

After consideration of the advantages, disadvantages and practicality of the nine OEL adjustment models identified in the literature, only three models were selected to be applied to usual work schedules and priority chemical substances encountered in the SAMI. These were three general formula models: the Brief and Scala, OSHA and Québec models. Although the Iuliucci model is also a general formula model, it is only applicable to a specific work schedule described by Iuliucci (12 h per day, and 4 days per week). The Iuliucci model can, therefore, not be applied to other work schedules, such as the three work schedules examples (WS1–WS3) described in the *Methods* section. Although pharmacokinetic-based models are considered more accurate compared to general formula models, the biological parameters required to apply these models in South Africa were not available for the 15 chemicals of interest in the current study. Figs. 3 and 4 show the approaches followed to calculate the RFs and OEL_A based on the Brief and Scala (RF_{B&S}), and OSHA (RF_{OSHA}) and Québec (RF_Q) models, respectively.

The calculated RFs and OEL_A based on the selected adjustment models for WS1, WS2 and WS3 are listed in Tables 5–7. WS1 consisted of 8 h per day for 7 consecutive workdays, followed by 7 rest days, WS2 was for 11.5 h per day following a cycle of 4D 4R 4 N 4R, and WS3 entailed 12 h per day for a cycle of 4D 3R 3D 4R. For each of the unusual work schedule examples (WS1–3), the RF_{B&S} was the same for the majority of the different chemical substances since the Brief and Scala model does not consider any pharmacokinetic parameters such as

Table 7

Reduction factors and adjusted Occupational Exposure Limits calculated for work schedule 3 (WS3) that consisted of 12 h per day for a cycle of 4D 3R 3D 4R (a 4-week cycle).

Nr	Chemical substance	Chemical formula	OEL _{8-h} hour	Units	Brief and Scala model		OSHA model			Québec model		
					RF _{B&S}	OEL _A	Adjustment category	RF _{OSHA}	OEL _A	Adjustment category	RF _Q	OEL _A
1	Arsenic (metal, organic and inorganic compounds)	As	0.01	mg/m ³	0.50	0.005	3	0.83	0.008	3	0.83	0.008
2	Benzene	C ₆ H ₆	1.00	ppm	0.50	0.50	3	0.83	0.83	3	0.83	0.83
3	Cobalt (elemental and inorganic compounds)	Co	0.05	mg/m ³	0.50	0.03	3	0.83	0.04	3	0.83	0.04
4	Carbon monoxide	CO	30.00	ppm	0.50	15.00	4	0.67	20.00	4	0.67	20.00
5	Coal dust*	—	2.00	mg/m ³	0.50	1.00	3	0.83	1.67	3	0.83	1.67
6	Hexavalent chromium compounds	Cr(VI)	0.05	mg/m ³	0.50	0.03	3	0.83	0.04	3	0.83	0.04
7	Iron oxide (dust and fumes; as Fe)	Fe ₂ O ₃	5.00	mg/m ³	0.50	2.50	3	0.83	4.17	3	0.83	4.17
8	Hydrogen sulphide	H ₂ S	10.00	ppm	0.50	5.00	1C	1.00	10.00	1C	1.00	10.00
9	Ammonia	NH ₃	25.00	ppm	1.00	25.00	1B	1.00	25.00	1B	1.00	25.00
10	Lead (elemental and inorganic compounds)	Pb	0.10	mg/m ³	0.50	0.05	3	0.83	0.08	3	0.83	0.08
11	PNOC	—		mg/m ³	0.50		1C	1.00		1C	1.00	
	Inhalable		10.00	mg/m ³		5.00			10.00			10.00
	Respirable		3.00			1.50			3.00			3.00
12	Silicon dioxide (crystalline silica)*	SiO ₂ *	0.10	mg/m ³	0.50	0.05	3	0.83	0.08	3	0.83	0.08
	Cristobalite											
	Quartz											
	Tridymite											
	Tripoli											
13	Titanium dioxide	TiO ₂		mg/m ³	0.50		1C	1.00		1C	1.00	
	Inhalable		10.00			5.00			10.00			10.00
	Respirable		5.00			2.50			5.00			5.00
14	Vanadium pentoxide	V ₂ O ₅		mg/m ³	0.50		1B	1.00		1B	1.00	
	Inhalable		0.50			0.25			0.50			0.50
	Fumes and respirable particulate		0.05			0.03			0.05			0.05
15	Wood dust	—		mg/m ³	0.50		3	0.83		3	0.83	
	Softwood		5.00			2.50			4.17			4.17
	Hardwood		1.00			0.50			0.83			0.83

Reported OELs are for inhalable particulates unless indicated otherwise. *respirable; D: day shift; OEL: Occupational Exposure Limit; OEL_A: adjusted OEL; OSHA: the Occupational Safety and Health Administration; PNOC: particles not otherwise classified (total dust); R: rest day; RF_{B&S}: reduction factor according to the Brief and Scala model; RF_{OSHA}: reduction factor according to the OSHA model; RF_Q: reduction factor according to the Québec model.

biological half-life. The uniform RF_{B&S} were 0.63, 0.54 and 0.50 for WS1 (Table 5), WS2 (Table 6) and WS3 (Table 7), respectively. The only exception in all three work schedule examples was for NH₃ which is classified as an irritant and required no adjustment. Therefore, the RF_{B&S} for NH₃ in WS1–WS3 was 1.00.

As expected, the RF_{OSHA} and RF_Q were the same for the 15 different chemical substances of individual work schedule example (Tables 5–7). This is because the chemical substances included in the present study have the same adjustment categories in both the OSHA and Québec models because the one model is based on the other (Verma, 2000). However, there are exceptions. For example, according to the OSHA model, LPG is grouped in Category 2 (Paustenbach, 2011), while the same substance is classified as Category 1C in the Québec model (Drolet, 2015). In contrast, to the Brief and Scala model, the OSHA and Québec models yielded different RFs for different chemical substances based on their adjustment categories. All Category 1 (A, B or C) chemical substances, which included NH₃ (1B), H₂S (1C), PNOC (1C), TiO₂ (1C) and V₂O₅ (1B), did not require any adjustment and consequently, the RF_{OSHA} and RF_Q were 1.00 across all three the work schedule examples (Table 5–7). None of the chemical substances in the present study were in Category 2. Rather, the majority of the substances including As, benzene, Co, coal dust, Cr(VI), Fe₂O₃, Pb, and SiO₂, were in Category 3 and required a weekly adjustment (Eq. 6). The RF_{OSHA} and RF_Q for these Category 3 chemical substances were 0.71, 0.87, and 0.83 for WS1 (Table 5), WS2 (Table 6) and WS3 (Table 7), respectively. Only one chemical substance, CO, was in Category 4. As per the OSHA and Québec

model guidelines, both the daily (Eq. 5) and weekly (Eq. 6) adjustments were calculated and the most conservative (i.e., lowest) RF was applied to provide the greatest worker protection. Based on this, the RF_{OSHA} and RF_Q for CO were 0.71 (WS1; Table 5), 0.70 (WS2; Table 6) and 0.67 (WS3; Table 7).

According to the “rules of thumb” stipulated by Paustenbach (2011), all the OEL_A were either equal to or lower than the standard OEL_{8-hour} (Tables 5–7). This means that adjusting the OELs currently used in the SAMI according to the proposed models will ensure an equivalent degree of protection for workers working unusual shifts compared to those works that have conventional work schedules of 8 h per day for 5 days a week or 40 h per week. Overall, the RFs calculated in the present study ranged from 0.54 to 1.00. These findings are in agreement with previous literature. Both Verma (2000) and Brodeur et al. (2001) reported RFs in the range of 0.50–1.00 for unusual work schedules examples. Verma (2000) evaluated unusual work schedule examples of (i) three 12-hours work shifts per week, followed by four 12-hours work shifts per week and (ii) four 10-hour work shifts per week, while Brodeur et al. (2001) calculated the RFs that would apply for work shifts ranging from 8 to 16 h per day and/or 40–60 h per week.

The approach followed in this study is also in line with a recent publication by Hartwig and the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (MAK Commission) (2023) that addressed the reduction of MAK values for extended work shifts in Germany. The authors proposed that linear concentration–time extrapolation should be used for substances

that cause systemic effects but with an unknown mechanism of action and half-life, while worst-case considerations are recommended for substances that act systemically and have a known mechanism of action and biological half-life (Hartwig & MAK Commission, 2023). Since the biological half-life of the 15 chemicals substances of the current study is unknown, the authors employed the Brief and Scala, OSHA, and Québec models. All three are linear models based on the assumption that toxicity is a function of concentration and time (Laparé et al., 2003). Hartwig and the MAK Commission (2023) concluded that for practical reasons linear concentration–time extrapolation is sufficient to prevent toxicity after prolonged exposure during unusual work schedules regardless of the substance's mechanism of action.

Lastly, three of the 15 chemicals investigated in this study are classified as Group (1) human carcinogens, including silica in the form of respirable crystalline silica (RCS), hexavalent chromium (Cr(VI)) compounds, and wood dust (IARC, 2012). Carcinogens are divided into two categories namely threshold and non-threshold carcinogens. The former has a level below which no carcinogenic effect is expected, while the latter hold the risk of cancer regardless of the level of exposure (Bevan and Harrison, 2017; Nohmi, 2018). In general, non-genotoxic carcinogenic chemicals are assumed to have a threshold, while genotoxic carcinogenic chemicals are assumed to not have a threshold (Nohmi, 2018). Based on this, RCS is considered a threshold carcinogen (Bevan and Harrison, 2017), while Cr(VI) compounds and wood dust are non-threshold carcinogens (Högberg & Järnberg, 2023). With non-threshold carcinogens, there is always a risk of developing cancer following exposure. However, if workers are exposed to lower concentrations of non-threshold carcinogenic chemical substances, they may have a lower risk of developing cancer. Therefore, an adjustment that will lower the OEL of carcinogens to which workers may be exposed is better than no adjustment. Therefore, it is still important to apply RFs to the OELs of carcinogens. The calculated RFs for all three unusual work schedule examples and models (Brief and Scala, OSHA and Québec) yielded more stringent OELs for the carcinogenic chemicals compared to the OEL_{8-hour} (Tables 5–7). The authors believe that these adjustments will ensure that workers are protected against carcinogenic chemicals as much as is practically feasible. This is also supported by Mutti (2023) who stated that zero risk for genotoxic carcinogens (i.e., non-threshold) is unlikely, therefore, keeping the risk as low as practically possible is the only realistic and achievable goal.

4. Conclusion

Adjusted OELs are necessary to ensure the health of workers exposed to airborne concentrations of chemical substances during unusual work schedules. Although there are different mathematical models available to calculate RFs, they can either be simple linear formulas or more complex pharmacokinetic-based models. After consideration of the advantages, disadvantages and practicality of the models, the Brief and Scala, OSHA and Québec models were selected to be applied to real-life examples of unusual work schedules found in the SAMI. The RF_{B&S}, RF_{OSHA} and RF_Q were subsequently used to calculate the OEL_A of 15 priority chemicals.

The Brief and Scala model (1975) was very simple to use and yielded the most conservative RFs that would provide the greatest worker protection. However, as in the case of the other general formula-based models the Brief and Scala model does not take the biological half-life of a chemical substance into account. Due to this, RF_{B&S} may

overestimate the degree to which the OELs should be lowered. On the other hand, although the OSHA and Québec models also do not account for a chemical substance's biological half-life, these models incorporate some pharmacokinetic components such as the primary adverse health effects of a substance.

In terms of toxicological relevance, pharmacokinetic-based models generate the most realistic RFs since they consider a substance's biological half-life. However, classic pharmacokinetic-based models such as those described by Mason and Dershin, Hickey and Reist, and Roach are limited by their assumption that the human body is one homogenous compartment. Moreover, multi-compartmental models such as PBPK models are data-intensive since they take physiological differences into account. Unfortunately, PBPK models are very specialised and often not suitable for generalised OEL adjustments. Moreover, the anatomical, physiological, biochemical, and physiochemical parameters required for pharmacokinetic based models are not available for many chemical substances encountered in the SAMI and therefore the use of such is not feasible. Since there is currently no clear legislation on how OELs should be adjusted for unusual work schedules in South Africa and no global consensus exists on which model to use, it is recommended that the OSHA or Québec model be used for OEL adjustments. Chemical substances listed in the MHSA (1996) should be compared with OSHA's classification of chemicals by primary adverse health effects and the Canadian Regulation Respecting Occupational Health and Safety (RROHS) document. The adjustment categories should be reviewed and modified if necessary, according to South Africa legislation. The authors are of the opinion that OELs adjusted in the manner described in this paper will improve the protection of workers with unusual work schedules in the SAMI.

Unfortunately, this study did have some limitations. The adjustment of OELs for workers who work overtime was not taken into consideration. In addition, the authors did not consider exposure to a mixture of chemicals. In the mining industry workers are exposed to multiple chemical hazards simultaneously which may cause additive, combined or synergistic effects depending on the primary adverse effects of the individual chemical substances. However, despite these limitations, this paper still contributes to the understanding of OEL adjustments for unusual work schedules in the mining industry.

CRedit authorship contribution statement

Ilzé Engelbrecht: Writing – review & editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Suranie Horn:** Writing – review & editing, Supervision, Conceptualization. **Cas J. Badenhorst:** Conceptualization. **Johan L. du Plessis:** Writing – review & editing, Supervision, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix

Appendix A. – Supplementary results

A.1 General formula models

General formula models are mostly derived from Haber's law which is based on the postulate that toxicity is a function of concentration and time (Eq. (A1)) (Brodeur et al., 2001):

$$k_e = \text{Concentration} \times \text{time} \quad (\text{A1})$$

Where k_e = a constant toxic effect.

This means that a toxic effect produced by a chemical substance is proportional to the duration and concentration of exposure to this substance (Laparé et al., 2003). However, outside a specific range, or for other chemical substances and conditions, the rule may not hold. Haber's law is only applicable to systemic toxicants and does not apply to irritants, sensitizers or carcinogens. Examples of OEL adjustment models based on Haber's law include the Brief and Scala, Iuliucci, OSHA and Québec models.

a) Brief and Scala model

Brief and Scala (1975) were the first to propose adjustments to OELs for unusual work schedules. The authors (1975) emphasised that unless worker exposure to some systemic toxicants was lowered, the daily dose would be greater, and due to the lesser time for recovery between exposures, peak tissue levels might be higher during unusual shifts than during normal shifts. For example, in a 12-hour workday, the period of exposure to chemical substances is 50 % higher than in an 8-hour workday, and the period of recovery between exposures is shortened by 25 % from 16 to 12 h (Paustenbach, 2011). This implies that repeated exposure during longer workdays might, in some cases, stress the detoxication mechanisms to a point that accumulation of a chemical substance might occur in target tissues, and that alternate pathways of metabolism might be initiated (Paustenbach, 2011). Consequently, there is uncertainty about the effects of exposure to chemical substances (Brief & Scala, 1975).

The Brief and Scala model considers the impact of the number of increased hours worked and the recovery time between exposure periods. In this model, daily- or weekly-based equations are used to determine RFs that are applied to the TWA exposure standard (Brief & Scala, 1975). Based on the work schedule, either the daily or weekly RF is calculated. When a worker worked less than 7 days in a row, the daily adjustment (Eq. (A2)) is used, while when a worker worked 8 h per day, 7 days per week the weekly adjustment (Eq. (A3)) is used. However, it is recommended that both the daily and weekly reduction factors be calculated, and the most stringent value should be considered for use.

Adjustment for daily or short-term exposure (Eq. A(2)):

$$RF_d = \frac{8}{h_d} \times \frac{24 - h_d}{16} \quad (\text{A2})$$

Where RF_d = daily reduction factor; h = hours worked per day (shift); 24 = number of hours in one day; and 16 = total exposure-free hours per day (for a standard workday).

Adjustment for weekly or long-term exposure (Eq. (A3)):

$$RF_w = \frac{40}{h_w} \times \frac{168 - h_w}{128} \quad (\text{A3})$$

Where RF_w = weekly reduction factor; h = hours worked per week (full roster cycle/consecutive workdays); 168 = number of hours in one week (7 days); and 128 = total exposure-free hours per week (for a standard 7-day week).

b) Iuliucci model

The Iuliucci model is similar to that of Brief and Scala. It takes the number of hours worked each day and number of days worked each week into account (Paustenbach, 2011). However, the model is only applicable to a specific work schedule described by Iuliucci (12 h per day, and 4 days per week) (Eq. (A4)):

$$RF = \frac{8 \text{ h worked}}{12 \text{ h worked}} \times \frac{12 \text{ h recovery}}{16 \text{ h recovery}} \times \frac{4 \text{ day work week}}{5 \text{ day work week}} \quad (\text{A4})$$

Where RF = reduction factor.

c) OSHA Model

As the name implies, this model was developed by OSHA. It is an empirical method based on observation rather than theory. Since the OSHA Model is based on Haber's Law, the model assumes that the magnitude of the toxic response of the chemical substance correlates to the concentration reaching the site of action of the agent (Brodeur et al., 2001; Laparé et al., 2003). It is designed to be applied to systemic toxic substances. Although the OSHA model is not a pharmacokinetic model it does incorporate some pharmacokinetic components by assigning health code numbers to chemical substances based on their primary health effects (Brodeur et al., 2001; Paustenbach, 2011). These health code numbers are then categorised into adjustment categories (Verma, 2000; Paustenbach, 2011). The categories are based on the primary type of health effects to be prevented, the biological half-life (if known), and the rationale for the limit of the chemical substance (Verma, 2000). Four categories are used to determine if any adjustment to the OEL is required, and if so, what equation is to be used (Paustenbach, 2011; AIOH, 2016):

Category 1 – Ceiling standards, mild irritants, and standards with technological limitations.

- Category 1A – Ceiling limit standard. Chemical substances in this category have a ceiling standard never to be exceeded at any time, and so, are independent of the length or frequency of work shifts. Examples include dichloroacetylene, formaldehyde, hydrogen chloride, iodine, ozone, potassium hydroxide, and natural mineral fibers (erionite) (Brodeur et al., 2001).
- Category 1B – Standards preventing mild irritants. This category includes chemical substances that cause irritation or those with an unpleasant smell. Since acute irritation or discomfort should be prevented no adjustment is applied. Examples include acetic acid, ammonia, natural mineral fibers (wollastonite as total and respirable dust), formic acid, and vinyl toluene (Brodeur et al., 2001; Paustenbach, 2011).
- Category 1C – Standards limited by technological feasibility. Chemical substances in this category include simple asphyxiants, substances presenting a safety risk or a very low health risk, substances whose half-life is less than 4 h, or for which standards are set by technological feasibility or good hygiene practices. Since these factors are independent of the length or frequency of work shifts, no adjustment is required. Examples include

chlorine, dichlorodifluoromethane, fibrous glass, methane, titanium dioxide (total dust), and zinc oxide (total dust) (Brodeur et al., 2001).

Category 2 – Acute toxicity standards.

The chemical substances in this category produce effects following short-term exposure. Therefore, these substances have OELs that prevent excessive accumulation of the substance in the body during 8 h of exposure on any given day. Consequently, a daily adjustment must be made to ensure that employees exposed to more than 8 h per day will not receive a dosage more than that intended by the standard (Eq. (A5)):

For daily adjustment (Category 2):

$$RF_d = \frac{8}{h_d} \quad (A5)$$

Where RF_d = daily reduction factor and h_d = hours worked per day (a value greater than 8).

However, it is important to note that for Category 2 substances the daily adjustment can only be made if the work shifts are all of the same length. If the number of hours worked per day differs between shifts, the TWAs must be adjusted for each work shift duration (Drolet, 2015). Examples of Category 2 chemical substances include gasoline, isopropyl alcohol, methyl silicate, nicotine, phosgene, welding fumes, and zinc chloride (fumes) (Brodeur et al., 2001; Paustenbach, 2011).

Category 3 – Cumulative toxicity standards.

This category includes chemical substances that produce effects following long-term exposure. These substances present a cumulative hazard. The OELs for these substances are designed to prevent excessive accumulation in the body resulting from many days or even from many years of exposure. Therefore, the OELs should be adjusted weekly to ensure that workers exposed to more than 40 h per week will not receive a dosage more than that intended by the OEL (Eq. (A6)):

For weekly adjustment (Category 3):

$$RF_w = \frac{40}{h_w} \quad (A6)$$

Where RF_w = weekly reduction factor and h_w = hours worked per week based on a repetitive work cycle (a value greater than 40).

As in the case of Category 2 substances with different length days, if work shifts are of unequal length from one shift to the next, the weighting must be done for each of the work shifts (Drolet, 2015). Examples of Category 3 chemical substances include coal dust, cobalt (metal, fume and dust as Co), refractory fibers (ceramics and others), lead and inorganic compound (dust and fumes as Pb), nickel (metal, soluble, and insoluble compounds as Ni), and silica (amorphous and fumes) (Brodeur et al., 2001; Paustenbach, 2011).

Category 4 – Acute and cumulative toxicity standards.

Chemical substances in this category include both acute and cumulative substances that produce effects following both short- and long-term exposure. In this case, the RF of both formulas is calculated, and the most conservative (i.e., lowest) is applied to provide the greatest protection. Examples of Category 4 chemical substances include acetonitrile, copper dust and mist (as Cu), carbon monoxide, dichlorofluoromethane, nitrobenzene, toluene, and styrene (monomer) (Brodeur et al., 2001; Paustenbach, 2011).

d) Québec model

The Québec model was developed in 1997 by a group of toxicologists from the Institut de recherche Robert-Sauvé en santé et en sécurité du travail (IRSST) and the University of Montréal (Firth & Drolet, 2014; Government of Western Australia, 2019). It is based on the OSHA model but attributes the most recent available pathological and toxicological information (Verma, 2000). To develop this model, issues of sensitization, skin irritation versus organ level toxicity, methemoglobin change, cholinesterase inhibition, toxicity on the reproductive system, and teratogenicity were assessed (Verma, 2000). The model uses an updated list of more than 700 substances listed in the Canadian Regulation Respecting Occupational Health and Safety (RROHS) document to categorise substances (Mellemsæther & Eide, 2016). Like the OSHA model, the Québec model is not based on pharmacokinetics, but it does take certain pharmacokinetic components into account (Verma, 2000). Moreover, the adjustment categories (Category 1A, 1B, 1C, 2, 3, and 4) are the same as those described for the OSHA model (Firth & Drolet, 2014). Currently, Canada uses the Québec model for the adjustment of OELs as TWAs into adjusted average exposure concentrations.

In Australia, the Department of Mines, Industry Regulation and Safety uses a modified Québec model (Government of Western Australia, 2019). For the modified Australian Québec model, the adjustment categories for individual chemical substances listed in the Québec Regulation were matched to corresponding chemical substances in Australia's Workplace Exposure Standards (WES) for Airborne Contaminants (Firth & Drolet, 2014; AIOH, 2016). Recent health effects were also reviewed, and the adjustment categories assigned by the IRSST were modified accordingly if the data suggested a different adjustment category (Firth & Drolet, 2013). For example, WESs with a peak limitation were identified and assigned as Category 1A, WESs with a carcinogen designation were identified and assigned Category 3 or 4 (except liquified petroleum gas, LPG, which remained in Category 1C), and WESs with a sensitiser designation were assigned Category 2, 3, or 4 (benzoyl peroxide remained Category 1B). In addition, for chemical substances that were in the WES but not in the Québec Regulation and vice versa, endpoint health effects and toxicology data were used to derive adjustment categories (Firth & Drolet, 2014). A complete list of the chemical substances with modified IRSST adjustment categories can be found in Firth and Drolet (2013).

A.2 Pharmacokinetic-based models

A.2.1 One-compartment models

The interaction between a chemical substance and the body following exposure is described using pharmacokinetics—the study of the absorption, distribution, metabolism, and excretion rates of drugs and toxicants. Pharmacokinetic models, also called toxicokinetic models, are therefore based on the fundamental principle of toxicology, which states that the intensity of a toxic effect is a function of the concentration of a toxic agent at the site of action (Laparé et al., 2003). Furthermore, pharmacokinetic models use scientific, substance-specific methodology based on the concept of 'body burden'. This means that these models acknowledge that the maximum body burden arising from a particular work schedule is a function of the

biological half-life of the chemical substance (Paustenbach, 2011). The biological half-life is the time it takes for half the substance to be eliminated from the cells, organs, or parts of the body where it produces its adverse health effects (Roach, 1978). Pharmacokinetic-based models are used to generate RFs based on the pharmacokinetic behaviour of the chemical substance as well as the number of hours worked each day and week (Paustenbach, 2011). Most pharmacokinetic-based models use a ‘one-compartment’ approach which assumes that the effect of exposure is isolated to a single site within the body. The body is therefore viewed as a single homogeneous box with a fixed volume. One-compartment models are the simplest uptake-excretion models (Hickey & Reist, 1977). There are four main one-compartment pharmacokinetic-based models namely the Mason and Dershin, Hickey and Reist, Roach, and MAHL model.

a) Mason and Dershin model

Mason and Dershin (1976) were the first to propose a pharmacokinetic model for the adjustment of exposure limits for unusual work shifts (Paustenbach, 2011). The Mason and Dershin model accounts for several important factors including the concentration of the chemical substance to which the individual is exposed, its physicochemical form, the rate of metabolism and excretion, as well as the distribution of the chemical substance in the body following absorption (Paustenbach, 2011).

b) Hickey and Reist model

The method published by Hickey and Reist (1977) describes the adjustment of exposure limits based on the number of hours worked each day, the number of hours worked each week, and the biological half-life of the chemical substance. Although the Hickey and Reist model was similar to that of Mason and Dershin, Hickey and Reist (1977) validated the pharmacokinetic model by comparing the results to biological data (Paustenbach, 2011). In the Hickey and Reist model, the biological elimination rate of a chemical substance (Eq. (A7)) is used to calculate the RF that should be applied:

$$k = \frac{(\ln 2)}{T_{1/2}} \quad (\text{A7})$$

Where k = biological elimination rate and $T_{1/2}$ = biological half-life.

Hickey and Reist model (Eq. (A8)):

$$RF = \frac{(1 - e^{-kt_{1n}})(1 - e^{-k(t_{1n}+t_{2n})n})(1 - e^{-kT_s})(1 - e^{-k(t_{1s}+t_{2s})})}{(1 - e^{-kt_{1s}})(1 - e^{-k(t_{1s}+t_{2s})m})(1 - e^{-kT_n})(1 - e^{-k(t_{1n}+t_{2n})})} \quad (\text{A8})$$

Where RF = reduction factor; e = Euler's Number (i.e., mathematical constant, 2.718); k = biological elimination rate; t_{1n} = length of a standard workday (i.e., 8 h); t_{2n} = length of the standard recovery period (i.e., 16 h); $t_{1n} + t_{2n}$ = length of a standard day (i.e., 24 h); t_n = length of a standard week (i.e., 168 h); n = number of workdays in a standard workweek (i.e., 5 days); t_{1s} = length of the extended shift workday (in hours); t_{2s} = length of the recovery period between extended shift workdays (in hours); $t_{1s} + t_{2s}$ = length of the extended shift “day” (usually, but not always 24 h); t_s = total length of the periodic work cycle (number of days worked and number of recovery days; in hours); and m = number of “work” days per “work” week in the extended work schedule.

c) Roach model

Roach (1978) also developed a pharmacokinetic model for OEL adjustments (Verma, 2000). However, a shortcoming identified for Roach's model is that the biological half-life is only available for a few chemical substances and therefore the worst-case scenario of half-lives must be applied to many substances (Verma, 2000).

Roach model (Eq. (A10)):

$$a = \frac{\log_e 2}{T_{1/2}} \quad (\text{A9})$$

$$RF = \frac{(1 - e^{-8a})(1 - e^{-120a})(1 - e^{-la})}{(1 - e^{-24a})(1 - e^{-168a})(1 - e^{-ma}) \sum e^{-na}} \quad (\text{A10})$$

Where RF = reduction factor; l = total number of hours for a complete work cycle; M = number of hours' duration of the work shift; N = number of hours from a prior work shift end to the shift end in question; e = Euler's Number (i.e., mathematical constant, 2.718); $T_{1/2}$ = biological half-life (in hours).

The Mason and Dershin, Hickey and Reist, and Roach models were independently developed but are in essence the same (Paustenbach, 2011). Therefore, all three models have the same assumptions, advantages and disadvantages (Table 4).

d) Maximum Adjustment Half-Life (MAHL) model

Due to the limitation of models that depend on the biological half-life of chemical substances, Armstrong et al., 2005 developed the Maximum Adjustment Half-Life (MAHL) model that is not dependent on substance-specific biological half-life data. By successively substituting a series of different biologic half-life values in a pharmacokinetic model, one may demonstrate that there is a maximum RF for the work schedule (Armstrong et al., 2005). This model, therefore, identifies the half-life that requires a maximum adjustment of the OELs for a given work schedule. This maximum adjustment half-life is not related to a particular chemical substance. Rather, it is for a hypothetical substance whose clearance rate leads to the greatest potential body burden (and thus requires the greatest RF) for the given work schedule. Thus, no toxic agent with any other (known or unknown) half-life will require a greater adjustment (Armstrong et al., 2005).

A.2.2 Multi-compartment models.

a) Physiologically based pharmacokinetic (PBPK) models

Physiologically based pharmacokinetic models are multi-compartmental models with a rigorous biological basis (Laparé et al., 2003). These models assume that individual organs or tissue groups are arranged as compartments in precise anatomical configurations connected by the cardiovascular system (Leung, 1992). Moreover, the transfer of chemical substances between the different compartments is governed by actual blood flow rates and tissue:blood partition coefficients (Leung, 1992). Physiologically based pharmacokinetic models are not based on new concepts but were first described in the literature by Teorell (1937). However, PBPK models were considered mathematically complex at the time and therefore the focus shifted to more simple linear models. Several decades later, Andersen et al., 1987 were the first authors to use PBPK modelling to adjust OELs for unusual work schedules.

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