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Extended work shifts and MAK values

MAK Value Documentation – Translation of the German version from 2022

A. Hartwig[1,*] MAK Commission[2,*]

1 *Chair of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Institute of Applied Biosciences, Department of Food Chemistry and Toxicology, Karlsruhe Institute of Technology (KIT), Adenauerring 20a, Building 50.41, 76131 Karlsruhe, Germany*

2 *Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area, Deutsche Forschungsgemeinschaft, Kennedyallee 40, 53175 Bonn, Germany*

* *email: A. Hartwig (andrea.hartwig@kit.edu), MAK Commission (arbeitsstoffkommission@dfg.de)*

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Abstract

MAK values (maximum concentrations at the workplace) are valid for exposure periods of 8 hours per day and 40 hours per week. In case of extended work shifts, it may be necessary to reduce the exposure concentration below the MAK value. This depends on the mechanism of action (either controlled by the concentration or by the concentration-time-product, C × T) and the half-life of the substance or its active metabolite. Publications addressing this issue were reviewed. In general, exposure levels do not need to be reduced for irritant substances that act primarily by a concentration-based mechanism. The use of linear C × T extrapolation is proposed for systemically acting substances with an unknown mechanism of action and half-life. The reduction of exposure levels based on worst-case considerations is recommended for systemically acting substances with a known mechanism of action and/or half-life. For practical reasons, linear C × T extrapolation as prescribed by DIN EN 689 is sufficient to prevent toxicity after extended work shifts irrespective of the mechanism of action of the substance. In any case, the BAT value (biological tolerance value) of the substance has to be observed.

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Introduction

MAK values are derived for an 8-hour working day and a 40-hour working week. However, in order to maintain continuous operations, a number of production facilities implemented shift systems with individual shifts lasting up to 12 hours. As a result, the average working week at these facilities may exceed 40 hours, with the hours worked in excess offset later by compensatory time off. The following evaluates the effects of working extended hours on the limit values at the workplace.

A survey carried out in 2015 found that 39% of 17 944 employed persons in 10 sectors worked up to 39 hours per week (Wöhrmann et al. 2016).

In 2013, weekly working hours of 37.7 hours were established by collective agreement for the chemical industry in Germany. However, 59% were working more hours than the contracted working time (Institut DGB-Index Gute Arbeit 2014).

Examples of shift systems

Examples of several different types of shift systems that are used in Germany are shown below (Bolt and Rutenfranz 1988):

4 shift groups: 1 × (7 × 8 hours), 1 × (6 × 8 hours), 2 × (4 × 8 hours)/week = average 42 hours/week, maximum 56 hours/week

4 shift groups: 4 × (2 × 12 hours + 2 days off) = average 42 hours/week (with 1 hour break = 38.5 hours/week), maximum 48 hours/week

4 shift groups: 2 × (6 × 8 hours + 1 × 12 hours), 1 × (6 × 8 hours), 1 × 7 days off = average 42 hours/week, maximum 60 hours/week

There are many other types of shift systems (DGUV 2009).

As a result, the hours worked may considerably exceed 8 hours a day or 40 hours a week.

Consequences for limit values

This issue was addressed by several authors who proposed different solutions to this problem (Armstrong et al. 2005; Bolt and Rutenfranz 1988; Brief and Scala 1975; Fiserova-Bergerova and Vlach 1997; Hickey and Reist 1977; Roach 1978; Saltzman 1988; Verma 2000).

In general, the effects of working longer hours on the limit value depend on the mechanism of action of the substance involved. The toxic effects of a substance or its critical metabolite are mainly dependent on either the concentration (C-dependent) or the concentration–time product (C × T-dependent) at the target site.

In the first case, the effect is not dependent on the duration of exposure. This applies to substances that are classified in Peak Limitation Category I of the List of MAK and BAT Values; for example, all substances that induce (sensory) irritation as their primary effect. In most cases, the MAK values of these substances do not have to be adjusted for the longer hours worked.

Substances classified in Peak Limitation Category II of the List of MAK and BAT Values that induce systemic toxicity as their primary effect are differentiated based on the dependency of the effects on concentration (C-dependent) or on the concentration–time product (C × T-dependent). This is largely determined by the toxicokinetics (half-life) of the substance or its critical metabolite. These relationships were modelled in the 1970s (Hickey and Reist 1977) and later (Fiserova-Bergerova and Vlach 1997) using a one-compartment toxicokinetic model. The consequences for the occupational exposure limits (in this case for different shift systems used in the United States) were derived mathematically using substances with half-lives of 1, 10 and 1000 hours (Fiserova-Bergerova and Vlach 1997). The authors

calculated reduction factors (RF) based on the half-life and the mechanism (C-dependent or C × T-dependent). The threshold limit values are then multiplied by these reduction factors to adjust for the longer hours worked (Table 1) (Fiserova-Bergerova and Vlach 1997).

Tab. 1 Reduction factors (RF) for four parameters of body burden for substances with systemic toxicity (Fiserova-Bergerova and Vlach 1997)

	highest reduction			
Parameter	**$t_{1/2}$ < 4 hours RF1**	**$t_{1/2}$ (hours)[a)]**	**RF2**	**$t_{1/2}$ > 20 days RF3**
concentration	1	6–18	1/2(8/T+40/W)	40/W
AUC_{exp}	8/T	3–14	8/T × 16(T+t)	8/T × 40/W
AUC_{day}	8/T		8/T	40/W
AUC_{week}	40/W		40/W	40/W

AUC_{exp}: cumulative exposure during the shift; AUC_{day}: cumulative exposure during a day; AUC_{week}: cumulative exposure during a week; $t_{1/2}$: half-life; T: length of the longest shift during the week (in hours); t: length of the shift that precedes or follows the longest shift (in hours); W: working week (in hours)
[a)] range of half-lives that lead to the lowest RF2

Table 1 shows the reduction factors for C-dependent substances (parameter "concentration" in Table 1) that were calculated based on the half-life ($t_{1/2}$) and the extended working day (T) or the extended working week (W). Threshold limit values do not need to be adjusted for substances with a half-life < 4 hours. According to the published figures, the reduction factor for substances with a half-life of 4 hours should be 0.9 instead of 1. However, this slight deviation is expected to have a negligible effect in practice.

In simplified terms, in the case of C × T-dependent substances (AUC_{exp}, AUC_{day}, AUC_{week} in Table 1), the ratio of the standard working day of 8 hours to the extended working day is decisive for the reduction factor (= 8/T) for substances with half-lives under 4 hours. For substances with half-lives over 20 days, the decisive variable is the ratio of the standard working week of 40 hours to the extended working week (= 40/W). The highest reduction is obtained for the parameter AUC_{exp}, i.e. the cumulative exposure during the shift. However, the usefulness of this parameter is questionable because threshold limit values are generally derived from animal studies in which the substance is administered daily at intervals of 24 hours and can act until the next dose is administered (this is equivalent to AUC_{day}).

These calculations can be used for weekly work cycles and for those cases when the hours at work plus the hours at rest = 24 hours (circadian rhythm). However, these requirements are not fulfilled by a 4-shift system with 12-hour shifts, because one cycle comprises 4 days instead of 7 days (2 work days, 2 rest days).

For these cases, Armstrong et al. (2005) published a formula that can be used to calculate reduction factors for systemically acting substances with a mechanism of action that is dependent on the concentration. The formula was developed based on the toxicokinetic model of Hickey and Reist (1977) and derives reduction factors for substances with known half-lives for use in extended shift systems. The calculations are based on the length of shift, the breaks between two shifts, the number of shifts per week and the number of days off per week. The authors found that the maximum reduction factor for an (extreme) system with twelve 12-hour shifts alternating with 12-hour recovery periods and 12 subsequent recovery days would be about 0.6.

Lower reduction factors are obtained for less extreme shift schedules: the reduction factor for a shift system with three to four 12-hour shifts per week was found to be equivalent to about 0.7 (see curve C in Figure 1 in Verma 2000).

Influence of shift work on the toxicokinetics/toxicodynamics of chemical substances (chronotoxicology)

Rats exhibited diurnal variation in susceptibility to some substances (particularly pharmaceuticals). Also in humans, similar variations were found in the hepatic metabolism of pharmaceuticals. These differences are attributed to the time point of food intake. A study with asbestos fibres revealed that clearance of the fibres occurred at a faster than normal rate in rats with a reversed day-night rhythm. The reasons for this are unknown (Bolt and Rutenfranz 1988).

Many other examples are presented in a recently published review. The authors suggest that further research is required and should be taken into consideration when determining the threshold limit values for shift work. However, the authors do not propose a specific approach (Smolensky et al. 2019).

A study in mice demonstrated that interruptions in the circadian rhythm promote tumour formation (Filipski and Lévi 2009).

Summary

The above calculations can be made only if the mechanism of action and half-life are known. This is often not the case. The following simplified worst-case assumptions are proposed for the derivation of a reduction factor for systemically acting substances:

Tab. 2 The value of the reduction factors (RF) depending on the mechanism and half-life of the substance (or its active metabolite)

Mechanism	$t_{1/2}$ unknown	$t_{1/2}$ known
unknown	linear C × T-extrapolation	RF = 40/W
C	RF = 0.7	RF = 0.6–1 using the formula of Armstrong et al. (2005)
C × T	RF = lower value of 8/T and 40/W (linear C × T-extrapolation)	< 20 days: RF = lower value of 8/T and 40/W (linear C × T-extrapolation)
		> 20 days: RF = 40/W
		>> 20 days (for example, biopersistent granular dusts): RF = 1 because cumulative exposure above the annual average is the same as for a 40-hour week

$t_{1/2}$: half-life; T: extended working day (in hours); W: extended working week (in hours)

Linear C × T extrapolation corresponds to the standard determination method according to DIN EN 689 (DIN 2020), which converts the exposure concentration of the substances to a shift length of 8 hours irrespective of their mechanism of action and their toxicokinetic properties. This is a pragmatic method that ensures compliance with the MAK value and its corresponding 40-hour concentration product when longer hours are worked. As data for the mechanism of action and the half-life are not available for most substances, the use of this method in practice is justified.

BAT values are derived either from the relationship between the body burden and critical levels of exposure or in correlation to the MAK value for an 8-hour exposure per work day. As adverse effects must not develop below the BAT value, the length of shift is irrelevant for this value. Therefore, the BAT value must always be observed.

Notes

Competing interests

The established rules and measures of the Commission to avoid conflicts of interest (www.dfg.de/mak/conflicts_interest) ensure that the content and conclusions of the publication are strictly science-based.

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