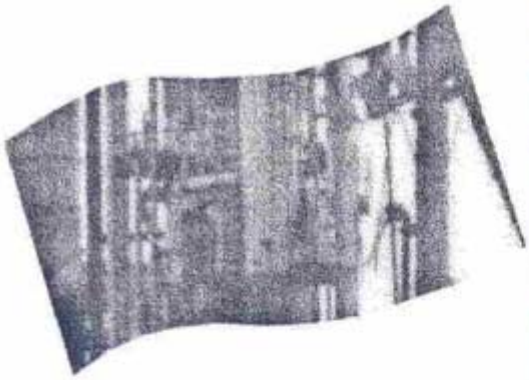
Adjustment of permissible exposure values to unusual work schedules



ÉTUDES ET RECHERCHES

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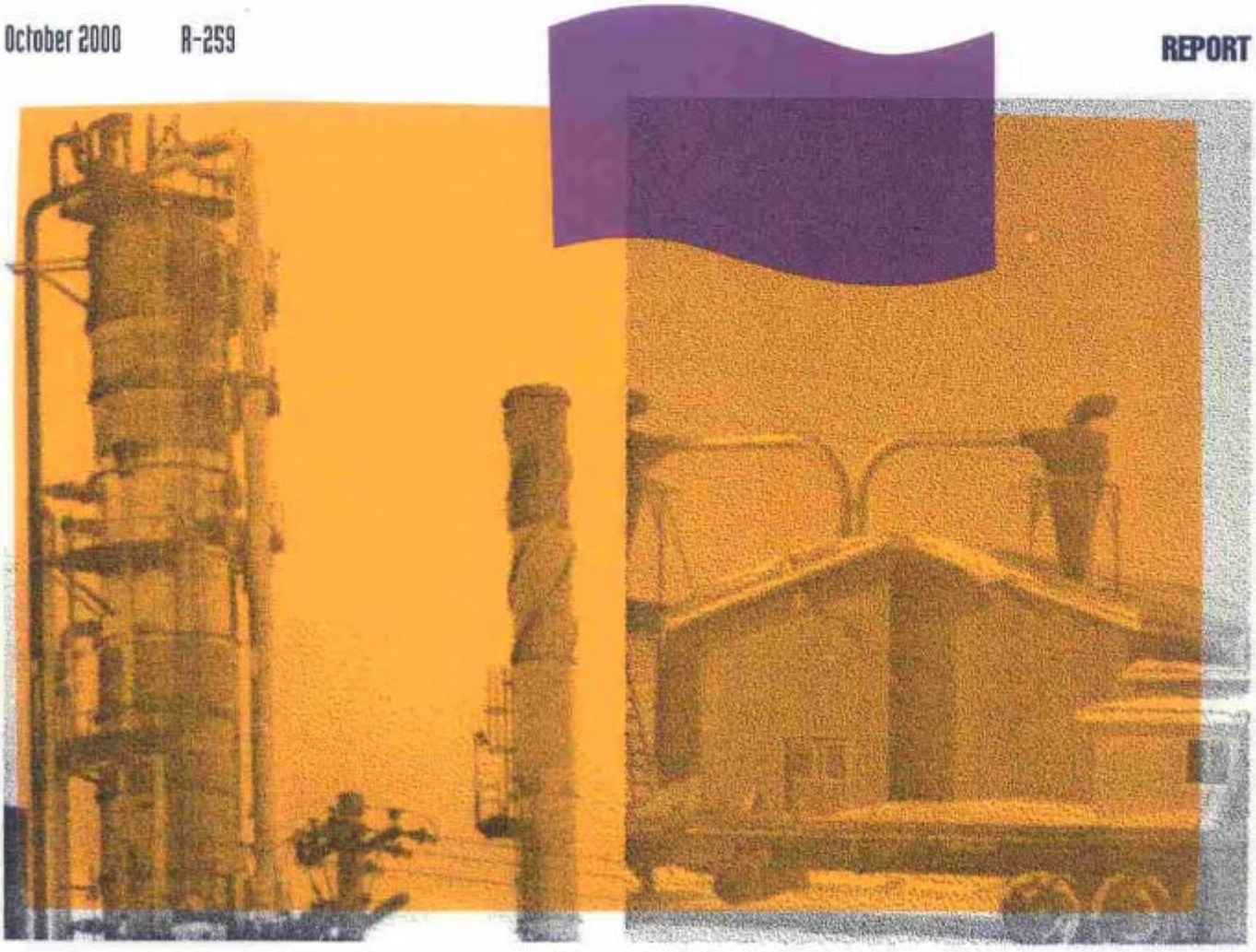
October 2000 R-259

REPORT



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Adjustment of permissible exposure values to unusual work schedules

ÉTUDES ET RECHERCHES

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October 2000

REPORT

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This study was financed by the IRSST. The conclusions and recommendations are those of the authors.

SUMMARY

This project was carried out in response to the request from the vice president, Programs and Consultancy of the CSST addressed to the IRSST: to carry out a study on the adjustment of permissible exposure values to unusual work schedules to support the work of Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (Appendix 1). Beforehand, the joint committee had established that the basic principle for adjusting permissible exposure values to unusual work schedules was to ensure an equivalent degree of protection for workers who have a conventional schedule of 8 hours per day, five days per week, and for workers with unusual work schedules (Appendix 2).

The goal of the project is to suggest to the Joint Committee, a method for adjusting the permissible exposure values for each substance in the Regulation respecting the quality of the work environment. These adjustments must apply to the exposure of workers with work schedules other than eight hours per day, five days per week, and must take into account the Quebec prevention context.

The IRSST entrusted the scientific management of the project to a steering committee of experts in this field (Appendix 3). The steering committee structured the methodological framework for the study (Appendix 4). Taking into consideration the guiding principle (whereby the adjustment principle should be based on toxicological considerations), the members of the steering committee recommended (Appendix 4, recommendation 2) that the logic of the Occupational Health and Safety Administration (OSHA), based on Haber's Law, be adopted as the basis for discussion of an eventual proposal by the IRSST.

OSHA's logic consists of assigning health code numbers (Appendix 5) to each of the substances in Schedule A of the regulation, and of linking these codes to prolonged work schedule categories (Appendix 6) on the basis of the "pertinent" pathology, meaning the one considered in establishing the permissible exposure values.

The project, entrusted to a team of researchers from the Université de Montréal and the IRSST, essentially consisted of a systematic validation, for each of the substances in Schedule A of the regulation, of the health code numbers and the prolonged work schedule category assigned by OSHA. The main points in the toxicological information collected for each of the substances in Schedule A of the regulation during the work was synthesized into a safety data sheet (Figure 1).

Starting with the principle that toxicokinetic methods for adjusting permissible exposure values are more rigourous from a scientific standpoint than empirical mathematical methods, including the OSHA approach, a study was also undertaken as part of the present project with the following objective: to determine, using different toxicokinetic approaches, the correction factors to be applied to the permissible exposure values for unusual exposure scenarios, and to compare the correction factors thus determined to those calculated using mathematical methods, such as that of

OSHA.

The results of this project take the following form:

1. First, a proposal from the steering committee suggesting that Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment use, for each of the substances in Schedule A taken individually, the prolonged work schedule category that is inspired by the OSHA method and which is identified on one of the 668 safety data sheets collected in Appendix II; the steering committee furthermore specifies the conditions for applying the adjustment;

2. Then, a confirmation that a method for adjusting the permissible exposure values that is based on the toxicokinetics of the contaminants results in correction factors that are less restrictive than those obtained using the OSHA method (Appendix I); the steering committee specifies that in the case of complex exposure scenarios, the kinetic approach is the only one by which an adjustment factor can be determined.

The steering committee ends by recommending that a permanent mechanism be implemented for adjusting the permissible exposure values to unusual work schedules.

1. INTRODUCTION

1.1 Issues

The vice president, Programs and Consultancy of the CSST asked the IRSST for a study focusing on the adjustment of permissible exposure values to unusual schedules to support the work of Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE) (Appendix 1). Subsequently, the Joint Committee agreed that the basic principle of adjusting exposure standards to unusual work schedules was to ensure an equivalent degree of protection for workers who have a conventional schedule of 8 hours per day, five days a week, and for workers with unusual work schedules, as stated in the document entitled: "Principe directeur sur l'établissement de normes d'exposition pour les horaires de travail non conventionnels" (Appendix 2).

In toxicological terms, for several chemical contaminants, an equilibrium occurs between the accumulation of a contaminant in the body while it is in the workplace, and the elimination of the contaminant when away from the workplace (this period is assumed to be without exposure) until a maximum body burden or an accumulation plateau is reached in the body. The time-weighted average exposure value (TWAEV) applicable to workers exposed to these contaminants must be modified for unusual schedules to ensure that the maximum body burden does not exceed the maximum body burden of a worker who has a conventional schedule. As a corollary, any means of exposure or any toxic action of a contaminant that is not linked in some way to the body burden requires no adjustment of the standard.

To fulfil this request, the IRSST proposed to the standing review committee an adjustment table for exposure standards for unusual work schedules for each of the substances in Schedule A of the RQWE. This proposal was to be formulated in consultation with Quebec and international experts in this field.

1.2 Current state of knowledge

The current knowledge on the adjustment of standards to unusual work schedules was recently summarized in three publications which are particularly applicable to the Quebec context (1,2,3). These publications describe the main methods for calculating the adjustment factors for permissible exposure values (PEV) in the case of substances that require an adjustment.

1.2.1 Brief and Scala equation

adjusted PEV = PEV x 8/h x (24 - h)/16
daily adjustment

adjusted PEV = PEV x 40/h x (168 - h)/128
weekly adjustment

where: h represents the exposure duration per day (daily adjustment) or per week (weekly adjustment).

1.2.2 Haber's Law (OSHA method)

adjusted PEV = PEV x 8/h
daily adjustment

adjusted PEV = PEV x 40/h
weekly adjustment

where: h represents the exposure duration per day (daily adjustment) or per week (weekly adjustment).

1.2.3 Toxicokinetic method (biological half-life ($T_{1/2}$))

$$\text{adjusted PEV} = \text{PEV} \times (1 - e^{-8k})(1 - e^{-120k}) / (1 - e^{-hk})(1 - e^{-24dk})$$

where k = substance elimination constant ($k = \ln 2 / T_{1/2}$);

h = duration in hours of the modified schedule;

d = number of days worked during the week according to the modified schedule.

Paustenbach (1) lists 25 substances for which a biological half life was measured and recommends the use of a half-life of 20 hours for the other substances of interest.

1.2.4 Toxicokinetic method (physiologically-based toxicokinetic models)

This is a more recent approach consisting of a case-by-case modeling of the distribution and the clearance of substances in the body using differential equations that include parameters of a physiological, physicochemical and metabolic nature (4).

In general, the theory of Brief and Scala produces the greatest reduction in the threshold limit value,

followed by the Haber method and the toxicokinetic methods. Therefore, for substance whose PEV is 100 ppm, for a 12-hour exposure period, Brodeur, Krishnan and Goyal (2) reported the following PEVs:

Brief and Scala	50 ppm
Haber	67 ppm
Toxicokinetic methods (biological half-life ($T_{1/2}$))	78 ppm
Toxicokinetic methods (physiologically-based models)	64 ppm

Of the simple methods for adjusting standards, the Brief and Scala method is the most conservative. The scientific data published to date seem to indicate that the Haber method, which was adopted by OSHA, generates values close to those for the physiologically-based toxicokinetic methods (4).

The OSHA method was proposed in 1979 (5). Paustenbach (1985) presented it in detail (6). The most recent version of the OSHA method dates from 1989 (7). Paustenbach (1994) again refers to it in his review article (1).

2. PROJECT OBJECTIVE

The goal of this project is to suggest to Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE), a method for adjusting the threshold limit values for each of the substances in the RQWE. These adjustments will apply to the exposure of workers with work schedules other than eight hours per day, five days per week, and must take into account the Quebec prevention context.

3. PROCESS

The IRSST entrusted the scientific management of the project to a steering committee of experts in this field. The steering committee, which met for the first time in June 1995 to set up the methodological framework for this study, arrived at the list of recommendations which is reproduced in Appendix 4.

Recommendation 1 (Appendix 4) therefore proposes that the steering committee's mandate be the following:

- to supervise the development process for a proposal for adjusting the threshold limit values to unusual schedules;
- to ensure the quality of the toxicological data and the content of the final proposal;

- to give advice on the applicability considerations listed in the activity description.

Taking into consideration the guiding principle, whereby the adjustment proposal should be based on toxicological considerations, the members of the steering committee recommended (recommendation 2, Appendix 4) that OSHA's logic, based on Haber's Law, as described by D.J. Paustenbach in "Patty's Industrial Hygiene and Toxicology" (1), be adopted as the basis for discussion of the IRSST's eventual proposals.

As specified in recommendation 3 (Appendix 4), OSHA's logic consists of assigning health code numbers (Appendix 5) to each of the substances in Schedule A of the RQWE and of linking these codes to prolonged work schedule categories (Appendix 6) based on the "pertinent" pathology, namely the one considered in establishing the permissible exposure values.

The project consisted essentially of a systematic validation, for each of the substances in Schedule A of the RQWE, of the health code number and the prolonged work schedule category assigned by OSHA. Beforehand, the wording of the health code numbers and prolonged work schedule categories was reviewed and was modified slightly to make it clearer and to better reflect the Quebec context.

3.1 Assigning a health code number (Appendix 5)

For each substance in Schedule A of the RQWE, it involved identifying, based on the most recent toxicological data, the pathologies that allow the pertinent effects to be defined, namely the critical effects that would lead to the assigning of a prolonged work schedule category. The pertinent effects retained belong to one of two classes, depending on whether they result from short-term exposure or long-term exposure.

The information used in assigning the health code numbers was taken mainly from secondary references. We therefore consulted the ACGIH document "TLVs and other occupational exposure values - 1995" presented on CD-ROM (8). It contains the toxicological data pertinent in establishing permissible exposure values, with supporting bibliographical references; it also contains data on the classification of carcinogens, as proposed by different international organizations. We also consulted the OSHA document "Chemical information manual" (9), as well as the books "Proctor and Hughes' Chemical Hazards of the Workplace" (10) and "Toxicologie industrielle et intoxications professionnelles" by Lauwerys (11).

During our work, we frequently made use of the CSST's Toxicological Index to obtain toxicological data as well as validated lists of substances classified according to their toxic properties.

Lastly, we consulted the primary sources in the toxicological literature as needed.

3.2 Assigning a prolonged work schedule category (Appendix 6)

This involves assigning, to each of the substances in Schedule A of the RQWE, a prolonged work schedule category that takes into account the pertinent toxic effects identified when a health code number is assigned. The prolonged work schedule categories retained are the same as those defined by OSHA.

3.3 Producing a technical data sheet

The main points in the toxicological data collected during the study for each of the substances in Schedule A of the RQWE were synthesized into a technical data sheet (recommendation 5, Appendix 4) based on the model used by a Quebec company (3). Figure 1 presents the data sheet and explains its parts.

3.4 Use of toxicokinetic models

The toxicokinetic methods for adjusting permissible exposure values are the most stringent from a scientific standpoint (1,2). They allow the exposure parameters to be adjusted in such a way that the concentration of the toxic substance at the site of action is not exceeded in unusual exposures. However, their use is limited by the fact that the adjustment calculation is based on one data, the biological half-life, which is available only for a limited number of substances.

The members of the steering committee recognized that over the short term, toxicokinetic models could not be used for a significant number of contaminants. They also noted that some data (1,2) seem to suggest that the adjustment factors calculated using toxicokinetic models for a limited number of substances are close to those calculated using the OSHA method. They therefore recommended (recommendation 6) that the project also address the use of toxicokinetic models for verifying the validity of application of any of the various adjustment models, in the case of substances where the biological parameters required for kinetic analysis are known.

A study was therefore carried out, as part of this project, with the following objective: to determine, based on different toxicokinetic approaches, the correction factors to be applied to the permissible exposure values for unusual exposure scenarios and to compare the correction factors thus determined to those calculated using empirical methods such as that of Brief and Scala and OSHA.

During the toxicokinetic study, three typical scenarios were used: 1) four consecutive 10-hour work days, followed by 3 days off; 2) three consecutive 12-hour work days, followed by four days off; 3) the complex 4/3 schedule, consisting of 12-hour work days, as defined in table 1 in Appendix I.

4. PROPOSAL FOR ADJUSTING PERMISSIBLE EXPOSURE VALUES TO UNUSUAL WORK SCHEDULES

4.1 General proposal

The steering committee suggests that Joint Committee 3.33.1 reviewing Schedule A of the RQWE use, for each of the substances in Schedule A, the prolonged work schedule category that is inspired by the OSHA method and identified on the individual technical data sheets presented in Appendix II.

4.2 Applying the adjustment

In the case of substances where the prolonged work schedule category requires that no adjustment be made, the permissible exposure values do not have to be adjusted, regardless of the type of work schedule.

In the case of substances where the prolonged work schedule category requires that an adjustment be made, the permissible exposure values are adjusted by solving one of the following two equations:

1) $F = 8/H_d$

(Substances that produce effects following short-term exposure)

2) $F = 40/H_w$

(Substances that produce effects following long-term exposure)

where: F = adjustment factor

H_d = exposure in hours per day

H_s = exposure in hours per week

In the case of substances that produce effects following short- as well as long-term exposure, the value of F must be calculated for each of the two equations; every day, the most stringent of the two adjustments is applied.

4.3 Application conditions

Adjustment of the permissible exposure values must be limited to the following conditions:

4.3.1 Work schedule covering a repetitive cycle of seven (7) consecutive days in which there is a period of at least two (2) consecutive days of recovery; for schedules that do not fulfil this

condition, the use of a toxicokinetic adjustment method is recommended;

4.3.2 Work shift whose exposure time is not less than four (4) hours nor greater than sixteen (16) hours.

It should be noted that the adjustment must never allow an exposure greater than the time-weighted average exposure value (TWAEV).

Short-term exposure values (STEV) are not adjusted.

4.4 Specific conditions

During the project, various questions dealing with toxicological interpretation problems arose and were submitted for discussion to the steering committee. Here is the result of the discussions.

4.4.1 Respiratory sensitizers (asthma)

The current state of knowledge is that respiratory system sensitization is probably linked to the total dose inhaled during an exposure period of a few or several days rather than only one day. As a result, an adjustment on a weekly rather than a daily basis is justified.

4.4.2 Skin sensitizers

Although the molecular immunological mechanism is not the same for skin sensitizers and respiratory sensitizers, it seems that skin sensitization is also linked to the total dose resulting from an exposure of a few or several days. Here again, adjustment on a weekly basis is justified.

4.4.3 Irritation versus toxicity in an organ

Substances frequently produce both irritation (local effect) and toxic effects in an organ or a physiological function (systemic effect). The difference, from an adjustment standpoint, is that the production of systemic toxic effects requires an adjustment of the permissible exposure values, which is not the case for irritation type effects. To choose between the types of effects, the ratio of the concentration needed to produce the systemic toxic effect and the time-weighted average exposure value (TWAEV) was calculated, where toxicological data were available. In the case where the ratio was equal to or less than 40, the systemic effect was chosen, with the result being that this choice imposed a daily or weekly adjustment, depending on the case.

4.4.4 Methemoglobinizing effects

Considering the fact that the biological exposure index for a methoglobinizing substance is 1.5% methemoglobinemia and given the fact that this value can easily be exceeded during short-term

exposure, an adjustment is justified on a daily basis for substances producing such effects.

4.4.5 Cholinesterase inhibition

Given the fact that it is important to prevent molecular lesions (cholinesterase inhibition) which may appear after short-term exposure, as well as toxic effects (the consequence of the molecular lesion which may appear after longer exposure), an adjustment is justified on either a daily or weekly basis, based on the most stringent correction criteria for substances producing such effects.

4.4.6 Toxicity on the reproductive system and teratogenicity

Given the great vulnerability of the developing embryo and fetus and the possibility that a teratogenic effect may be produced by short-term exposure, an adjustment is justified on a daily basis for this type of effect. However, in the case of a toxic effect on the reproductive system, as in the case of a reduction in fertility, an adjustment on a weekly basis seems justified.

4.5 The case of biological exposure indices

To the question, "Must biological exposure indices be adjusted for unusual schedules?", a qualified answer must be given. Such an answer has already been formulated in section 4 of a report produced by the IRSST (reference 3):

- If the biological index is in the form of a biochemical parameter with a value of a toxic effect threshold (cholinesterase inhibition, carboxyhemoglobinemia, erythrocyte protoporphyrins), no adjustment needs to be made.

- The same is true for any measurement of the concentration of a substance in a biological fluid (blood lead content, volatile substance in expired air) when the value assigned to the biological index is comparable to a tolerable limit value, namely a threshold value which can provide a direct evaluation of the health risk..

- However, the same conclusion does not apply in the case of biological exposure indices whose values includes a time dimension. In fact, since they depend on the exposure time, a reevaluation of these urinary biological exposure indices seems useful in the case of unusual work schedules.

4.6 The case of multiple exposures

The steering committee recognized that, in the case of exposure to more than one substance, part III of the RQWE entitled "Daily exposure to several substances" should apply. To do this, T, the time-weighted average exposure value permitted under part I of Schedule A, must be replaced by T_a, the time-weighted average exposure value adjusted to the unusual schedule for each of the substances

present simultaneously.

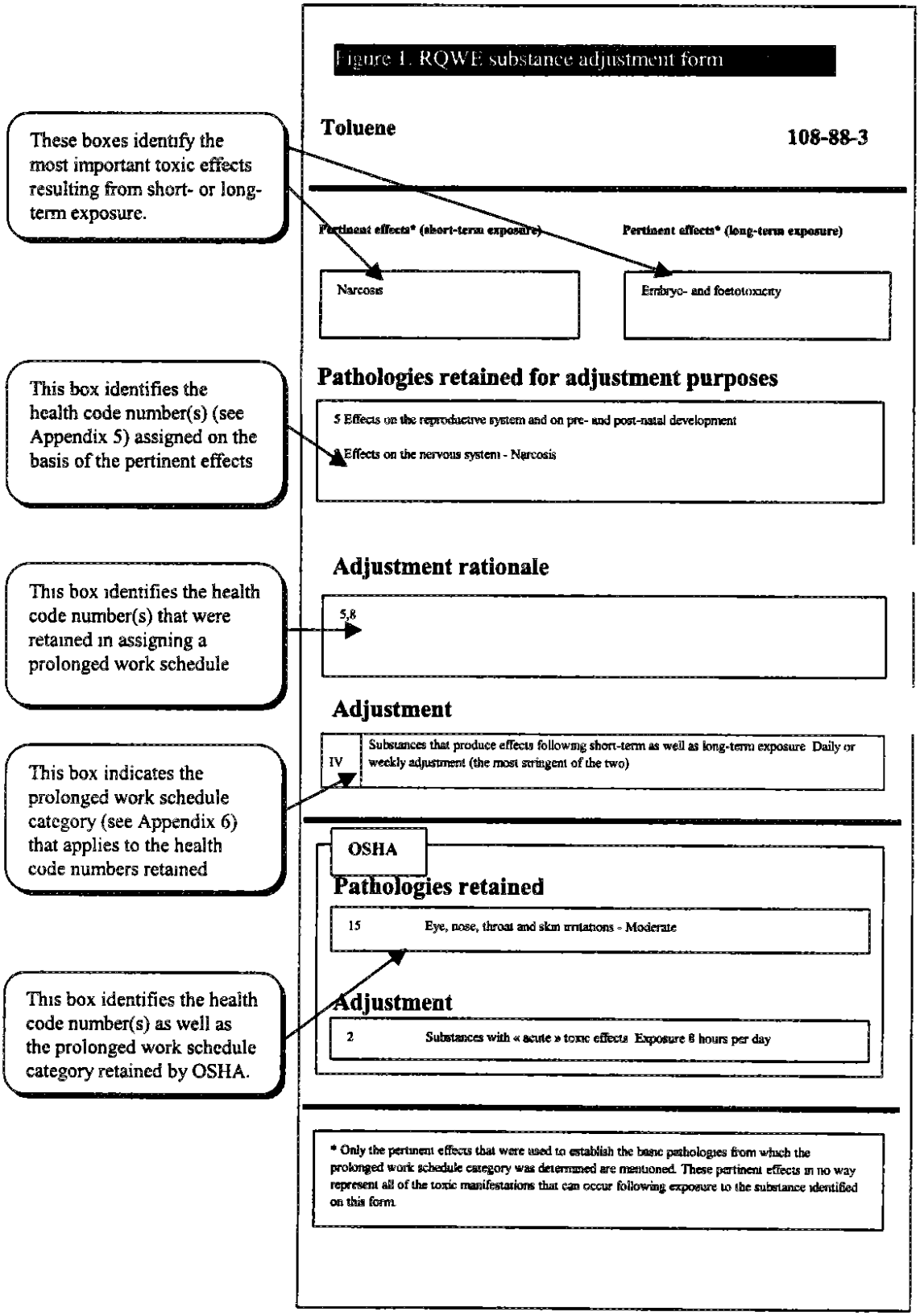
4.7 Results of the toxicokinetic analysis (Appendix I)

The results obtained indicate that the use of a method based on contaminant toxicokinetics to adjust the permissible exposure values, produces correction factors that are less stringent than those obtained using the OSHA method.

When a substance's half-life is known, the use of graphs developed by Hickey and Reist (6) using a toxicokinetic approach is a rapid and reliable means of establishing a correction factor. This approach is however limited to simple and repetitive scenarios. In the case of more complex exposure scenarios, such as the scenario corresponding to a 4/3 schedule, a one-compartment model can be developed that will allow a correction factor to be established.

4.8 Project follow-up

The steering committee recommends that a permanent mechanism be implemented for adjusting the permissible exposure values to unusual work schedules so that the current work can be amended as new knowledge emerges on the toxicity of a substance in Schedule A of the RQWE.


These boxes identify the most important toxic effects resulting from short- or long-term exposure.
This box identifies the health code number(s) (see Appendix 5) assigned on the basis of the pertinent effects
This box identifies the health code number(s) that were retained in assigning a prolonged work schedule
This box indicates the prolonged work schedule category (see Appendix 6) that applies to the health code numbers retained
This box identifies the health code number(s) as well as the prolonged work schedule category retained by OSHA.
Figure 1. RQWE substance adjustment form
Toluene
108-88-3
Pertinent effects* (short-term exposure)
Pertinent effects* (long-term exposure)
Narcosis
Embryo- and foetotoxicity
Pathologies retained for adjustment purposes
5 Effects on the reproductive system and on pre- and post-natal development
8 Effects on the nervous system - Narcosis
Adjustment rationale
5,8
Adjustment
IV
Substances that produce effects following short-term as well as long-term exposure Daily or weekly adjustment (the most stringent of the two)
OSHA
Pathologies retained
15
Eye, nose, throat and skin irritations - Moderate
Adjustment
2
Substances with « acute » toxic effects Exposure 8 hours per day
* Only the pertinent effects that were used to establish the basic pathologies from which the prolonged work schedule category was determined are mentioned. These pertinent effects in no way represent all of the toxic manifestations that can occur following exposure to the substance identified on this form.

APPENDIX 1. SPECIFICATIONS (without appendices and tables)

Title	Adjustment of permissible exposure values to unusual work schedules
Person in charge	Guy Perrault/ IRSST; Jules Brodeur / Université de Montréal and the other members of the steering committee

1. **Project summary** (limited to the space on this page)

- **Health and safety problem and project pertinence**

The CSST asked the IRSST to carry out a study on variable schedules to support the work of Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE) (Appendix 1). The Joint Committee agreed that the basic principle of adjusting exposure standards to unusual work schedules was to **guarantee an equivalent degree of protection for workers with a conventional schedule of 8 hours per day, five days per week, and for workers with unusual schedules,** as expressed in the document entitled "Principe directeur sur l'établissement de normes d'exposition pour les horaires de travail non conventionnels" (Appendix 2).

- **Methodology**

The IRSST created a steering committee to plan the development of the project and to supervise its execution. This steering committee proposed using the logic suggested by the American organization OSHA as inspiration; validating and updating the toxicological content by means of a group or groups of experts in industrial toxicology; and using data from toxicokinetic principles to validate the adjustment criteria for each of the substances in Schedule A of the RQWE where the existing data allow it. The IRSST provides logistical support to the steering committee.

- **Expected results**

The final report will contain validated health number assignment tables for each of the substances in the RQWE with identification of the primary pathology, validated tables for determining the prolonged work schedule categories, and a recommendation on adjustment criteria (equation) by products or groups of products. For each of the substances, a data sheet will summarize the data pertinent to the adjustment of the threshold limit value. Computer media will provide access to all of the data, the adjustment calculations, and the updating of the toxicological content.

- **Expected practical results**

A satisfactory response, that is usable in the field, to a request by the CSST to the IRSST for a study whose goal is better protection of the health of workers who are exposed to chemicals during unusual work schedules.

2. Detailed description of the project (Add additional pages if necessary)

Issues and pertinence of the occupational health and safety project

The vice president, Programs and Consultancy at the CSST asked the IRSST for a study on unusual schedules to support the work of Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE) (Appendix 1). Subsequently, the Joint Committee agreed that the basic principle of adjusting exposure standards to unusual work schedules was to **guarantee an equivalent degree of protection for workers with a conventional schedule of 8 hours per day, five days per week, and for workers with unusual work schedules**, as expressed in the document entitled "Principe directeur sur l'établissement des normes d'exposition pour les horaires de travail non conventionnels" (Appendix 2).

In toxicological terms, for several chemical contaminants, an equilibrium occurs between the accumulation of a contaminant in the body during its presence in the work environment and the elimination of the contaminant when not in the workplace (this period is assumed to be without exposure) until a maximum body burden or accumulation plateau is reached in the body. The time-weighted average exposure value (TWAEV) applicable to workers exposed to these contaminants must be modified for unusual work schedules to **ensure that the maximum body burden does not exceed the maximum body burden reached by a worker with a conventional work schedule**. As a corollary, any means of exposure or any toxic action of a contaminant that is not linked in some way to the body burden, does not result in any adjustment of the standard.

To comply with this request, the IRSST proposes suggesting to the standing review committee, an exposure-standard adjustment table for unusual work schedules for each of the substances in Schedule A of the RQWE. This proposal will be formulated in consultation with Quebec and international experts in this field.

7. Current knowledge

The current knowledge on the adjustment of standards to unusual work schedules was recently summarized in three publications that are particularly applicable to the Quebec context (1,2,3). To plan the response to the request, namely to suggest an adjustment table for each of the substances in Schedule A to the Standing Review Committee for Schedule A, the IRSST assembled a steering committee whose mandate, during its first meeting, was to establish a consensus on the best way to fulfil the objective in a reasonable period of time of one year. The participants (Appendix 3)

arrived at the list of recommendations which is reproduced in Appendix 4.

Recommendation 2 suggests that the OSHA (Occupational Safety and Health Administration) approach be adopted as the basis for discussion on eventual IRSST proposals on the adjustment of threshold limit values to unusual work schedules. Recommendation 3 explains that the OSHA approach consists of assigning health code numbers (Appendix 5) to each of the substances in Schedule A of the RQWE, and of linking these codes to prolonged work schedule categories (Appendix 6) based on the "main" pathology, namely the one that was considered in establishing or recommending permissible exposure values.

By applying recommendation 3 to the application of the OSHA approach, a table (Appendix 6) can be developed that links 554 substances in Schedule A of the RQWE to OSHA health code numbers (4) by specifying, using numbers 1, 2, 3, etc., where the health code numbers and the substances intersect, the level of importance of this class of pathology in relation to the assignment of the limit value. The 114 other substances (Appendix 7) are not included in OSHA's health code number assignment list. Of these 114 substances, the IRSST does not provide analysis service for 62 substances, which indicates a lesser interest in the Quebec context, for these substances at least.

The prolonged work schedule categories (1,5), as determined by OSHA for each of the 554 substances for which health code numbers have been assigned, are summarized in Appendix 8:

Table 8.1 Substances with no recommended adjustment.

Table 8.2 Substances with a recommended daily adjustment.

Table 8.3 Substances with a recommended weekly adjustment.

Table 8.4 Substances where an adjustment is recommended based on the more stringent of the daily or weekly calculation.

The IRSST's data base which was used in preparing tables 8.1 to 8.4 also contains the German data (6) dealing with the toxic effects of several contaminants. It should be noted that the German procedures do not use these categories of effects to determine adjustments to standards for unusual work schedules, but instead apply other provisions of their regulations such as limits in the number and frequency of short-term exposures. The carcinogenicity classifications of the International Agency for Research on Cancer (IARC) will be added to this data base for purposes of comparison

with OSHA data. The two systems can be used for a first validation of the health code numbers. The prolonged work schedule categories were determined by OSHA in 1979 and 1989 (1,5). To our knowledge, no group of toxicology experts has reviewed or updated this list in the last few years. Also, a good number of substances (163) are found in table 8.4, where the OSHA suggestion of choosing the weekly or daily average that gives the more stringent adjustment does result in application and interpretation difficulties. There would be a definite advantage in reducing the number of substances in this category or of supplying the clients with a computer tool by which they could easily obtain a reliable answer.

The main methods for calculating adjustment factors for permissible exposure values (PEV), in the case of substances that require an adjustment, are the following (1,2,3):

Haber's Law

adjusted PEV = PEV x 8/h	daily adjustment
adjusted PEV = PEV x 40/h	weekly adjustment

Brief and Scala equation

adjusted PEV = PEV x 8/h x (24 - h)/16	daily adjustment
adjusted PEV = PEV x 40/h x (168 - h)/128	weekly adjustment

where h is the exposure duration per day (daily adjustment) or per week (weekly adjustment).

Toxicokinetic methods (biological half-life ($T_{1/2}$))

$$\text{adjusted PEV} = \text{PEV} \times (1 - e^{-8k})\,(1 - e^{-120k}) / (1 - e^{-hk})\,(1 - e^{-24dk})$$

where k = substance elimination constant ($k = \ln 2 / T_{1/2}$);

h = duration of the modified schedule in hours;

d = number of days worked during the week according to the modified

schedule.

Paustenbach (1) lists 25 substances for which a biological half-life was measured and recommends the use of a half-life of 20 hours for the other substances of interest. The articles that describe these evaluations of half-life date from 1962 to 1982. The Germans, however, classified 220 substances on the basis of their half-life (less than 2 hours, between 2 and eight hours, and more than 8 hours). Several references (1,2) recommend the use of physiologically-based toxicokinetic models as fields of research to be given priority.

Toxicokinetic methods (physiologically-based toxicokinetic models)

Case-by-case modeling of the distribution and clearance of the substances in the body using differential equations that include parameters of a physiologic, physicochemical and metabolic nature (7).

In general, the theory of Brief and Scala provides the greatest reduction in the threshold limit value, followed by Haber's method and the toxicokinetic methods. Therefore, for styrene whose PEV is 100 ppm, for a 12-hour exposure period, Brodeur, Krishnan and Goyal (2) reported the following PEVs:

Brief and Scala	50 ppm
Haber	67 ppm
Toxicokinetic methods (biological half-life ($T_{1/2}$))	78 ppm
Toxicokinetic methods (physiologically-based models)	64 ppm

Of the simple methods for adjusting standards, the Brief and Scala method is the most conservative. The scientific data published to date seem to indicate that the Haber method, which was adopted by OSHA, gives values close to the physiologically-based toxicokinetic methods (7).

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8. Research hypotheses

The goal of this project is to suggest to Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE), a method of adjusting the threshold limit values for each of the substances in the RQWE. These adjustments apply to the exposure of workers with work schedules other than eight hours per day, five days per week, and should take into account the Quebec prevention context.

9. Proposed methodology and process

For example: epidemiology, prospective study, semi-experimental study, action research, etc., by justifying the approach and the techniques that one intends to use, including computer media, as need be.

It is a study in which the IRSST entrusts the scientific management to a steering committee of experts in this field. The steering committee met for the first time in June 1995 to set up the methodological framework for this study in the form of proposals (Appendix 4), where one aspect, of the "literature review" type was covered in section 7. Some other recommendations are of a methodological nature and form the framework for the methodology.

Recommendation 1 (Appendix 4) proposes that the steering committee's mandate be the following:

- to supervise the development process for a proposal for adjusting threshold limit values to unusual work schedules;

- to ensure the quality of the toxicological information and the content of the final proposal;

- to give advice on the applicability considerations listed in the activity description.

The state of current knowledge reflects all the knowledge accumulated over the years in the context of the references mentioned, which can be used as a starting point in developing the adjustment proposal. However, the committee is of the opinion that the toxicological data on each of the substances must correspond to current knowledge and that the reasoning justifying the recommendations for each of the substances must be available. Recommendation 5 proposes a validation of the health code numbers and the subsequent assigning of the prolonged work schedule category by one or more groups of toxicology experts who would proceed to update the scientific

and technical data, substance by substance, and to document the bases for coding. To do this, a technical data sheet developed from the model used in reference 3 will be produced for each substance in the RQWE by this group of experts. The use of a single group of experts who have already done research and published in this field would provide the steering committee with a uniform approach and response. The toxicological index, and the IRSST and CSST information libraries will participate in collecting the toxicological data.

The steering committee also proposes asking the group(s) of experts to suggest a means of using toxicokinetic models to verify the validity of application of the adjustment factors for substances whose biological parameters or half-lives are known or become known, and to make a more general proposal on the Haber, Brief and Scala or toxicokinetic adjustment methods for all of the substances in tables 8.2 and 8.3. In the opinion of the members of the steering committee, when scientific data are available, the toxicokinetic models would serve as validation of the means of applying the proposed adjustment for the substances in the RQWE while the proposal is being developed, and as need be, during later application of the means of adjustment. A mechanism will be proposed by the IRSST and the CSST's Toxicological Index for carrying out this future validation as part of the existing computer links with private and public occupational health and safety networks. Given that the basic toxicological information has been compiled in a data base, it would be preferable if the same compilation work were carried out on the validated information and the prolonged work schedule categories. It would then be relatively easy to introduce, during the computer compilation, the required equations for adjusting the threshold limit values for each substance, regardless of their simplicity or complexity. This would first provide the client who is electronically linked to the IRSST or the Toxicological Index with a rapid and reliable answer, and second, allow an automatic validation of the results using a toxicokinetic method where possible.

The steering committee has also drawn up recommendations on certain applicability parameters for the adjustments to the standards, and particularly the application to biological indices, the specific case of "allergenic" or "sensitizing" substances, the context of widespread daily exposure to several substances, and the excursion limits. A preliminary position of the committee is formulated in recommendations 7 - 10 (Appendix 4). In particular, recommendation 8 on "allergenic" or "sensitizing" substances for the respiratory system or the skin will eventually be dealt with again in the form of a request for a study (other than that of adjusting threshold limit values) to formulate a separate proposal to Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment. The other proposals will be discussed again while the IRSST's proposal is being developed and will be included in the final report.

11. Valorization

Once the research has been completed, what are the expected valorization or transfer activities, and the level of involvement of the project leader and the team?

Once the work has been completed, the final report will be sent by the IRSST to Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE).

12. Activity schedule

Indicate the main steps in the project and the report presentation dates.

The final report will be deposited at the IRSST one year after the start of the work.

APPENDIX 2. GUIDING PRINCIPLE

GUIDING PRINCIPLE FOR ESTABLISHING EXPOSURE STANDARDS FOR UNUSUAL WORK SCHEDULES

Even when clinical data on humans and toxicological data on animals are lacking, it is realistic to believe that the adoption of unusual work schedules could result in an increased health risk, if the permissible exposure values for certain (several) chemical substances are not adjusted (1).

The basic principle for adjusting exposure standards to unusual work schedules is therefore to **ensure an equivalent degree of protection for workers with conventional schedule of 8 hours per day, five days per week, and for workers with unusual work schedules.**

The process of establishing these adjustments of standards therefore requires a prior consensus on the scope of permissible threshold limit values.

The American organization ACGIH (American Conference of Governmental Industrial Hygienists) specifies that the standards that it suggests under the acronym **TLV7** refer to concentrations of substances in the air and represent the conditions under which, in all likelihood, almost all of the workers may be exposed, day after day, without harmful effects (2).

This statement corresponds to the assertion that a body burden exists for a substance, below which a toxic effect is not expected. For several substances, an equilibrium occurs between the accumulation of the substance in the body while it is in the workplace, and the elimination of the substance when it is not (this period is assumed to be without exposure) until a stable body burden or accumulation plateau is reached in the body. The time-weighted average exposure value (TWAEV) applicable to workers exposed to these substances must be modified for unusual work schedules to **ensure that the maximum body burden does not exceed the maximum body burden reached by a worker with a conventional work schedule.** As a corollary, any means of exposure or any toxic action of a substance that is not linked in some way to the body burden, requires no adjustment of the standard.

APPENDIX 3. PARTICIPANTS IN THE STEERING COMMITTEE MEETINGS

Members of the steering committee

Dr. Jules Brodeur, toxicologist, Université de Montréal;

Dr. Jean-Luc Malo, lung specialist, Hôpital du Sacré-Coeur;

Dr. Perrine Hoet, Unité de toxicologie industrielle et de médecine du travail, Université de Louvain, Brussels, Belgium

Dr. Pierre O. Droz, Institut universitaire romand de Santé au Travail, Lausanne, Suisse

Dr. Guy Perrault, IRSST.

Observers

Dr. Robert Tardif, Université de Montréal;

François Lemay, Information processing; Madeleine Bourdhouxe, Work Organization; Daniel Drolet and Dr. Ginette Truchon, Hygiene and Toxicology, IRSST;

Céline Lemieux, CSST, chair of Joint Committee 3.33.1 reviewing Schedule A of the Regulation respecting the quality of the work environment (RQWE);

Dr. Ada Vyskocil, Toxicologist, Université de Montréal;

Gilles Lapointe, Toxicological Index, CSST.

APPENDIX 4. RECOMMENDATIONS OF THE STEERING COMMITTEE ON PROJECT EXECUTION

RECOMMENDATIONS OF THE MEMBERS OF THE STEERING COMMITTEE

1. The members agreed on the steering committee's mandate:

   - to supervise the development process for an adjustment proposal for threshold limit values for unusual work schedules;

   - to ensure the quality of the toxicological data and the content of the final proposal;

   - to give advice on the applicability considerations listed in the activity description.

2. Taking into consideration:

   - the request for a systematic adjustment proposal for threshold limit values (TLVs) for all substances in Schedule A of the RQWE;

   - the guiding principle whereby the adjustment proposal should ideally be based on toxicological considerations;

   - the members recommend that the OSHA logic as described by Denis J. Paustenbach in "Patty's Industrial Hygiene and Toxicology (1994) 3rd Edition, edited by R.L. Harris, L.J. Cralley, and L.V. Cralley. Vol. III, Part A, p. 191-348", be adopted as the basis for discussion of eventual IRSST proposals.

3. This OSHA logic consists of assigning health code numbers (Appendix 1) to each substance in Schedule A of the RQWE and of linking these codes to prolonged work schedule categories (Appendix 2) based on the "main" pathology, namely the one that was considered in establishing or recommending the permissible exposure values.

4. As a starting point, this table of pathologies should be improved by using the following as a basis:

- the IARC (International Agency for Research on Cancer)
- the German prolonged work schedule category assignments related to:

  the classification for peak exposure categories;

  the classification for feto-embryo damage risk;

  the classification of germ cell mutagens

as summarized in the ACGIH document "Guide to Occupational Exposure Values - 1994".

5. The health code numbers and the subsequent assignment of the prolonged work schedule category should also be validated by one or more groups of experts, by proceeding substance by substance and by establishing a technical data sheet for each, based on the model used in the ALCAN document entitled "Recommandations Alcan relatives aux facteurs d'ajustement des valeurs limites d'exposition (VLE) pour les horaires prolongés. Octobre 1994."

6. Since it is unlikely that the toxicokinetic models can be used over the short-term for a significant number of contaminants and since the first results seem to indicate that the adjustment factors calculated by the toxicokinetic models are, in practice for a limited number of substances, close to the adjustments calculated using the Haber method, it is proposed that the study also cover the use of toxicokinetic models to verify the validity of application of adjustment factors in the case of substances whose biological parameters or half-lives are or become known. The IRSST should establish, following its proposal on the adjustment of PEVs, means of applying this validation according to toxicokinetic models.

7. The biological exposure indices that are proposed for information purposes in the IRSST document entitled "Guide de surveillance biologique - Prélèvement et interprétation des résultats, 1994", or all biological exposure indices. However, eventual biological indices based on the dose/effect relationship would not be adjusted.

8. The members of the steering committee would like to emphasize that several "allergenic" or "sensitizing" substances for the respiratory system or the skin are not standardized. To promote the prevention of pathologies caused by these products, the committee recommends that an intervention strategy accompanied by identification lists for these products be

introduced into the document entitled: "Sampling Guide for Air Contaminants in the Workplace, Document T-06, 1994" or into any other document intended for this purpose.

9. In the case of exposure to more than one substance, Part III of the RQWE entitled "DAILY EXPOSURE TO SEVERAL SUBSTANCES" should apply by replacing T, the time-weighted average exposure value permitted under part 1 of the Schedule, with T_a, the time-weighted average exposure value adjusted to the unusual work schedule for each of the substances simultaneously present.

10. The excursion limits for substances with no short-term exposure value as well as the frequency of the exposures between the TWAEV and the STEV should not be adjusted unless justified by toxicological considerations.

Appendix 5

List of health code numbers defined by OSHA

Code	Brief description
1	Carcinogenic effect detected in humans (Designation C1 in RQWE)
2	Carcinogenic effect suspected in humans (Designation C2 in RQWE); mutagenic effect
3	Effects following long-term exposure - systems other than nervous, respiratory, blood and reproductive system
4	Effects following short-term exposure - other than teratogenic, narcotic, respiratory, methemoglobinizing
5	Effects on reproductive system and on pre- and post-natal development
6	Effects on nervous system - cholinesterase inhibition
7	Effects on nervous system - other than narcosis and cholinesterase inhibition
8	Effects on the nervous system - Narcosis
9	Respiratory effects - Asthma
10	Respiratory effects following long-term exposure, other than asthma
11	Respiratory effects following short-term exposure
12	Hematologic effects - other than methemoglobinizing effects
13	Methemoglobinizing hematological effects
14	Marked irritation of the skin and/or mucous membranes
15	Moderate irritation of the skin and/or mucous membranes
16	Slight irritation of the skin and/or mucous membranes
17	Simple asphyxia
18	Explosive or flammable substances, or those with another safety risk
19	Substances with a slight health risk
20	Smelly substances with a very slight health risk

Appendix 6

Assigning prolonged work schedule categories according to OSHA

Category	Assignment criteria	Adjustment
1A	Substances governed by a ceiling value	No adjustment
1B	Irritating or smelly substances	No adjustment
1C	Simple asphyxiants, substances with a safety risk or very slight health risk. Technological limitations	No adjustment
II	Substances that produce effects following short-term exposure	Daily adjustment
III	Substances that produce effects following long-term exposure	Weekly adjustment
IV	Substances that produce effects following short- as well as long-term exposure	Daily or weekly adjustment (the more stringent of the two)

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