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Emergency Exposure Indices for Industrial Chemicals

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ERRATUM

In Tables A3-1 (p.53), A3-3 (p.54) and A3-4 (p.55), the figures in the columns headed ppm (mg/m3) are in fact **ppm**.

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SUMMARY

This report examines the criteria for defining indices of exposure which could be used as guidance on the potential health effects from accidental chemical releases. It develops guidelines for their setting and use and provides examples for a few representative chemicals. Effects on the natural environment were deliberately excluded from consideration.

It was considered that the indices should relate to the whole population, including the very young and the elderly, the pregnant and those who are ill but not those whose health is so unstable that the outcome of their illness is unlikely to be related to the degree of chemical exposure. Three exposure indices were identified separating four zones of effect, thus

Death/Permanent Incapacity	*Disability*	*Discomfort*	*Detectability*
EEI-3	EEI-2	EEI-1	

$EEI(t_1)$-1 is thus defined as "That airborne concentration for exposures lasting up to a specified exposure time (t_1) <u>below</u> which direct toxic effects are unlikely to lead to *DISCOMFORT* in the exposed population (including susceptible but excluding hypersusceptible groups) and above which, as the concentration increases, *DISCOMFORT* would become increasingly more common." and $EEI(t_2)$-2 and $EEI(t_3)$-3 for *DISABILITY* and *DEATH/PERMANENT INCAPACITY* respectively are defined similarly.

Guidance is given on the collection of experimental and human data, the evaluation of its quality and relevance, and on the selection of data for use in setting EEIs. Data on the toxic effects of exposure can be analysed in many ways; thus graphical, mathematical or computer techniques can be used. Various ways of deriving EEIs are considered and one, for chlorine, is worked through in detail as an example.

Expression of toxicological data in terms of numerical indices involves assumptions and simplifications of which those who use them must be aware. EEIs are only appropriate for excluding the likelihood of specified health consequences in the situation of accidental release and cannot be used for quantitative risk assessment purposes. The accuracy of EEIs in this predictive role will be greatest if toxicological data are available which relate to the relevant exposure duration.

It is possible to apply dispersion models iteratively or to plot exposure/time profiles for points of interest to determine the most appropriate exposure duration to use when setting EEIs. In relation to the use of EEIs, the isopleth envelope - the line surrounding successive concentration "contours" - defines an area outside which the effects relative to that EEI (i.e., Death/Permanent Incapacity, Disability or Discomfort) are unlikely to occur.

In order to test the comprehensibility of the EEI concept and the ECETOC guidance for setting them, a "ring test" was conducted to evaluate the consistency of values produced by different groups. Participants were asked to set EEIs for 15, 30 and 60 minute exposures (where possible) for phosphine, acrylonitrile and hydrogen fluoride. Eleven groups of one or, at best, a few people participated; there was considerable variability in the values. In general this variability resulted from different opinions on the validity or relevance of particular data. The variability would be overcome if EEIs were set by a larger, multidisciplinary group or by discussions between the several groups who had derived indices for the same chemical.

A. INTRODUCTION

In the field of occupational health and hygiene, atmospheric concentration limits have been established for a large number of gases, vapours and particulates to aid in the protection of workers' health. These concentration limits, generically termed "occupational exposure limits" (OELs), have a recognised place in evaluating and controlling occupational exposures to airborne chemicals. Some OELs refer to concentrations (8 hour - TWA) averaged over a normal working day and are set to protect against repeated exposures occurring over a working lifetime: other limits, such as Short Term Exposure Limits (STELs), are set to protect against the acute-toxic effects produced (e.g. ACGIH, 1989; Appendix 1).

To protect the health of communities from the effects of air pollution, more stringent standards have been promulgated for a smaller number of airborne substances which arise from industrial discharges to atmosphere, vehicle exhausts, domestic chimneys, farming and other activities (e.g. WHO, 1972). In the control of industrial discharges to the atmosphere the technique of mathematical modelling has been used to estimate the dispersion of discharges from industrial stacks under variable stack height, discharge concentration, volume rates and velocities and meteorological conditions. Models have been used to design stacks which will achieve adequate dilution of discharges before they reach ground level.

Over recent decades, during which standards for control of the workplace and the general environment have become more stringent, there have been a number of serious accidents resulting in chemical emissions which have involved the communities in the area surrounding the release. In 1976 at Seveso in Italy, an area of several hundred hectares was contaminated with 2,3,7,8-tetrachloro-dibenzodioxin (TCDD). Over 200 families were evacuated, 175 individuals developed chloracne and a large number of animals died and/or were disposed of to prevent TCDD entering the food-chain (Homberger et al., 1979). At Bhopal in India, in 1984, the release of methyl isocyanate is believed to have killed about 2,000 people and to have produced injury to the eyes and respiratory

system of 10,000 - 20,000 individuals (Newman-Taylor, personal communication). Accidents such as these led authorities to develop legislation ("Seveso" Directive) on hazardous chemical installations (EEC, 1982, 1987, 1988). Over the same period of time, the availability of computers encouraged extension of the use of mathematical dispersion models in predicting the dispersion of atmospheric discharges in situations where there had been accidental release at ground level. These models may present their output as "contour lines" or "isopleths" of equal concentration which move with time. The term "isopleth" is used in this sense throughout this report. Alternatively, models may present the concentration at a specific point as a function of time.

Under legislation such as that developed from the "Seveso" directive, the management of installations which constitute major accident hazards has been required:

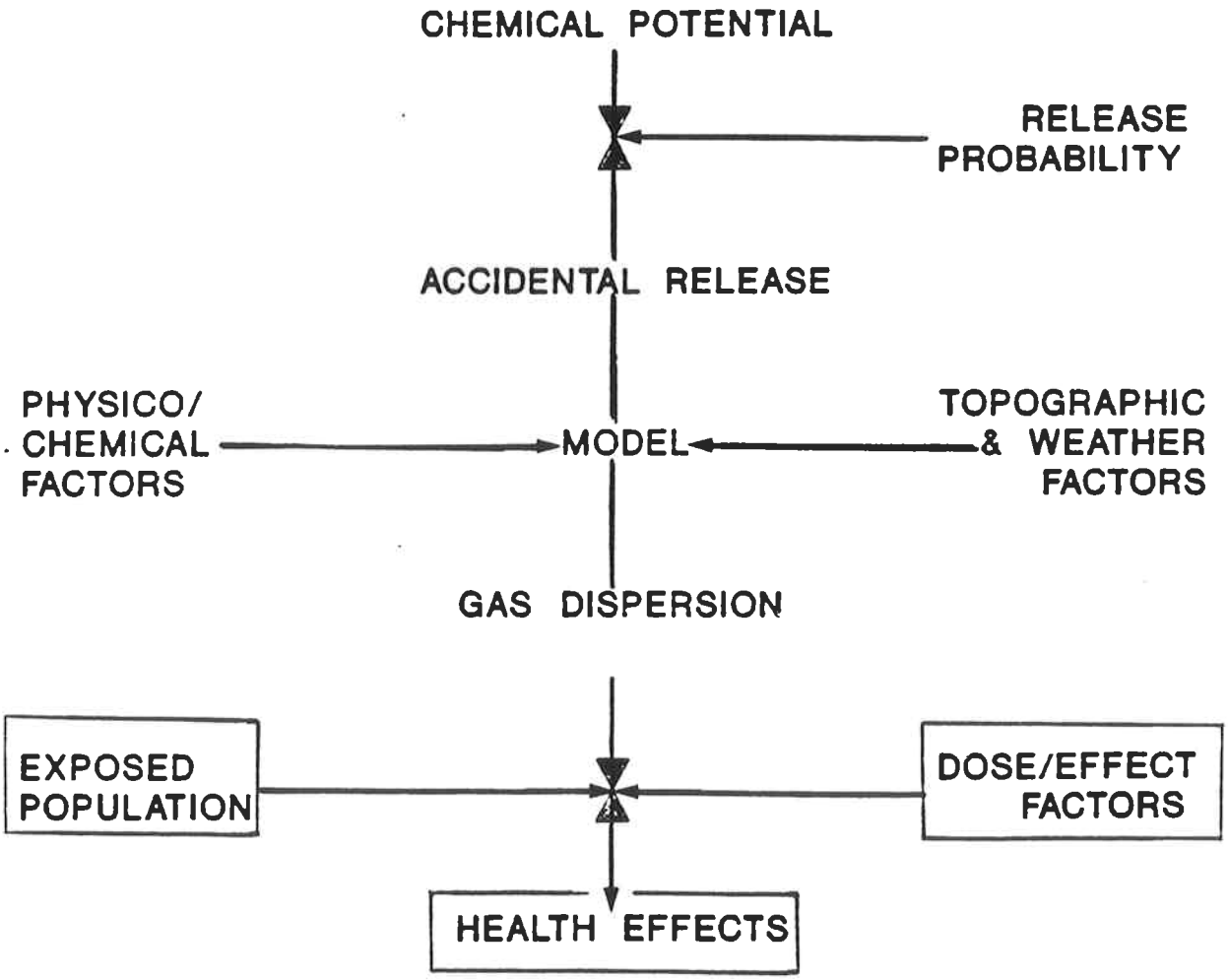
- to assess and minimise the probability of an accident,
- to prepare (in conjunction with local authorities and emergency services) plans to mitigate its consequences and,
- to advise residents near such installations of the nature of the hazard and the measures taken to reduce the risks and the plans prepared to minimise the consequences of any accident.

Such action requires an evaluation not only of the probability of a release but also of its consequences in terms of effects on human life and health, environmental damage and material loss.

The effects on human health of an accidental release will depend on the toxicity of the substance, the concentration of substance in the atmosphere, the period of exposure and the distribution of people in the area surrounding the installation. The concentration in the atmosphere, as a function of time, will depend on the quantity released, the meteorological and other physical conditions including topography, obstacles, etc.. Mathematical models have been developed which help to predict the concentrations of gas or vapour occurring at different times at any point in the neighbourhood of an accidental release (cf Appendix 2). If these estimates are combined with data on population distribution, the numbers of individuals who may become exposed to

various concentrations of substance can be assessed. To predict the severity of their injuries, knowledge of the adverse effects on health of various degrees of exposure to the substance is required.

The relationship of release, dispersion, exposure and health effects can be expressed in the following manner:



This report is concerned only with the factors contained in boxes.

The severity of an injury suffered by an individual will depend on:

- the actual exposure rather than the predicted exposure,
- the susceptibility to the effects of the chemical.

In relation to the first factor, the difference between actual exposure and predicted exposure will depend on the accuracy of knowledge on the quantity and rate of release, the reliability of the model and the local conditions which may produce deviations from the predictions, e.g. the immediate topography and whether the person is indoors or outdoors. In relation to the second factor, susceptibility may be influenced by age, nutritional state, preexisting illness, etc.. It is not therefore possible to predict the severity of the injury of a particular individual; "average" predictions for populations are more feasible.

The Scientific Committee of ECETOC recognised that there was a need for advice on how to derive exposure limits which could be used in evaluating the potential health effects on populations of airborne releases (of gases, vapours and dusts) of the type which could occur in major accidents. A Task Force was set up with the following Terms of Reference:

- to examine criteria for the defining of one or more exposure indices for both workers and the general population which can be used as guidance on the potential health effects resulting from accidental chemical release;

- to develop guidelines for setting such indices;

- to develop guidelines for use of such indices;

- to provide examples of indices for a few representative chemicals.

Effects on the natural environment were excluded although it was recognised that these are important when evaluating the total damage caused by any release and determining the necessary remedial actions. The factors required for evaluating the direct effects on human health are different from those considered when assessing the health effects arising from exposure to

contaminated food or drinking water, or when assessing damage to plant and animal life.

Various atmospheric limits had been produced by several authorities for different purposes and these are detailed in Appendix 1. None of them was suitable as emergency exposure indices (Alexeeff et al., 1989). The basic concepts of suitable indices were therefore defined and the indices were termed "Emergency Exposure Indices" (EEIs). A closely similar concept was developed in parallel by the conjoint activities of the American Industrial Hygiene Association and Organisational Research Counsellors, Inc.. Their exercise has resulted in the definition of Emergency Response Planning Guidelines (ERPGs) and an administrative procedure for developing ERPGs for individual chemicals.

It was not the objective of this report to produce an extensive list of Emergency Exposure Indices for individual compounds, rather to recommend their definition and a procedure for setting them (Appendix 3) and to advise on their proper use. Steps have been taken to test the validity of the procedure by examining the consistency of figures produced by a number of groups who work in the field and who were provided with uniform data sets on the candidate chemicals (subsequently reported in Appendix 4).

EEIs as discussed in this report are intended to provide advice on the concentrations of gas etc. which, if not exceeded over the specified period of exposure, will avoid the clinical effects of interest. They do not provide evidence on the concentrations which will be needed to produce these effects. EEIs are therefore inappropriate for quantitative risk assessment (expressing the expected frequency of a clinical effect) and cannot be used for this purpose.

B. CRITERIA FOR ESTABLISHMENT OF EMERGENCY EXPOSURE INDICES

1. *CONCEPTS*

Any numerical index of toxic effect or any standard which is set to protect against toxic effects must reflect the relationship between:

- the population potentially exposed (i),
- the degree and pattern of exposure (ii),
- the nature and severity of the toxic effect(s) anticipated (iii),
- the proportion of those exposed who are subject to toxic effect(s) (iv).

Thus LC_{50} values refer to a specific animal species (i), an exposure concentration for a specified time (ii), the nature of the toxic effect is death (iii) and the proportion affected is 50% (iv). The TLV-STEL* values refer to workers (i), represent the exposure for 10-15 minutes by inhalation (ii), which is expected to be without significant toxic effects (iii) and in nearly all subjects (iv).

These four concepts necessary in establishing a definition for EEIs and the question of safety factors are considered in turn.

1.1. Population

The population concerned in any industrial accident involving the release of hazardous substances is the work force within the premises and the general public who live or work in the vicinity. The general public will contain groups who may be more susceptible to chemical exposure than the average person, e.g. the elderly, the young, the pregnant and those with minor acute illness or chronic illness compatible with participation in normal daily activities. The TF considered that EEIs set should take into account such susceptible groups but not more seriously debilitated, hyper-

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* Threshold Limit Values - Short Term Exposure Limits (ACGIH)

susceptible groups, e.g. those with pneumonia or myocardial infarction. Hypersusceptible groups of people have been excluded from this exercise because:

- such individuals are considered to be in a grave and unstable health condition and the outcome of their illness will not primarily be related to the degree of exposure. (When potentially exposed as a consequence of a major chemical release hypersusceptible people should, as a high priority, receive medical attention as a precautionary measure);
- data from experimental studies will not, normally, accurately predict the health effects of a chemical in a hypersusceptible individual.

Previous schemes have adopted similar criteria (Subcommittee Toxicity of the Dutch Committee for Prevention of Disasters by Hazardous Substances, 1974; AIHA, 1988).

1.2. Exposure

Following an accidental release of a quantity of a chemical, the concentration at any point to which the chemical disperses will be influenced by meteorological conditions and topography. As the gas-cloud passes and disperses the concentration at a particular point will generally rise to a maximum which will be sustained for a period and thereafter will fall towards zero. Indices of exposure could be the peak concentration, the average concentration over a specified time period or $\int_0^\infty C(t)dt$ (where C(t) is the instantaneous concentration at time t) or some other function of concentration and time.

It was considered that the most practical descriptors of exposure would be the exposure duration and a concentration which was not exceeded during the exposure. Emergency Exposure Indices would be most useful if the exposure period or periods to which they refer were of a duration pertinent to realistic scenarios for the installation under consideration. The description of these scenarios should incorporate both the evolution

of release over time, as determined by product inventory, isolation and other mitigating devices, and dispersion factors as determined by meteorological and topographical conditions. In some cases, the exposure period will be fairly clear and similar for a wide range of concentrations. This will be the case when release is uniform and ceases abruptly and wind velocity is high. In other cases, exposure duration will vary considerably according to concentration of interest and in these cases an iterative process must be used to establish the appropriate duration for each EEI, beginning with an arbitrary period.

EEIs (for each toxic effect (see B.1.3)) should be established where the data allow it for a number of exposure periods up to 1 hour so that values most appropriate to predicted exposure periods may be chosen (few exposures will exceed 1 hour in duration).

Alternatively, the relationship between the EEI and time could be established (either as an equation or graphically) so that the EEI could be estimated for any relevant exposure period. Values should not be established where the data cannot support them and, where an equation or graphical relationship is established, the range of exposure durations for which it is considered valid must be defined.

1.3. Nature and Severity of Toxic Effects

Toxic effects can be of many different types and each can occur with varying degrees of severity. The type of exposure occurring in industrial accidents showed that the effects of importance are those that can occur in man following an acute exposure to an atmosphere containing the substance. Systemic effects will result chiefly from inhalation: local effects will involve the eyes, respiratory epithelium and skin.

In view of the public concern regarding carcinogens, the exclusion of carcinogenic effects from consideration in setting EEIs requires some comment. The TF recognised the importance of cancer as an endpoint but gave weight to the evidence showing that the probability of it occurring as a result of a single, short (accidental) exposure is extremely low.

The risk to the population would thus be small compared with that arising from the acutely hazardous effects of chemicals. The exclusion of cancer as an endpoint in setting EEIs does not reduce the protection of the public because EEIs are predictive in nature, rather than protective. With carcinogens as with other hazardous chemicals, the protection of the public will be achieved by substitution, inventory reduction and safe and secure storage and systems to minimise releases and reduce exposures should they occur. EEIs for carcinogens should be set on the basis of acute effects and it must be recognised that their role is confined to the prediction of the occurrence of acute effects.

There are limitless possibilities for describing the grades of severity of the immediate toxic effects of acute exposures. It is essential in defining EEIs that each should indicate a type of toxic effect which could clearly be seen to require a particular type of practical response. This approach is related conceptually to the clinical practice of triage in casualty management. In common with others working in this field (AIHA, 1988; Illing, 1989; Baxter et al., 1989), a need was recognised for three indices to represent the transitions between four graded effects.

Death/Permanent Incapacity is the most severe effect for which an exposure index could be provided; it is easily defined and is used by society to judge the severity of accidents. Two other grades of effect - disability and discomfort - though less well defined, place distinct demands on emergency and health care services. The term *disability* is used here to indicate that persons will require assistance or that effects of exposure will be more severe and/or prolonged without it. Persons suffering *discomfort*, though distressed and possibly requesting assistance, will not be dependent on it for minimising the severity or duration of the effect of exposure. Exposure insufficient to cause discomfort or adverse health effects may nevertheless be perceived by means of smell, taste or sensations (mild sensory irritation) which are not uncomfortable. This awareness of exposure might lead to anxiety and complaints and constitutes what is termed here *detectability*. Except for *death*, these graded categories of effect are not sharply demarcated but each merges into adjacent categories. The characteristics of the categories are set out

below:

CATEGORY	CHARACTERISTICS
DEATH/PERMANENT INCAPACITY	Death/Permanent Incapacity occurring either immediately or soon after exposure or a permanent loss of a necessary faculty (e.g. blindness) resulting in serious restriction of normal social or economic activity. The possibility of surgical correction (e.g. corneal grafting) does not affect "permanence".
DISABILITY	External assistance is needed because: - persons are disabled by exposure and cannot take actions necessary to protect themselves or escape and/or - exposed persons acquire an illness or condition - of which the outcome or duration can be significantly modified by treatment or nursing care, - with permanent or long-lasting residual effects including effects on the outcome of an existing or subsequent pregnancy.
DISCOMFORT	Exposed persons may request assistance but their condition, though unpleasant and possibly amenable to symptomatic relief - does not produce disablement, - does not result in permanent or long-lasting effects, - is not modified as regards outcome and duration by treatment or nursing care.
DETECTABILITY	Exposed persons may make complaints or enquiries or may express anxiety but exposure, if perceived at all, will be perceived only by smell, taste, sight or by sensations (mild sensory irritation) which does not persist after exposure ceases. There are no direct effects of exposure on health.

Clearly, in triage terms, clinical effort will be directed particularly to persons in the *disability* category.

1.4. Proportion of the Exposed Population showing each Category of Toxic Effect

EEIs should indicate exposures (defined in B.1.2.) which would be thresholds for the occurrence of *death/permanent incapacity, disability or discomfort* (defined in B.1.3.) in the population (defined in B.1.1.). At such a threshold concentration, a small proportion of the population might exhibit effects.

Precision in defining "a small proportion" is impossible and unnecessary because:

- the categories of effect are not precisely demarcated;
- the data available for setting EEIs are imprecise and derived from various sources, including experiments and clinical observations. (Usually these were not designed for the purpose of setting EEIs);
- the incidence of effects at EEI exposures will depend on the proportion of susceptible people in the population and this is variable and uncertain;
- the response will depend on the actual pattern of exposure rather than the predicted exposure category;
- models used to predict the pattern of exposure provide information which is inherently imprecise.

1.5. Safety Factors

No safety factors should be incorporated into EEIs or applied to them. This is because EEI values are intended to predict thresholds for discomfort or health hazard for people rather than to define acceptable exposure levels for health protection. In practice, because the pattern of exposure will almost always lead to effects less severe than those arising from constant exposure to the EEI concentration for the relevant period, a safety factor is inherent in the exposure measure (B.1.2, above). In addition, data used in the setting of EEIs will generally be used conservatively (e.g. use of most sensitive species, see C.5.4). This

will usually mean that if an EEI is not exceeded, the effects it indicates should not be observed.

2. *TERMINOLOGY*

The term Emergency Exposure Index (EEI) was chosen because it signifies the situation to which they are applicable without implying restrictions on the uses to which they may be put. The word "index" suggests the essential low precision of the values determined for them.

The term Emergency Exposure Index should be regarded as a generic term which relates to terms such as ERPG in the same way that the generic term Occupational Exposure Limit relates to terms such as TLV (Threshold Limit Value, ACGIH), MAK (Maximale Arbeitsplatz Konzentration, FRG) or OES (Occupational Exposure Standard, UK-HSE).

Although neither the name ERPG nor the precise definitions used by the ORC/AIHA were adopted, EEIs for 60 minute exposure durations set on the basis of the present document will generally be similar to those developed when working to ORC/AIHA definitions.

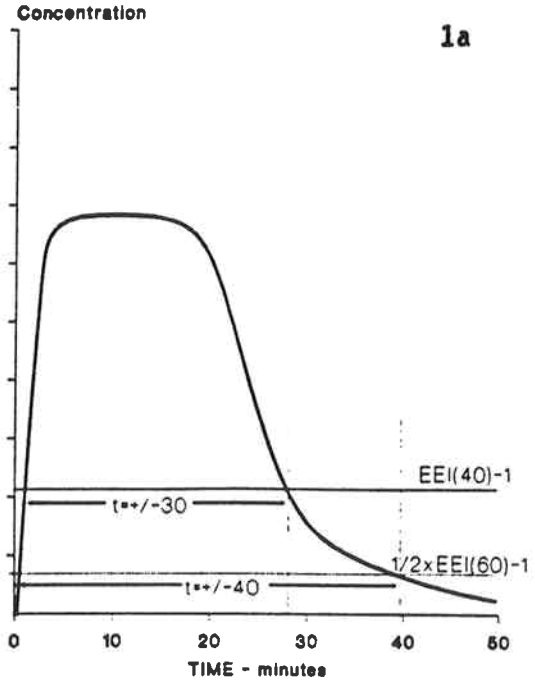
It is suggested that the format for specifying EEI should be as follows:

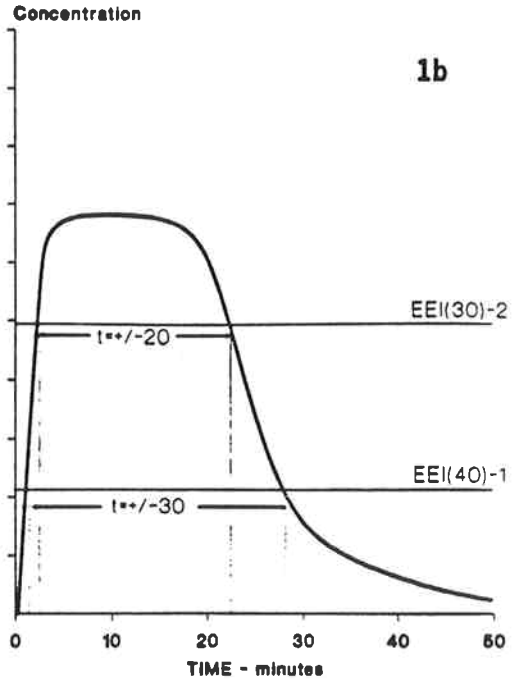
$$EEI(t_N)\text{-}N\ (ABCD)$$

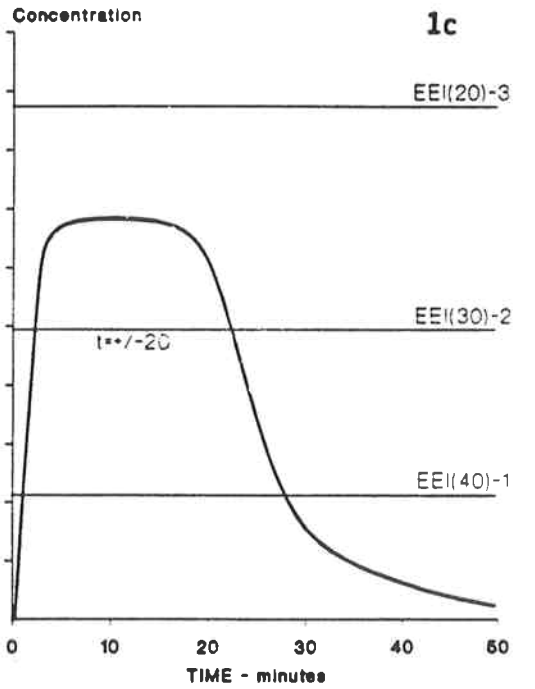
where t_N is the duration in minutes for which the EEI for effect N was established;

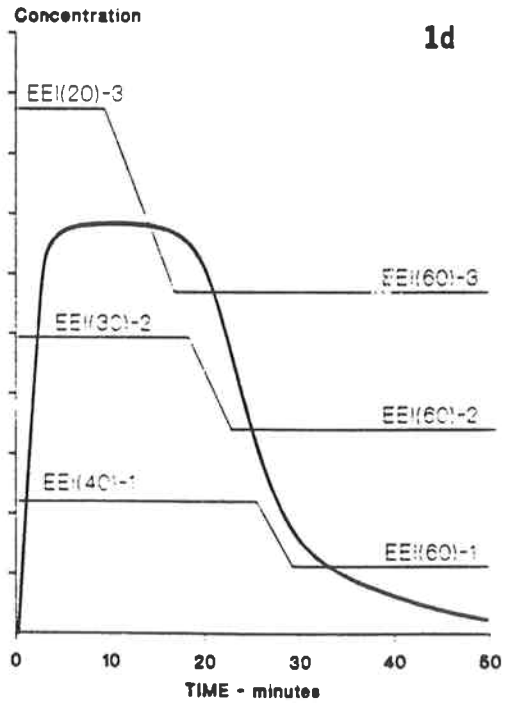
N is 1, 2 or 3 to indicate the effects Discomfort, Disability or Death/Permanent Incapacity, respectively;

ABCD is the Name or Acronym of the responsible institution.









Legend Figures 1a, b, c, d

Each curve illustrates the concentration of a released gas at a particular point varying over time. The initial rapid rise is followed by a plateau and an asymptotic decrease to zero.

1a. Discomfort considerations. The duration of exposure (t_1) relating to discomfort is the time over which ½ EEI(60)-1 is exceeded. This is approximately 40 minutes and there is a possibility of discomfort occurring, since the peak concentration exceeds EEI(40)-1. The time (t_2) that EEI(40)-1 is exceeded (30') is taken to be the exposure duration for disability considerations - see Figure 1-b.

1b. Disability Considerations. The duration of exposure (t_1) relating to disability is the time over which the EEI(t_1)-1 is exceeded, shown in Figure 1-a to be about 30'. In this case there is a possibility of disability occurring, since the peak concentration exceeds EEI(30)-2. The time (t_2) that EEI(30)-2 is exceeded (about 20') is the duration of exposure for death/permanent incapacity considerations - see Figure 1-c.

1c. Death/permanent Incapacity Considerations. The duration of exposure (t_1) relating to death/permanent incapacity is the time over which EEI(t_2)-2 is exceeded, shown in Figure 1-b to be about 20'. Death/permanent incapacity are unlikely to occur, since the peak concentration does not attain EEI(20)-3. Compare with Figure 1-d.

1d. Effect of Allowing Exposure Time Selection on Mortality/Permanent Incapacity Prediction. A fixed exposure time of 60' would result in death/permanent incapacity being considered possible. Selection of appropriate exposure times results in a less conservative prediction which would be expected to be more accurate.

3. *DEFINITIONS*

Emergency Exposure Indices are therefore defined as follows :

Emergency Exposure Index-1 (EEI(t_1)-1)

That airborne concentration for exposures lasting up to a specified time (t_1) below which direct toxic effects are unlikely to lead to *discomfort** in the exposed population (including susceptible but excluding hypersusceptible groups) and above which, as the concentration increases, discomfort would become increasingly more common.

Emergency Exposure Index-2 (EEI(t_2)-2)

That airborne concentration for exposures lasting up to a specified time (t_2) below which direct toxic effects are unlikely to lead to *disability** (the need for rescue or treatment) in the exposed population (including susceptible but excluding hypersusceptible groups) and above which, as the concentration increases, disability would become increasingly more common.

Emergency Exposure Index-3 (EEI(t_3)-3)

That airborne concentration for exposures lasting up to a specified time (t_3) below which direct toxic effects are unlikely to lead to *death/ permanent incapacity** in the exposed population (including susceptible but excluding hypersusceptible groups) and above which, as the concentration increases, death/permanent incapacity would become increasingly more common.

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* as characterised in section B.1.3.

4. *THE EXPOSURE DURATION*

The definitions imply that each effect is unlikely to be observed provided that neither the EEI concentration value nor the chosen exposure period for which the EEI was set is exceeded.

4.1. Deciding the Exposure Period for Open-air Releases

The duration of exposure is not a simple concept. Firstly, a gas or vapour cloud may persist unpredictably in hollows, sheltered areas and other local irregularities. No systematic allowance can be made for this but the possibility must be borne in mind (particularly for heavy vapours and gases) in any considerations of major releases. Secondly, particularly in still conditions, concentrations may approach zero asymptotically. It is therefore necessary to select for each EEI a low concentration below which the exposure period can be disregarded.

It is suggested that for EEI-1, EEI-2 and EEI-3 values, the corresponding "insignificant" concentrations should be ½ EEI(60)-1, EEI(t_1)-1 and EEI(t_2)-2 respectively. The successive application of these is shown in Figures 1-a, -b, and -c which illustrate the concentration of released gas with increasing time.

In all cases there is an initial rapid rise in concentration followed by an asymptotic decrease to zero. When assessing the possiblity for discomfort (figure 1-a) the duration of exposure (t_1) is the time over which 1/2 EEI(60)-1 is exceeded. This is approximately 40 minutes; there is a possibility that discomfort will occur as the peak concentration exceeds EEI(40)-1. The time (t_2) that EEI(40)-1 is exceeded (30 minutes) is taken to be the exposure duration for disability concentrations.

The concept for a disability concentration occurring is when the peak concentration exceeds EEI(30)-2 (figure 1-b). The time (t_3) that EEI(30)-2 is exceeded (about 20 minutes) is the duration of exposure leading to death/permanent incapacity considerations further illustrated in figure 1-c. In this latter case death/permanent disability is unlikely

to occur as the peak concentration does not attain EEI(20)-3. This situation should be compared to that illustrated in figure 1-d which examines the hypothetical effect of changing exposure time selection on the death/permanent incapacity prediction. With a fixed exposure time of 60 minutes death/permanent incapacity would be considered possible; selection of appropriate exposure times results in a less conservative prediction which would be expected to be more accurate.

If successive isopleths (isoconcentration contours) for a particular EEI are plotted at successive time intervals on a series of parallel lines (representing the wind direction), the maximum duration of exposure can be determined from the intervals between the times the cloud reaches and passes particular points (Appendix 2, fig A2-1). If the isopleths are drawn for the EEI(60)-1 the area outside the isopleth envelope (the envelope enclosing all successive isopleths) represents the area of ground where the EEIs are at no time exceeded and therefore the area where no adverse effects are likely to occur following an emission. Alternatively, dispersion models may produce concentration-time diagrams which can be used to determine the appropriate EEI exposure duration for a particular point (Appendix 2, fig A2-2).

The choice of duration of exposure in this way may be restricted by the availability of EEI values for short exposures because of lack of data.

4.2. The Exposure Period for Releases into Confined Spaces

EEIs might legitimately be applied to the release of gases or vapours into confined spaces such as buildings. In this case, the time-course for the concentration must be estimated on the basis of release and ventilation data. The exposure duration may be found to be the evacuation time rather than the time until the concentration falls to near-zero; if disability could occur within the evacuation time the health effects would be greater. Such a situation might require provision of improved escape routes or the availability of personal protection of some kind.

4.3. Implication of the Definitions

The implications of the definitions of EEIs when used in conjunction with dispersion models are as follows:

EEI(t_1)-1

Provided that the duration of significant exposure (>½ EEI(60)-1) does not exceed t_1, discomfort will be unlikely in an area outside the envelope of successive isopleths calculated for the EEI(t_1)-1 value. Discomfort would not necessarily occur within that area, but it might.

EEI(t_2)-2

Provided that the duration of significant exposure (> EEI(t_1)-1) does not exceed t_2 disabling effects would not be expected outside the isopleth envelope at EEI(t_2)-2. Within this envelope disablement would not necessarily occur, but it might.

EEI(t_3)-3

Provided that the duration of significant exposure (>EEI(t_2)-2) does not exceed t_3 death/permanent incapacity would not be expected outside the isopleth envelope at EEI(t_3)-3. Within this envelope death/permanent incapacity would not necessarily occur, but it might.

4.4. Other Situations

There may be other situations in which EEIs would have applications. Their suitability for any such applications should be established carefully and with a full understanding of the principles underlying the definitions.

It is again emphasised that EEIs used in this process are intended to provide advice on the concentrations of gas etc. which, if not exceeded over the selected period of exposure, will avoid *death/permanent incapacity*, *disability* or *discomfort*, and not on the concentrations which will be needed to produce those effects.

C. GUIDELINES FOR SETTING EMERGENCY EXPOSURE INDICES (EEI)

1. *DATA COLLECTION*

Ideally the data from which EEIs are set would be well-documented descriptions of the clinical effects seen in a representative sample of the general population exposed to accurately measured concentrations of the substance under consideration for relevant exposure periods. In practice such data never exist. Reliance has to be placed on toxicological data from animal studies and clinical data, usually from workplace accidents. It is essential that a thorough literature search be conducted for data relating both to accidental and experimental human exposures and to toxicological studies. Although the most immediately or directly applicable data will come from reports of acute inhalation studies in animals and man, the search should not be confined to these but widened to include all routes of exposure and all exposure periods. Where the reports of inhalation studies are scant (or inadequate), this subsidiary information may be helpful and in all cases will provide confirmatory information on the overall toxicity of the substance. In some circumstances, for example where the data available on the chemical itself are inadequate, data relating to a close chemical analogue may contribute significantly to the information to be considered.

All data sources should be consulted, including the published scientific literature and any unpublished information from industry and public bodies. Every attempt should be made to obtain the full text of original articles in order to extract the detail of the experimental conditions and results. Secondary information sources should be used only when original articles cannot be obtained.

2. *EVALUATION OF THE DATA QUALITY AND RELEVANCE OF REPORTS*

Once reports have been identified, the value of each should be judged against a number of criteria:

- the adequacy of the description of methods, results, statistical analysis, atmospheric analysis, etc.;

- the degree of detailed information on,

  - findings in individuals and groups of individuals,
  - the qualitative and quantitative description of effects,
  - the degree of exposure and variability of exposure of individuals or groups,
  - dose/response relationships for each effect;

- the relevance of the study, in particular the relevance of,

  - the experimental species used,
  - the route(s) of exposure of experimental animals,
  - the duration and pattern of exposure (whether of animals or man) to the duration and pattern relating to EEIs,
  - the duration of the post-exposure period of observation to the types of adverse effects seen;

- the degree to which the findings are consistent with findings in other valid experimental and human studies.

It is appropriate to reject part or all of the data in any study on the basis of the above criteria if serious inadequacies are identified. If it is decided to reject data, the reasons for the action should be documented, if only for audit purposes.

3. *SELECTION OF RELEVANT DATA*

Data relevant to each of the Emergency Exposure Indices should be extracted from reports. Both quantitative and qualitative data should be collected which relate to each of the following effects:

- death/permanent incapacity;
- disability, e.g. pathological effects in the lung or clinical observations indicative of severe respiratory impairment;
- discomfort, e.g. significant sensory irritation;
- detection, e.g. smell, transient irritation.

The data describing individual effects should be considered from three points of view:

- the relationship between the dose and each effect, with the primary objective of determining either the threshold concentration or the highest no-effect level;
- whether the severity of the response is more related to the cumulative dose received (i.e. concentration x time) or is more related to the absolute exposure concentration (i.e. independent of time);
- in cases where cumulative exposure is the predominant factor, the influence of the duration of exposure on the dose-response relationship.

4. *THE CONTRIBUTION OF HUMAN DATA*

Human data may be available from three types of study:

- effects observed following accidental exposures;
- experimental studies in volunteers;
- epidemiological studies.

4.1. Accidental Exposures

Reports may be available on the health effects of accidental acute or prolonged exposures to substances during their development, production, use or disposal. These reports generally consist of a description of the circumstances of exposure, the presenting symptoms, the clinical signs, the results of medical tests (e.g. X-rays, haematological and biochemical tests) and the outcome of any treatment. Sometimes, the degree and duration of exposure are known or can be judged with confidence (e.g. by

reconstruction of the accident). More often than not reliable evidence about the true extent of exposure is lacking; such data must therefore be used with care when setting EEIs.

4.2. Experimental Studies

Information is occasionally available from experimental studies in which human volunteers have been exposed to known atmospheric concentrations of a substance for known periods or have been exposed by the oral or dermal route to known quantities of substance. Their subjective and objective clinical responses are usually noted before, during and after recovery from the exposure. Such findings are generally of value only in setting the EEI-1, since the experiments must be designed to avoid causing any significant damage to health. When using such information, it must be recognised that the volunteers are usually highly selected and their physical and other characteristics and health are likely not to be truly representative of the population at risk.

The evaluation of experimental human data should include consideration of both the pre- and post-exposure health of subjects, their clinical symptoms and signs and other medical findings. It will also include making expert judgements about the likelihood, nature and extent of exposure and the feasibility that the observed effects are causally related to exposure. Such evaluations must be made conjointly by those experienced in occupational medicine, hygiene and toxicology.

Human studies may also provide information on the more subjective aspects of perception (odour, taste, nuisance), as well as indicate the possibilities of medical treatment.

4.3. Epidemiological Studies

Epidemiological studies relating to substances used in industry may be useful in setting EEIs, but more frequently they are not since they usually describe the effects of long-term exposures which are of little relevance to those which occur in industrial accidents.

5. *THE CONTRIBUTION OF ANIMAL DATA*

5.1. Studies of Different Types

The most relevant animal data will be obtained from acute inhalation experiments because:

- they indicate those toxicants which have a direct toxic action on the respiratory tract;

- the rate of uptake by the inhalation route is more relevant than that by other routes when the effects are systemic (toxic to internal tissues after absorption);

- such experiments are usually able to show the correlations between exposure duration, atmospheric concentration and resultant toxic effects.

Acute studies using other routes of administration (e.g. oral, dermal) can provide supporting data, particularly for systemic toxicants (ECETOC, 1984). For such data it is necessary to relate the oral or dermal dose to the inhaled dose of the substance. Knowledge of the metabolism and pharmacokinetics of the substance by each route of exposure is necessary before such data can be used with any degree of confidence. Where no inhalation data are available on a substance, it may be most appropriate to initiate testing in order to generate the data required.

When considering the use of data from exposure routes other than inhalation, the following should be noted:

- For compounds acting directly on the surface membranes of the respiratory tract, estimation of the inhalation toxicity from oral or dermal toxicity studies leads to an underestimation of their potency.

- Substances absorbed via the lungs may not undergo significant metabolism before reaching the heart, central nervous system and other

target organs or tissues. Substances administered orally may be incompletely absorbed, or altered by digestion or metabolism in the intestinal mucosa or liver before entering the systemic circulation and reaching the target organs. Thus the effects of inhaled and orally administered substances will often be quantitatively or qualitatively different.

- The cumulative dose of a chemical administered by inhalation is usually proportional to the product of the exposure period and the atmospheric concentration while the dose enters the body gradually throughout the period of exposure. A substance administered by other routes may be absorbed over shorter or longer periods of time and may thus produce totally different blood and organ concentrations. Equivalent doses by the various routes may therefore lead to different peak blood and organ concentrations, resulting in variations in the toxic effects.

5.2. Indicators of Lethal/Permanently Disabling Effects in Man from Acute Animal Exposures

When considering the lethal concentration for establishing the EEI-3, both the time of death and the possible cause of death of animals should be examined with a view to judging the possible benefits of treatment in man. In the absence of data from which to judge the likely success of treating human cases it would be reasonable to take deaths occurring during exposure or within 48 hours as indicating the EEI-3 concentrations and to assume that deaths occurring after that time could be prevented by treatment, i.e. indicative of the EEI-2 concentrations.

Permanent incapacity is difficult to predict. The question of carcinogens has already been considered (cf B.1.2). Scarring of the cornea and lungs leading to blindness and severe restrictive pulmonary disease are the most likely causes of permanent incapacity and these will be most likely with severe irritants. Nevertheless human experience is invaluable in such instances, since it is known that chlorine, though irritant, seldom provokes a severe fibrotic reaction in the lungs.

5.3. Indicators of Non-Lethal Effects in Man from Acute Animal Exposure

Non-lethal effects are judged from clinical, pathological and functional changes occurring following acute exposure of animals. The following animal findings may be indicative of:

Disability

- deaths occurring more than 48 hrs after cessation of exposure,
- pulmonary oedema and major pathological changes in the respiratory system, short of permanent fibrosis,
- neurotoxic effects including significant CNS depression,
- evidence of severe changes to other organs e.g. liver, kidney,
- cardiovascular effects e.g. cardiac sensitisation, hypotension,
- severe lachrymatory effects or corneal damage, short of severe scarring,
- corrosive effects on the skin,
- effects on the blood e.g. severe methaemoglobinaemia or carboxyhaemoglobinaemia,
- evidence of teratogenic or foetotoxic activity;

Discomfort

- all effects reversible within 24 hrs without treatment,
- moderate to severe skin irritation,
- moderate eye irritation,
- respiratory irritation as shown by a significant decrease in respiration rate or nasal discharge,
- piloerection and other evidence of increased autonomic nervous system activity;

Detection

- evidence that animals had recognised the presence of an atmospheric contaminant e.g. increased motility, rubbing of eyes, or minor changes in the pattern or rate of respiration.

Where a substance is either known or suspected to cause teratogenic or foetotoxic effects, the possibility must be considered that these effects could be manifest in man as a result of a single exposure to a concentration below that causing other effects associated with an EEI(t)-2. Where this is so, it must be reflected in the figure set for the EEI(t)-2. In such circumstances, specific information as to the nature of the toxic effect should be made available to those concerned.

Most data on non-lethal effects (*disability*, *discomfort*) in animals will come from repeated exposure studies. Chronic or cumulative actions of the chemical may produce effects at lower exposure levels than after single exposure. On the other hand, perception (odour detection, irritation) may be reduced after prolonged or repeated exposure. Thus data from repeated exposure can overestimate as well as underestimate the non-lethal effects and should be used with care.

5.4. Species Variability

It is advisable to consider data separately for each species and then to identify and consider the significance and possible causes of any marked species differences in sensitivity before deciding whether any of the species is likely to give a more accurate prediction than others of the effects in man. Where there is uncertainty, the data from the most sensitive species should be used in developing the EEIs. There are limited circumstances where it would be appropriate to use data from another species, thus:

- where there is a substantial body of human data which contradicts the data from the most sensitive animal species;

- where substantial data from the majority of a (less sensitive) species are in good agreement with the data for man;

- where it is known that, for a particular effect, the most sensitive animal species is not an appropriate model for man;

- where it is known that, (because of marked differences in absorption, metabolism or excretion of the substance) the most sensitive species is not relevant for man.

6. *ORDERING, USE AND PRESENTATION OF THE DATA*

6.1. Ordering of Data

Having identified and evaluated the valid and potentially useful information, it should be ordered in a logical fashion.

It is recommended that, for each toxic effect category, the data be considered species by species, giving priority to observations in man and to inhalation studies, where available. A data-set might be arranged in the following way:

Death/Permanent Incapacity
- inhalation data from human experience,
- inhalation data from all available animal studies,
- data (if applicable) by other routes of administration in animals;

Disability for each type of abnormality recognised e.g. lung damage,
- inhalation data from human experience,
- inhalation data from all available animal studies,
- data (if applicable) by other routes of administration in different animal species;

Discomfort for each type of abnormality recognised e.g. irritation of respiratory tract,
- inhalation data from human experience,
- inhalation data from all available animal studies,
- data (if applicable) by other routes of administration in different animal species;

Detection for each sensory modality recognised e.g. irritation of eyes,

- inhalation data from human experience,
- inhalation data from all available animal studies.

6.2. Use and Presentation of the Data

The ultimate aim of the exercise is to describe the incidence of each adverse effect as a function of the degree of exposure and its duration, in order to estimate the level of exposure which is the threshold for each effect at the duration of exposure under consideration.

Consequently it is necessary to consider each set of data in terms of its time/concentration relationship, as far as it is possible. In some cases data will be insufficient; then a judgement of the threshold concentration will be based on experience. In other cases the threshold concentration might be estimated by analysis of data using, for example:

- log concentration/log time graphs (see Appendix 3),
- appropriate computer programmes to allow statistical analysis or graphical display of the data.

Before presenting the data for each effect it is necessary to consider species, concentration, exposure time and the quality of the data. Those data which cannot properly be considered in this way (e.g. when duration of exposure is not known) should be discarded. Data points lying significantly outside the range of the majority should be reviewed and, where possible, the reasons for the difference identified. Such data points may be discarded if there are reasonable grounds for so doing.

Other limits, such as occupational exposure limits (e.g. TLV and MAK values) should not be directly incorporated into the assessment. Nevertheless the documentation used to establish them, which is often published, may contain data which can be used to establish EEIs.

6.2.1. The use of Haber's law. Haber's law has been used to describe the relationship between the constant atmospheric concentration (C) of a toxic gas or vapour and duration of exposure (t) resulting in a particular toxic endpoint (e.g. LC_{50}). The original law $C.t = k$ has been modified to a more generally applicable form:

$$C^n.t = K$$

where C = concentration,
t = time,
K = constant and
n = a number > 0

or $$n \log C = -\log t + k'$$ where $k' = \log K$

Such a relationship is expressed as a straight line of slope 1/n on a log C vs log t plot. The linearity of such a plot for a particular effect and response will indicate the applicability of Haber's law in that situation. Haber's law is known to apply to some toxic gases and vapours but in others, particularly where exposure leads to effects arising from the direct action at the site of initial contact, the toxic effect may be more closely related to the peak concentration. For many substances, there is no simple relationship.

If calculations based on Haber's law are made to interpolate or extrapolate data to concentrations and times not actually studied experimentally, it must be remembered that - for a given substance - different toxic mechanisms may be responsible for producing the various abnormalities being considered and different dose-effect relationships may apply to them. As a general rule it is not possible to use Haber's law to deduce the threshold of an effect for an exposure period shorter than that used in the relevant experimental studies. It may be acceptable to calculate a threshold for longer periods of exposure than that studied (for example the threshold for a 2 hrs exposure from data from a 1 hr exposure) since such an extrapolation can be expected to overestimate the threshold for the effect. Extrapolation to periods shorter than those used experimentally should be used only where there is adequate information on the mechanism of toxic action.

When using this approach it should be remembered that, for a given toxicant, the mechanisms of action leading to each category of effect (i.e. *death, disability* etc.) may well be different. Thus any relationship established for one effect may not be applicable to the other effects. Care must therefore be taken in transposing a relationship derived for one effect (e.g. death) to data referring to a second effect (e.g. discomfort).

Where the quality of data in individual experiments permit, the use of Probit analysis may be appropriate for examining dose-response data (Finney, 1971). In some cases there may be sufficient confidence in the data to make an estimate of the threshold concentrations (i.e. Effect Concentration 1%) at various time points for the effect under consideration. It also gives information as to the value of n in modification of Haber's law and allows extrapolations of the data to be made for exposure periods greater than the range of the experimental data. More pragmatic estimates can often be made with data of lesser quality by using log C/log t plots and determining the relationship by eye. However, this approach will clearly lead to lower confidence in the accuracy of the estimate. In most instances available data will not be of a sufficient quality to allow statistical treatment.

6.2.2. Optimising Estimates of Concentration as a Function of Exposure Time for a Particular Lethal Response (e.g. LC_{50}, LC_1). Where several acute inhalational toxicity experiments have been performed in a particular species, each comprising groups of animals exposed to a particular concentration for a particular time and having a measured mortality, it may be possible to combine all of the data sets using suitable statistical procedures, e.g. probit analysis, in order to produce an overall estimate of the relationship between LC_{50} (or LC_1, $LC_{0.1}$ etc.) and time of exposure from which a more reliable estimate of the value at a particular time may be made. Thus a line on the Log C vs Log t plot (see Appendix 3) representing the function so obtained for a low lethality relevant to the setting of an EEI-3 may be a useful contribution to a critical scientific review. The choice of the low mortality value, the weight given to such data in comparison with data

from man or other species in which there may be insufficient data for such an analysis and the extent to which it is legitimate to extrapolate beyond any studied exposure duration are critical judgements requiring the opinion of experts in more than one discipline.

6.2.3. Priority of human data. The importance of human data is emphasised. When considering such data particular attention must be given to the accuracy of the estimates of exposure concentrations. In many cases it will be found that no direct measurement of concentration has been made but that exposure levels will have been inferred from minimal information. Such estimates are often the primary cause of discrepancies between information obtained in man and that from animal studies in which exposure concentrations are usually measured and are therefore more reliable.

EEIs can be derived from human data alone if it is scientifically sound. If this is not the case, it must be supplemented by data from animal studies.

6.2.4. The use of safety factors. It is not considered necessary to apply a safety factor when estimating the threshold for any specific effect in man from the thresholds as determined or estimated in animals.

6.3. Example

Appendix 3 consists of a worked example of the way in which data may be used to determine EEIs. Chlorine was chosen as this chemical has been reasonably well studied over a number of years (cf Appendix 3).

It is emphasised that the EEIs were derived from the data quoted; other competent groups with access to other data may reach different conclusions about appropriate values for the EEI(t)-1, -2 and -3 for chlorine.

6.4. Ring Test

In order to test the comprehensibility of the EEI concept and the procedures used in the above example a "ring test" was conducted to evaluate the consistency of values produced by different groups. Participants were asked to set EEIs for 15, 30 and 60 minute exposures (where possible) for phosphine, acrylonitrile and hydrogen fluoride. The results are given in appendix 4. Eleven groups of one, or at best a few people participated; there was considerable variability in the values. In general this variability resulted from different opinions on the validity or relevance of particular data. The variability would be overcome if EEIs were set by a larger, multi- disciplinary group or by discussions between the several groups who had derived indices for the same chemical.

7. *THE NEED FOR FURTHER TESTING*

In some circumstances, especially where there are no human data or experimental animal inhalation studies, it may not be possible to set an EEI. In such cases it is recommended that proposals for conducting relevant studies are formulated.

The design of such studies would differ from those of standard safety evaluations since they should be tailored to produce information appropriate to the estimation of an EEI. For example, an acute inhalation study conducted to the current OECD protocol would not be appropriate since a range of exposure times (e.g. between 5 and 120 minutes) and a range of exposure concentrations would be required to allow the threshold of all acute effects to be determined as a function of time.

8. *THE NEED FOR REVIEW*

EEIs should be regularly reviewed to take into account any new data from animal studies or from human experience.

D. GUIDELINES ON THE USE OF EMERGENCY EXPOSURE INDICES

1. *THE PRACTICAL APPLICATION OF EEIs*

EEIs can be applied to situations arising from an actual or conceivable accidental release of chemicals but they cannot be used in isolation. Normally, they will be applied predictively to estimate the potential for human health effects resulting from credible release scenarios at existing or planned chemical installations. In many instances judgements based on knowledge or experience may enable their estimation to be simplified. The procedure for the use of EEIs is quite complex and a thorough understanding of this complexity is necessary to avoid their inappropriate use or application. Evaluation of the consequences of a release to the open air involves seven stages:

- definition of the accident scenario and determination of all relevant characteristics of the release as a function of time;

- definition of the meteorological conditions to be considered;

- selection an appropriate dispersion model/system;

- determination of the time-concentration relations* at the points of interest,

- deciding which of the effect categories, *Death/Permanent Incapacity*, *Disability* and/or *Discomfort*, and therefore which of the EEIs, are under consideration;

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* At any point involved in the passage of a cloud of gas or vapour, the concentration will increase to a maximum and then decrease towards zero. To visualise the dispersion of the gas cloud, the dispersion can be expressed two-dimensionally as a family of concentration-time plots for different places (Fig A2-2) or as a family of concentration-place curves (isopleths) for different times (Fig A2-1).

- determination of the exposure duration at the points of interest for the selected effect category (cf B.4.1);

- drawing (constructing) concentration-time plots at points of interest or isopleth envelopes for EEIs of interest to determine the impact of exposures resulting from the accidental release.

It is again emphasised that EEIs used in this process are intended to provide advice on the concentrations of gas etc. which, if not exceeded over the selected period of exposure, will avoid *death/permanent incapacity, disability* or *discomfort*, and not on the concentrations which will be needed to produce those effects. Therefore EEIs cannot be used for quantitative risk assessment (expressing the expected frequency of a clinical effect).

2. *THE USE AND MISUSE OF EEIs*

EEIs have been designed specifically to provide practical information on the health hazards associated with single, accidental exposures to chemical substances in a form appropriate for several purposes. In association with information produced by mathematical dispersion modelling, they can be used to predict or exclude possible effects on the health of those who may be exposed in areas around the release site. Such predictions are of value in:

- estimating the possible health effects of accidental releases in existing or proposed situations;

- evaluating the need for measures to reduce adverse health consequences in the general population and workers at the site of a potential release so as to avoid a catastrophic outcome, e.g. by inventory control, changes in plant design, construction or operation, siting of escape areas;

- in co-operation with public authorities, establishing and maintaining contingency procedures to minimise the effect of accidents that may nevertheless occur (CEFIC, 1987, 1989);

- on-site and off-site emergency response planning to ensure effective deployment of emergency services.

Not all indices will be equally relevant to these situations.

A distinction should be drawn between

- planning the emergency response to an accidental release considered credible from an existing installation and,

- planning the location and design of a new installation to meet safety criteria acceptable to society.

For the former purpose, all three EEIs are appropriate. For the latter, society should choose the health effect which is just unacceptable in the context of the improbability of the cause. If this corresponds to one of the EEIs proposed, then this EEI may have a contribution to decisions regarding permission for new installations. If society chooses an endpoint which is different from those chosen in this report, a different index would be required, but the principles of its setting and use would be similar to those described in this report for EEIs.

It is emphasised that EEIs should not be used as assessments of health risk in other exposure situations or for purposes other than those outlined above. There is inevitably a considerable degree of uncertainty attached to EEI figures and, while they will be sufficiently accurate for use in emergency planning, they cannot be applied to the evaluation of health hazards in other exposure situations without reconsideration of the suitability of the human and animal data on which they have been based (cf C.4.2.,C.4.3).

In particular EEIs cannot be used to evaluate:

- occupational exposures resulting from normal operations;

- effects of repeated exposures on health;

- effects on the environment (other living organisms, food, animal foodstuffs, etc);

- ambient air quality;

- toxic effects of exposure to the combustion products of the chemical,

  [some chemicals produce combustion products (e.g. HCN, HCl) which, in specific cases will present a greater hazard than the parent substance, when it is known that a substance will, when burned, produce products of toxicological significance, their impact on the EEI should be considered as a separate exercise];

- the numerical probability of any particular health outcome.

3. *PROBLEMS ASSOCIATED WITH THE USE OF EEIs*

3.1. The Uncertainty of Effects within Isopleth Envelopes

The total area in which any EEI is exceeded is the envelope enclosing the sequential isopleths (cf B.4.1, Fig. A2-1). This shows isopleths for a selected concentration at 6 successive time periods and the envelope enclosing all areas where that concentration has been exceeded. If that concentration is the EEI(60)-1, it will be unlikely that discomfort will be experienced in areas outside the envelope. Nevertheless within the envelope there will be areas where the EEI (60)-1 level is experienced for periods less - and sometimes much less - than 60 minutes and in these areas also it is possible that no discomfort will be experienced.

There will be a similar state of affairs when envelopes for the isopleths for the EEI(60)-2 and EEI(60)-3 concentrations are plotted.

Thus setting EEIs for a standard period of time (e.g. 60 minutes) and using an envelope to delineate all areas covered by that concentration can produce an exaggerated view of the area in which health may be put at

risk. Where individual isopleths show that the realistic exposure period is shorter (or in some cases larger) than 1 hr, then a more accurate picture of the likely hazard areas will be produced using EEIs set for the shorter or longer period.

3.2. Exposure to Mixtures of Substances

It must be recognised that following an accidental release exposure may not be to a single substance but to a mixture of two or more substances. Where there is a potential for mixed exposure it may be possible in some cases to base the evaluation on the most toxic component of the mixture, knowing that control of its hazard will automatically control the hazard of other components. In other cases, where it is clear from the toxicity of the components that each acts independently of the others, it may be possible to set EEIs for individual components and predict the areas covered by calculating their isopleths. In a limited number of cases components of a mixture may act synergistically and, if so, EEIs would need to be set taking this toxicological phenomenon into account. In the vast majority of the cases there will be insufficient data from which to decide whether components act independently or (more rarely) synergistically. In those cases it is safest to assume that their toxicity will be additive. Developing EEIs for mixtures will be extremely complex and done only rarely, not only because because of the difficulties of judging the toxic hazards of mixtures, but also of the uncertainty about the composition of any mixture and the fact that the proportions of components may vary with time and at different places after release.

3.3. Other Uncertainties

It is imperative that those setting and using EEIs recognise that the conclusions that can be drawn from them are inherently imprecise because of the uncertainties outlined previously. The imprecision arises from the facts that:

- EEIs do not demarcate sharply between effects but represent broad transition zones;

- the data used in setting EEIs are usually imperfect and this will lead to uncertainty in the resulting values;

- individual dispersion models are not perfect and different mathematical models often produce different results;

- models depend upon input data, e.g. on the quantity and rate of release of a chemical and on the meteorological conditions as well as the local topographical features which cause deviations from predicted concentrations even where models and their input conditions are broadly accurate (cf Appendix 2);

- population characteristics, such as nutritional status, endemic disease and genetic factors may cause a particular susceptibility or resistance in population affected by a chemical release;

- considerable differences in effect may result from the type of housing in the area affected and the extent to which people are able to escape indoors.

When developing plans for avoiding or mitigating the potential health effects of a chemical release, EEIs should be used with care and with a thorough understanding of the uncertainties involved. It is essential that EEIs are used only by competent persons or groups with experience in the interpretation of toxicological and clinical data in man, in the prediction of credible release scenarios and in mathematical dispersion modelling.

E. CONCLUSIONS

There is a need for Emergency Exposure Indices in planning emergency responses and there is general agreement that there are three effect criteria to be considered. The definitions of these adopted by ECETOC differ slightly from those in the AIHA ERPG programme. This difference is not considered likely to effect the choice of exposure levels for each effect as there is a large measure of agreement between the ECETOC EEI concepts and the ERPG concepts.

Despite the simplicity of the single exposure period of 60 minutes adopted by the AIHA, ECETOC considers that EEIs should be set for exposure periods appropriate to the accidental release for each health effect for which they are to be used. In practice, ERPGs and EEIs set for a 60 minute exposure period can be considered as virtually identical.

It is possible that one EEI or an index derived similarly for a more relevant endpoint could contribute to decisions regarding the acceptability of an installation in a community.

From experience in the preparation of Appendix 3 and the experience of the ring test (appendix 4), it is clear that setting EEIs is a complex and time-consuming task which needs to be undertaken by one or more expert multi-disciplinary groups in which a consensus can be reached about the validity and relevance of individual data points which may be critical to the setting of EEIs. In many cases, data are likely to be inadequate and additional data may have to be generated. The setting of EEIs is thus a costly exercise; it should not wastefully be duplicated. Steps should be taken to consider carefully the need to co-ordinate the development of EEIs and to gain for them an international approval.

EEIs are a part of a complex process involving the definition of accident scenarios, the estimation of their probability of occurrence, the modelling of gas dispersion and the extrapolation of dose-effect data across time, different endpoints and species. The process is inherently imprecise and continuing

efforts for improvement will be required in all aspects of the process and in the interfaces between them.

The Ring test demonstrated the comprehensibility of the EEI concepts and the usefulness of the guidance. Though concordance between participants was not as close as might have been wished, an analysis of the reasons for disagreement indicated that these would readily have been resolved by discussion between the groups.

A separate exercise would be necessary to evaluate threshold concentrations for use in evaluating the impact of accidental releases on the natural environment.

F. RECOMMENDATIONS

1. When EEIs are to be set, this should be done by a multidisciplinary team using techniques similar to those outlined in this document.

2. There should be rigorous search for and evaluation of data prior to the selection of data of suitable validity and relevance for setting EEIs.

3. The EEI setting process should be meticulously documented so that the procedure adopted and judgements made are evident.

4. Where data prove inadequate to set one or more EEIs for one or more exposure times, no value should be set until additional data are available.

5. Protocols for tests which can provide information appropriate for setting EEIs should be developed.

6. Where separate groups arrive at different EEI values these should be resolved by scientific consultation rather than an averaging process.

7. Dispersion models need calibration or modification for use at low concentrations, such as those of EEIs, where factors such as adsorption which are not normally included in the model become important.

8. Groups developing EEIs in accordance with the concepts and definitions of this document are encouraged to use the notation suggested in this document, including appending the name, initials or acronym of any authority accrediting the values.

9. Consideration should be given to the advisability of developing EEIs on an international basis.

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APPENDIX 1

EXISTING SHORT-TERM LIMITS

Titles and Acronyms	Responsible Organisation	Definition	Aims	Notes
Threshold Limit Value Short-Term Exposure Limit TLV-STEL	American Conference of Governmental Industrial Hygienists (ACGIH) (1989 -1990)	15 minute time weighted average concentration in the working environment	To prevent irritation, chronic or irreversible tissue damage or narcosis of a degree which will increase the likelihood of accidental injury, impair self rescue or reduce work efficiency in the workplace environment.	The limit should not be exceeded in the workplace. Exposures should not exceed 15 minutes and should not be repeated more than 4 times daily. There should be at least 1 hour between successive exposures at the STEL.
Threshold Limit Value TLV-C (ceiling)	ACGIH (1989 - 1990)	A concentration that should not be exceeded during any part of the day in the working environment.	To prevent over-exposure to substances which rapidly produce adverse or immediately lethal effects (e.g. irritant vapours) in the workplace.	If instantaneous monitoring is not possible, sampling may be over a 15 minute period except for substances producing effects over a shorter period.
Emergency Exposure Limits EEL	Toxicology Committee of the American Industrial Hygiene Society (AIHA, 1964)	Concentration of contaminants that can be tolerated without adversely affecting health, but not necessarily without discomfort or other evidence of irritation or intoxication in or around the workplace.	Intended as guidance in planning the management of emergencies involving a single accidental release of substances into the atmosphere in and around the workplace. For use in mathematical models used to predict down-wind concentrations.	EEL should not be exceeded except to prevent more serious hazard. Will not protect hypersensitive individuals. Values given for 5, 15, 30 and 60 minutes exposure.

APPENDIX 1 (cont. 1)

EXISTING SHORT-TERM LIMITS

Titles and Acronyms	Responsible Organisation	Definition	Aims	Notes
Emergency Exposure Limits - EEL later called Emergency Exposure Guidance Limits - EEGL	U.S. Nat. Acad. Sci./Nat. Res. Council Committee on Toxicology (AIHA, 1964, 1966; NAS/NRC, 1986)	As above	As above, but on substances of interest to the U.S. Dept. of Defence	As above, but takes increase in ventilation rate into account during the emergencies. Ventilation rates of 50, 40 and 30 l/min assumed in estimating EELs for 10, 30 and 60 minutes exposure.
Emergency Tolerance Limits - ETL	U.S. Aerospace Industry (Ricca, 1966, 1970)	Concentrations which may be detectable sensory perception but will not cause intolerable respiratory or dermal irritation, pathological changes or residual symptoms in 95% of the healthy adult population in or around the workplace.	Intended for use in planning and controlling normal operations, i.e. predictable short-term exposures which may be repeated infrequently in the workplace.	The limit should not be exceeded during normal operations, and reached infrequently.
EPEL (Eenmalige Populatie Expositie Limiet) (Single Population Exposure Limit)	Toxicity Sub-Committee of the Committee for prevention of Disaster by Hazardous Substances (Netherlands) (De Saeger, 1988)	Maximum concentrations of toxic substances, tolerable to the general public for short periods of exposure. Exposure may occasionally cause serious discomfort or other quickly reversible effects.	To provide an aid to planning for emergencies involving accidental release of substances into the general environment, and for, e.g. selecting sites for industrial development, residential areas and for storage processing and transport.	Safety factors of 2 used to cover differences between animals and man and between healthy and susceptible humans. Values estimated for 30, 60 and 120 minutes exposure. More serious effects expected if PEL is exceeded by factor of 2-4.

APPENDIX 1 (cont. 2)

EXISTING SHORT-TERM LIMITS

Titles and Acronyms	Responsible Organisation	Definition	Aims	Notes
Short-term Public Emergency Guidance Level SPEGEL	National Research Council (NAS/NRC, 1986)	Suitable concentration for unpredicted, single short term, embergency exposure for general public.	To take into account the wide range of susceptibility of the general public.	SPEGEL are generally set out at 0 - 0.5 times the EEGL. See EELs.
Immediately Dangerous to Health (IDLH)	NIOSH (1985)	The IDLH represents the maximum concentration from which one could escape within 30 minutes withou any escape-impairing symptoms, or any irreversible health effects.	The IDLH level is defined for the purpose of respirator selection.	

APPENDIX 1 (cont. 3)

EXISTING SHORT-TERM LIMITS

Titles and Acronyms	Responsible Organisation	Definition	Aims	Notes
Emergency Response Planning Guidelines ERPGs	ERPG Committee of the American Industrial Hygiene Association (AIHA, 1987)	ERPG-3: The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing life-threatening health effects. EPRG-2: The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action. ERPG-1: The maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to one hour without experiencing other than mild, transient adverse health effects or without perceiving a clearly defined objectionable odour.	The ERPG Guideline values are intended to provide estimates of concentration ranges where one reasonably might anticipate observing adverse effects as described in the definitions ERPG-1, ERPG-2 and ERPG-3 as a consequence of exposure to the specific substance.	

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APPENDIX 2

GAS DISPERSION MODELS

The behaviour of a pollutant in the atmosphere (its dispersion) is influenced by the type of pollutant, the manner of its release, the stability of the atmospheric conditions, the type of terrain, the wind speed and direction and other factors. The choice of dispersion model will depend on the nature of the problem under examination and, to some extent, on the preference of the modeller for particular models (Pasquill, 1961).

Over the past years, much experimental work has been done to validate these dispersion models. A number of mathematical techniques are now available for the prediction of dispersion, both for instantaneous releases and for continuous releases from a fixed point. The models are rather complicated. They must be able to simulate dense gas releases, which may be instantaneous, transient (for various times) or continuous, and isothermal or non-isothermal. Such is the complexity of these models that, even with modern computers, the computation time precludes their use in reaching judgements at the time of a release. Accordingly, they are used predictively in a range of representative release and meteorological circumstances. Models are divided into 'box-models' and 'K-models' depending on the modelling and computational techniques and they can be 2- or 3-dimensional.

The output of dispersion models may either be in the form of isopleths at ground level at successive moments in time (Fig. A2-1) or in the form of concentration-time profiles at one or more particular points (Fig. A2-2).

To determine the total area in which a defined concentration will be exceeded, the gas cloud development has to be determined over the time of release plus the time taken to lower the concentration below that defined. Figure A2-1 shows a typical example of the successive isopleths of gas dispersion following a release lasting 15 minutes. The envelope enclosing all these isopleths give the total area where the isopleth concentration will be exceeded.

The accuracy of results is influenced by the choice of model, which is itself determined by the type of emission source, the meteorological conditions and the type of assessment envisaged. In general, different models give results within an order of magnitude (mostly within a factor 2 or 3) of each other. The error arising from the terms used to describe the source and the meteorological conditions can amount to an order of magnitude or greater (Havens, 1986).

Most models in common use have been calibrated and tested for high concentrations - for example that of the lower explosive limit. At low concentrations and long distances, especially at low wind speeds with the consequent long travel times, the accuracy of most models is questionable. At a windspeed of e.g. 1 m/sec it will take molecules half an hour to reach a distance of 1800 m. During this long travel time, the concentration can be reduced by chemical reaction with moisture, adsorption, rain out or phototransformation. These effects are more significant at low concentrations and for strong reactants or oxidants. There may be a need to recalibrate models or develop new models with improved accuracy at low concentrations such as those of the EEIs.

Figure A2-1 : Succession and Development of Dispersion Clouds through Space at Successive Times - Choice of Exposure Duration

The following figure illustrates serial isopleths for an EEI(t) produced by a dispersion model producing its output as isopleths. They have been plotted on parallel lines representing the wind direction. Vertical double arrows represent exposure durations which are not exceeded at various positions down-wind. For example, at the position of the double arrow marked "t<15", exposure at the EEI had not begun at 10 mins but was ended at 25 minutes, so the duration of exposure at that position for that EEI was less than 15 minutes. In this case, exposure to the EEI(t) never lasts more than 20 minutes. If the isopleths represent the EEI(60) concentration, the dispersion can be re-modelled to plot the isopleths for EEI(20). These isopleths will be smaller, and the duration of exposure to EEI(20) may never exceed 15'. The model can be re-run to plot isopleths at EEI(15), and so on (iteratively) until the duration of exposure matches the EEI used at the position of interest.

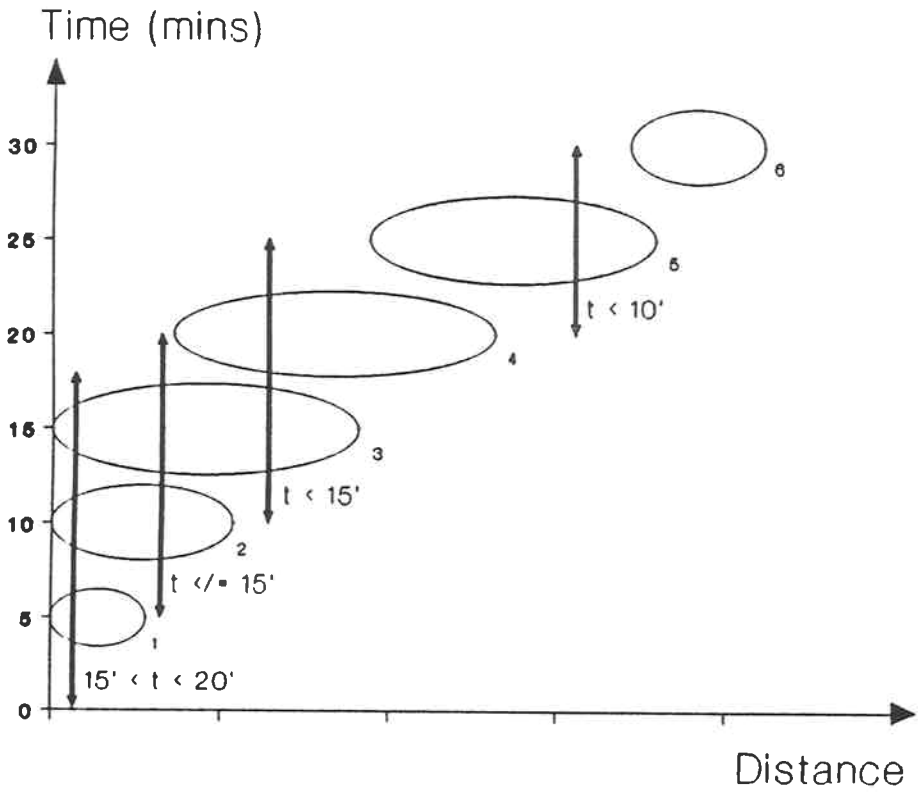
The lower figure illustrates the concept of the EEI envelope for the isopleths arranged on the same axis.

Figure A2-2 : Succession and Development of Concentration Profiles through Time at Different Places

This figure illustrates 3 concentration-time profiles for 3 positions down-wind from a source of emission as might be produced by a modelling system producing this kind of output. The duration of exposure at a particular concentration can be estimated directly from the profile for a position of interest.

FIGURE A2-1

Succession and Development of Dispersion Clouds through Space at Successive Times - Choice of Exposure Duration



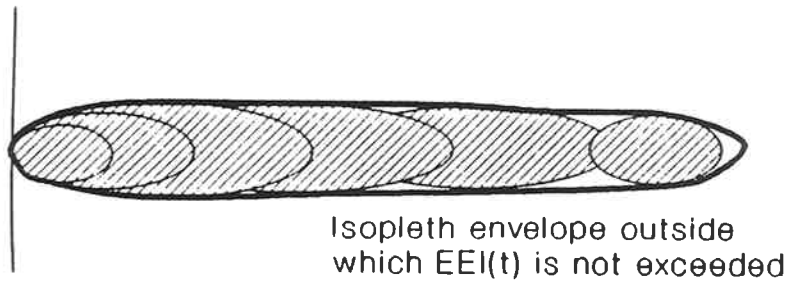
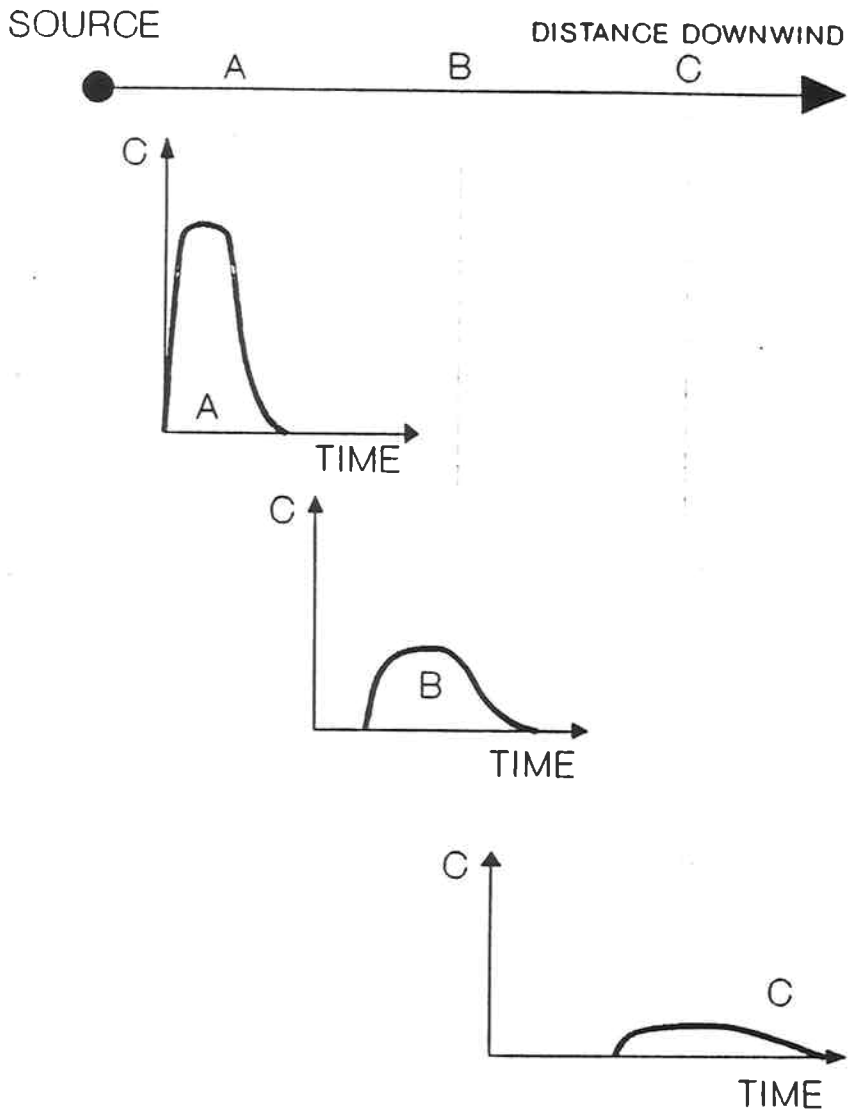


FIGURE A2-2

Succession and Development of Concentration Profiles through Time at Different Places



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APPENDIX 3

ILLUSTRATIVE EXAMPLE OF SETTING EEIs

Chlorine has been selected as an example of how EEIs may be set since a moderate amount of toxicological and human data are available on its acute effects. It is emphasised that the EEI figures have been derived by one small group of scientists using the method of analysis of data described in this report; other groups using different methods and having access to other data may well recommend other figures for one or more of the EEIs.

Within the principles set out in section D, there are many ways in which data can be brought together to facilitate their evaluation in the setting of EEIs. In this example, for each of the effects (*Death/Permanent Incapacity, Disability, Discomfort*) it was decided to plot on a log C vs log t diagram (C : concentration and t: duration of exposure) the results of experiments and observations relevant to the particular effect. The purpose is to map the regions representing "effect" exposures and "no-effect" exposures.

Ideally, this would result in a situation illustrated in fig. A3-1a in which all "effect" points (●) lie in a region above and to the right of a line representing the threshold exposures for the effect, and all "no-effect" points (o) in a region below and to the left.

In practice, mapping data from many experiments results in points which are not so clearly separated (Fig. A3-1b). In such a case, detailed consideration must be given to the reliability and strength of evidence represented by each point and the best scientific judgement used in deciding the rectilinearity of the line representing threshold exposures, and its position. The intercept of this line on the ordinate at (say) 60 minutes represents the EEI(60) corresponding to the effect under consideration (Fig. A3-1a).

EEI-3 (*Death/Permanent Incapacity*)

Adequate human mortality/exposure data are not available. Mammalian inhalation data are relatively plentiful. Table A3-1 lists the lowest observed effect exposures and highest no-observed effect exposures for acute inhalational toxicity in mice, the most sensitive species. Table A3-2 lists LC_{50}s found in a number of inhalation tests in mice.

The data from Tables A3-1 and A3-2 are plotted in Figure A3-2. The effect - and no - effect areas were not clearly demarcated and it was decided to insert a rectilinear threshold exposure line which lies below all "effect" points and above as many "no - effect" points as possible.

The intercepts on the ordinates at 60, 30 and 15 minutes indicate that the EEI(60) - 3 for chlorine would be 25 ppm (75 mg/m^3), the EEI(30)-3 would be 60 ppm (180 mg/m^3) and the EEI(15)-3 would be 130 ppm (390 mg/m^3).

EEI-2 (*Disability*)

Toxicological and clinical data are relatively sparse. The lowest observed effect exposures and highest no-effect exposures from all data considered relevant are listed in Table A3-3. Results of studies by routes other than

inhalation indicate that chlorine has no important effects apart from its irritancy. Data from Table A3-3 are plotted in Figure A3-3.

The rectilinear threshold line which lies below all disabling effects points and above as many points giving less than disabling effects, gives an intercepts lead to an EEI(60)- 2 of 3 ppm (9 mg/m^3), an EEI(30)-2 of 4.5 ppm (13.5 mg/m^3) and an EEI(15)-2 of 7ppm (21 mg/m^3).

EEI-1 *(Discomfort)*

Data considered relevant to discomfort without disability are displayed for all species in Table 4 and Fig 4. The line drawn is the highest line below all effect points. The common occupational exposure limit of 1 ppm for 8 hours has been marked as a NOEL. It should however be noted that certain authorities (NIOSH, 1976; WHO, 1984; ACGIH, 1987) regard 1 ppm as 'obviously irritant' and causing 'respiratory discomfort', though it is accepted that permanent health effects and disability do not result from lifelong exposure to this level. The TF took the view that it was reasonable that the threshold for discomfort should be relatively independent of exposure duration for a simple irritant, and, in view of the possibility of a wider range of susceptibilities in the general population compared with the employed population and of the doubt as whether 1 ppm is a no-discomfort level, the TF took the value of the EEI(60)-1 to be 0.4 ppm (1.2 mg/m^3), that of EEI(30)-1 to be 0.45 ppm (1.35 mg/m^3) and EEI(15)-1 to be 0.48 ppm (1.44 mg/m^3).

Conclusions

The data and the method of assessing these data led the TF to derive the following EEIs:

EEI(60)-3 = 25 ppm (75 mg/m^3)

EEI(60)-2 = 3 ppm (9 mg/m^3)

EEI(60)-1 = 0.4 ppm (1.2 mg/m^3)

Values for other times can be derived from Figures A3-2, A3-3 and A3-4. More data-points would be necessary in the concentration range 5-30 ppm to produce more reliable figures for exposures in the region of one hour. Observations would need to be specifically designed to yield information regarding disability and discomfort.

There are many ways in which data might be evaluated to produce EEIs. The above example is only one technique which was considered useful for a substance on which there was a relatively large amount of data. The example should not be taken as a recommending this technique for all other substances. Combined data from simple acute mortality studies will seldom justify sophisticated statistical analysis and a uniform mechanistic approach will inhibit the application of appropriate scientific and medical judgement which is the basis on which EEIs must generally be set.

TABLE A3-1

Exposure to Chlorine - Death
Species: Mice

Reference	Concentration ppm (mg/m3)	Exposure (minutes)	Mortality* (%)
Zwart (1987)	801	10	30
	741	10	0
Silver et al. (1942)	380	10	10
Bitron and Aharonson (1978)	290	6	0
	290	9	40
	170	22	14
	170	14	0
Schlagbauer and Henschler (1967)	62-69	30	10
	55	30	0
	10	180	80
	10	360	90

* including delayed death

TABLE A3-2

Exposure to Chlorine - Death
Species: Mice

Reference	No/Sex	Exposure (minutes)	LC50 ppm
Zwart (1987)	30M + 30F	10	1033
Silver et al. (1942)	300 M	10	674
Lipton and Rotariu (1941)	20 (not spec.)	10	628
Silver and McGrath (1942)	?	10	597/524
Alarie (1980)	?	10	300
Bitron and Aharonson (1978)	?	11	290
Zwart (1987)	30M + 30F	30	496
Schlagbauer and Henschler (1967)	80F	30	127
Bitron and Aharonson (1978)	?	55	170
Vernot et al. (1977)	?	60	137

M = Male F = Female ? = unknown

TABLE A3-3

Exposure to Chlorine - Serious Health Effects

Reference	Species	Concentration ppm (mg/m3)	Time	Effect
Zwart (1987)	mouse	569	10m	lung weight (14d)
Weedon et al. (1940)	mouse	250	60m	lachrymation
Schlagbauer and Henschler (1967)	mouse	55	30m	minor residual epithelial damage (8-10d)
Zwart (1987)	rat	8700	5m	residual lung pathology
		564	30m	at 14 days
		560	60m	
Winternitz et al. (1920)	dog	164	30m	lung pathology (>15d)
Barbour (1919)	dog	180-200	30m	symptoms after exposure
		25-30	30m	irritancy during exposure
Barrow and Smith (1975)	rabbit	50	30m	lung function
Cralley (1942)	rabbit	30	5m)	irreversible ciliostasis
	(in vitro)	18-20	10m)	
		200	<1m)	reversible ciliostasis
		20	25m)	
Lehman (1887)	rabbit	33	"hours"	Atelectasis
		18	<5h	NOEL
	cat	18	3-5h	cough and pathology
		1	7.5h	<disability
	guinea pig	33	3.5h	pathology
Rotman et al. (1965)	man	1	8h	lung function (24h
Anglen (1981)				disabling)
		2	2h	NOEL
		0.5	8h	NOEL
Chang and Barrow (1984)	rat	10.9	10m	RD50
Barrow and Steinhagen (1982)	rat	25.0	10m	RD50
Barrow et al. (1977)	mouse	19	2m	RD50
		10	10m	delayed recovery
		9.3	10m	RD50
Various	man	4	<1h	intolerable conc.
Tatarelli (1946)	man	34	15m	severely affected
Charan et al. (1985)	man	1000	<few	hospitalised/no deaths

NOEL = no observable effect level
m = minutes h = hours

Note on RD50 : Barrow et al. (1977) suggested that a concentration capable of producing a 50 % decrease in respiratory rate (RD50) in animals would induce intolerable irritation and would be incapacitating to humans.

TABLE A3-4

Exposure to Chlorine - Minor Health Effects

Reference	Species	Concentration ppm (mg/m3)	Time	Effect
Barrow et al. (1977)	mouse	19	2m	RD50
		9.3	10m	RD50
		0.7	10m	threshold for irritation
Chang and Barrow (1984)	rat	10.9	10m	RD50
Barrow and Steinhagen (1982)	rat	25	10m	RD50
Ponomereva et al. (1980)	rat	0.4	4h	irritation threshold
Lehmann (1887)	cat	1	7.5h	irritation only
	rabbit) guinea pig)	18	5h	first irritant effects
ACGIH (1987)	man	0.5	8h	TLV-TWA*
		1	8h	TLV-TWA -
		3	10m	TLV-STEL
		1	10m	TLV-STEL*
Matt (1889)	man	≥1.3	5-16m	irritation
Beck (1959)	man	≥1	30	discomfort
		0.36	n.a.**	? discomfort
		<0.3	n.a.**	sensory irritation
Rupp and Henschler (1967)	man	≥0.5	15-50m	discomfort
		≤0.2	n.a.**	sensory irritation

m = minutes h = hours

* Notice of intended change 1987-88

** n.a. = not applicable

Note on RD50 : Barrow et al. (1977) suggested that a concentration capable of producing a 50 % decrease in respiratory rate (RD50) in animals would induce intolerable irritation and would be incapacitating to humans.

Figure A3-1a,b

Illustration of ideal (a) and likely (b) distribution of data points (● = effect, o = no-effect) on Log C (ppm) vs Log t plot for a particular effect

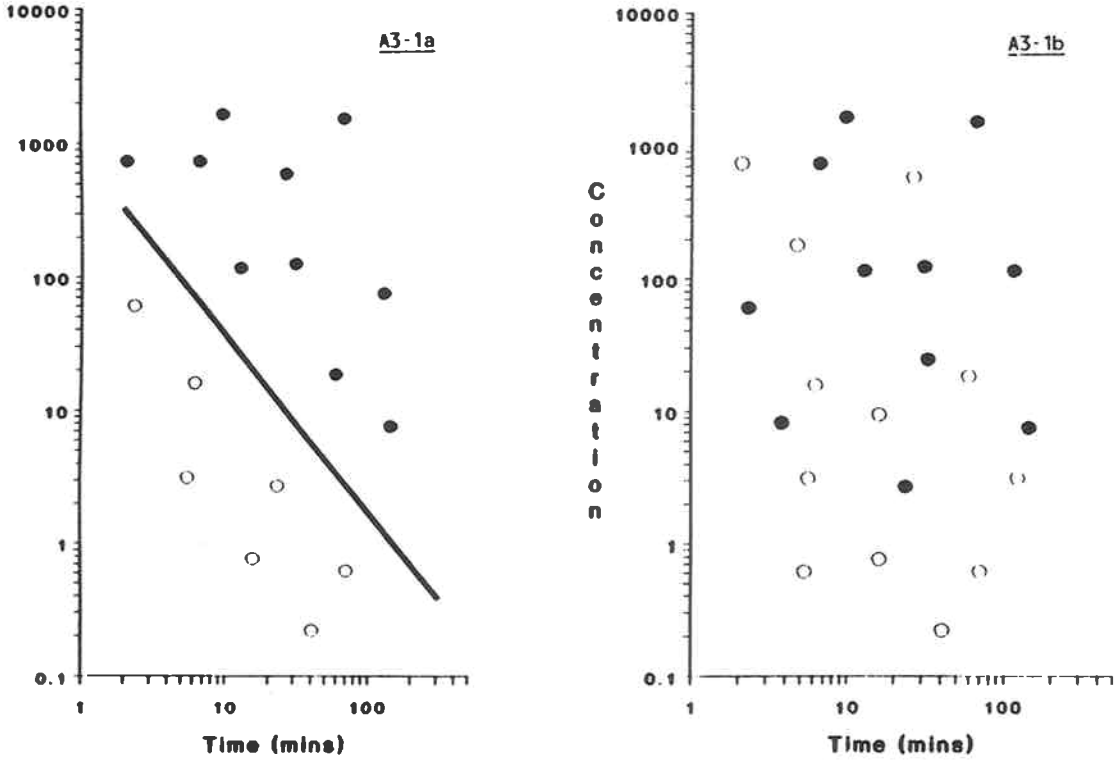


Figure A3-2

Log C (ppm) vs Log t plot for various response rates for lethality in mice

The thin line is the LC_{50} vs time relationship. The thick line passes under all effect points and above as many no-effect points as possible and is regarded as the EEI-3 vs time relationship.

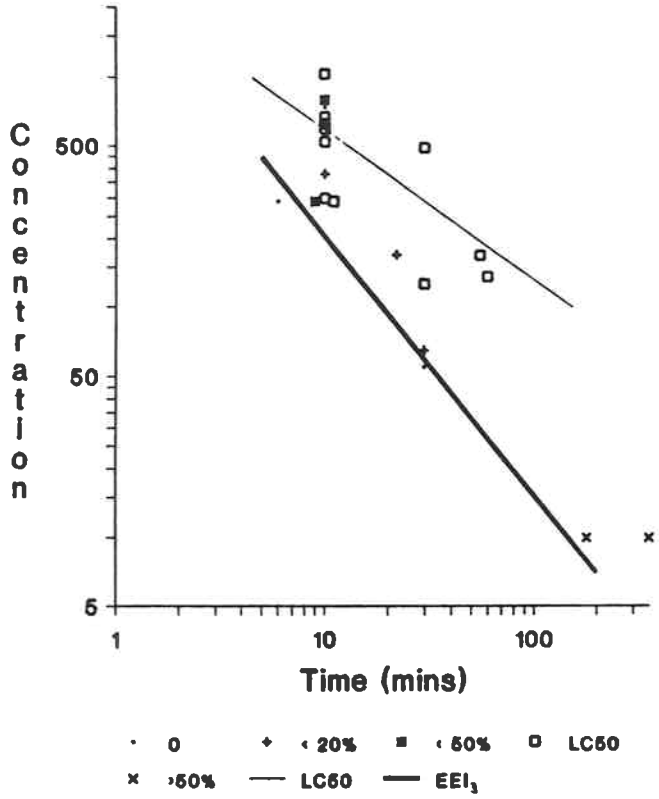


Figure A3-3

Log C (ppm) vs Log t plot for disabling effects in various species

The thick line passes under all effect points and above as many no-effect points as possible and is regarded as the EEI-2 vs time relationship.

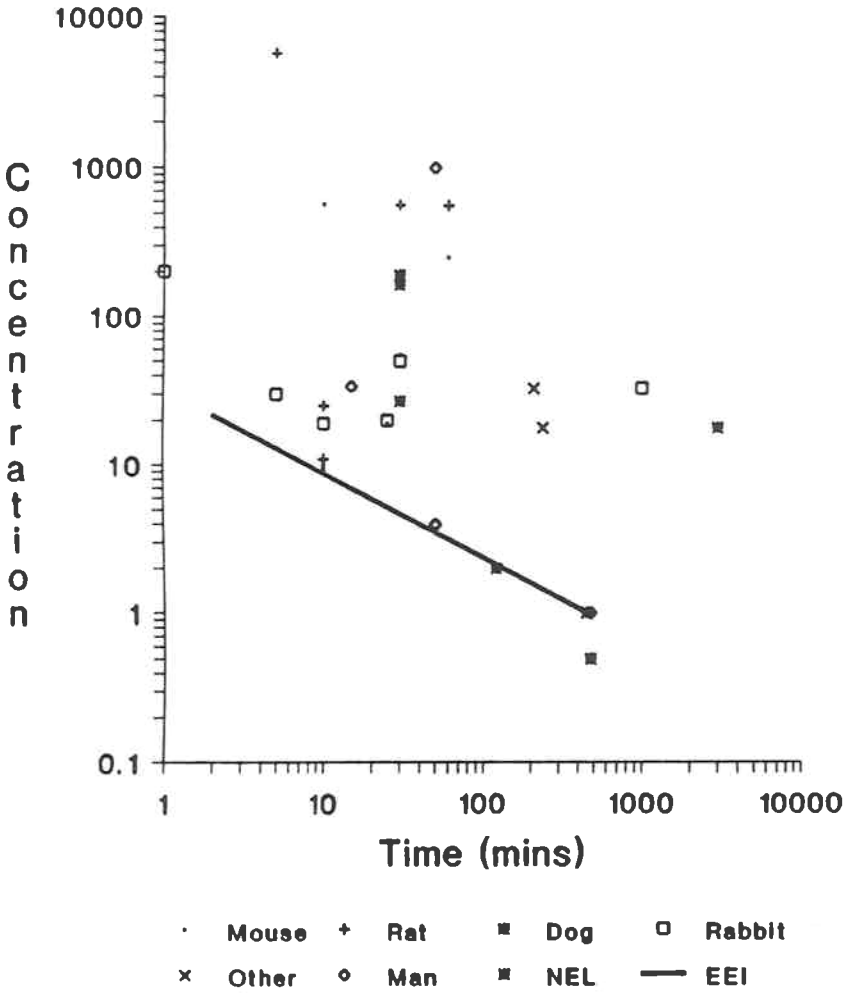
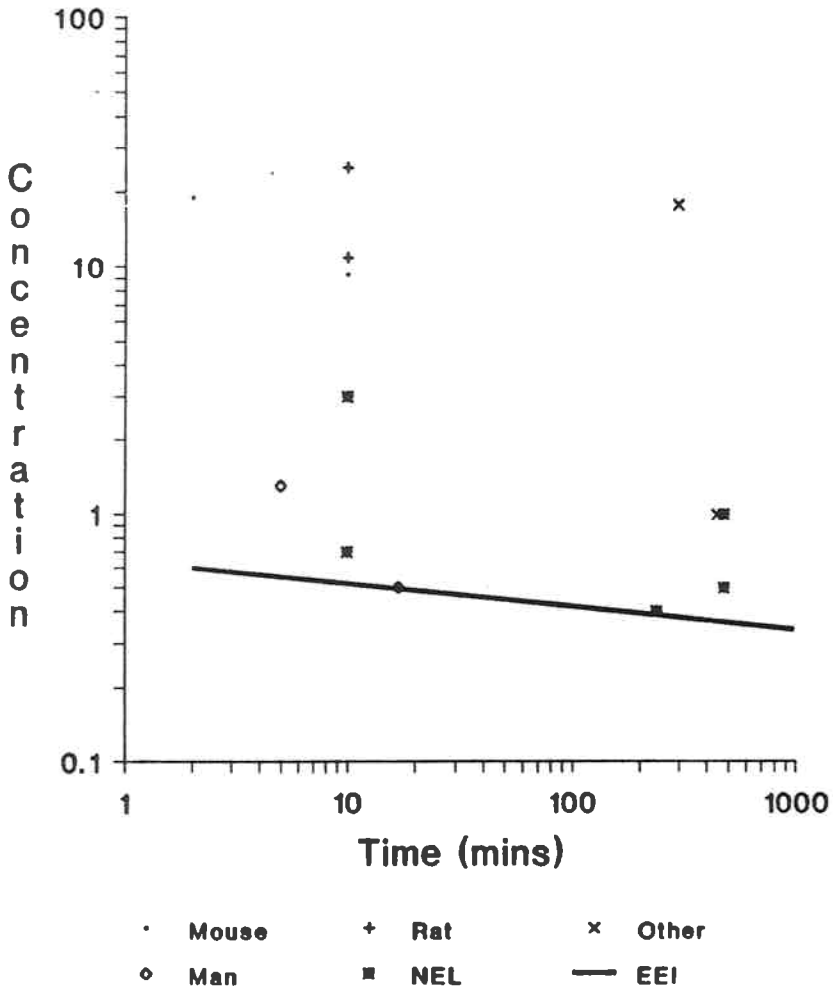


Figure A3-4

Log C (ppm) vs Log t plot for discomfort in various species

The thick line passes under all effect points and above as many no-effect points as possible and is regarded as the EEI-3 vs time relationship.



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APPENDIX 4

EXAMINATION OF THE RESULTS OF THE RING TEST OF SETTING EEIs ACCORDING TO THE TASK FORCE'S DRAFT RECOMMENDATIONS

1. *INTRODUCTION*

While guidance is provided on the setting of EEIs, there was no way of judging whether, and to what extent, consistent EEI figures would be set by different professional groups, except by direct investigation. A ring-test was therefore carried out to determine the practical problems experienced in following the guidelines, to examine the inter-group variability and, if possible, its origins. The intention was that the guidelines could be modified to help overcome any problems and reduce the variability.

2. *METHODS*

ECETOC member companies were invited by letter to participate by deriving EEIs for three chemicals in accordance with the ECETOC guidelines. The chemicals selected, phosphine (PH_3), acrylonitrile (AN) and hydrogen fluoride (HF) represented materials which (in the vapour phase) were mainly toxic, both toxic and irritant or mainly irritant. Each participant was sent the latest draft of the report (not materially different from this report) and reference lists and as many of the original toxicological and clinical papers that could be obtained for each chemical. The references are included in the bibliography to this Appendix.

Each participant was asked to derive EEIs for 15, 30 and 60 minutes where this was considered possible. If they used data in addition to that supplied, they were asked to indicate this. Participants undertook the work between March and December 1989.

Where results were received as ppm, these were converted to mg/m^3 by multiplying by 1.41, 2.2 & 0.83 for PH3, AN & HF respectively.

For the purpose of Table A4-1, numbers which are not averages were simplified to 2 significant figures.

3. *RESULTS*

11 ECETOC members submitted values derived using the method of the draft report. The reports varied widely in the details provided about the methods used. In some cases, only the EEIs were given, in others a scholarly critical review of the literature was provided. In most cases, the limits had been set by one or a very few people rather than by a multidisciplinary group. Several respondents commented on the paucity of data, particularly for phosphine.

While some respondents commented on the difficulty of the task and the complexity of the issues discussed in the technical report, there did not appear to be any serious misconceptions arising from the report. One company (A) produced results which seemed consistently high; they were asked to review their results for a systematic error, such as using the reciprocal

of conversion factors, but none was found and their results were included as received.

The values provided by the 11 companies are given in Table A4-1. In general, the distribution of values was skewed suggesting that the distribution was log-normal.

The number of missing values in each column of Table A4-1 is a measure of the difficulty experienced with setting that particular EEI for that particular substance. This is illustrated by the number of values submitted by the participants as a function of the chemical, the EEI and the exposure period (Fig. A4-1). It is clear that it was found difficult to set EEIs for shorter exposure periods.

The relationships for the EEI values and exposure time were plotted on a log-log scale (Fig. A4-2a,b,c). It should be pointed out that this is for illustrative purposes only; any kind of averaging process is usually inappropriate in setting EEIs (see discussion). In general, the relationship was monotonic and approximately rectilinear. Where this is not the case, it is usually because the number of estimates contributing to the mean is not the same in each case.

The suggested EEI values for phosphine are illustrated on a logC - logt plot on which are also plotted most of the datapoints for the relevant effects which were available (Figs. A4-3 - A4-5). It is clear that there are few datapoints in the region of the plot where the EEIs lie and there is a tendency for the straight line relationships derived by the respondents to do one of two things: either to pivot about a point (presumably considered to represent exposure conditions reliably representing a threshold for the relevant effect), or to be parallel and positioned in accordance with the relevance or reliability ascribed to a particular datapoint.

4. *DISCUSSION*

At first sight, the variability in the results was disappointing. The coefficient of variation (derived from the arithmetic mean and standard deviation) was generally in the range 100 - 200% and, typically, suggested results ranged over at least an order of magnitude. It was not possible to find a clear pattern of variability with substance, EEI or exposure time; the coefficient of variation for EEI-2 for HF was consistently high at all time periods but this was entirely caused by the values from company A.

It is noteworthy that, even for the substances chosen on which there are no more data than would be the case with most newer chemicals, only slightly more than 50% of the values requested could be derived with less than a third of the values for 15 minute exposure.

Irrespective of the appropriateness of the experimental observations and of the reliability of the data for setting EEIs, it is clear from Figs A4-3 - A4-5 that the data are not in the most appropriate area of the logC - logt plot to make EEIs easy to set; the values represent extrapolations from surrogate effects in surrogate species exposed to excessive concentrations for excessive durations.

Nevertheless, Figs A4-3 - A4-5 also indicate that there was considerable agreement about the slope of the line on the logC - logt plot. The positioning of this line highlights whether a particular data point (such as an outlying LC50 value indicated by an arrow in Fig A4-5) can be ignored or whether it should be considered. Such differences cannot be resolved by an averaging process. It is necessary to achieve a consensus on the evaluation of such critical datapoints by scientific discussion.

It is anticipated that, if the ring-test participants were brought together to discuss their proposals with a view to agreeing values, most of the variability would disappear and any remaining would result from personal judgements about the margin of safety expected from the figures.

It is recommended that, as far as possible, EEIs should be set either by a group larger than that used by the participants (in which the necessary discussions can take place) or should be set by several (smaller) groups who should then harmonise their positions by scientific negotiation.

This could be tested by bringing together the participants in the Ring Test with a view to reaching an agreed position on the EEIs for phosphine, acrylonitrile and hydrogen fluoride.

Until this is done, it is not considered appropriate to regard the average of the ring test values or any individual value as an established EEI of any of the three chemicals and certainly none carries the recommendation of ECETOC.

Otherwise, the Task Force took the view that the concepts underlying EEIs and the methodology of setting them were satisfactorily described in the technical report.

TABLE A4-1

EEIs mg/m3

PH3	(15)-1	(30)-1	(60)-1	(15)-2	(30)-2	(60)-2	(15)-3	(30)-3	(60)-3
A						170			350
B			1			14			140
C									
D		20	10		100	50		200	100
E									
F			1			3			110
G			1			7			14
H			14		70	70		560	170
I	7	7	3	22	13	4	85	35	14
J	42	21	10	270	160	85	420	210	110
K	15	10	5	75	50	25	100	75	50
AM 1)	21	14	6	122	78	48	202	217	117
CV % 2)	86	49	87	106	69	115	94	96	88
GM 3)	16	13	4	77	59	23	153	144	77

AN	(15)-1	(30)-1	(60)-1	(15)-2	(30)-2	(60)-2	(15)-3	(30)-3	(60)-3
A		1400		5500	2600	1300	8800	4400	2000
B									
C								660	520
D		100	50		200	100		500	250
E									22
F			30			75			400
G			44			170			440
H	44	35	26		500	290		880	440
I	48	43	40	180	130	120	1100	370	280
J	550	390	280	990	550	330	3300	1500	660
K	200	150	100	500	400	300	600	600	500
AM 1)	210	357	81	1793	736	337	3438	1278	549
CV % 2)	113	151	110	139	129	121	110	112	97
GM 3)	123	152	57	839	442	220	2068	887	364

HF	(15)-1	(30)-1	(60)-1	(15)-2	(30)-2	(60)-2	(15)-3	(30)-3	(60)-3
A	2			600	400	300	1075	642	400
B									
C	8	8	8				830	420	210
D		15	7		25	15		50	50
E			8			17			42
F			1			25			80
G			4			17			42
H	5	4	3	46	37	29	330	170	79
I	2	2	2	23	18	17	370	230	190
J	12	10	7	54	42	33	170	100	62
K	20	10	5	50	40	25	75	60	50
AM 1)	8	8	5	155	94	53	476	238	120
CV % 2)	80	54	51	161	160	175	82	92	96
GM 3)	6	7	4	70	47	28	334	163	88

1) Arithmetic Mean 2) Coefficient of Variation (= SD x 100/AM) 3) Geometric Mean

FIGURE A4-1

Number of responses (out of 99 possible) as a function of chemical, EEI and time period

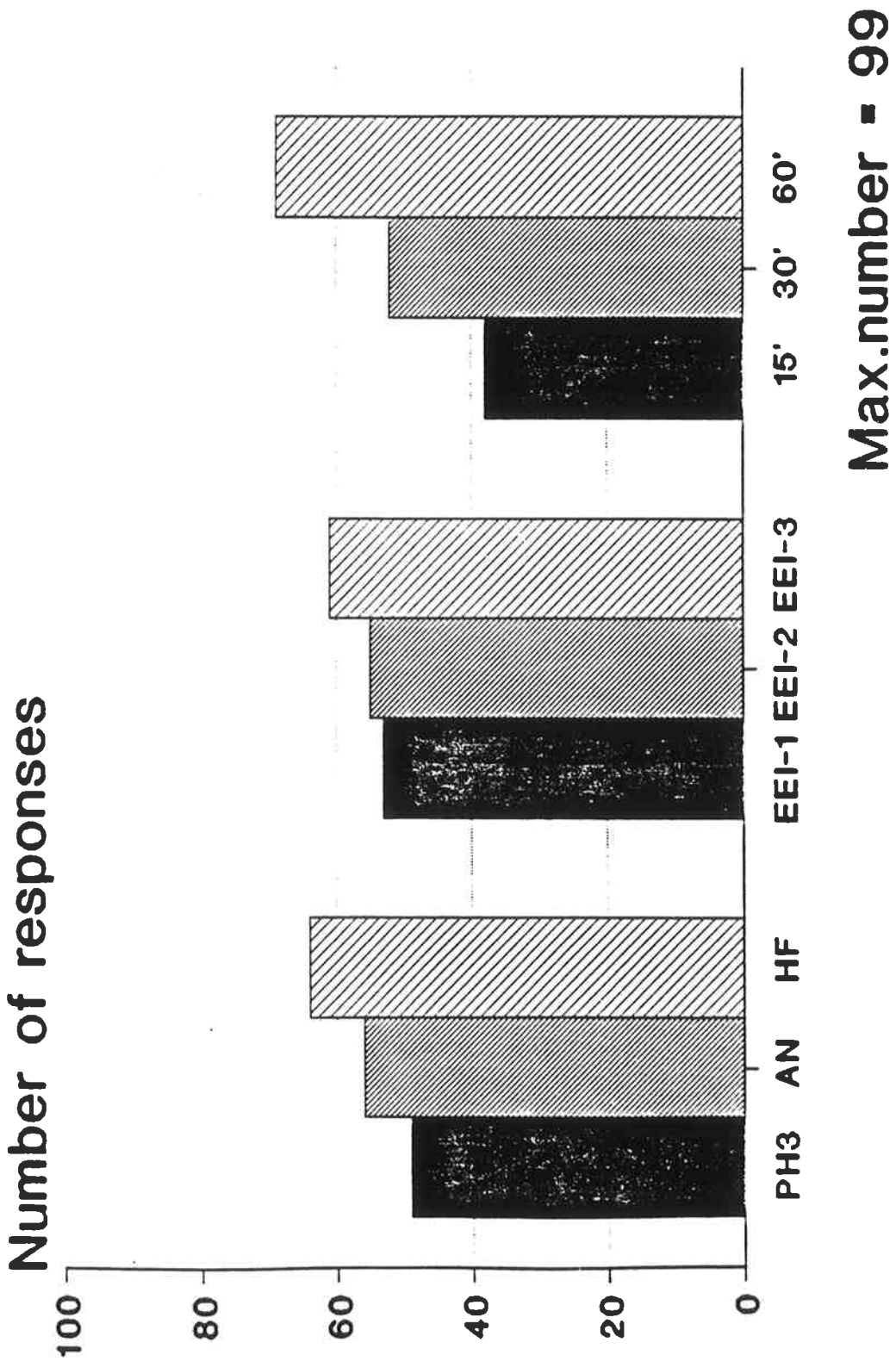


FIGURE A4-2a,b,c

Geometric mean of submitted values for each EEI for three time periods for each of the three chemicals

FIGURE A4-2a

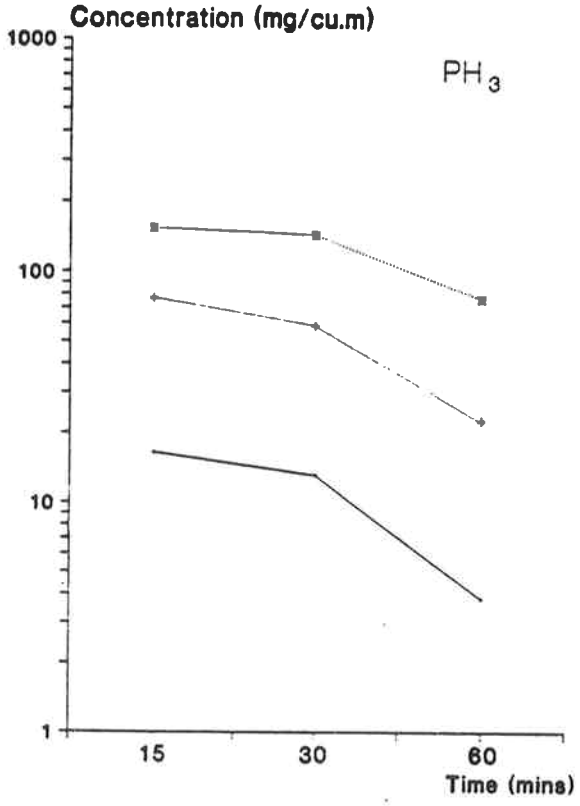


FIGURE A4-2b

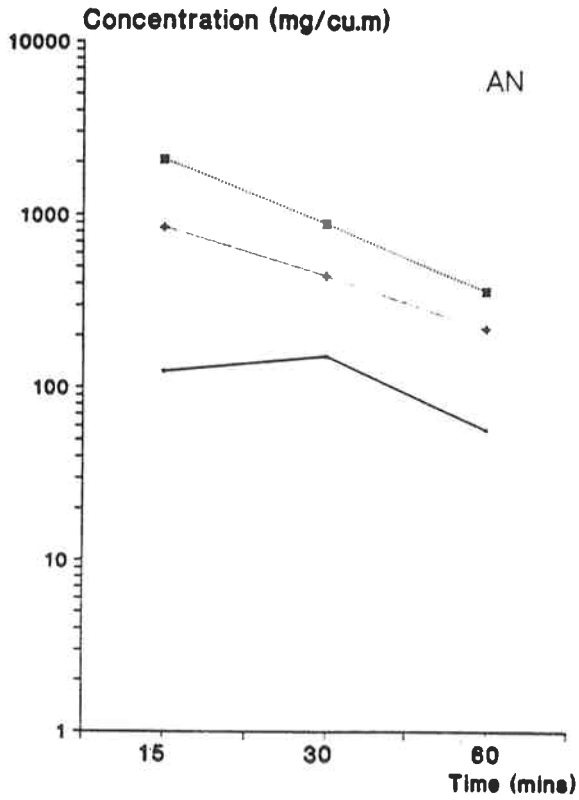


FIGURE A4-2c

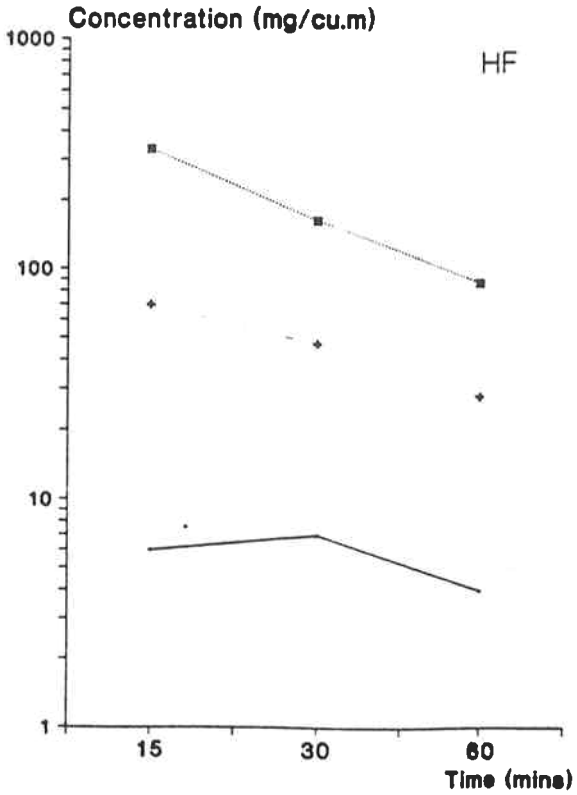


FIGURE A4-3a,b,c

These figures indicate for phosphine how the EEI values (*) lie in a different region of the Log C vs Log t plot from that where the data is to be found.

Figure A4-3a
PHOSPHINE
Emergency Exposure Index 1 : Discomfort

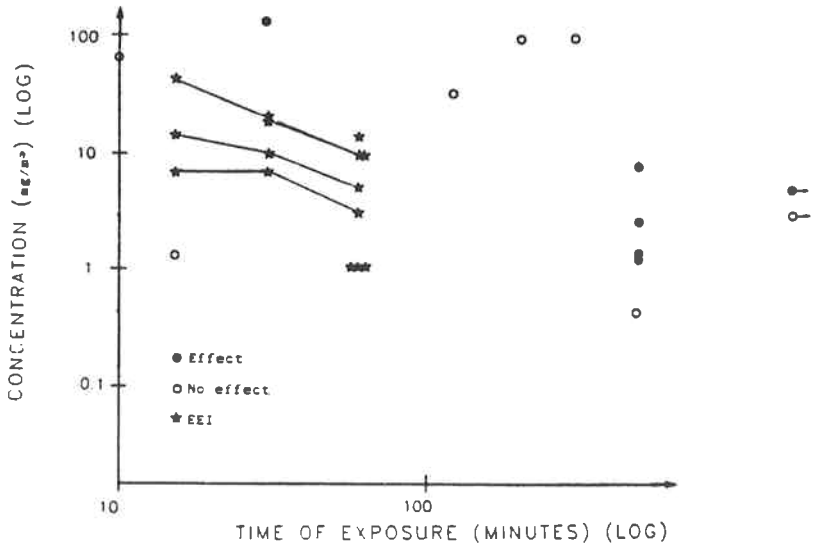


Figure A4-3b
PHOSPHINE
Emergency Exposure Index 2 : Disability

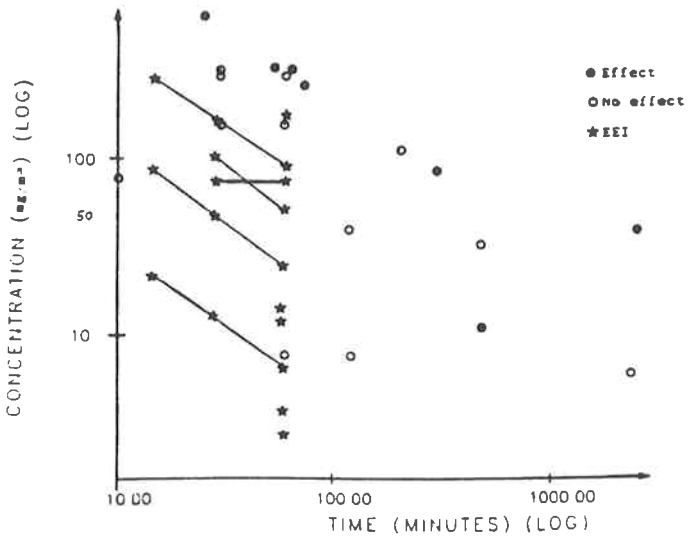
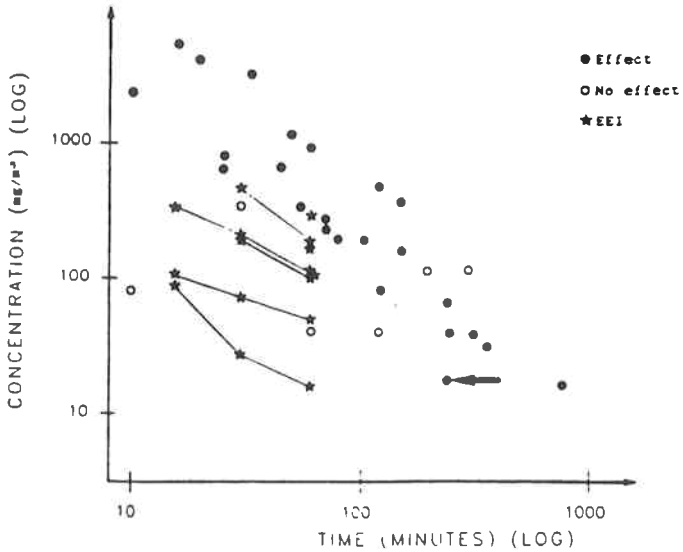


Figure A4-3c
PHOSPHINE
Emergency Exposure Index 3 : Death



APPENDIX 5

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No.5	Joint Assessment of Commodity Chemicals, Vinylidene Chloride
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