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OCCUPATIONAL AND CONSUMER EXPOSURE ASSESSMENTS

ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Paris 1993

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ENVIRONMENT MONOGRAPHS

The Environment Monograph series is designed to make available to a wide readership selected technical reports prepared by the OECD Environment Directorate. The Joint Meeting of the Chemicals Group and Management Committee recommended that this report be derestricted. It has been made public under the authority of the Secretary-General. Copies of Environment Monographs on a limited basis can be forwarded on request.

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Summary

This Environment Monograph is based on the outcome of the OECD Workshop on Occupational and Consumer Exposure Assessments held in Orlando, Florida, on 19-21 February 1992. The Workshop was sponsored by the United States Environmental Protection Agency.

The measurement of occupational and consumer exposure contributes to the data set on which to base the overall assessment of the potential hazard posed by chemicals to human health. Often such measurements are lacking. Therefore, in order to screen chemicals so that resources can be directed towards those which present the greatest problems, realistic estimations of human exposure need to be made.

This document offers a choice of possible approaches for assessing occupational and consumer exposure, by both the dermal and inhalation routes, primarily to chemicals produced in high volumes and for which only limited data are available. For some of these approaches, programs on computer diskettes are available.

The use of actual measured data is recommended, but where these are not available the approaches presented here can be adapted to using calculated values or data from analogous or surrogate chemicals.

The purpose of the exposure assessment is to obtain the Estimated Human Exposure level. In combination with the assessment of health effects based on toxicity studies, the Estimated Human Exposure level can be used to judge whether further action in relation to the chemicals is required. It is recommended that exposure to, and toxicity of, the chemicals be analysed together: thus the amount of detail required for the one will be dictated, to a large extent, by the severity of the other. The approaches presented encompass the range from qualitative to sophisticated quantitative assessments.

In the occupational setting, exposure by the inhalation route has received by far the most attention. For many chemicals, atmospheric standards exist, either on a national or international basis, which quantify both the permitted levels and duration of exposure. The situation is not so well defined for the dermal route of exposure. The Workshop recommended that further research be conducted into methods for assessing such exposures, and that the results of this work be widely disseminated.

Résumé

Cette monographie sur l'environnement s'appuie sur les résultats d'un atelier de l'OCDE sur l'évaluation de l'exposition des travailleurs et consommateurs. Cet atelier a eu lieu a Orlando en Floride du 19 au 21 février grâce au soutien de l'agence américaine pour la protection de l'environnement (US-EPA).

Les données chiffrées de l'exposition des travailleurs et consommateurs ont leur place dans l'ensemble des données à l'aide desquelles une évaluation générale des dangers potentiels de produits chimiques pour la santé humaine est effectuée. La plupart du temps ces données chiffrées manquent et elles doivent être remplacées par des valeurs obtenues par estimation quand il s'agit de dépister les substances qui présentent les problèmes les plus aigus et qui nécessitent par conséquent une évaluation en priorité.

Ce document contient une sélection de méthodes permettant d'évaluer l'exposition, par inhalation ainsi que par voie cutanée, des travailleurs et consommateurs aux produits chimiques, principalement ceux qui sont produits en grand volume et pour lesquels il manque des données. Des programmes informatisés existent pour certaines de ces méthodes.

En l'absence de données réelles obtenues par mesure, et pour aboutir à une valeur d'estimation, on peut procéder de deux façons distinctes et complémentaires. La première façon consiste a calculer l'exposition à partir de propriétés physiques fondamentales. L'autre façon consiste à utiliser des données réelles obtenues pour des substances qui, bien que différentes, présentent des schémas d'exposition analogues.

En comparant les niveaux d'exposition obtenus par estimation avec les résultats d'études toxicologiques, on peut conclure à l'opportunité ou non d'une action ultérieure pour un produit ainsi évalué. Il est recommandé d'analyser ensemble l'exposition et la toxicité. Ainsi le volume de données requises pour l'un sera dicté par la sévérité de l'autre. Les méthodes actuelles couvrent un large éventail, allant de méthodes largement qualitatives à d'autres permettant une quantification poussée.

S'agissant du lieu de travail, l'exposition par inhalation est celle qui, de loin, a reçu l'attention la plus grande. Des normes d'exposition nationales et internationales, tant pour la concentration permise que pour la durée de l'exposition, ont été établies pour de nombreuses substances. En ce qui concerne la voie cutanée, la situation est moins bien définie et l'atelier a recommandé que des recherches plus approfondies soient entreprises afin d'élaborer des méthodes d'évaluation. En outre l'atelier a recommandé que les résultats de ces recherches soient largement diffusés.

1. Introduction

One component of the OECD Existing Chemicals Programme is data collection on, and assessment of, those High Production Volume (HPV) chemicals for which Member countries have found little or no readily available information when searching their databases and the open scientific literature. To assist in this task, Member countries have agreed various data elements which they considered essential, though not exclusive, for making an initial assessment of these chemicals. Collectively, these elements are known as the Screening Information Data Set (SIDS), a list of which is at Annex VI, and the chemicals subjected to this procedure are the SIDS chemicals. In order to share the burden of data collection and, as necessary, testing to complete any given parameter, Member countries in collaboration with industry volunteer to "sponsor" the various SIDS chemicals. When all such data have been gathered and collated, the chemicals are assessed as to whether they are of immediate concern for human health and/or the environment and thereby warrant further action.

One parameter of the SIDS is focused on exposure to the chemicals. This document addresses some of the current procedures employed in making an initial assessment of occupational and consumer exposure.

2. Background

This document has been prepared for use by those Member countries sponsoring chemicals for data collection, testing and assessment under the OECD Existing Chemicals Programme. It is intended to be of assistance in the initial assessment of the occupational and consumer exposure to those HPV chemicals for which full SIDS data are available. It is based mainly on the results of the OECD/US EPA Workshop on Occupational and Consumer Exposure Assessments held in Orlando, Florida, in February 1992 and on comments subsequently received from Member countries, international organisations and other interested bodies. It is therefore believed to represent the current "state-of-the-art" as regards the assessment of occupational and consumer exposure.

It should be stressed that the guidance contained in this document is provisional and will be modified in the light of further comments from, and use made by, Member countries and the outcome of discussions at future SIDS Initial Assessment Meetings.

The objective of any occupational and consumer exposure assessment is to calculate a *"realistic"* Estimated Human Exposure (EHE) level, expressed in terms of dose per unit weight, e.g. mg/kg, based on data contained within the full SIDS Dossier for the "sponsored" chemical. This level can then be compared with the results obtained from conducting the Initial Assessment of Health Effects and a judgement made as to whether the chemical presents a cause for concern and the possibility of further action. For consistency within assessments, when calculating the human exposure level, in the absence of evidence to the

contrary, there may be a need to standardise some of the appropriate physiological parameters. In this respect it is suggested to assume that:

(a) an adult weighs 70 kg;
(b) the respiratory volume is 10 m^3 (i.e. 10,000 litres) per working day (eight hours);
(c) the consumer respiratory volume is 15 litres per minute.

Other factors that should be obtained before assessing exposure relate to the physical state of the chemical and its weight fraction in any product or formulation that is professionally used. If the chemical is also present in consumer products, an appropriate adjustment should be made to the EHE.

3. Occupational Exposure

For exposure via the inhalation route, some chemicals may have been assigned a national or company-based occupational exposure limit (e.g. TLV, MAK, OES, etc.), perhaps even further refined to encompass short-term limits or ceiling values. Whenever possible these levels, preferably expressed as **mg/m^3** rather than **ppm**, should be used as the basis for calculating the EHE. In other cases actual monitoring data, both personal and background, may be available and can, after suitable statistical treatment (e.g. geometric mean and standard deviation), be used in a similar manner. The overall procedure should be repeated for all the various production processes and uses made of the chosen chemical and, from a knowledge of frequency and duration of exposure, the results of the "worst case" highlighted. The knowledge that technical or personal protective equipment is required may assist in formulating one's views.

However, for the majority of SIDS chemicals it is anticipated that *"real"* data will *not* be available and hence "estimation" methods will need to be used. Three such methods, as proposed by the United States, the United Kingdom and Germany, have been identified. They have varying levels of detail, and Member countries are free to choose from them. These are attached as Annexes I-III. These methods rely on a knowledge of similar production processes and use patterns and/or on the physical-chemical properties of the "sponsored" or a "surrogate" chemical. Thus where "real" data are missing for a chosen chemical it may be possible to substitute data from another chemical meeting the criteria mentioned above. In all these methods the amount of detail and level of sophistication required for a "quantitative" estimation depends to some extent on the toxicity of the chemical. Therefore, the occupational exposure (and consumer exposure) assessment should not be conducted in isolation. For example, a chemical showing low toxicity may require only qualitative or, at most, semi-quantitative exposure estimation. In those cases where a chemical is also incorporated into a consumer product, the occupational or professional exposure should be supplemented by the appropriate component of the consumer exposure assessment in calculating the overall EHE. The situation is not so clear-cut regarding dermal exposure, and only the model used by the US EPA addresses this point. Indeed one of the conclusions of the Orlando workshop was that more work was needed in this area and that Member countries should share their experiences. Such information will be invaluable in updating this guidance, for both occupational and consumer exposure.

Overview of the Models for Estimating Occupational Exposure (Annexes I-III)

The US EPA submission (**Annex I** to this Workshop Report) provides a number of model approaches whose applicability relies on some knowledge of production and use scenarios in the United States (e.g. the NIOSH National Occupational Exposure Survey). The identification of critical unit operations during manufacture and use, leading to significant exposure scenarios, allows a degree of specificity in the assessment. However, some reservations as to the applicability of the models in circumstances of more modest resources or expertise could restrict their use.[1]

The UK HSE submission (**Annex II**) illustrates a possible approach based on a structured logic tree using analogous exposure data. Its future development into a simple, validated "expert system" for screening purposes is attractive, particularly as the ultimate choice of exposure databases could be adapted to national needs. In the first instance, the UK National Exposure Database (NEDB) could be a relevant tool in the development of this approach. The classifications based on physical and (apparent) toxicological properties and containment levels will need careful definition for more general future use.

The German BAU submission (**Annex III**) offers a generally qualitative screening approach based on common knowledge of the exposure situations in different areas of use and on an example of "mass balance" calculations. This could be a particularly relevant screening tool when there is an early indication that a high degree of sophistication is unlikely to be warranted.

4. Consumer Exposure

Much of the foregoing can also be applied to the assessment of consumer exposure, in that: the objective, when combined with any possible occupational exposure, is to calculate an EHE; "real" data are to be preferred; and the toxicity of the chemical should be brought to bear on the level of detail required. Again, for most SIDS chemicals it is expected that "estimation" methods will be required. Two have been identified. One of these, as used by the US EPA, is available on computer diskette. Although a synopsis is attached as **Annex IV**, further details on its use are best obtained from the incorporated files, most of which are "menu-driven". The other method is presented in a discussion paper from the Netherlands, attached as **Annex V**. Unlike in the occupational setting where, to a greater or lesser extent, some exposure is bound to occur, there will of course be no requirement to undertake an exposure assessment if the chemical is not present in a consumer product. Product registers and inventories, etc. will need to be consulted, perhaps with assistance from other Member countries, to check if this is indeed the case. There may, however, be a need to incorporate other factors such as presence in drinking water in obtaining an overall EHE.

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[1] Copies of the Appendices referred to in Annex I can be obtained through the OECD. Contact the Environmental Health and Safety Division of the OECD Environment Directorate.

Overview of the Models for Estimating Consumer Exposure (Annexes IV and V)

The methods proposed by the US EPA, as described in Annex IV, are on a computer diskette which contains the SCIES, AMEM, FLUSH and DERMAL procedures.[1]

SCIES is a Screening-level Consumer Inhalation Exposure Software program for the passive and active annual average inhalation exposure to components of consumer products.

AMEM is an estimation model for assessing migration of a chemical from a polymer and the inhalation exposure.

FLUSH is a program for estimating concentrations of chemicals in surface waters that may result from disposal of consumer products containing these chemicals into household wastewater. It also provides estimates of human exposure from ingestion of drinking water and fish that may become contaminated by these household wastewater releases.

DERMAL is a program which allows estimation of dermal exposure, in terms of potential dose rate, for contact with (1) a film of liquid deposited on the skin, (2) dusts and powders, and (3) chemicals contained in or adhering to solid matrices.

The proposed model from the Netherlands (Annex V) is self-explanatory. It allows input of selected values or, in certain circumstances, allows a "default" value to be chosen. This model has also been submitted for publication in the scientific literature in order to elicit further comments.

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[1] Further details on the use of these programs may be obtained from:

Dr Elizabeth Bryan
US Environmental Protection Agency
Exposure Evaluation Division
401 M Street, S.W.
Washington, D.C. 20460

Fax: (1-202) 260-0018

Annex I

Approaches for Developing Screening Quality Estimates of Occupational Exposure Used by the US EPA's Office of Pollution Prevention and Toxics, and their Applicability to the OECD SIDS Programme

United States Environmental Protection Agency
Office of Pollution Prevention and Toxics

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Appendix O	Compilation of Engineering and Other Control Methods
Appendix P	US New Chemical Assessment Methods for Estimating the Release from Nitrogen Blanket Transfer

[1] Copies of these Appendices can be obtained through the OECD. Please contact the OECD Environment Directorate, Environmental Health and Safety Division, 2 rue André-Pascal, 75775 Paris Cedex 16, France. Fax: (33-1) 45.24.16.75.

1. Introduction

The information needed to assess the potential for occupational exposure to a chemical substance includes information on the size of the population, the physical-chemical properties of the chemical substance, the chemical processes in which the substance is handled (including specific unit operations), the frequency and duration of exposure, the specific activities performed by the workers handling the substance, and control measures (local exhaust ventilation, general mechanical ventilation) or other personal protective equipment (respirators, chemical protective clothing) used. Ideally, information specific to the substance under consideration would be used in all evaluations to assess occupational exposure. If a complete set of representative information is available, a comprehensive assessment of occupational exposure can be developed. It is generally preferable to use monitoring data based on personal samples rather than general area samples, modelling or assessments based on analogy to similar chemicals to estimate inhalation exposure. When the intent of the monitoring is to determine the exposure of a worker or group of workers, personal samples taken in a worker's breathing zone and samples in the areas adjacent to the activities are usually preferred over general area samples.

For predicting dermal exposure, monitoring data are generally preferred to modelling techniques, although monitoring methods for estimating dermal exposure have not been standardized and interpretation of the data may be difficult. Assessments based on specific worker activities for specific processes are necessary to account for variations in magnitude of exposure, frequency, or duration. For example, one would expect occupational exposure to be quite different for a manual packaging operation than for an automated packaging operation for the same substance.

For the chemicals for which the Organisation for Economic Co-operation and Development (OECD) Screening Information Data Set (SIDS) data is available, it is likely that complete, representative information will not be available, and an ideal assessment will not be possible. When representative information is not available, screening quality occupational exposure assessments may present results in terms of a "typical" or average exposure, "bounding" estimates of exposure, etc., depending on the type of assessment and the intended use of the assessment. The bounding estimate of exposure is an estimate of exposure which is higher than the individual in the exposure distribution with the highest exposure. Thus, exposure is not likely to be greater than the bounding estimate. This is useful in determining whether further resources need to be devoted to the assessment of occupational exposure. If there are no concerns at the bounding estimate, it may be possible to drop the substance from further review. This will allow resources to be better focused on other assessments or other chemical substances. If bounding estimates of exposure are of concern, further analysis to characterize exposure may be necessary. The assumptions and methods used to predict occupational exposure should be critically evaluated to determine how representative they are of the majority of the situations in which exposure occurs.

In evaluating assessments of occupational exposure, it is important to understand the type of assessment developed (e.g. typical or bounding estimate) and all assumptions, uncertainty and bias associated with the monitoring data and/or models or other approaches used.

2. Approaches and Data Sources Used to Estimate Occupational Exposure to New Chemical Substances

Generally, exposure via inhalation and dermal contact are the primary routes of occupational exposure, although exposure can also result from ingestion if good hygienic practices are not followed. The basic approach in developing an assessment of occupational exposure entails gathering data and information to address the following:

- What is the population of potentially exposed individuals?
- What are the magnitude, frequency and duration of inhalation and dermal exposure?
- What personal protective equipment and control methods are used to reduce or mitigate exposure?
- How effective are they at reducing exposure?

Of primary importance in developing the assessment of occupational exposure is a full understanding of the processes or unit operations during which exposure occurs and the associated worker activities which result in exposure. Once all of the processes or unit operations have been identified, the specific worker activities associated with each operation or process should be defined. This is of primary importance as there may be high variability in the occupational exposure for a group of individuals due to seasonal variations, interday or intraday variations, changes in the process or in worker activities at one facility, etc., and operations may vary between one facility and the next.

Once the worker activities for each process or operation are identified, the next step is to determine the population potentially exposed, and the magnitude, frequency, and duration of their exposure. Defining the population of potentially exposed individuals can be difficult or impossible if information on the production volume, number of sites where the substance is used, process descriptions and descriptions of worker activities is not available. Another area of potential uncertainty is the magnitude of the exposure. Without information on the process and associated worker activities, it may be difficult to estimate the airborne concentration of a substance, and quantify the potential for inhalation or dermal exposure. In such cases a bounding estimate may be possible. In addition, it may be difficult or impossible to estimate the frequency and duration of exposure without information on the process, operations and worker activities.

Finally, an assessment of the impact of personal protective equipment, engineering and other methods of control on exposure is developed. There can be a great deal of uncertainty associated with the assessment of control technologies. For example, the performance of personal protective equipment (e.g. respirators, chemical protective clothing, etc.) depends on whether the equipment is properly selected for the hazards identified, is properly maintained, stored, and properly fitted and used. The protection afforded by the equipment can be substantially reduced if improperly used or maintained. Often, training of workers in the proper use of personal protective equipment is required to ensure that misuse or improper use does not occur.

Engineering controls such as general mechanical ventilation, local exhaust ventilation, isolation or enclosure of an operation, etc. are preferred over the use of personal protective equipment if the exposure cannot be reduced at the source via elimination or substitution of

a less hazardous substance. Engineering controls are usually designed to control emissions from a specific process, operation, or piece of equipment, prior to their escape into the work environment. The effectiveness of the engineering controls will vary from one operation to the next depending on the design specifications of the hood or capture device, ductwork, fan, air cleaning device, etc. In addition, the equipment installation, maintenance practice, use, hood-to-source location, worker intervention, etc. may affect the operating efficiency. These factors and the lack of documentation on the effectiveness of engineering controls make it very difficult to assess their impact on the potential for occupational exposure.

2.1 Selected Sources of Occupational Exposure Data and Information

Data sources which contain specific information on worker exposure and supporting documentation are most useful. Some relevant data sources which contain information and data on occupational exposure include the Occupational Safety and Health Administration's (OSHA) Integrated Management Information System, National Institute for Occupational Safety and Health (NIOSH) National Occupational Exposure Survey (NOES), NIOSH Health Hazard Evaluations (HHEs) and NIOSH Industrywide Studies (IWS). In addition, various documents are available to assist in the evaluation of the effectiveness of personal protective equipment and to identify relevant engineering and other methods of control.

2.1.1 OSHA Integrated Management Information System

This system contains over 77,000 exposure measurements and is probably the largest source of accurate exposure data in the world. The system contains exposure measurements organized by industry and process, and judgments by compliance officers who are experts in industrial hygiene. In addition, the number of workers represented by each measurement is included. The system is computer readable. Appendix A contains an example of information found in the OSHA Integrated Management Information System (IMIS).

2.1.2 NIOSH National Occupational Exposure Survey

The National Occupational Exposure Survey (NOES) of 1981-1983 was initiated by NIOSH to address a critical and continuing need for information on nationwide patterns of occupational exposures to potential health hazards. The NOES consisted of on-site observational surveys in a sample of nearly 5,000 establishments which have been selected to represent most sectors of the American workforce covered by the Occupational Safety and Health Act. The database contains the results of this survey.

A two-stage sampling strategy was employed to construct the sample of establishments to be surveyed. The first stage resulted in the selection of 98 geographical areas, or primary sampling units. The geographical areas chosen in the first stage had relatively higher concentrations of those industries which were included in the target population. The second stage of sampling produced lists of establishments with 2,500 or more employees not included in the first stage of sampling, and were treated separately in order to maintain more nearly equal probabilities of selection across establishments.

First stage selection of geographical areas was accomplished by random selection from strata defined by geography, number of employees, and concentration of establishments. It employed systematic sampling from a list of establishments ordered by number of employees and Standard Industrial Classification (SIC). The second stage sample was

enlarged by 25 per cent, and establishments in this enlarged sample were screened by telephone to determine eligibility for inclusion in the survey. A total of 4,490 establishments were ultimately surveyed in the NOES. Substitutions were made for establishments which fell outside the scope of the survey, and inspection warrants were obtained and enforced where necessary. The effective refusal rate among establishments selected for inclusion in the survey was 0.3 per cent.

Two stages of ratio estimation were used in the process of projecting survey data to national statistics. Variances of the estimates were calculated using the method of balanced repeated replications. Appendix B contains additional information on the NIOSH National Occupational Exposure Survey.

2.1.3 NIOSH Health Hazard Evaluations

Health Hazard Evaluations, which are prepared by the Hazard Evaluations and Technical Assistance Branch of NIOSH, often contain well-documented occupational exposure measurements as well as a description of the operations and processes studied. The investigations are conducted under the Occupational Safety and Health Act of 1970, which authorizes an investigation to be conducted following a written request from any employer or authorized representative of employees, to determine whether any substance normally found in the place of employment has potentially toxic effects in such concentrations as used or found. Where appropriate, recommendations are made for controlling and mitigating potential exposures and hazards. Appendix C contains a recent NIOSH Health Hazard Evaluation.

2.1.4 NIOSH Industrywide Studies

The Industrywide Study Branch of NIOSH assesses whether specific occupational exposures of certain worker groups are associated with adverse health consequences. Study designs vary (cohort, case control, proportionate mortality, cross-sectional incidence, reproductive questionnaire) depending on the question to be addressed and availability of data. The majority of the Industrywide Studies are reports of industrial hygiene surveys during short one- to two-day surveys at plant sites to evaluate their suitability for industrywide studies. There is no or limited sampling during walk-through surveys. In-depth survey reports document detailed exposure information obtained during a one-week survey of a plant site. There is usually extensive air sampling data contained in an in-depth survey report. Appendix D contains information on the NIOSH Industrywide Studies.

2.1.5 Industrial Process Profiles and Other Documents Developed to Support Premanufacture Notification (PMN) Review

Industrial process profiles were developed under contract to support the review of new chemical submissions. The profiles describe the application of chemicals, exposure to and possible routes of environmental release of chemicals used in selected applications, such as metal treatment, printing, etc. Appendix E contains a listing of the Industrial Process Profiles developed to date.

3. Overview of Techniques Used to Estimate Occupational Exposure in the US New Chemicals Program

Because of the lack of specific information on industrial processes and worker activities for the SIDS chemicals, the existing data sources, databases and reference materials may not provide enough information for OECD Member countries to estimate occupational exposure for the SIDS chemicals. In the absence of any relevant data with which to estimate occupational exposure to the SIDS chemicals, it may be appropriate to use methodology and approaches used in the New Chemicals programs of the Member countries.

Screening quality assessments of occupational exposure are developed during the US New Chemical or Premanufacture Notice (PMN) review program. The New Chemicals Program requires the submitting company to provide information in a standard format with which the EPA will assess the potential for occupational exposure. The information provided to EPA that is relevant to the assessment of occupational exposure includes the following:

1) yearly production volume;

2) number of sites and days per year of operation;

3) description of the chemical processes (including unit operations) during manufacture, processing and use;

4) worker activities, protective equipment and engineering controls used, the physical form of the substance during the activity, the number of workers exposed, and the maximum duration in hours/day and days/year.

In addition, if not provided in the submission, EPA estimates the vapor pressure and physical form during manufacture, processing, and end use of the substance. Using this information, and any additional relevant information provided in the submission, an assessment of occupational exposure during manufacture, processing and use is developed.

3.1 Methods for Estimating Inhalation Exposure

The amount of substance inhaled by a worker is a function of many variables including the airborne concentration of the substance, the amount of time spent in an atmosphere containing the substance, the breathing rate of the worker, the worker activity or job performed, the physical and chemical properties of the substance, the temperature changes, seasonal changes, and the effectiveness of engineering controls or personal protective equipment in protecting the worker. Many of these variables also affect the amount of substance available via dermal contact.

Worker inhalation exposure is best determined using personal monitoring measurements for workers performing the job under study while being exposed to "typical" pollutant levels. Since monitoring data are seldom available for new chemicals, other methods are often relied on to assess worker exposures. Predictions of the expected airborne concentration of a substance may be based on monitoring data for analogous substances, OSHA Permissible Exposure Limits (PELs) for substances present in the workplace, and mass balance models.

The methods or approaches used to assess the potential for inhalation exposure include the following, in decreasing order of preference:

1) using monitoring data to assess the potential for occupational exposure to the chemical substance;

2) using occupational exposure data for an analogous substance during similar processes or operations and similar worker activities;

3) using generic scenarios based on available information and data for a specific industrial process;

4) using regulatory standards (OSHA Permissible Exposure Limits) for analogous substances or substances present in the same workplace as the new chemical to calculate the upper bound of the airborne concentration;

5) using mass balance models to estimate inhalation exposure to vapors.

Often, more than one method is appropriate for assessing occupational exposure for new chemical substances with several different uses. The selection of which method to use depends on the data available with which to predict exposure for the specific exposure scenario of interest. The preferred approach is to use monitoring data for typical conditions for the exposure scenario of interest to predict exposure to the new chemical substance. The hierarchical preference of one method over another is based on the preference for the use of either monitoring data or information which characterizes exposure for the specific substance or an analogous substance for the exposure scenario of interest. If no data or information which characterize the exposure are available, other methods such as assuming compliance with a regulatory standard, or using mass balance models to predict exposure, are used. Each method is explained in more detail below.

3.1.1 Using Monitoring Data to Estimate Inhalation Exposure

When monitoring data on occupational exposure are available, the utility of the data is evaluated following the process described in Guidelines for Statistical Analysis of Occupational Exposure Data, developed under contract for the US Environmental Protection Agency's Office of Toxic Substances. Appendix F contains a brief description of these Guidelines. The quality of the exposure data available for occupational exposure assessments varies from poorly characterized, summary data to well-characterized sets of individual data points. In almost all instances, the quantity of available data is limited. The guidelines describe the treatment of uncertainties, assumptions, and biases in the data. With the assistance of an industrial hygienist and a statistician, the Guidelines can be used to categorize the data and perform the statistical analysis. The Guidelines are currently undergoing peer review. In the absence of monitoring data on the new chemical substance itself, various other methods or approaches are used to estimate occupational exposure.

3.1.2 Using Information on Analogous Substances to Estimate Inhalation Exposure

The airborne concentration of vapors and particulates may be estimated using personal monitoring measurements for analogous chemicals or processes. In each case, similarities must exist in physical-chemical properties of the chemicals, nature of the workplace environment, quantities of material handled, and worker activities associated with the use of the chemical.

Although estimates of airborne concentrations may be based on analogous chemicals or processes, caution should be used when making the analogy. If the exposure calculations based on analogous chemicals or processes exceed the regulatory limits or other consensus standards, the assessment may not be realistic, and the assumptions or calculation methods should be checked for their validity. Appendix G contains the US New Chemicals methodology for estimating airborne concentrations of vapors from analogous data.

When using an analogy for particulates, the following parameters should be judged to be similar: hygroscopicity, moisture content, density, particle shape, particle size and distribution, and static buildup potential. Whenever available, particle size information for the new chemical should be obtained. This information may be presented in several different ways, from a complete particle size distribution to the limited identification of average size or per cent of particulates above or below certain cutoff sizes. Depending on the type of data submitted, the particle size information may be used to more completely characterize the exposure to the worker. The data should represent the PMN particle size distribution at the potential exposure points.

If properly collected and analysed, particle size information may be used to identify the per cent of particles in the respirable range. The definition of respirable particulates varies, although the most commonly used method of measuring respirable particulates involves using a cyclone with a cutoff size of 10 μm; this effectively defines the respirable particulates as those particles less than 10 μm in diameter. Another definition of respirable particulates is those particles with an aerodynamic diameter of 3.5 μm or less. These particles are expected to reach the alveolated gas exchange portions of the human respiratory system, where they may be absorbed. Almost all particulates that are inhaled and are larger than the respirable size are deposited in the upper respiratory tract. Those which deposit in the nasopharynx behind the nasal hairs tend to be carried downward to the throat. Those which deposit in tracheobronchial system are carried upward to epiglottis. Those particles that are larger than the respirable particles tend to be ingested.

3.1.3 Using Generic Scenarios to Estimate Inhalation Exposure

The generic scenarios contain information on typical assumptions used in predicting inhalation exposure to a new chemical substances, for certain specific uses and industries. The scenarios are developed based on past new chemical cases and other data sources such as those discussed herein. The generic scenarios have been developed by the US EPA's Office of Toxic Substances, and have not been peer-reviewed. For inhalation exposure, the methodology is generally based on using analogy to similar chemical substances (such as in a spray application), using regulatory standards (such as for particulate exposure), or using models for predicting exposure to vapors. A listing of the generic scenarios being developed and available generic scenarios are included in Appendix H.

3.1.4 Using Regulatory Standards to Estimate Inhalation Exposure

When occupational exposure data are not available for the new chemical substance, OSHA Permissible Exposure Limits (PELs) are frequently used to estimate occupational exposure to solids during operations such as spray coating or solids handling. Use of a regulatory standard to estimate inhalation exposure for a new chemical substance assumes that the facility is covered by the standard, and is in compliance with the regulatory standard. The assessor should carefully consider these assumptions, as there are currently several different OSHA standards with different requirements and PELs for different workplaces (General Industry (Part 1910), Shipyards (Part 1915), Marine Terminals (Part 1917), Longshoring (Part 1918), Construction (Part 1926), Agriculture (Part 1928), etc. and OSHA does not inspect workplaces with fewer than 11 employees.

The OSHA PEL for Particulates, Not Otherwise Regulated, 15 mg/m^3 total dust as an 8-hour time-weighted average (TWA) (29 CFR 1910.1000, Table Z-I-A), is frequently used to estimate particulate exposure for new chemical substances. Data collected by OSHA and NIOSH for total dust exposures have been tabulated by Standard Industrial Code (SIC) (Mitre, 1985). The tabulation of the mean exposure supports the use of 15 mg/m^3 to represent the airborne concentration of total dust in the worker's breathing zone as a substitute for specific data.

The OSHA PEL for oil mists of 5 mg/m^3 as an 8-hour TWA is frequently used if data is lacking to describe exposures to oil mists generated in operations such as metalworking or similar operations. To calculate exposure to the new chemical substance, the appropriate OSHA PEL is corrected by the weight fraction of the PMN chemical in the solids or oil.

3.1.5 Using Mass Balance Models to Estimate Inhalation Exposure to Vapors

When monitoring data or information on analogous chemicals are not available, the US New Chemicals Program uses mass-balance or "box" models to predict airborne concentrations and inhalation exposure. These models are most applicable for vapor and gaseous emissions because vapors follow currents freely and are not influenced by gravity. The model frequently used to estimate inhalation exposure is based on the mass balance of a substance in an enclosed space. The airborne concentration of the contaminant is a function of the source generation rate and the volumetric ventilation rate within the space. Depending on the worker activity for which exposure is being predicted, the source generation rate is either based on the rate of evaporation from a pool of liquid or the displacement of saturated vapor from an enclosed space. Using the source generation rate and some simplifying assumptions, the airborne concentration of the contaminant during transfer and loading operations and for sampling and open surface operations can be estimated.

Worker exposures can be influenced by many variables: 1) degree of automation, 2) employee work practices, 3) equipment design, age, and frequency of maintenance, 4) container and closure design, 5) ventilation type and rate, 6) employee use of protective equipment, 7) effectiveness of emission control devices, and 8) product flammability. These factors and the simplifying assumptions must be carefully considered before estimating worker exposure using these models. This is especially true if the default parameters are used to represent worst and typical conditions in the workplace. One check of the models is that good design of equipment keeps concentration below 25 per cent of the Lower Explosive Limit (LEL). A reasonable worst case assumption should not exceed good design practice. For PMN chemicals, however, the LEL or operating practices may not be known. The models

have not been peer-reviewed, but have been submitted for presentation at the 1992 American Industrial Hygiene Conference and Exposition. The models commonly used in the US New Chemicals Program are contained in Appendix I.

3.2 Methods for Estimating Dermal Exposure

In comparison to inhalation exposure, the assessment methodology for predicting dermal exposure is relatively simplistic. To assess the potential for dermal contact with a chemical, it is necessary to identify the activity where potential contact may occur, the likelihood of contact, the frequency of contact, the potential surface area of contact, the physical state of the contacted substance, associated chemicals, and the likelihood and effectiveness of the use of personal protective equipment such as chemical protective clothing. With this information, appropriate assumptions can be made to complete the assessment.

In the US New Chemicals Program, for liquids and many solids such as powders, granules, or flakes, a quantitative estimate of contact is made using the methodology presented in Appendix J. However, for materials such as gases, cast solids, or corrosives, a qualitative estimate is made using the following guidelines:

- *Corrosives* -- For new chemicals determined to be corrosive or for mixtures with pH greater than 12 or less than 2, express contact as negligible due to the corrosive nature of the substance or associated compounds. Consider contact points at which corrosivity may not apply, as in dilute solutions, and quantify for them as needed.

- *High temperatures* -- Express contact as negligible for materials that are at temperatures above 140°F. Consider contact points at which temperature would not be a factor.

- *Cast solids/PMN in matrices* -- Do not quantify contact. If the material is manually transferred, acknowledge that some surface contact may occur.

- *"Dry" surface coatings (e.g. fiber spin finishes)* -- If manual handling is necessary and there is an indication that the material may abrade from the surface, quantify contact with fingers/palms as appropriate.

- *Gases/vapors* -- Do not quantify contact, but acknowledge that some dermal contact will occur in the absence of protective clothing.

Qualitative estimates for the new chemical describe dermal exposure using the following exposure categories:

- *None* -- This is used to describe workers who have no chance of dermal contact during normal job activities.

- *Very low* -- This is used to describe workers who during typical job activities would have no dermal exposure but who, on occasion, may have short periods of exposure after which all contact surfaces would be washed.

- *Incidental contact* -- This is used to describe workers who during typical job activities have occasional dermal contact of a minor nature.

- *Intermittent contact* -- This is used to describe workers who during typical job activities have dermal contact such as splashes, wiping with contaminated rags, contact with contaminated tools, or surfaces. Contact may be with either liquids or solids.

- *Routine contact* -- This is used to describe workers who during typical job activities routinely have dermal contact not including immersion in a liquid.

- *Routine immersion* -- This is used to describe workers who typically immerse their hand(s) into a liquid.

Worker practices and the use of dermal personal protective equipment are strongly dependent on the industry under study. Therefore, when making qualitative estimates it is important to obtain as much current information on work practices in the industry as possible.

3.3 Methods to Evaluate the Effectiveness of Personal Protective Equipment

The primary types of personal protective equipment used to reduce worker exposure are gloves and respirators. Aprons, coveralls, goggles, and face shields also may be used where necessary. It can be extremely difficult to evaluate the effectiveness of personal protective equipment for chemicals, and with the lack of information on new chemicals, the task is even more difficult.

3.3.1 Gloves and Chemical Protective Clothing

The ability to predict glove use practices, especially for end-users of a chemical, is poorly established. Glove protection depends both on glove selection and work practices. Therefore, it is difficult to define the level of protection resulting from the general use of gloves. There are no gloves available that are totally impervious to chemicals. Also, there are no existing models to predict the degree of protection offered by a glove of a particular material when used in contact with a specific chemical. However, if gloves are properly selected and appropriately used (considering available information on permeation, penetration, degradation, and frequency of replacement), their use will significantly reduce exposure. The Guidelines for the Selection of Chemical Protective Clothing (A.D. Little, 1985) is a comprehensive document containing tables of recommendations to aid and facilitate the selection of chemical protective clothing.

The effectiveness of gloves is a function of characteristics of the glove, the type of chemical to which exposure may occur, the conditions of exposure, and the activities of the worker. The physical environment is an important consideration as gloves are often composed of polymeric materials that may be stressed, punctured, or otherwise damaged in actual use.

EPA has had an ongoing research project to assist in the assessment of the permeation of new chemical substances through glove materials. This research has resulted in the development of test methods to measure glove permeation during intermittent contact, the development of a computer model to predict permeation of certain chemicals through selected polymeric materials commonly used in chemical protective clothing, and research to improve the standard test methodology for measuring the permeation of substances through gloves. The computer model requires chemical-specific input: molecular weight, density, and

vapor pressure or molecular structure of the chemical. The model also incorporates specialized versions for certain chemical groups for which it requires more detailed input resulting in a more accurate prediction. The output is a cumulative amount of chemical permeating through the material over time, presented as mass per surface area for a designated period. The model also provides breakthrough times. Appendix K contains information on the model used to predict glove permeation rates for new chemical substances. A method to measure permeation through chemical protective clothing under intermittent chemical contact was also developed (see Appendix L). In addition, permeation was measured for selected acrylate compounds.

The results of the research were used to develop a guidance manual which is used to assess the permeation of new chemicals through polymeric materials. The US New Chemicals Program may require glove permeation testing to be conducted for new chemicals. These tools are used in determining the feasibility of requiring glove permeation testing, and evaluating permeation data submitted for new chemicals. The methodology used by the US to evaluate the permeation of new chemicals through chemical protective clothing material is provided as Appendix M.

3.3.2 Respiratory Protection

Respiratory protection for new chemicals presents some unique and complicated problems for the assessment and control of occupational exposure. Often, the potential for inhalation exposure is a primary concern for the workers who handle new chemicals, often in conjunction with other contaminants present in the work environment. For new chemical substances regulated within the United States, respirators must be properly selected, fitted, maintained, and used, in accordance with OSHA and NIOSH regulations for respirators. The NIOSH Certified Equipment List (NIOSH, 1991) is updated periodically and contains a listing of respirators and components which have been certified by NIOSH as of December 31, 1990 under 30 CFR 11. In addition, for new chemical substances, testing of organic vapor cartridge service life may be required to ensure that the respirator selected is appropriate.

Selection of an appropriate respirator is difficult without information on the acceptable exposure limit, warning properties, etc. Therefore, for new chemicals, classes or categories of respirators are selected, and the rationale of selection is clearly presented. It also must be remembered that wearing a respirator is often a burden to a worker performing tasks. Not all worker activities or types of respirators are amenable to use of respirators over extended periods of time. These and other factors are important considerations in the selection and use of respirators for new chemical substances. The NIOSH Assigned Protection Factors for respirators, and the NIOSH recommendations included in the Guide to Industrial Respiratory Protection (NIOSH, 1987) and the Strategy for Recommending Respirators for Control of Exposures to Substances Undergoing Premanufacturing Notification (PMN) Review (W.R. Myers, ND) are used in selecting types or classes of respirators for new chemical substances. Information from the Strategy for Recommending Respiratory Protection for PMN substances is contained in Appendix N.

3.4 Methods for Evaluating Engineering and Other Controls

If the contaminant cannot be eliminated or controlled at the source of generation, by engineering alone or in combination with other methods of control such as administrative controls, changes in work practices are generally preferred over the use of personal protective equipment for controlling occupational exposure. The rationale is that engineering and other

controls, when properly designed for the system or operation and considering the worker interaction, will minimize the dispersion of the contaminant into the workplace air, thereby reducing the exposure at the source of generation. In contrast, personal protective equipment is an attempt to provide a barrier between the worker and the contaminant to reduce or eliminate occupational exposure. There are many types of controls used in reducing or eliminating occupational exposure, although local exhaust ventilation and the use of nitrogen blanketing are commonly seen in the New Chemicals Program. The methodology for evaluating the effectiveness of nitrogen blanketing and considerations for local exhaust ventilation are presented below.

3.4.1 Local Exhaust Ventilation

Local exhaust ventilation (LEV), in addition to general ventilation, is the primary control used to reduce worker exposure to chemicals. If LEV is used for a specific activity, the specifications of the control for new chemicals is be compared to the recommendations made by ACGIH in Industrial Ventilation: A Manual of Recommended Practice (ACGIH, 1986). Although a qualitative determination of control use can be made, it will usually not be possible to account quantitatively for a reduction in exposure due to the use of local exhaust ventilation. A compilation of types of engineering and other methods of control for selected industries commonly seen in the New Chemicals Program was prepared under contract for the EPA (IT Corporation, 1991). Appendix O contains information on this document.

The actual reduction in worker exposure from the use of LEV is not a simple relationship. It is dependent on several factors:

- the design capture efficiency of the LEV system;
- the work practices of the employee;
- air currents in the work area;
- other process-specific factors such as dragout or sudden releases; and
- actual maintenance of the LEV system over time.

The design capture efficiency is primarily dependent on hood design and exhaust volume. The best hood design is one that encloses or confines the process. This is not always possible when worker access to the process is considered. Exhaust volumes (or face velocities) presented in the ACGIH ventilation manual for a similar process should be compared with information supplied by the new chemical submission to ensure that adequate face velocity will be used in the design.

The addition of a LEV system can affect the work practices of the employee. Enclosure of the process can cause changes in work practices that may make the LEV less effective. The LEV design should never allow the breathing zone of the worker to pass between the pollutant source and the exhaust.

Air currents in the work place from other processes, natural ventilation, general ventilation, or movement in the area can reduce the effectiveness of an LEV system. All possible cross currents should be minimized.

Process-specific factors such as dragout can cause the chemical to be carried out of the capture zone of the LEV system, thus decreasing its efficiency. Processes that release sudden surges of hot gases or vapors must design the LEV system to account for these releases. Finally most LEV systems are not maintained at peak efficiency throughout their life. If a system is older, the questions of design parameters such as face velocity versus actual parameters should be addressed.

One process where standard LEV design can obtain very high efficiencies is the use of lay-on or slot LEV to control worker exposure during drum filling. In a series of tests on LEV use in drum filling performed for OTS, capture efficiencies were between 99 to 100 per cent when the ACGIH design flow rate was used (PEI, 1987). The efficiency of the lay-on and slot LEV systems in drum filling operations generally was independent of the concentration of emissions leaving the drum. The efficiency was affected by the fill rate that determines the emission velocity at the drum bung hole.

3.4.2 Nitrogen Blanketing

Chemicals that are extremely volatile or that react with water or air on contact are often loaded into shipping containers under a nitrogen blanket. This handling procedure (known as nitrogen blanketing, padding, or purging) displaces air and moisture and therefore prevents degradation of the chemical. A report was prepared for the EPA describing the process and work activities associated with the procedure for selected chemical substances (Mitre, 1984), including the methodology for estimating the release from nitrogen blanket transfer. Appendix P contains the methodology for estimating ambient releases from nitrogen blanket transfer.

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Annex II

The Estimation of Occupational Exposure to Chemicals

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Note: This paper is a personal contribution directed towards assisting discussion. It does not necessarily reflect the views of the author's parent organisation, The Health and Safety Executive (UK).

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Annex One Tentative Application of Empirical Procedure to SIDS Data 48

Summary

A primary objective of chemicals safety assessment is to provide an indication of the extent of concern, or of reassurance, over prevailing standards of control. Occupational exposure is finite and determinable, but the variability of real data is large. Estimates of received dose are correspondingly imprecise and it is necessary to address the issue of the precision required in relation to the decisions that are to be made, such as prioritisation of further work.

In the absence of real data, estimates of occupational exposure can in principle be derived from two distinct but complementary procedures, a calculus based on fundamental properties and an expert system approach relying on analogy with real data. Both techniques require similar validation. The choice between them would depend on criteria, including the cost of application and whether the precision is adequate for the assessment purpose. The basis for development and validation of the analytical approach is discussed, and a cursory analysis of certain SIDS data sets is used to illustrate the potential application.[1]

1. Introduction

The concepts of hazard and risk assessment are fundamental in any strategy which is to result in effective action to ensure the safe use of chemicals in society. Rigorous definitions of the terms "hazard" and "risk" perhaps matter less than the imperative that the procedures adopted succeed in focusing attention on real priorities and allow for balanced decisions on any appropriate control measures. This is by necessity a dynamic and iterative process: proof of safe or unsafe is very rarely absolute, but any assessment scheme must allow for judgements to be made.

A fundamental concept in occupational health/hygiene was first enunciated by Paracelsus in the early sixteenth century: *sola dosis facit venum* -- only the dose makes the poison. This is the direct antecedent of much contemporary work in toxicology and epidemiology, when the quest for a no observed adverse effect level (NOAEL) or the dose-response threshold in an exposed population is a leading goal. However without a satisfactory indicator of human exposure, observations on the hazard cannot lead to sensible judgements on how the attendant risks should be managed.

Real data are always preferable to predictions, simulations or models, but their absence cannot excuse inaction. It is perhaps an indictment, with widely shared responsibility, that despite decades of economic and profitable exploitation of many chemicals we still find ourselves at the stage of having to make either theoretical or empirical estimations of the exposures that have been and are occurring.

Exposure is a wide term, and even with the qualification *occupational* is not amenable to any simple or comprehensive description. In classical terms, focus is given to the different routes of absorption, viz. inhalation, dermal and ingestion.

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[1] The basic concept outlined in this paper has been substantially developed into an expert system for estimating exposure. This paper should be seen as an early evolutionary stage in the development of this expert system.

Although in principle these are quantifiable, the assessment of risk can be constrained by the uncertainty of commensurate factors, including:

- non-occupational exposure (e.g. dietary levels of cadmium);
- synergism on co-exposure to other agents;
- lifestyle, predisposing human factors, etc.

For the purposes of this paper, emphasis is placed on the inhalation route of occupational exposure as, in quantification terms, it is frequently the route of lead impact and concern. It is assumed that ingestion can only be considered significant in conditions of *prima facie* unsatisfactory basic hygiene beyond the scope of this study. The dermal route of absorption is of widely varying significance, heavily influenced by mitigating factors such as protective clothing or, on the other hand, confounding factors such as the failure in some quarters to adopt even the most basic standards of occupational hygiene which are the norm in other quarters. It is in this rather unsatisfactory context that inhalation exposure emerges as the primary indicator of occupational exposure, especially in circumstances where there is little evidence of acute effects on health and, correspondingly in the absence of actual assessment, limited perceived imperative to adopt specific control measures.

2. Variables in Exposure

It is perhaps useful to start by stating an obvious fact, that no single number can ever be an adequate description of occupational exposure to a chemical. On the other hand, to retreat behind a subjective presentation of exposure quantification couched in broad ranges, perhaps covering several orders of magnitude of dose without adequate qualification, does little to assist an assessment/management objective. In a practical world the regulator or the assessor, deprived of a simple numeric of the "true" exposure, would be provided with a robust and validated estimation procedure on which reasonable conclusions could be justified. Before considering how a balance between theory and empiricism can be struck in developing such a procedure, it is necessary to review real experience of some of the variables which influence exposure.

Occupational exposure is a result of a complex equation of both dependent and independent variables. It is fairly obvious that the potential for exposure is influenced by properties such as volatility or particle size. We would for example expect the potential exposure to, say, acetone to be of a different order of magnitude from that to glycerol. Similarly, the handling of a micronised dry powdered aromatic amine dye complex would result in a rather different exposure as compared with handling the same chemical in pellet form or dispersed in a solution. Direct manufacture as compared to use may clearly introduce different bases for assessment.

A fully contained process plant would be likely to give rise to much smaller exposures to any chemical irrespective of physical-chemical properties in contrast to a relatively uncontained process design. For example exposure to vinyl chloride monomer during production and polymerisation is likely to be a couple of orders of magnitude lower than that to toluene during rubber processing. A paint product intended to be sprayed presents, evidently, a different potential for exposure from that of one to be applied by brush.

Human factors is rather a wide term, incorporating a variety of individual, organisational and cultural attitudes which influence perceptions of acceptable practice. For example the degree of training, supervision and provision of protective clothing may vary widely both within and between different industry sectors (e.g. chemical and waste reclamation/disposal industries). The rating of different industries can also vary widely between different countries, due both to different technology bases or infrastructure and perceptions of relative performance.

Although this analysis may already present an adequate challenge to those who seek to estimate and rationalise occupational exposure, there are additional factors which need to be considered. Of prime importance is that derived from knowledge or experience of the toxicological effects of exposure and in particular those that present acute challenges to health. Serious central nervous system (CNS) disturbance or respiratory tract or skin/eye irritation are illustrations of effects that would in practice lead to control standards which would mitigate what in other circumstances would appear to be a "normal" degree of exposure. Additional complications are introduced by the (widely varying) appreciation of the potential for chronic impacts on human health. Although there has been much progress, an international consensus of the interpretation and consequences for human health of, for example, carcinogens, mutagens and reproductive toxicants identified in animal toxicological research is still some distance away. The current reality is that there remains some divergence, even at the national level, on the imperatives which influence the required degree of control of exposure.

The occupational hygiene profession has recognised for several decades that there are many workplace variables which influence any received exposure [e.g. HSE (1989)]. Primary variables include:

(a) the number of sources from which the contaminant is released;

(b) the rates of release from each source;

(c) the type and position of each source;

(d) the dispersion or mixing of the contaminant in the air of the workroom, as influenced by local ventilation and random movements or turbulence in the air;

(e) the ambient conditions, particularly for outdoor operations, where factors such as wind speed, direction and air temperature are important factors.

It is also possible to codify inter and intra variations between processes, shifts and individuals and to compensate for errors in actual sampling and analytical techniques.

Modelling of these variables is complex, particularly when considered in the context of human factors and, for example, a more sophisticated analysis of physical-chemical property influences. The latter presents a technically interesting range of problems involving fundamental physics and fluid dynamics. For example, the evaporation of mixed solvents from a paint substrate has an important time variable due to different volatilities which are also dependent on differential permeation rates through a rheologically dynamic paint skin.

It is beyond the purpose of this paper to develop such concepts of variability further, but their recognition is still important in identifying strategies to obtain meaningful estimates of exposure. In occupational hygiene there have been, perhaps, two fundamental and interactive influences on determining acceptable practice:

(a) the measurement and analysis of real (personal) exposure data as a basis for interpretation and assessment;

(b) the development and use of occupational exposure limits based on scientific evidence in order to impose a crucial constraint on acceptable exposure variability.

Within the constraints imposed, it is generally accepted that certain occupational exposure data can be described in terms of standard statistical distribution models and, in particular, the log-normal distribution (e.g. NIOSH 1975, HSE 1989).

The key index of variability is given by the geometric standard deviation. Even within narrowly defined homogeneous data groups, these have been shown to vary from around 1.2 to in excess of 3 (NIOSH 1975). Few analyses appear to have been done on truly heterogeneous groups representing exposure, in different industries and circumstances, to the same substance. It is unlikely that mixing such diverse data could do much more than illustrate the obvious point that non-random variations at process level would be expected to yield a polymodal distribution heavily disguised by inter-group biases.

With the composite experience built up over several decades of applying occupational hygiene procedures, it may still be possible in principle to predict occupational exposure to a specified substance within a spectrum bounded by:

"poor" - "normal" - "good"

Clearly these terms are not objective and usually relate to some pre-existing standard. However if it is possible to codify real exposure data and historical experience within such a range there is then a possibility of developing descriptors or criteria for specifying different bands to which one could classify a specific chemical. This concept will be developed at Section 5.

3. Precision Required in Estimates

It is important to consider briefly what should be the required precision in estimating occupational exposure. It has been argued earlier that we could be faced with two initial options -- a single number or an indeterminate but very wide range -- neither of which offer any real basis for decisions. If we reject these approaches it may be helpful to consider first just what range of judgements need to be made through the assessment process. A simple scenario would be to address the ratio:

$$\frac{\text{Index of Toxic Dose (NOAEL)}}{\text{Index of Occupational Exposure Dose}} = R$$

If the objective was to contribute to a prioritisation procedure the most basic analysis could have the following end points:

R < 1	=	highest priority
R >> 1 (say >10)	=	lowest priority

It would be artificial to produce a strict ranking order, but candidate chemicals could by this process be structured into different bands reflecting the degree of concern and thereby the urgency in refining the data set, conducting more formalised risk assessment and proposing appropriate control action.

From the description at Section 2 of the uncertainties involved in producing a real quantification of actual exposure it has to be argued that the banding of decision criteria has to be correspondingly crude. Perhaps the best that can be achieved for a prioritisation programme would be a classification into high, medium or low priority. If this premise is accepted then it follows that the precision and reliability of the exposure estimate need only be commensurate with the weighting given to it in reaching judgements for future action. It would therefore be sensible to approach the issue of exposure estimation on the basis of classification into relatively broad exposure bands of perhaps an order of magnitude difference, and to resist the temptation to attempt artificially to refine the estimate.

4. Possible Approaches to Exposure Estimation

There would appear to be two distinct but not fundamentally independent alternative strategies to exposure estimation:

(a) *Deterministic/theoretical*, based on the development of modelling equations which under specified initial conditions and simplifying assumptions can yield a reasonably objective and relative (to other substances) estimate of exposure by all relevant routes.

(b) *Analogical/empirical*, based on a structured codification of past and current experience which, through a set of rules derived from an expert system approach, can produce estimates of exposure which would be expected to reflect real circumstances (i.e. amenable to validation by real data).

Either of the above approaches could in principle prove satisfactory in realising the stated objectives of an assessment procedure, provided these have been adequately specified. Both would require a degree of validation to support the underlying assumptions. If it was necessary to choose between them, of crucial significance would be consideration of the precision required and the degree of expertise (and cost) necessary to apply the technique.

Different deterministic models have been applied by regulatory authorities internationally, including Germany (new substances), UK (pesticides) and the United States (various applications). However little attention has apparently been given to developing the alternative approach using analogous experience. It is nevertheless widely practised at various stages of chemical assessment where a degree of expert judgement is relied upon.

Simple statements such as:

"this seems very like ...";

"On the basis of what is known of X, I would expect ...";

"This must have a similar mechanism to Y, and would merit a similar approach"

are commonplace in any real assessment system (including specifying the boundary conditions and assumptions of deterministic models or interpreting toxicological data). It is, however, the overt use of subjective judgement without adequate codification or validation which has rendered the approach less than fully satisfactory in the "regulatory" context.

The rest of this paper explores whether it could be possible to develop the empirical approach for exposure estimation, and then indicates in general terms how it could be applied to current OECD SIDS data sets.

5. Exposure Estimation by Analogy with Current Knowledge

Section 2 has sought to identify certain factors which influence occupational exposure. It is clear that exposure is not governed by simple physical variables alone, such as the vapour pressure at processing temperatures. Not all influencing factors are determinable (and some may be inherently irrational), and any meaningful estimation procedure has to incorporate basic assumptions and simplifications. Nevertheless, if the exercise is to be meaningful a degree of quantification is necessary and this must stand the challenge of appearing to be reasonable and defensible.

Section 2 considered the effect of different parameters on exposure. Clearly these parameters are not entirely independent, but nevertheless it is useful to consider the combined effect of containment levels and physical properties on exposure. **Figure 1** shows schematically the relationship between these parameters.

This simplified representation largely ignores the important human factors except in so far as they are incorporated into the "containment" category. But it is perhaps an intuitively useful starting point. What it seeks to represent in three dimensions is that, as the potential for a substance to become airborne (e.g. volatility) increases and the degree of process containment is relaxed, the potential for exposure also increases. The question is to see how such a basic concept can be refined and quantified meaningfully.

Figure 1 uses a banding approach for the levels of containment. Possible definitions for these levels are given in **Table 1**.

Band or level A represents the highest level of containment. The X-axis, physical properties, will largely depend on the volatility of the compound, but as discussed in Section 2 other factors may also need to be considered, such as dustiness. Handling a granular or liquid reactive dye will result in much lower exposure than the use of a finely powdered dye.

Table 1 **Possible definitions for levels of containment**

Level	Process type
A	Fully contained plant
B	Small quantities -- good local exhaust ventilation Larger quantities -- local exhaust ventilation
C	Large evaporation areas -- no containment of LEV
D	Spray application

Figure 1 **Exposure as a function of containment level and physical properties**

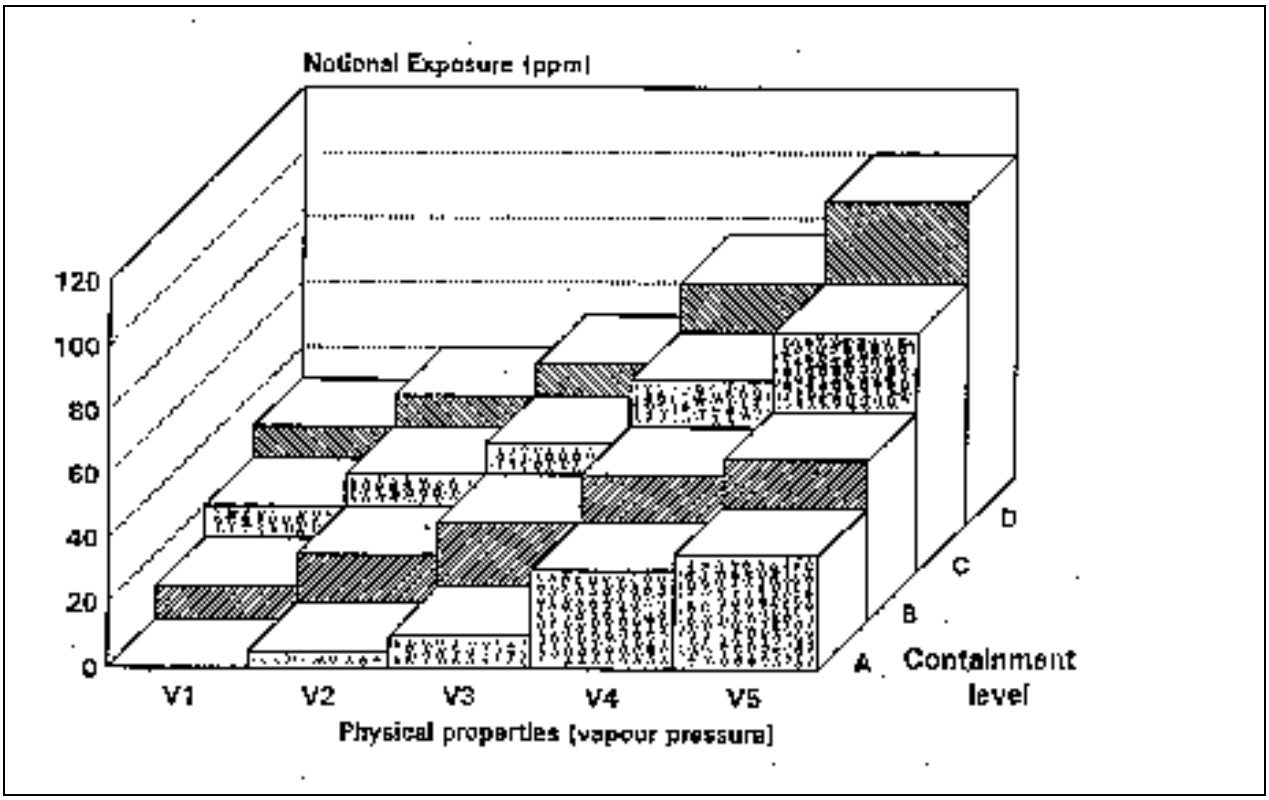


Figure 1 introduces the obvious observation that, say, production of an isocyanate prepolymer in a closed reactor system would have a rather different exposure potential from applying a two-pack polyurethane paint by spray. In the absence of knowledge of process design and use circumstances, it may be possible to do little more than assume that Band B represents a pragmatic indication of normal conditions.

The scheme presented in Figure 1 can be used to assess exposure for substances which are considered to be non- or only mildly toxic. Such substances are unlikely to have occupational exposure limits and conditions of use, i.e. containment level, and physical properties are likely the determinant factors in exposure levels. The estimation of exposure for 1,2 -pentadiene, example D in **Annex One**, gives an example of this type of approach.

However many commonly used substances have known toxic properties and some have been assigned occupational exposure limits. For these substances users will, or should have, made a conscious effort to control exposure to limit adverse health effects. In these circumstances, physical properties are unlikely to be an important determinant in exposure. The nature of the adverse effects will influence the level of exposure limits and in turn the level of exposure. Conformity to limits varies between different users of substances within one country; there will be correspondingly greater variations between countries. **Figure 2** gives a three-dimensional representation of toxicological effects and containment performance. The terms for containment performance have to be seen in the context of known exposure limits or, in the absence of a limit, by analogy with other substances with comparable toxic effects.

The categorisation of toxic effects is a starting point for an analogical approach and examination of Structure-Activity Relationships; attempts to push the model too far will almost certainly throw up anomalies. With that caveat, **Table 2** attempts to illustrate categorisation of toxic effects.

Figures 1 and 2 demonstrate that it is conceptually possible to obtain a structured correlation of the key variables that will influence exposure. They also introduce a first indication of how exposure quantification could be derived from analyses of real data using a well validated occupational exposure database which links exposure to the relevant bands that have been identified. Such data from known substances could then be satisfactorily applied to others by analogy with specified conditions on the bands chosen. What would emerge is not a single number, but a statistically qualified exposure distribution estimate.

The next step (currently in progress, December 1991) is to validate the subjective exposure categories using a comprehensive database of real exposures [National Exposure Database (NEDB), HSE 1989] and to perform regression and cluster analysis of certain physical properties biased by some derived index of toxicity. The use of simple Structure-Activity Relationships (SARs) can also be considered.

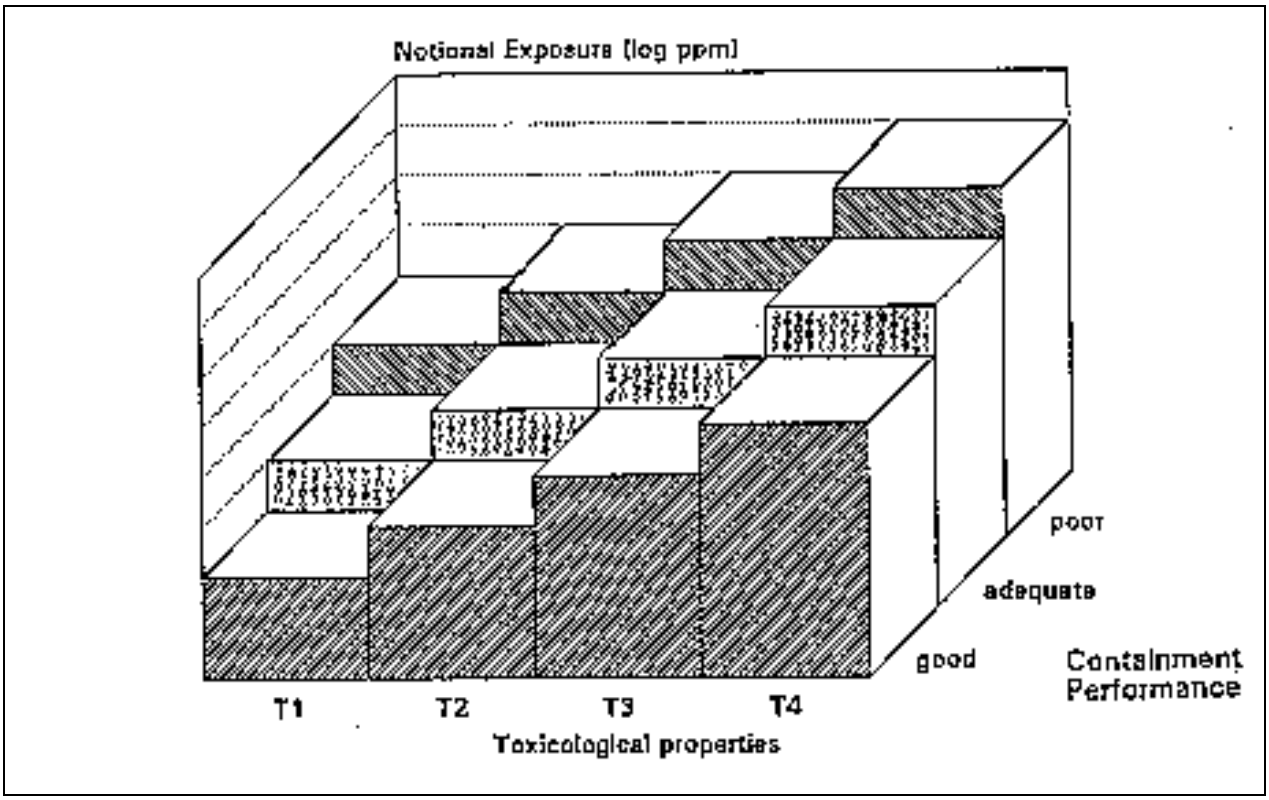
The approach is based on the hypothesis that an expert system based on prior experience and analogy can be codified and tested against real data and thereby satisfactorily extended or extrapolated to a wide range of other chemicals. It is probably easier to consider first volatile substances in volume units (ppm) and then convert to the more useful mass units (mg/m^3). Aerosols and particles in air present more difficulty, and it is likely that the precision of the estimate will be correspondingly cruder, but again the real data will illustrate the variability to be expected.

Table 2 **Toxicity classfication**

Category	Indicative classification*	Examples
T1	Very toxic (including some carcinogens)	Bischloromethyl ether Acrylonitrile Dimethyl nitrosamine Arsenic trioxide
T2	Toxic (including serious chronic irreversible effects)	Diisocyanates Cadmium Mercury
T3	Harmful/irritant (including moderate acute/chronic effects)	Tricholoreothylene n-Hexane Toluene
T4	Low toxicity/not classifed	Chlorofluorocarbons Acetone Diethyl ether

* *Note: This classification is not intended to mirror precisely that used in European Community Directives.*

Figure 2 **Exposure as a function of toxicological properties and containment standard**



6. Tentative Application of Empirical Procedure to SIDS Data

Whilst work is undertaken to develop and validate the evaluation procedure outlined in Section 5, it is rather impertinent (or perhaps foolhardy) to present a subjective and crude assessment. However, as the procedure is based on the application of expert knowledge by analogy, it may nevertheless be useful to indicate the general approach. Accordingly, Annex One includes an assessment of the first four OECD "Category 1" chemicals with basic SIDS data in dossiers. It needs to be stressed that this is no more than an attempt by the author to provide a useful contribution for discussion whilst a more rigorous approach is developed. The evaluation at Annex One incorporates a significant degree of caution over the validity of any estimate, with potential exposures normally ranging over 2 orders of magnitude. In one case (1,3-pentadiene) it concludes that real exposure data -- which would appear to exist -- would be much more reliable than any estimate. In the other cases a subjective judgement is made, on a paucity of information, as to the likely containment performance of process plant during manufacture and use. It is clear that such judgements are necessary if a meaningful estimate is to be given, but the technical basis is highly tenuous.

Only real occupational exposure data (airborne and biological) can provide a satisfactory basis for evaluating any estimate. It is clearly possible to do this in a control study where the data are available. Otherwise the estimate can only provide a challenge to those who have the ability to produce new data for comparison.

References

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NIOSH (1975) Exposure measurement Action Level and Occupational Environmental Variability, National Institute for Occupational Safety and Health. PB 267 509.

NEDB HSE (1989) The HSE National Exposure Database (NEDB), Burns D.K. and Beaumont, P.L., Ann Occ. Hyg. 36:1-14.

Annex One

Tentative Application of Empirical Procedure to SIDS Data

A. Triethyl phosphate

Triethyl phosphate is manufactured in fully contained plant. A significant proportion of its uses would be expected to be conducted under similar standards of control. However certain applications, such as a flame retardant in plastics, could introduce a wider exposure potential (e.g. plastic extrusion at moderate or high temperatures). Similarly use as an intermediate in the pharmaceutical, pesticide and lacquer industries would be expected to involve low volume process plant with emission or exposure controls dictated by other considerations (e.g. other intermediates).

The toxicity profile available is generally reassuring, with no indications of immediate acute (e.g. severe irritation) or chronic effects which would introduce impracticalities for controlling exposure. However this basic information is hardly adequate to make any firm judgement. (Is there significant anticholinesterase activity, for example?)

The physical-chemical data indicate a moderate volatility, with potential for vapour in air concentrations to arise outside of contained plant. The substrates vapour concentration at 25^{o}C is in the order of 400 ppm (3,000 mg/m^{3}). The rate of hydrolysis in air should be noted, but this is probably not of immediate relevance except to indicate that future consideration should be given to assessing the toxicity of the decomposition product, diethylphosphate. Although the n-octanol/water partition coefficient would indicate only a limited contribution to exposure from skin absorption, the application as a plasticiser/fire retardant would suggest that some assessment of potential consumer exposure would be requested.

Overall, the volatility and other physical-chemical data would suggest, at a first order, that potential analogues could be substances such as phenol, nitrobenzene, aniline or certain glycol ethers. This would place the potential occupational exposure range (8-hour time weighted average) as follows:

Poor	Normal	Good
10 ppm	1 ppm	< 0.1 ppm
75 mg/m^{3}	7.5 mg/m^{3}	< 0.75 mg/m^{3}

In the majority of contained applications, occupational exposure over a shift would on this basis be unlikely to exceed 0.75 mg/m^3. Assuming inhalation of 10 m^3 of air in an eight-hour shift, this would translate to a maximum daily (24-hour) dose of 7.5 mg. The potential for exposure to higher concentrations (up to x 100) during applications in non-contained plant and, in particular, in higher temperature applications should be noted.

B. Camphene

Camphene appears to be manufactured and used mainly on a large scale in what would be fairly standard contained plant. There is very little information about the conditions of downstream use, but it is noted that 80 to 90 per cent is used to produce isobornylacetate.

The toxicity profile gives virtually no indication of significant acute or chronic effects that would mitigate exposure. However, by analogy to other complex hydrocarbons and in particular noting the application as a fragrance material, it is possible that sensory perception and irritation at higher concentrations would be relevant.

The physical-chemical data indicate a substance with a relatively narrow liquid temperature range but with an appreciable vapour pressure in the solid phase. Sublimation is an obvious potential property.

Overall, the physical-chemical data would suggest, as a first order, potential analogues such as o- and p-dichlorobenzene, with the vapour pressure at the lower end of a range which would include certain single aromatic hydrocarbons (e.g. styrene), low molecular weight glycol ethers, and isophorone. This would place the potential occupational exposure range as follows:

Poor	Normal	Good
10 ppm	1 ppm	< 0.1 ppm
55 mg/m^3	5.5 mg/m^3	0.55 mg/m^3

As the type of plant used in bulk operations is likely to be contained, but with potential for vapour releases during loading, etc., this would suggest a representative occupational exposure over a shift to be around 5.5 mg/m^3. Assuming inhalation of 10 m^3 of air during an eight-hour shift, this would translate to a maximum daily dose of approximately 55 mg. The potential for exposure to concentrations considerably higher, particularly in consideration of any process-dependent emissions of particulate material and skin contamination, should be noted.

C. Benzeneamine, 3-nitro

The SIDS data on this relatively simple chemical are surprisingly sparse and give little basis for assessment. By analogy with other aromatic amines, one would expect moderate to high toxicity, with acute effects such as methaemoglobinaemia and liver/kidney dysfunction being strong mitigating influences on exposure. It is not possible to speculate if control/containment could be further influenced by considerations of genotoxicity and related chronic effects on health. Skin absorption is likely to be an important source of potential exposure.

Using analogues such as methylene dianiline on the basis of physical-chemical properties, a *very crude* first estimate of potential exposure would be:

Poor	Normal	Good
> 1 ppm	0.1 ppm	< 0.01 ppm
6 mg/m^3	0.6 mg/m^3	0.06 mg/m^3

The "normal" figure would equate to an average daily occupational dose of 6 mg, with the likelihood that skin absorption could increase this by a factor of 2 or more. However, it must be stressed that without airborne and biological monitoring data little confidence could be placed in this estimate.

D. 1,2,-pentadiene

This is a major commodity petrochemical product, with the specification of process design likely to be dictated by its low boiling point and flashpoint rather than immediate considerations of toxicity. The lack of toxicity data is, perhaps, not surprising although the single *in vitro* genotoxicity study results are somewhat reassuring despite the close structural similarity with butadiene.

The SIDS data include an estimated occupational exposure (8 hr TWA) of 0.07 ppm (0.198 mg/m^3) in air. This seems impressively low and would indicate an unusually high standard of process containment. However, bearing in mind the comments in Section 2 of the main paper on the variability of exposure, particularly over diverse operations and exposure conditions, it would be unsatisfactory to base the assessment on this single number. Nevertheless it is plausible that such a figure could represent the geometric mean in an intermittently exposed population. The potential for skin absorption is likely to be low in most circumstances.

In this case, it would be much more satisfactory to invite Exxon to elaborate on the occupational exposure data rather than speculate by analogy or theoretical calculation.

Annex III

Occupational Exposure Assessment for Selected SIDS Chemicals

A Contribution from the Federal Institute for Occupational Safety and Health, Germany

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Introduction

The OECD Workshop on Occupational and Consumer Exposure Assessments in Orlando has the objective to identify methods and procedures which can be used to differentiate among selected SIDS chemicals in terms of human exposure in the occupational and consumer settings. Member countries have been requested to demonstrate exposure methodologies using the basic data sets of nine selected Phase 1 chemicals.

The following presents a simple approach to categorise substances according to their exposure potential at the workplace on a screening level of assessment.

Exposure Elements

Direct human exposure of workers who come into contact with chemical substances will be discussed in this paper up to the absorption interface, i.e. the point at which a substance may be absorbed by the organism. The term exposure is described by the following elements:

- the route of exposure;
- the extent of exposure;
- the characteristics of the exposed population.

The route of exposure refers to the way a worker is exposed to a substance, i.e. by inhalation and/or by dermal contact. Information on the route of exposure can be derived from the physical-chemical properties of the substance. The vapour pressure, as a measure of a chemical's tendency to volatilise from the liquid or solid phase to the gas phase, is the most important property in determining the potential for inhalation exposure. Also the physical form of a substance has to be taken into account. Powdered substances may be easily inhaled during certain operations. Besides the physical-chemical properties, the type of use pattern may influence the route of exposure, e.g. if substances are applied in spraying operations.

The extent of exposure results from a combination of level, duration (hours per day) and frequency (number of days per year) of exposure. The level of exposure is influenced by different factors such as the physical-chemical properties of the substance, the process conditions, and the use of safety control measures. Duration and frequency of exposure depend upon the technical process and the manufactured volume of the substance.

The characteristics of the exposed population include the number and sex of the workers exposed. Information on the exposed populations can be derived from statistical data.

The Methods of Assessment

For the chosen chemicals, the route of exposure is determined and a coarse classification of the exposure potential is given. The route of exposure is assessed on the basis of the physical-chemical properties of the substances. Dermal exposure is expected for all substances under review because skin contact with liquids or solids is likely at open handling of the substances. The

potential for inhalation exposure is dependent on the vapour pressure and the physical form of the substance. As no information on the physical form was included in the SIDS, an inhalation exposure is assumed for all substances that are solids. For liquid substances the vapour pressure is used in the assessment. An inhalation exposure is assumed if the vapour pressure is more than 1 Pa.

To differentiate the substances according to their exposure potential in a quantitative manner, detailed information on the exact type of use, e.g. the process and operating conditions, is necessary. As such detailed information was not provided by the SIDS dossiers, only a coarse classification of the exposure potential in terms of "high", "medium" and "low" can be made, based on common knowledge of exposure levels, occupational health and safety control measures, and worker populations in different areas of use.

Substances used in the chemical industry, e.g. as intermediates, present a relative low exposure potential. They are generally used in closed systems. Open handling of these substances is limited to only a few activities, health and safety control measures are obligatory, and the number of exposed workers is small.

Substances used in general industry, e.g. additives in the plastic manufacturing industry or dyestuffs in the textile industry, are classified as having a medium exposure potential. Only certain groups of workers with knowledge of the processes come into contact with these substances. The level of exposure is normally limited due to technical protective measures.

Substances used as components in formulations for the skilled trade or agricultural area, e.g. components of detergents, cleaners, cosmetics or paints, exhibit a relatively high exposure potential. After industrial production the products have a wide dispersive use. Uncontrolled exposure and a large number of exposed workers are common characteristics in this use area.

In addition to the classification of exposure potential described above, a theoretical calculation of possible airborne concentrations at the workplace is performed for all liquid substances. The calculation is based on the mass transfer of a substance through the liquid/gas phase boundary and the assumption that the substance becomes completely mixed with the workplace atmosphere after evaporation. The theoretical concentration ($\mathbf{C_i}$) is calculated according to the following equation [1]:

$$\mathbf{C_i} = n_i \, (1 - \exp(-S \cdot t)) / (S \cdot V)$$

where: n_i [mol/h] = mass of evaporated substance
S [h^{-1}] = ventilation rate
V [m^3] = volume of the room
t [h] = time of evaporation

The mass of evaporated substance is calculated according to:

$$n_i = (F \cdot P_s \cdot ß) / (R \cdot T)$$

where:
- F [m^3] = evaporation surface
- P_s [Torr] = vapour pressure of the substance
- ß [m/h] = mass transfer coefficient
- R [Torr m^3/K mol] = universal gas constant
- T [K] = temperature of the gas phase

The calculation is performed using the same standard default parameters for all substances:

room volume:	100 m^3
evaporation surface:	0.02 m^2
ventilation rate:	1 h^{-1}
mass transfer coefficient:	8.7 m/h
evaporation time:	100 min

The results of the calculation give a quite good impression of possible airborne concentrations at the workplace.

Conclusions

The information given in the SIDS dossiers is rather insufficient to assess workplace exposure in a quantitative manner. Therefore the exposure potential of the selected chemicals is assessed only on a screening level, using data on the physical-chemical properties and the use of the substances. For comparison of exposure and toxicological data, e.g. in a hazard assessment process, a more precise evaluation of the exposure situation is needed. To this end detailed information on the exact type of use is necessary. Predictions of the exposure potential in terms of level, duration and frequency of exposure can then be made using published data for the substance under review or analogous substances with similar use pattern.

References

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Annex IV

Screening Level Consumer Exposure Assessments

United States Environmental Protection Agency

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1. Background

Screening level exposure and dose assessments for new and existing chemicals are integral to the determination of whether action on a given chemical is warranted. If warranted, the assessments help determine what aspects should be considered, e.g. should testing be requested for a certain health endpoint.

Ideally, these assessments might be based on monitoring data for the media for which exposure and dose are being assessed, and for the time period of interest to the assessor. For the most part, these data are insufficient, difficult to obtain, or non-existent, necessitating estimation of exposure and dose. Therefore, a scenario approach is often used. In this approach the assessor defines the exposure situation that is to be evaluated and then uses professional judgement, simulation models, data on analogs, and the like to estimate the exposures and doses that are expected to be associated with that scenario.

Where possible, available information is used to the maximum extent. For example, product surveys that describe the frequency of use and quantity used of a consumer product have been developed by EPA for consumer products that are frequently encountered during assessments for new chemicals. For consumer products less frequently seen, assessors may use survey data that are more general; however, those tend to be qualitative rather than quantitative.

The following presents methods and data recommendations for estimating exposures and doses of chemicals in consumer products. Methods for estimating inhalation, dermal contact, and ingestion are presented. The methods represent the evolution of analytical tools developed to address consumer use situations.

1.1 Calculation of Exposure and Dose

This section presents methods and data needed to estimate exposure and dose. Frequency of use and quantity used are two essential parameters required in developing estimates for the inhalation, dermal, and ingestion routes. Section 1.2 provides information to aid the assessor in determining frequency of use and quantity used. Methods for estimating inhalation exposure and dose are found in Section 1.3. Section 1.4 presents methods for assessing the dermal route, while Section 1.5 cites methods for assessing the ingestion route.

1.2 Frequency of Use and Quantity Used

EPA surveys that report information on frequency of use, quantity used, and duration of exposure are available for use on consumer products that are frequently seen during review of new and existing chemicals. One such survey is the National Usage Survey of Household Cleaning Products. This survey reports the frequency of use for 14 cleaning tasks by the person most often performing that task; the brand of product; the type (aerosol, powder, liquid); any protective measures used; and the hours spent performing the task. A list of sources for product use frequency and use quantity is presented in Section 1.7.

Market research reports also are useful, although somewhat limited, sources of data on product use frequency. One readily available series of market research reports is the Simmons Market Research Bureau (SMRB) reports. SMRB reports provide data on frequency of purchase, number of buyers, and demographics of the buying population. The data cover a wide range of consumer products by product type and brand. The reports do not report the frequency of use by

the user nor the quantity used. In this respect, the SMRB reports are more qualitative than quantitative.

1.3 Inhalation Exposure

Human exposure is defined as the contact between an agent such as a chemical and the outer boundary of a person. Units of exposure are concentration multiplied by the time of contact. For inhalation exposures, typical units are ppm - hr and mg/m^3 - hr.

Chemical substances present in ambient air as gases or vapors may be inhaled, thus contributing to potential dose via the lungs. Although a significant fraction of the inhaled chemical may be exhaled, this fraction is chemical-specific and thus not easily predicted. For this reason, potential dose estimates for gases and vapors are based on the entire quantity of inhaled chemical. The general definition of potential dose is the amount of a chemical contained in material ingested, air breathed, or bulk material applied to the skin. Units of dose (potential or otherwise) are expressed as a mass. Dose rates (potential or otherwise) are expressed as mass over time; typical examples are mg/yr or for lifetime average daily dose (LADD), mg/kg/day.

Calculation of Exposure Concentration: The Office of Toxic Substances (OTS) screening level assessment of inhalation exposure/dose for chemicals in consumer products involves the use of a two-zone mass balance model. The model calculates zonal concentrations for five-minute time steps during and after the interval of use. The resulting peak and average concentrations in the two zones form the basis for the estimates of concentrations to which a user (active) and non-user (passive) person is exposed. The active person exposure has two components, the exposure from active use of the product, and the subsequent passive exposure. The mathematical derivation for these exposures is presented in Attachment A (not included in this document).

Determining the concentrations of the chemical substance in a zone requires knowledge of its emission rate from the consumer product. One way to estimate this, when it is not known, is first calculating volatility (a function of molecular weight and vapor pressure) of the chemical. A relationship has been developed correlating the time required for 90 per cent of a chemical to evaporate with the vapor pressure and molecular weight of pure chemicals (Chinn, 1981). Chinn (1981) found that a linear relationship existed between the logarithms of the time required for 90 per cent evaporation and the volatility of a chemical.

Chinn (1981) manipulated the ideal gas law to obtain an expression for the volatility of a compound. Chinn then found that the logarithm of the volatility correlates linearly with the logarithm of the time required for 90 per cent evaporation of pure chemicals as determined by the Shell thin film evaporometer at 25°C and 0 per cent relative humidity for 40 chemicals. The measured evaporation times and physical properties of the 40 chemicals used in developing this correlation and the mathematical theory are presented in Attachment A (not included).

Although this method has not undergone extensive peer review, Chinn (1981) reported that it performed well when compared with results of field trials. This correlation does, however, depend on the test method used to establish the evaporation time; therefore, other test methods may give different results. However, this was the only suitable correlation identified at the time this model was put together.

The Chin method along with the amount of product used, weight fraction of the chemical of interest, and duration of product use are used to estimate the chemical emission rate for the model.

Calculation of Potential Dose: Estimating the potential dose requires the estimation of exposure concentration, knowledge of the individual's breathing rate, duration of contact with the contaminant, and frequency of use. Breathing rates vary from individual to individual and according to activity. The common default breathing rate is 1.1 m^3/hr based on an average adult during a 24-hr period. The basic equation for estimating the potential dose rate via inhaltion for the active person (defined as the person actively using the consumer product) is as follows:

$$IPD_A = [(Conc_A \times IH_A \times DUR_A) + (CONC_B \times IH_p \times (INT - DUR_A)] \; X \; FREQ$$

where:

IPD_A	=	Active potential dose rate (mg/yr)
$CONC_A$	=	Average active concentration, active person (mg/m^3)
IH_A	=	Active inhalation rate (m^3/hr)
DUR_A	=	Duration of active use (hr)
$CONC_B$	=	Average passive concentration, active person (mg/m^3)
IH_p	=	Passive inhalation rate (m^3/hr)
INT	=	Interval between uses (hr)
FREQ	=	Frequency of use (events/yr)

The basic equation for estimating the potential dose rate via inhalation for the passive person (person not using the consumer product but having contact with it via inhalation) is as follows:

$$IPD_p = CONC_p \times IH_p \times DUR_p \; X \; FREQ$$

where:

IPD_p	=	Passive potential dose rate
DUR_p	=	Duration of passive contact (hr)
$CONC_p$	=	Average concentration, passive person (mg/m^3)

The mathematical derivation for calculation of dose and the default parameters used in frequently seen scenarios is presented in the SCIES documentation (Attachment A, not included).

Polymer Migration Model: Assessing inhalation exposures to chemicals that migrate from polymeric materials such as PVC pipe and television cabinets can be accomplished using the Polymer Migration Model (AMEM). Examples of chemical uses in polymer systems are as plasticizers and flame retardants. Chemicals used in these capacities often have low molecular weights and are capable of migrating through the polymeric structure to the air phase, thus becoming available for consumer contact.

In order to assess contact with migrating chemicals, a model based on Fick's laws of diffusion and mass transfer theories was developed by Arthur D. Little in 1984. This model is developed and discussed in detail in *Methodology for Estimating the Migration of Additives and Impurities from Polymeric Materials*, Vol. 11 of *Methods for Assessing Exposure to Chemical Substance* (Arthur D. Little, 1990). The model takes into account the characteristics of the

polymer, the migrant, the phase external to the polymer, and the interactions among these three entities. The migration model developed in 1984 was updated in 1989 to include partitioning and external boundary layer effects and diffusion into a solid external phase.

AMEM will calculate the fraction of the chemical which is expected migrate from the polymer under the conditions specified. Although AMEM is most often used to estimate the weight fraction that has migrated to the air phase, it may also be used to estimate migration to a liquid phase as discussed later.

1.4 Dermal Exposure/Dose

The sections that follow delineate methods that can be used to estimate dermal exposure and dose occurring via three pathways: (1) contact with a film of liquid deposited on the skin; (2) contact with dusts and powders deposited on the skin; and (3) contact with chemical substances contained in or adhering to solid matrices. A method for assessing contact during immersion of skin in liquids is not presented. The major problem with attempting to assess contact during immersion of skin in liquids is that the portion of the entire mass of the chemical substance in the solution that is in contact with the receptor is not known.

(1) Contact with a Film of Liquid Deposited on the Skin

Most significant, quantifiable dermal consumer exposure scenarios involve liquid films on the skin. For each use of the product, the assessor determines the mass of liquid deposited on the skin by multiplying (1) the estimated volume of liquid deposited by (2) the estimated concentration of the subject chemical substance in the liquid deposited on the skin. This, multiplied by the number of annual contact events, yields total mass per year.

The product obtained by multiplying (1) the area of skin likely to be in contact with the liquid during ordinary use by (2) the film thickness is an estimate of the volume of liquid deposited on the skin. The film thickness of a liquid can be determined using the following equation:

$$\textit{Film thickness}\ (cm) = \frac{\textit{amount of liquid retained on skin}\ (mg/cm^2)}{\textit{density of liquid}\ (g/cm^3)\ x\ 1000\ (mg/g)}$$

Experimentally determined values of the amount of liquid retained on hands are presented in *Methods for Estimating the Retention of Chemical Liquids on Hands*, Volume 13 of *Methods for Assessing Exposure to Chemical Substances* (Versar, 1985).

An estimate of the concentration of the subject chemical substance on the skin is derived by multiplying together: (1) the weight fraction (WF) of the chemical substance in the product, (2) the density (DSY) of the formulation, and (3) the dilution factor (DIL), or fraction of formulation present as used by the consumer during the contact event.

The basic equation for estimating the annual rate for dermal potential dose (potential dose is defined as the amount of bulk material applied to the skin) via a liquid film is as follows:

$$DPD = WF \times DSY \times DIL \times T \times AV \times FQ$$

where:

DPD	=	annual rate for dermal potential dose (mg/yr)
WF	=	weight fraction of chemical substance in product (unitless)
DSY	=	density of formulation (mg/cm^3)
DIL	=	dilution fraction (unitless)
T	=	film thickness of liquid on the skin surface (cm)
AV	=	skin surface area exposed per event (cm^2/event)
FQ	=	frequency of events per year (events/yr).

The variables of this equation are determined as follows:

- The weight fraction (WF) of a chemical substance in a formulation can sometimes be obtained from the product label. Other sources of information that may be needed to determine the weight fraction are presented in *Methods for Assessing Consumer Exposure to Chemical Substance*, Vol. 7 of *Methods for Assessing Exposure to Chemical Substances* (Versar, 1987). A generic approach for determining the weight fraction of a chemical substance based on knowledge of its function in a product can also be used. This generic approach and values for the weight fraction of functional components in select consumer products are presented in *Standard Scenarios for Estimating Exposure to Chemical Substances During Use of a Consumer Product*, Vols. I and II (Versar, 1986).

- The density (DSY) of the formulation can sometimes be obtained from the product label. It can also be easily determined experimentally if the product is available. Densities for specific chemical substances can be obtained from references listed in *Methods for Assessing Consumer Exposure to Chemical Substance* (Versar, 1987).

- The dilution fraction (DIL) is the quotient obtained from dividing the mass of product by the mass of substance in which this mass of product is diluted. The dilution fraction can sometimes be determined from information on the product label. Products that are used undiluted are assigned a value of 1.0 for dilution fraction.

- The film thickness of a liquid on the skin (T) is the quotient obtained by dividing the mass of liquid retained per square centimeter (cm^2) of skin surface by the density of the liquid as used by the consumer. Values for film thickness of selected liquids under various experimental conditions are based on data from *Methods for Estimating the Retention of Chemical Liquids on Hands* (Versar, 1985). To assess contact with liquids that are not listed in the above reference, one can use data for the liquid that most closely resembles the liquid for which one is trying to assess contact. Two physical properties that can be used to compare liquids are kinematic viscosity and density. Values for kinematic viscosity and density can be obtained from references listed in *Methods for Assessing Consumer Exposure to Chemical Substance* (Versar, 1987).

- The exposed skin surface area (AV) can be ascertained from judgement as to regions of the body likely to be exposed during use of the product and from generic values for skin surface area presented in *Methods for Assessing Consumer Exposure to Chemical Substance* (Versar, 1987).

(2) Contact with Dusts and Powders Deposited on the Skin

Contact with dusts and powders is similar to contact with liquid films, since it involves the deposition of a limited, quantifiable amount of product on the skin. The parameter dust adherence (DA), however, replaces the film thickness (T) and density (DSY) parameters required in the previous equation for estimating dermal potential dose to liquid films. The dust adherence parameter is expressed in units of mass per unit of skin surface area and, unlike liquid films, does not require a density factor to convert volume to mass.

The basic equation for estimating the annual dermal rate for potential dose from dusts and powders deposited on skin is as follows:

$$DPD = WF \times AV \times DA \times FQ$$

where:

DPD	=	annual rate for dermal potential dose (mg/year)
WF	=	weight fraction of chemical substance in product (unitless)
AV	=	skin surface area exposed per event (cm^2/event)
DA	=	dust adherence (mg/cm^2)
FQ	=	frequency of events per year (events/year)

Methods for determining the variables WF, AV and FQ, were delineated in Versar, 1987. Data on dust adherence to skin (DA) are limited. The following experimental values for dust adherence were reported by the Toxic Substances Control Commission of the State of Michigan (Harger, 1979):

- vacuum cleaner dust sieved through an 80-mesh screen adheres to human hands at 3.44 mg/cm^2;
- dust of the clay mineral kaolin adheres to hands at 2.77 mg/cm^2;
- commercial potting soil adheres to hands at 1.45 mg/cm^2.

The conditions of the experiment were not reported. Since the research was performed to support predictions of occupational contact with the chemical, 4,4'-methylenebis(2-chloroaniline) (MBOCA), and since occupational contact is likely to yield maximum saturation of the skin, it is assumed that the experimental conditions were designed to encourage maximum dust adherence (Versar, 1982). It is not known, however, which physical or chemical properties of a powdered substance determine the extent of its adherence to skin; therefore, it is not possible to predict the extent to which the three substances tested may represent commonly encountered household products (e.g. powdered detergent).

Driver et al. (1989) conducted soil adherence experiments which involved measuring the adherence of dried soils of various types to the hands of adult males under a laboratory setting. Driver et al. (1989) measured average adherences of 1.40 mg/cm^2 for particle sizes less than 150 μm, 0.95 mg/cm^2 for particle sizes less than 250 μm, and 0.58 mg/cm^2 for unsieved soils.

Until more data become available, the value for vacuum cleaner dust can be used as an upper limit. Substances that are lipophilic, are surfactants, or tend to clump in the presence of skin moisture may adhere to a greater extent. However, since maximum adherence is probably rare in most household exposure scenarios, the value for vacuum cleaner dust probably represents dust adherence under reasonable worst case conditions.

(3) Skin Contact with Chemical Substances Contained in or Adhering to Solid Matrices

The primary application for assessing skin contact with chemical substances contained in or adhering to solid matrices is the assessment of contact to substances in clothing. Contact with substances in clothing can be divided into substances contaminating clothing, such as detergent residuals, and substances that are ingredients of clothing, such as dyes. In the case of both dyes and residues, the fraction transferred to the skin must be known to accurately assess dermal contact. The tendency for chemical substances to transfer to skin varies with the quantity of residue or dye on the fabric, the specific chemical substance being transferred from the fabric to the skin, physical and chemical properties of the skin surface being contacted, and duration of skin contact with the substance being transferred. No experimental data regarding transfer of residues or dyes to skin have been found. As a result of a lack of data for this parameter, arbitrary values for per cent transfer during contact must be used.

In an assessment of consumer exposure to sodium LAS (linear alkanesulfonate surfactant) in detergent products, Procter & Gamble (1981 as cited in JRB, 1982) calculated dermal absorption of sodium LAS in detergent residues on clothing using an arbitrary transfer factor for detergent residue of 10 per cent (0.10) (JRB, 1982). The equation below is suggested for estimating the annual rate for dermal potential dose to chemical substances in residues or to dyes and other chemicals on clothing in cases where the amount of chemical substance deposited on the fabric surface is known or can be estimated. This equation is adapted from an equation used by Procter & Gamble to determine dermal absorption of sodium LAS present in detergent residues on clothing.

$$DPD = ADF \times TF \times AV \times FQ \times WF$$

where:

DPD	=	annual rate for dermal potential dose (mg/year)
ADF	=	amount of product or residue deposited on the fabric surface (mg/cm^2)
TF	=	fraction of residue transferred to the skin per exposure event ($event^{-1}$)
AV	=	area of skin surface exposed (cm^2)
FQ	=	frequency of events per year (events/year)
WF	=	weight fraction of chemical substance of interest in product or residue. (This value is equal to 1 where the product or residue is the chemical of interest.)

Note that for substances formulated to adhere to fabric, such as dyes, an arbitrary transfer factor of 10 per cent for a given exposure event would probably yield a vast overestimate of dermal contact under most conditions. It is suggested that the assessor arbitrarily assume the percentage of dye that would be lost during a lifetime of wearings. The assessor can then assume that a major portion of the dye would be lost when the fabric is washed. The remaining fraction of dye could then be assumed to be lost during fabric wear. Information regarding the typical lifetime of the cloth item, and on the number of times that an individual would contact or wear the item, could be used to estimate the fraction of dye transferred to the skin per event. Some of this information can be found in *The Generic PMN Report on Surfactants* (JRB, 1982), prepared for the Exposure Evaluation Division of the Office of Pesticides and Toxic Substances of the US Environmental Protection Agency. Trade associations representing the textile industry may also be a source for this information.

1.5 Ingestion Exposure/Dose

Methods for assessing exposure and dose resulting from ingestion are delineated in this section for two pathways: (1) ingestion of chemical substances leached out of objects used in the mouth, or (2) ingestion from unintentionally swallowing liquids used in the mouth.

(1) Ingestion of Chemical Substances Leached Out of Objects Designed to be Used in the Mouth

Athletic mouth guards, pacifiers and teethers can serve as sources of chemical substances that can be ingested. For example, children place teethers and/or pacifiers in their mouths and suck or chew on them. In the process, chemical substances may leach or diffuse from the object into saliva and may subsequently be swallowed. Exposure and dose for this pathway can be estimated if experimental data on the rate of leaching of the chemical substance from the object into saliva are available or estimated using the Polymer Migration Model for release into a liquid phase. Estimates based on this model may underestimate or overestimate actual exposure because the liquid phase is water. The basic equation for estimating the annual rate for ingestion potential dose to a chemical substance that has leached out of an object used in the mouth is as follows:

$$IPD = LR \times SAO \times D \times F$$

where:

IPD	=	annual rate for ingestion potential dose (mass/year)
LR	=	experimentally determined or estimated leaching rate of the chemical substance from the object into saliva (mass/hr/cm^2)
SAO	=	surface area of the object being placed in mouth (cm^2)
D	=	duration of exposure event (hours/event)
F	=	annual frequency of exposure events (events/year)

(2) Ingestion Exposure from Unintentionally Swallowing Liquids Used in the Mouth

Toothpaste and mouthwash are examples of consumer products intended to be used in the mouth but not intended to be consumed. The basic equation for estimating the annual rate for ingestion potential dose to chemical substances present in liquids used in the mouth that are swallowed unintentionally is as follows:

$$IPD = WF \times M \times LUS \times F$$

where:

IPD	=	annual rate for ingestion potential dose (mass/year)
WF	=	weight fraction of chemical substance in liquid (unitless)
M	=	mass of liquid used per exposure event (mass/event)
LUS	=	fraction of liquid used in the mouth that is swallowed unintentionally (unitless)
F	=	annual frequency of exposure events (events/year)

A major limitation of this method is that there are no data to support any generalization regarding the proportion of liquids used in the mouth that may be swallowed unintentionally. Consequently, an arbitrary value must be selected for this parameter.

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Annex V

Estimation of Consumer Exposures to Chemicals: Application of Simple Models

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1. Introduction

The objective of the OECD Workshop on Occupational and Consumer Exposure Assessments is to identify methods and procedures which can be used to differentiate among selected existing substances (SIDS chemicals) in terms of human exposure in the occupational and consumer setting. Nine example substances have been chosen from the Phase 1 SIDS chemicals for which exposure assessments can be submitted. For some chemicals only the basic SIDS data were included in the dossiers, whereas for others these data were supplemented with more detailed information on occupational or consumer exposure. Data from product registers have been included.

The nine example substances are:

1. 3-nitrobenzenamine (99-09-2)
2. camphene (79-92-5)
3. triethylphosphate (78-40-0)
4. 1,3-pentadiene (504-60-9)
5. dodecanedioic acid (693-23-2)
6. copper, [29H,31H-phthalocyaninato-(2)-] (147-14-8)
7. octamethylcyclotetrasiloxane (556-67-2)
8. 2-[2-(2-butoxyethoxy)ethoxy]-ethanol (143-22-6)
9. 2,2,4-trimethyl-1,3-pentanediol monoisobutyrate (25265-77-4)

This document deals with consumer exposure only. It is the opinion of the authors of this contribution towards the Workshop that an exposure assessment is an integral component of a hazard assessment. Therefore, a method is presented for an *a priori* hazard assessment of consumer products, including the assessment of the external and internal exposure, the determination of no-effect levels for man, and the calculation of hazard quotients.

Unfortunately, the SIDS data provided for the nine example substances did not include the sections relevant to derive no-effect levels for man (Section 4 of this paper). Therefore, only the general method for this derivation and for the final hazard assessment (Section 5) can be presented.

2. Estimation of the External Exposure

Compound 1

Use:

In the data sheet provided, the use is indicated as "dyestuffs". It is assumed that this means that the substance is a raw material for the preparation of dyestuffs. Consumers are not expected to be exposed to this substance as such.

Compound 2

Use:

The substance is mainly used as an intermediate for which no consumer exposure is expected. Consumers can be exposed to the substance if used as fragrance material. The type of products is not specified. Exposure of consumers is expected to be negligible.

Compound 3

Use:

The substance can be used as a catalyst and intermediate for which no consumer exposure is expected. The substance is also used as solvent, flame retardant, and plasticizer in mainly plastic materials (the compound is available in the matrix), as well as in pharmaceuticals, pesticides and lacquers.

Exposure estimates:

a. Flame retardant in plastic materials

It is assumed that this type of additives will be used for articles like TV's, radios, computers and so on, and in plastics used in motor cars, planes etc. Evaporation will be dependent on the vapour pressure, both at ambient temperature and at the temperature at usage. Evaporation will be at the maximum just after production because of evaporation from surfaces. Migration of these substances is expected to be very low. Consumers will be exposed by inhalation; dermal exposure is considered negligible. The concentration in living areas of consumers is very hard to establish, so very rough estimates need be made:

Vapour pressure (Pa)	Concentration (mg/m^3)	Exposure period (days/year)
< 0.0001	0	365
0.0001-0.1	0.001	150
>0.1	0.01	50

Exposure period and frequency points at a chronic exposure scenario (Section 3.1.3):

The vapour pressure of compound 3 is given as 0.0039 Pa at 20°C (ambient temperature) and 0.17 Pa at 99.2°C (maximum temperature of usage is estimated at 35 °C) (SIDS data).

C_{ihl} = 0.001 mg/m^3

b. Plasticizer in plastic materials

It is assumed that migration of additives for polymers like PVC is of more importance than for additives like flame retardants. Most evaporation will also take place during the first month of usage. Dermal contact with plasticized PVC will occur regularly and migration is not unlikely. Some oral intake is conceivable due to the fact that people put plastic articles in their mouth (on purpose or by habit) and because of hand-mouth contact.

Inhalation:

The amount of plastic with plasticizer in living areas is difficult to establish, so again only a rough estimate can be made:

Vapour pressure (Pa)	Concentration (mg/m^3)	Exposure period (days/year)
< 0.0001	0.001	365
0.0001-0.01	0.01	365
>0.01	0.1	365

Exposure period and frequency points at a chronic exposure scenario (Section 3.1.3):

The vapour pressure of compound 3 is given as 0.0039 Pa at 20°C (ambient temperature) and 0.17 Pa at 99.2°C (maximum temperature of usage is estimated at 35 °C) (SIDS data).

C_{ihl} = 0.01 mg/m^3

Dermal exposure:

Contact area: 25% hands
Weight fraction (wf): 0.3
Density (ρ): 1000 mg/cm^3
Exposure period: 15 minutes/event
Exposure frequency: 150 events/year

Exposure period and frequency point at a subchronic exposure scenario (Section 3.1.3):

$C_{derm} = wf \cdot \rho$ = 300 mg/cm^3

Oral exposure:

Contact area food (S): 20 cm^2
Weight fraction (wf): 0.3
Density (ρ): 1000 mg/cm^3
Thickness of contact layer T: 0.01 cm
Migration from article (m): 0.01%
Exposure frequency: 10 events/year

Exposure frequency points at a subchronic exposure scenario (Section 3.1.3):

C_{orl} = S · T · wf · ρ · m /S · T · ρ = 0.006/200 mg/mg food = 30 mg/kg food
I_{orl} = 200 mg food

Compound 4

Use:

The substance can be used as chemical intermediate. Consumers are not expected to be exposed to this substance as such.

Compound 5

Use:

The substance can be used as chemical intermediate. Consumers are not expected to be exposed to this substance as such.

Compound 6

Use:

The substance is a pigment for use in inks, paints and plastics.

Exposure estimates:

a. Pigment for use in inks and paints

It is assumed that consumers will be exposed chiefly by dermal contact. The exposure frequency and duration point at acute exposure. Hands (25 per cent of the surface) will be exposed. Inhalation will be insignificant considering the low vapour pressure. Oral exposure may occur by hand-mouth contact or via food, but probably at a very low rate. The concentration of the substance in inks and paints is reported as maximally 40 per cent (wf).

Surface area of hands (25%): 210 cm^2
C_{derm} = wf · ρ = 40% = 40 mg/cm^3

(The density of inks and paints, ρ, is assumed to be 1000 mg/cm^3.)

b. Pigment for use in plastics

Evaporation will be dependent on the vapour pressure, both at ambient temperature and at the temperature at usage. In view of the vapour pressure, inhalation exposure is inconceivable for consumers. Migration of these substances is expected to be very low: dermal exposure is considered negligible.

C_{ihl} = 0 mg/m^3

Compound 7

Use:

The substance is mainly used as an intermediate for which no consumer exposure is expected. The data sheet further reports use as a base propellant in spray cleaners. Other uses are as a surfactant in detergents (powder, liquid, oven cleaners), as a defoamer in inks, paints and lubricant fluids, and as carrier solvent in deodorants/antiperspirants.

Exposure estimates:

a. Use as base propellant in spray cleaners

Exposure can occur by inhalation and dermally. It is assumed that all the substance used per event will evaporate, and that 5 per cent will end up on the skin of the hands.

Inhalation:

Content of spray can (c): 200,000 mg
Fraction used/event (f): 25%
Weight fraction (wf): 15%
Volume of room (V): 15 m^3
Exposure frequency: 50 events/year
Exposure duration: 10 minutes

Exposure period and frequency point at a subchronic exposure scenario (Section 3.1.3):

$C_{ihl} = c \cdot f \cdot wf / V = 500\ mg/m^3$

Dermal exposure:

Content of spray can (c): 200,000 mg
Fraction used/event (f_1): 25%
Weight fraction (wf): 15%
Fraction on skin (f_2): 5%
Surface area hands (S): 840 cm^2
Thickness film layer (T): 0.01 cm
Exposure frequency: 50 events/year
Exposure duration: 10 seconds

Exposure period and frequency point at a subchronic exposure scenario (Section 3.1.3):

$C_{derm} = c \cdot f_1 \cdot f_2 \cdot wf /S \cdot T = 45\ mg/cm^3$

b. Use as surfactant in detergents

Exposure will be mainly dermally.

Dermal exposure:

Amount used per event (a): 5000 mg
Weight fraction (wf): 23%
Fraction on skin (f): 1%
Volume of water used (V): 5000 cm^3
Exposure frequency: once daily
Exposure period: 15 minutes/event

Exposure period and frequency point at a subchronic exposure scenario (Section 3.1.3):

$C_{derm} = a \cdot wf \cdot f / V = 0.002\ mg/cm^3$

c. Defoamer in inks, paints and lubricant fluids

Exposure will be mainly via the dermal route. However, considering the weight fractions of the substance in consumer products, exposure must be considered insignificant with respect to health risks.

d. Carrier in deodorants/antiperspirants

Exposure will be via the dermal and inhalatory route.

Dermal exposure:

Amount used per event (a): 1000 mg
Weight fraction (wf): 70%
Fraction on skin (f): 100% (no evaporation assumed)
Thickness of contact layer T: 0.01 cm
Surface area armpits: 400 cm^2 (estimated)
Exposure frequency: once daily
Exposure period: 24 hours/day

Exposure period and frequency point at a chronic exposure scenario (Section 3.1.3):

$C_{derm} = a \cdot wf \cdot f / S \cdot T = 175\ mg/cm^3$

Inhalation exposure:

Amount used per event (a): 1000 mg
Weight fraction (wf): 70%
Fraction evaporated (f): 100%
Volume of room (V): 15 m^3
Exposure frequency: once daily
Exposure period: 10 minutes

Exposure period and frequency point at a chronic exposure scenario (Section 3.1.3):

$C_{ihl} = a \cdot wf / V = 47\ mg/m^3$

Compound 8

Use:

The substance is used as a solvent in brake fluids and in ink fluids.

Exposure estimate:

Consumers can be exposed dermally to the substance in inks. Hands only (25 per cent of surface) will be exposed. Inhalation exposure is expected to be minimal in view of the vapour pressure of the compound.

Contact area hands (25%): 210 cm^2
Weight fraction (wf): 0.6
Density (ρ): 1000 mg/cm^3
Exposure period: 15 minutes/event
Exposure frequency: 15 events/year

Exposure period and frequency point at a subchronic exposure scenario (Section 3.1.3):

$C_{derm} = wf \cdot \rho = 600\ mg/cm^3$

Compound 9

Use:

The substance is used as an intermediate for plasticizers for which no consumer exposure is expected. It is further used as coalescing agent in latex paints and as solvent in inks.

Exposure estimates:

Consumers can be exposed dermally to the substance in paints and inks. Inhalation exposure is expected to be minimal in view of the vapour pressure of the compound. Oral exposure may occur by hand-mouth contact or via food, but probably at a very low rate.

a. Use as coalescing agent in paints

The exposure frequency and duration point at acute exposure. Hands only will be exposed. The concentration of the substance in paints is reported as maximally 3 per cent (wf).

$C_{derm} = wf \cdot \rho = 3\ \% = 30\ mg/cm^3$

(The density of paint, ρ, is assumed to be 1000 mg/cm^3.)

b. Use as solvent in inks

The exposure frequency and duration points at acute exposure. Hands will be partly exposed (25 per cent of surface). The concentration of the substance in inks is reported as maximally 60 per cent (wf).

Contact area of hands (25%): 210 cm^2

$C_{derm} = wf \cdot \rho = 60\% = 600\ mg/cm^3$

(The density of ink, ρ, is assumed to be 1000 mg/cm^3.)

3. Estimation of the Internal Exposure

3.1 General approach

3.1.1 Introduction

Exposure -- or more precisely external exposure or intake -- can be defined as the quantity of a substance reaching a receptor. In man, this receptor can be the epithelium of the gastrointestinal tract in case of ingestion, the pulmonary epithelium in case of inhalation, and the skin in case of dermal contact. The internal exposure or uptake can be defined as the quantity of a substance which has been absorbed, i.e. which has passed these receptors into the systemic circulation. Bioavailability then is defined as the fraction of the external dose which has been absorbed.

The hazard assessment for chemical substances to which consumers are exposed can be based on a comparison between estimated exposure and appropriate no-effect levels for man. In addition, several categories of substances may deserve special attention. The common factor for these categories is that they are regulated already. They include proven (category 1 and 2) carcinogenic (R45 or R49), mutagenic (R46) and teratogenic (R47) substances, blacklisted cosmetics, food additives, and food contaminants migrating from packaging materials. These categories should be tagged. Non-regulated categories which need to be tagged are individual substances and preparations classified as corrosive (R34 or 35) and/or sensitizing (R42 or 43). According to EC criteria, preparations need not be classified for sensitizing properties if they contain less than 1 per cent of a sensitizing substance. Preparations need not be classified for corrosive properties if they contain less than 1 per cent of a corrosive substance with R35, or less than 5 per cent of a corrosive substance with R34.

Food contaminants of environmental origin are not discussed here.

3.1.2 Scope of the exposure estimations

Consumers can be exposed to individual substances, preparations (mixtures or solutions composed of two or more substances), and substances embedded in a solid matrix (article). They receive chemical doses via the oral, dermal and inhalation route. Not counting accidental intoxications, inhalation is probably the most important source of exposure.

Information on the use and function of a substance must be available in the data set provided. Subsequently, it can be decided to which product group the substance belongs, whether consumers will be exposed and, if so, which exposure route(s), exposure frequency and duration need to be be considered for the exposure assessment. This information has been presented in Section 2, along with estimates for the concentration of substances in products which can be ingested (C_{orl}) and/or come into contact with the skin (C_{derm}), and estimates for the air concentration of substances (C_{ihl}). It must be emphasized that these estimates pertain to situations with obvious risks of human exposure. In all other conceivable situations exposure is assumed to be zero until further work shows that this is a serious underestimation.

The exposure estimates are restricted to direct use by consumers, assuming that post-use exposure will be less significant. Abuse and accidental intoxications are not considered, but careless use is.

3.1.3 Frequency and duration of exposure

Exposure can be judged to be acute, subchronic (short-term), or chronic as related to the exposure schedules in experimental animal studies:

- Acute exposure is considered to include exposure periods up to two days and exposure frequencies up to seven events per year. If more than seven exposures of up to two days in duration occur, the exposure is characterized as subchronic. Additional indirect exposure is considered irrelevant. Acute intoxication via dermal exposure is infrequent in the consumer setting, but must be considered for occupational exposure.

- Subchronic exposure is considered to include periods from three to 14 days per year, and exposure frequencies up to seven times per year. If more than seven exposures of from three to 14 days occur, the exposure is characterized as chronic. Additional indirect exposure is considered irrelevant.

- Chronic exposure is considered to include periods from 15 days per year onwards. Additional indirect exposure may be important.

3.1.4 Inhalation exposure

Man can be exposed to gases, aerosols and solid particles. The fraction of a substance that will be bioavailable cannot be easily predicted, especially for aerosols and solid particles. It is a function of vapour pressure, solubility, particle size, particle shape, air velocity, ventilation rate, and the fact whether nose or mouth breathing is used. Although a significant fraction of an inhaled substance may be exhaled, initial exposure estimates for gases and vapours can be based on the assumption that the total amount inhaled is bioavailable:

$$U_{ihl} = C_{ihl} \cdot V \cdot t \cdot B_{ihl} / BW \qquad (1)$$

with: U_{ihl} = estimated uptake by inhalation [mg/kg bw/period]
C_{ihl} = average air concentration [mg/m^3]
V = ventilation rate of an adult male or a six-year-old child at a light activity level [0.8 m^3/hour] (US EPA, 1989; de Nijs & Vermeire, 1990)
t = period of time of exposure event [hour]; for (sub)chronic exposure the period is taken to be 24 hours resulting in a ventilation rate of 20 m^3/day
B_{ihl} = bioavailability for inhalation: in the absence of data this factor is assumed to be 0.75 (Linders, 1990)
BW = body weight for the average adult [71 kg] (de Nijs & Vermeire)

Airborne particulates in inhaled air only partially enter the respiratory system. Once inhaled, the particles may undergo deposition or may be exhaled without deposition. This so-called aspiration efficiency drops slowly for particle sizes over 10 μm. Only particles small enough to reach the alveolar region are available for absorption. Other deposited particles can be taken to be cleared to the pharynx and swallowed. The above formula for gases and vapours can be adapted for particulates as follows:

$$U_{ihl,\ lung} = C_{ihl} \cdot V \cdot t \cdot B_{ihl} \cdot R / BW \quad (2)$$

$$U_{ihl,\ git} = C_{ihl} \cdot V \cdot t \cdot B_{ihl} \cdot NR / BW \text{ (see 3.1.6)} \quad (3)$$

with: $U_{ihl,\ lung}$ = estimated uptake via the lungs following inhalation [mg/kg bw/period]
$U_{ihl,\ git}$ = estimated uptake via the gastrointestinal tract following inhalation [mg/kg bw/period]
C_{ihl} = average air concentration [mg/m^3]
R = respirable fraction which is the fraction of all inhaled particles deposited in the alveoli, depending on particle size distribution; in the absence of data on particle size this fraction can be assumed to be 1. If data on particle size are known, R can be assumed to be 1 for mass median aerodynamic (MMAD) diameters below 10 μm and 0 for MMADs above 10 μm.
NR = non-respirable fraction; equal to 1 - R

3.1.5 Dermal exposure

The skin can be exposed to substances in liquids, dusts, powders, solids, gases, vapours and aerosols. Exposure of the skin to gases, vapours, aerosols and solids will not be discussed within the framework of this ranking exercise because a quantitative exposure estimate would present too many difficulties and is also expected to be of minor importance. In case of dermal exposure to substances in liquids, dusts and powders, the substance, unless present in pure form, must leach or diffuse out of a matrix. Prediction of the matrix effects is too complex at present. For a worst case analysis, one can merely assume the matrix effect to be absent.

Dermal exposure is the quantity of a substance that will be in contact with the skin. This means that a film thickness has to be established, i.e. the layer of liquid, dust or powder which is supposed to be in direct contact with the skin. The thickness of this layer is assumed to be 0.01 cm. The fraction of a substance which is available for absorption from this layer through the skin is difficult to estimate. It is a function of the solubility of the substance in water and fat, its polarity and molecular size on the one hand, and, on the other hand, environmental factors and skin-dependent variables. In the present estimations only substance-related factors can be considered.

The bioavailability can be assumed to be zero for substances with a log K_{ow} below -1 and over 5 or a relative molecular mass over 700 or a $LD_{50, dermal}/LD_{50, oral}$ ratio greater than 10. In all other cases total absorption is assumed.

$$U_{derm} = C_{derm} \cdot T \cdot S \cdot B_{derm} / BW \quad (4)$$

with:
- U_{derm} = estimated uptake via the skin [mg/kg bw/day]
- C_{derm} = concentration of the substance in the contact layer [mg/cm^3]; in case a percentage (by volume) of the substance in the product is given, this concentration is equal to the product of that percentage and the density of the product [$cm^3/cm^3 \cdot mg/cm^3$]
- T = thickness of film layer [cm]; assumed to be 0.01 cm
- S = skin surface area of an average adult male exposed [cm^2]: see **Table 1**
- B_{derm} = bioavailability for dermal exposure: see above
- BW = body weight for the average adult [71 kg] (de Nijs & Vermeire, 1990)

Table 1 **Mean surface area by body part for the adult male (US EPA, 1989)**

Body part	Mean surface area (cm^2)
Head	1180
Trunk	5690
Upper extremities	3190
Arms	2280
Upper arms	1430
Forearms	1140
Hands	840
Lower extremities	6360
Legs	5060
Thighs	1980
Lower legs	2070
Feet	1120
Total	19 400

3.1.6 Oral exposure

Consumers may ingest contaminants or additives in food products or substances in saliva migrating from preparations (e.g. cosmetics) or solid materials (textiles, toys).

$$U_{orl1} = C_{orl} \cdot I_p \cdot B_{orl} / BW \quad (5)$$

with:
- U_{orl} = estimated oral uptake [mg/kg bw/event for acute exposures and mg/kg/day for (sub)chronic exposures]
- C_{orl} = average concentration in product [mg/kg]
- I_p = amount of product ingested [kg/event for acute exposures and kg/day for (sub)chronic exposures]; for food contaminants and additives, mean daily intakes can be found in de Nijs & Vermeire (1990) which have been derived from WVC (1988)
- B_{orl} = bioavailability for oral exposure; in the absence of data this factor is assumed to be 1
- BW = body weight for the average adult [71 kg] (de Nijs & Vermeire, 1990)

Humans may also ingest the non-respirable fraction of inhaled airborne particulates, as discussed in Section 3.1.4:

$$U_{orl2} = U_{ihl,\ git} = C_{ihl} \cdot V \cdot t \cdot B_{ihl} \cdot NR / BW \quad (6)$$

3.2 Exposure calculations for the examples

Compound 3

3a. Flame retardant in plastic materials

Inhalation:

C_{ihl} = 0.001 mg/m^3, chronic, vapour
U_{ihl} = 0.0002 mg/kg bw/day for adult

3b. Plasticizer in plastic materials

Inhalation:

C_{ihl} = 0.01 mg/m^3, chronic, vapour
U_{ihl} = 0.002 mg/kg bw/day for adult

Dermal:

C_{derm} = 300 mg/cm^3, subchronic
U_{derm} = 8.9 mg/kg bw/day

Oral:

C_{orl} = 30 mg/kg food, subchronic
U_{orl} = 0.08 mg/kg bw/day

Compound 6

6a. Pigment for use in inks and paints

Dermal:

C_{derm} = 40 mg/cm^3
U_{derm} = 1.2 mg/kg bw/event

Compound 7

7a. Use as base propellant in spray cleaners

Inhalation:

C_{ihl} = 500 mg/m^3, subchronic, aerosol
U_{ihl} = 143 mg/kg bw/day for adult

Dermal:

C_{derm} = 45 mg/cm^3, subchronic
U_{derm} = 0 (no bioavailability, log K_{ow} < -1, see 3.1.5)

7b. Use as surfactant in detergents

Dermal:

C_{derm} = 0.002 mg/m^3, subchronic
U_{derm} = 0 (no bioavailability, log K_{ow} < -1, see 3.1.5)

7c. Carrier in deodorants/antiperspirants

Dermal:

C_{derm} = 175 mg/cm^3, chronic
U_{derm} = 0 (no bioavailability, log K_{ow} < -1, see 3.1.5)

Inhalation:

C_{ihl} = 47 mg/m^3, chronic, aerosol
U_{ihl} = 13 mg/kg bw/day

Compound 8

Use as a solvent in inks

Dermal:

C_{derm} = 600 mg/cm^3, subchronic
U_{derm} = 18 mg/kg bw/day

Compound 9

9a. Use as coalescing agent in paints

Dermal:

C_{derm} = 30 mg/cm^3, acute
U_{derm} = 4 mg/kg bw/event

9b. Use as solvent in inks

Dermal:

C_{derm} = 600 mg/cm^3, acute
U_{derm} = 18 mg/kg/event

4. Estimation of No-effect Concentrations

4.1 General approach

4.1.1 Introduction

Hazard assessment for man can be based on a comparison of a predicted exposure level and an exposure level at which no or a certain degree of effects, thought to be acceptable, are expected. In addition, the number of people at risk may be considered as well as the occurrence of special risk groups. In the following, this approach will be discussed, starting with the derivation of no- or acceptable effect levels through the process of hazard identification and dose-response assessment. With regard to (sub)chronic exposure, a distinction needs to be made between non-genotoxic substances and genotoxic substances.

4.1.2 Derivation of an acute no-effect level

In case of acute exposure hazard, ranking will be based on the quotient of the estimated total uptake for the event and a suitable indication of a no-effect level on uptake basis for acute exposure, which should be based on the LD_{50} or LC_{50} because no other acute toxicity data are available. Data on the slope of the dose-response curve usually are also not provided and, in any case, are based on mortality and not on general toxicity. It is proposed to assume that man is equally sensitive to acute exposure of substances as experimental animals, and that the no-effect level $NEL_{man,\ acute}$ can be derived from the EC classification as shown in **Table 2**.

Table 2 **Derivation of the $NEL_{man,acute}$ from acute toxicity tests with animals**

Acute toxicity EC class	Criteria for classification		$NEL_{man,\ acute}$	
	oral exposure [mg/kg bw]	inhalation exposure [10^3 mg/m^3]	oral exposure [mg/kg bw]	inhalation exposure [10^3 mg/m^3]
very toxic	$LD_{50} \leq 25$	$LC_{50} \leq 0.5$	0.2	0.005
toxic	$25 < LD_{50} \leq 200$	$0.5 < LC_{50} \leq 2$	2	0.05
harmful	$200 < LD_{50} \leq 2000$	$2 < LC_{50} \leq 20$	25	0.5
unclassified	$LD_{50} > 2000$	$LC_{50} > 20$	200	2

The derivation of the $NEL_{man, acute}$ is based on the assumption that at the logarithmically equidistant doses or concentrations chosen, no mortality and (almost) no adverse effects will be shown given the usual slope of dose-response curves for acute toxicity, which is approximately 2-8 (e.g. in case of an exceptionally shallow dose-response curve with a slope of 2, a decrease in log dose by one unit would mean a decrease in mortality by two probit units such as occurs in a decrease in mortality from 50 per cent to approximately 2 per cent). For example: Substances with an LD_{50} above 2000 mg/kg bw (log value 3.3) are assumed not to cause adverse effects at a dose of 200 mg/kg bw (log value 2.3) or, in other words, substances which need not be classified for acute toxicity according to EC criteria are assumed to have a $NEL_{man, acute}$ one order of magnitude lower. This $NEL_{man, acute}$ is then equivalent to the acute toxicity class borderline between harmful and toxic.

4.1.3 Derivation of a (sub)chronic no-effect level

4.1.3.1 Non-genotoxic substances

Introduction

It is assumed that the EC data set contains data from which a no observed adverse effect level (NOAEL) can be derived from subchronic (28-day or 90-day) tests, or occasionally from chronic tests for substances which cannot be classified as genotoxic carcinogens (R45 or R49 or R40[1]) and/or genotoxic (R46 or R40). Occasionally, human studies may be available to derive a NOAEL.

Derivation of a NOAEL from experimental animal data

Concepts

Human toxicological data on substances are often not available, and therefore the potential of a substance to cause effects following prolonged exposure is derived from results of tests on animals. One of the basic assumptions is that humans and mammals are similar in relative susceptibility to toxic chemicals. With respect to (sub)chronic toxicity, it is the aim of the hazard evaluation to identify the most critical adverse effect following prolonged exposure and to establish the relation between the dose, time, severity of effects (dose- and time-effect elation), and response (dose- and time-response relation) of the experimental animal. "Dose" specifies the amount of a chemical administered. The term "effect" applies to the extent of biological changes, and response can be defined as the incidence rate of effects. If possible, the data obtained need be evaluated vis-à-vis their significance to man.

For non-genotoxic effects, a certain substantial deviation from a statistically distributed normal value must be attained before a particular effect in an organism is manifested, resulting in a threshold dose for this effect. In some cases compensatory mechanisms, e.g. saturable

[1] The EC R40 class also contains nongenotoxic carcinogens; a NOAEL is assumed to exist for these substances.

detoxification by microsomal enzymes or feedback systems in endocrinology, may be responsible for the existence of a threshold dose. The subthreshold dose for the most critical effect in one test is called the Dose Without Effect (DWE) and is the highest exposure level without adverse, i.e. toxicologically relevant, effects. Effects regarded as non-adverse can still occur below this Dose Without Effect. The threshold dose, i.e. the lowest exposure level in one test at which the most critical adverse effect is occurring, is called the Lowest Effect Dose (LED).

If more than one test is available, the overall evaluation leads to the selection of the most critical test. Unless a particular animal model is clearly not relevant to man, the most critical test is the most sensitive test on the most sensitive species, assuming that man is at least as sensitive as this animal species. This approach applies when the tests are of similar duration and quality. If not, the evaluation usually concentrates on the longer test and/or the test of better quality. However, in case of compensatory mechanisms, effects observed in tests of short duration may not be seen in long-term tests: an example of such an effect is a decrease in thyroid hormones.

The overall DWE is widely known as the no observed adverse effect level (NOAEL). The dose without any effect is called the no observed effect level (NOEL) or no-effect level (NEL), and the lowest critical effect dose the lowest observed adverse effect level (LOAEL).

Derivation of an NOAEL

Guidance in selecting an NOAEL from subchronic and chronic animal tests can be obtained from publications of the Dutch Health Council (HC, 1985a and 1989), the International Programme on Chemical Safety (IPCS, 1978; 1987; 1970), and the US Environmental Protection Agency (US EPA, 1986), as summarized in Vermeire et al. (1992).

Extrapolation

A no-effect level (NEL) for man needs to be extrapolated from an NOAEL for experimental animals or from human data using a fixed safety factor. This NEL_{man} can be compared to the predicted exposure level. Hazard ranking can be based on the quotient of the predicted exposure level and the NEL_{man}.

The value of the safety factor depends on the number of uncertainties involved. It is a product of uncertainty factors:

- a factor of 10 to account for intraspecies variation;
- a factor of 10 to account for interspecies variation;
- a factor of 10 to account for uncertainty as a result of extrapolation from a lowest observed adverse effect level (LOAEL), if no NOAEL can be derived;
- a factor of 10 for uncertainty as a result of extrapolation from a subchronic test to a chronic NOAEL; this factor need not be applied to substances which are metabolized and excreted at a high rate; obviously this factor also need not be applied in case a subchronic NEL is needed, as in the case of subchronic consumer exposure;
- extra uncertainty factors for other sources of variation, e.g. in case of poorly conducted tests; these extra sources of variation will be ignored in the priority setting system.

For a priory hazard assessment, it is recommended to apply the safety factors as indicated in **Tables 3 and 4**.

Acute data and LOAEL's from human data are considered inadequate for the derivation of a NEL_{man}. In general, if data are lacking for the derivation of the NEL_{man} according to the standard procedure described above, a default NEL_{man} may be used for a priority hazard assessment. This default NEL_{man} is conservatively fixed at 0.1 μg/kg bw/day or 0.4 $\mu g/m^3$ air for both subchronic and chronic exposure.

Table 3 **Safety factors for the extrapolation of the NOAEL to the subchronic NEL_{man}**

Information available	Safety factor
NOAEL from subchronic animal test	100
LOAEL from subchronic animal test	1000
NOAEL from subchronic human data	10

Table 4 **Safety factors for the extrapolation of the NOAEL to the chronic NEL_{man}**

Information available	Safety factor
NOAEL from chronic animal test	100
LOAEL from chronic animal test	1000
NOAEL from subchronic animal test	1000
LOAEL from subchronic animal test	10 000
NOAEL from chronic human data	10
NOAEL from subchronic human data	100

4.1.3.2 Genotoxic substances

For substances which can be classified as genotoxic carcinogens, an acceptable risk level for man may be extrapolated from the available carcinogenicity test(s) on experimental animals or from epidemiological data on man. It is proposed to extrapolate to the the Negligible Risk (NR) level (1 : 10^6/lifetime) (MHPPEP, 1990). Substances which cannot yet be classified with respect to carcinogenicity because of the absence of data, but are classified as genotoxic, should for practical purposes be regarded as genotoxic carcinogens. In such cases it is not possible to extrapolate towards a certain risk level for the individual substance by the methods available. For these substances -- and for classified genotoxic carcinogens without data suitable for extrapolation -- it is proposed to determine a fixed risk level for each relevant route of exposure on the basis of the lowest calculated risk level of a reasonable number of classified genotoxic carcinogens.

Data concerning the classified genotoxic carcinogens can be found in **Table 5**. Based on these data, the general NR level is proposed to be an intake of 0.02 μg/kg bw/day for ingestion and an air concentration of 0.002 μg/m^3 for inhalation exposure. These risk levels can be compared to the predicted exposure level. Risk ranking can be based on the quotient of the predicted exposure level and the NR level.

Table 5 **Negligible Risk (NR) levels for classified genotoxic carcinogens (Vermeire et al., 1990 and 1991)**

Compound	Negligible Risk level			
	Oral exposure [μg/kg bw/day]	Ref.	Inhalation exposure [μg/m^3]	Ref.
acrylonitril			0.037	2
benzene	0.017	1	0.12	2
epichlorohydrin			0.002	2
ethylene oxide			0.024	2
1,2-dichloroethane	0.14	1	0.48	1
propylene oxide			0.90	2
vinyl chloride	0.035	1	1.0	1
benzo(a)pyrene	0.02	1		
phenanthrene	0.20	1		
Range	0.017-0.20		0.002-1.0	

4.1.3.3 Conversions

Conversion factors for diet studies

The relation of mg/kg diet (ppm) to mg/kg body weight is shown in **Table 6**:

Table 6 **Relation of mg/kg diet to mg/kg body weight (Lehman, 1954)**

Animal	Weight (kg)	Food consumed g/day	Conversion factor ppm to mg/kg bw/day
mouse	0.02	3	0.15
rat (young)	0.10	10	0.10
rat (old)	0.40	20	0.05
guinea pig	0.75	30	0.04
rabbit	2.0	60	0.03

Correction for exposure frequency

In case of continuous exposure the $NOAEL_{rat,\ subacute,\ inh}$, which is usually derived from an experiment with an intermittent exposure schedule, needs to be converted to a continuous NOAEL:

$$NOAEL_{inh,\ continuous} = NOAEL_{inh,\ intermittent} \cdot (x/24) \cdot (y/7) \quad (7)$$

with: x = hours/day of intermittent exposure
y = days/week of intermittent exposure

Conversion with respect to route of exposure

An inhalatory $NEL_{man,\ ihl}$ can be converted to an oral $NEL_{man,\ oral}$ or vice versa, using the following formula:

$$NEL_{man,\ ihl} \cdot V \cdot t \cdot B_{ihl} = NEL_{man,\ oral} \cdot B_{oral} \cdot BW \quad (8)$$

4.2 No-effect levels for the example substances

Compound 3

Requirements:
- $NEL_{man,\ chronic,\ ihl}$ = chronic inhalatory no-effect level
- $NEL_{man,\ subchronic,\ ihl}$ = subchronic inhalatory no-effect level
- $NEL_{man,\ subchronic,\ derm}$ = subchronic dermal no-effect level

Values: No SIDS data available (see Introduction)

Compound 6

Requirement: $NEL_{man,\ acute,\ derm}$ = acute dermal no-effect level

Values: No SIDS data available (see Introduction)

Compound 7

Requirements:
- $NEL_{man,\ subchronic,\ ihl}$ = subchronic inhalatory no-effect level
- $NEL_{man,\ subchronic,\ derm}$ = subchronic dermal no-effect level
- $NEL_{man,\ chronic,\ ihl}$ = chronic inhalatory no-effect level
- $NEL_{man,\ chronic,\ derm}$ = chronic dermal no-effect level

Values: No SIDS data available (see Introduction)

Compound 8

Requirement: $NEL_{man,\ subchronic,\ derm}$ = subchronic dermal no-effect level

Values: No SIDS data available (see Introduction)

Compound 9

Requirement: $NEL_{man,\ acute,\ derm}$ = acute, dermal, no-effect level

Values: No SIDS data available (see Introduction)

5. Calculating Hazard Quotients

5.1 General approach

5.1.1 Acute exposure

Hazard ranking will be based on the quotient Q of the estimated total uptake for the event and a suitable indication of a no-effect level on uptake basis for acute inhalation or oral exposure.

Inhalation route:

$$Q_{acute,\ ihl} = C_{ihl} / NEL_{man,\ acute,\ ihl} \quad (9)$$

with: $NEL_{man,\ acute,\ ihl}$ = no-effect level for acute inhalation exposure of man [mg/m^3]

For further explanation of the notations used, see formula 1 (Section 3.1.4)

Dermal route:

$$Q_{acute,\ derm} = C_{derm} / NEL_{man,\ acute,\ derm}$$

with: $NEL_{man,\ acute,\ derm}$ = no-effect level for acute dermal exposure [mg/kg bw]

A dermal $NEL_{man,\ acute,\ derm}$ can be derived from the $NEL_{man,\ acute,\ oral}$ or the $NEL_{man,\ acute,\ ihl}$ (see 4.1.2) as follows:

$$Q_{acute,\ derm} = U_{derm} / NEL_{man,\ acute,\ oral} \cdot B_{oral} \quad (14)$$

or

$$Q_{acute,\ derm} = U_{derm} / NEL_{man,\ acute,\ ihl} \cdot V \cdot t \cdot B_{ihl} / BW \quad (15)$$

Oral route:

$$Q_{acute,\ oral} = U_{orl1} / NELman,\ acute,\ oral \cdot B_{oral} \quad (10)$$

or

$$Q_{acute,\ oral} = U_{orl2} / NEL_{man,\ acute,\ oral} \cdot B_{oral} \quad (11)$$

with: $NEL_{man,\ acute,\ oral}$ = no-effect level for acute oral exposure of man [mg/kg bw]

For further explanation of the notations used, see formula 5 (Section 3.1.6).

5.1.2 Subchronic exposure

Hazard ranking will be based on the quotient Q of the estimated average daily uptake and the subchronic no-effect level for man on uptake basis derived from subchronic (up to 90-day) toxicity data (no extrapolation to chronic exposure).

Inhalation:

$$Q_{subchronic,\ ihl} = C_{ihl} / NEL_{man,\ subchronic,\ ihl} \quad (12)$$

with: $NEL_{man,\ subchronic,\ ihl}$ = no-effect level for subacute inhalation exposure of man [mg/m^3]

For further explanation of the notations used, see formula 1 (Section 3.1.4).

Dermal route:

$$Q_{subchronic,\ derm} = DU_{derm} / NEL_{man,\ subchronic,\ derm} \cdot B_{derm} \quad (13)$$

with: DU_{derm} = estimated average daily dermal uptake

For further explanation of the notations used, see formula 4 (Section 3.1.5).

In case a dermal $NEL_{man,\ subchronic,\ derm}$ is not available, the $NEL_{man,\ subchronic,\ oral}$ or the $NEL_{man,\ subchronic,\ ihl}$ can be used as follows:

$$Q_{subchronic,\ derm} = DU_{derm} / NEL_{man,\ subchronic,\ oral} \cdot B_{oral} \quad (14)$$

or

$$Q_{subchronic,\ derm} = DU_{derm} / NEL_{man,\ subchronic,\ ihl} \cdot V \cdot t \cdot B_{lhl} / BW \quad (15)$$

Local effects can only be dealt with qualitatively, taking into account the concentration of the substance in a product and the irritating and sensitizing potential of this substance. At present, it does not seem possible to incorporate the presence of such properties in a quantitative priority ranking scheme.

Oral route:

$$Q_{subchronic,\ oral} = DU_{orlx} / NEL_{man,\ subchronic,\ oral} \cdot B_{oral} \quad (16)$$

with: DU_{orlx} = estimated average daily oral uptake
x = 1 or 2

For further explanation of the notations used, see formula 5 (section 3.1.6).

5.1.3 Chronic exposure

Hazard ranking will be based on the quotient of the estimated average daily uptake, including indirect exposure, and the chronic no-effect level for man $NEL_{man,\ chronic}$ on an uptake basis, derived from semi-chronic (extrapolated to chronic exposure) or chronic toxicity data, or on the quotient of the total average daily uptake and the negligible risk level (NR).

Inhalation exposure:

$$Q_{chronic} = [DI_t \cdot B_{oral} + DU_{ihl}] / NEL_{man,\ chronic,\ ihl} \cdot B_{ihl} \quad (17)$$

with DU_{ihl} = estimated average daily inhalatory uptake
DI_t = predicted total daily intake [mg/kg bw/day]
$NEL_{man,\ chronic,\ ihl}$ = no-effect level for chronic inhalation exposure of man [mg/m^3]

For further explanation of the notations used, see formula 1 (Section 3.1.4).

The $NEL_{man,\ chronic,\ ihl}$ should be based on a NOAEL for continuously exposed experimental animals. For conversions, see Section 4.1.3.3.

The same formula can be applied to genotoxic carcinogens using NR levels.

Dermal exposure:

$$Q_{chronic,\ derm} = [DI_t \cdot B_{oral} + DU_{derm}] / NEL_{man,\ chronic,\ derm} \cdot B_{derm} \quad (18)$$

with: DU_{derm} = estimated average daily dermal uptake
$NEL_{man,\ chronic,\ derm}$ = no-effect level for chronic dermal exposure of man [mg/kg bw/day]

For further explanation of the notations used, see formula 4 (Section 3.1.5).

The $NEL_{man,\ chronic,\ derm}$ should be based on a NOAEL for continuously exposed experimental animals. In case a dermal $NEL_{man,\ chronic,\ derm}$ is not available, the $NEL_{man,\ chronic,\ oral}$ or the $NEL_{man,\ chronic,\ ihl}$ can be used. For conversions, see 4.1.3.3.

The same formulae can be applied to genotoxic carcinogens using NR levels.

Oral exposure:

$$Q_{chronic,\ oral} = [DI_t \cdot B_{oral} + DU_{orlx}] / NEL_{man,\ chronic,\ orl} \cdot B_{orl} \quad (19)$$

with: DU_{orlx} = estimated average daily oral uptake
x = 1 or 2

$NEL_{man,\ chronic,\ orl}$ = no-effect level for chronic oral exposure of man [mg/kg bw/day]

For further explanation of the notations used, see formulas 5 and 6 (Section 3.1.6).

The same formula can be applied to genotoxic carcinogens using NR levels.

5.2 Hazard quotients for the example substances

The final hazard assessment cannot be presented, as the essential SIDS data have not been provided (see Introduction).

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Annex VI

Screening Information Data Set (SIDS)

1. Chemical Identity:

CAS number;
Name;
Structural formula.

2. Physical-chemical Data:

Melting point;
Boiling point;
Vapour pressure;
Partition coefficient: n-octanol/water;
Water solubility.

3. Sources and Levels of Exposure:

Production ranges expressed as tonnes per annum;
Categories and types of use.

4. Environmental Fate and Pathways:

Aerobic biodegradability;
Abiotic degradability (hydrolysis and photodegradation by estimation);
Estimates of environmental fate, pathways and concentrations (including Henry's Law constant as calculated from physical-chemical data, aerosolisation, volatilisation, soil adsorption and desorption calculated using structure activity relationships).

5. Ecotoxicological Data:

Acute toxicity to fish;
Prolonged toxicity to daphnids;
Toxicity to algae.
If significant exposure is expected in the terrestrial environmental compartment, efforts should be made to perform appropriate terrestrial toxicity tests. In addition, when aquatic toxicity testing is not possible (e.g. in the case of insolubility of the test chemicals) efforts should also be made to perform terrestrial toxicity tests.

6. Toxicological Data:

Acute toxicity;
Repeated dose toxicity;
Genetic toxicity (two end points, generally point mutation and chromsumal aberrations);
Reproductive toxicity (including fertility and development toxicity).

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