NATIONAL INSTITUTE OF PUBLIC HEALTH AND ENVIRONMENTAL PROTECTION
BILTHOVEN, THE NETHERLANDS

Report no. 679101 009

THE DERIVATION OF PRELIMINARY MAXIMUM PERMISSIBLE CONCENTRATIONS OF VOLATILE COMPOUNDS IN AIR

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July 1993

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This research was carried out on behalf of the Directorate-General for Environmental Protection, Directorate of Chemicals, Safety, and Radiation Protection, in the frame of the project Integrated quality objectives for water, soil and air (Quality objectives and risks, project no. 679101)

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PREFACE

This report contains results of research carried out in the framework of the project 'Setting integrated environmental quality objectives'. The results have been discussed in the 'Setting integrated environmental quality objectives advisory group'. Members thereof are C.W.M. Bodar (Health Council of The Netherlands), J.H.M. de Bruijn (Ministry of Housing, Physical Planning and the Environment), J.H. Canton (National Institute of Public Health and Environmental Protection), C.A.J. Denneman (Ministry of Housing, Physical Planning and the Environment), J.W. Everts (Ministry of Transport, Public Works and Water Management; Tidal Waters Division), M.P.M. Janssen (National Institute of Public Health and Environmental Protection), P. Leeuwangh (Winand Staring Centre for Integrated Land, Soil and Water Research), W. Ma (Institute for Forestry and Nature Research), E.J. van de Plassche (National Institute of Public Health and Environmental Protection), P.B.M. Stortelder (Ministry of Transport, Public Works and Water Management; Institute for Inland Water Management and Waste Water Treatment), J. Struijs (National Institute of Public Health and Environmental Protection), M. Vossen (Ministry of Transport, Public Works and Water Management; Institute for Inland Water Management and Waste Water Treatment), and J. van Wensem (Technical Soil Protection Committee).

ACKNOWLEDGEMENTS

The derivation of preliminary Maximum Permissible Concentrations in this report was performed in consultation with four (eco)toxicological advisors: L. v. Bree (Laboratory of Toxicology of the National Institute of Public Health and Environmental Protection), J.H. Canton, mrs. J.E.M. v. Koten-Vermeulen and F.X.R. v. Leeuwen (all from the Toxicology Advisory Centre of National Institute of Public Health and Environmental Protection). Their contribution to the development of the methodology used in this study and to the evaluation and selection of the collected data is greatly acknowledged.

CONTENTS

SUMMARY

In the sub-project 'Volatile Compounds', part of the project 'Setting integrated environmental quality objectives' Maximum Permissible Concentrations (MPC's) are derived for 46 volatile substances for water, sediment, soil and air. These MPC's are used for setting integrated environmental quality objectives (i.e. limit and target values). In case of the derivation of MPC's in air a step-wise approach was used. First, preliminary MPC's are derived based on information from reviews only. These preliminary MPC's will be harmonized with the ones for water, sediment and soil. If it can be concluded that the preliminary MPC in air leads to exceedance of a MPC in another compartment, the preliminary MPC in air will be re-evaluated. The present report contains the results of the derivation of these preliminary MPC's. Therefore preliminary MPC's in air were derived aiming at the protection of man as well as the ecosystem: the MPC_{human} and MPC_{eco}, respectively. Both MPC's are compared and one will be selected as the preliminary MPC in air used for harmonziation.

For derivation of the MPC_{human} the selected volatile compounds can be divided into two groups. The first group contains 12 compounds for which limit- and/or target values have already been set by the Ministry of Housing, Physical Planning and the Environment. For these compounds the data set was only updated, to see if recent studies necessitate a re-evaluation of the limit and /or target value. It was concluded however that this was not the case. Therefore the limit and/or target values will be used for harmonization of the MPC's for the different compartments.

The second group comprises 34 compounds, for which no limit and/or target values have been set. For these compounds toxicological data were collected from reviews. It should be emphasised that this concerns a first screening: in many cases it is difficult to assess the reliability of the information presented in reviews. Uncertainty factors, applied on results from toxicological studies (a NOAEL of LOAEL) were therefore applied rather rigid. A more flexible, compound-dependent approach could not be realized within the timeframe of this first screening. For 24 compounds a preliminary MPC_{human} could be derived.

For the derivation of a MPC_{eco} ecotoxicological data were collected from reviews. The modified EPA method was used to derive a preliminary MPC_{eco}. For 35 compounds a MPC_{eco} could be derived. For the other 11 compounds no useful ecotoxicological data were available.

Comparing the MPC_{eco} and MPC_{human} it could be concluded that the latter MPC is always lower than the other one. This means that for these compounds the MPC_{human} will be used as the preliminary MPC in air used for harmonization. For 3 compounds, i.e. 1,3-dichloropropane, 2,3-dichloropropene and ethylene, the MPC_{eco} will be used as the preliminary MPC in air because no MPC_{human} could be derived. For 3 compounds, i.e. 3- and 4-monochlorotoluene and pentachloroethane, no preliminary MPC in air could be derived at all because no (eco)toxicological information was available.

SAMENVATTING

In het deelproject 'Vluchtige Stoffen' dat onderdeel uitmaakt van het project Integrale Normstelling Stoffen (INS), worden voor 46 vluchtige verbindingen Maximaal Toelaatbare Risiconivo's (MTR's) afgeleid voor water, sediment, bodem en lucht. Deze MTR's dienen als basis voor het vaststellen van integrale milieukwaliteitsdoelstellingen (grens- en streefwaarden). Voor het bepalen van MTR's voor lucht is gekozen voor een stapsgewijze benadering. Hierbij worden eerst voorlopige MTR's afgeleid, d.w.z. dat alleen gebruik is gemaakt van informatie uit reviews. Deze voorlopige MTR's voor lucht zullen vervolgens afgestemd worden met de MTR's voor water, sediment en bodem (intercompartimentale afstemming). Indien hieruit naar voren komt dat de voorlopige MTR voor de lucht leidt tot een overschrijding van de MTR in een ander compartiment, zal een nadere evaluatie plaatsvinden van de voorlopige MTR voor de lucht. Het voorliggende rapport bevat de resultaten van de afleiding van deze voorlopige MTR waarden voor lucht. Hierbij is zowel ter bescherming van de mens als het milieu een voorlopige MTR afgeleid: de MTR_{humaan} en MTR_{eco}. Deze waarden zijn vervolgens met elkaar vergeleken waarna de voorlopige MTR voor lucht gekozen is, die gebruikt zal gaan worden voor de intercompartimentale afstemming.

Voor het afleiden van voorlopige MTR_{humaan}'s kunnen de geselecteerde vluchtige verbindingen in twee groepen worden verdeeld. De eerste groep bestaat uit 12 stoffen waarvoor reeds (al dan niet wettelijk vastgelegde) grens- en/of streefwaarden zijn vastgesteld door het ministerie van VROM. Voor deze verbindingen zijn alleen meer recente gegevens verzameld uit reviews, om te bezien of er reden is voor aanpassing van deze grens- en/of streefwaarden. Dit bleek niet het geval te zijn. De grens- en/of streefwaarden zullen dan ook gebruikt worden voor de intercompartimentale afstemming.

De tweede groep bevat 34 verbindingen waarvoor geen grens- en/of streefwaarden bestaan. Voor deze verbindingen zijn uit reviews toxiciteitsgegevens verzameld, waaruit zo mogelijk voorlopige MTR_{humaan}'s afgeleid zijn. Benadrukt dient te worden dat het een eerste screening van deze stoffen betreft: bij het gebruik maken van reviews kan de betrouwbaarheid van de daar beschreven informatie moeilijk beoordeeld worden. Om deze reden zijn vrij rigide onzekerheidsfactoren toegepast voor het afleiden van een MTR_{humaan} uit de resultaten van een toxicologische studie (NOAEL of LOAEL). Een meer flexibele, stofafhankelijke aanpak was binnen het kader van deze snelle screening niet mogelijk. Voor 24 verbindingen was het mogelijk een voorlopige MTR_{humaan} af te leiden. Voor de overige stoffen waren onvoldoende of geen gegevens beschikbaar.

Na verzameling van ecotoxicologische gegevens uit reviews, zijn zo mogelijk voorlopige MTR_{eco}'s afgeleid met behulp van de gemodificeerde EPA methode. Voor 35 verbindingen is een voorlopige MTR_{eco} afgeleid, terwijl voor de overige 11 stoffen geen bruikbare toxiciteitsgegevens beschikbaar waren. Bij vergelijking van de MTR_{eco} en MTR_{humaan}'s, blijkt de MTR_{humaan} in alle gevallen lager te zijn dan de MTR_{eco}. Dit betekent dat de MTR_{humaan} gebruikt zal worden voor de intercompartimentale afstemming. Voor 3 stoffen, nl. 1,3-dichloorpropaan, 2,3-dichloorpropeen en ethyleen, zal de voorlopige MTR_{eco} gebruikt worden omdat geen MTR_{humaan} kon worden afgeleid. Voor 3 stoffen, nl. 3- en 4 monochloortolueen en pentachloorethaan, kon überhaupt geen voorlopige MTR voor de lucht bepaald worden aangezien geen (eco)toxicologische informatie beschikbaar was voor het afleiden van een MTR_{eco} of MTR_{humaan}.

1. INTRODUCTION

1.1 The project 'Setting integrated environmental quality objectives'

In 1989 the project 'Setting environmental quality objectives' started. Aim is to derive integrated environmental quality objectives for air, water, sediment and soil for a great number of compounds, based on the risk philosophy of the Ministry of Housing, Physical Planning, and Environment. [1, 2] The project is carried out by the National Institute of Public Health and Environmental Protection. The first project 'MILBOWA' resulted in the report 'Desire for levels'. [3] In this report a methodology was proposed for deriving quality objectives for water, sediment and soil for several compounds like heavy metals, chlorophenols, pesticides and polycyclic aromatics. The method consisted of determining Maximum Permissible Concentrations (MPC's) for the various compartments by applying extrapolation methods to ecotoxicological data, followed by harmonization of the MPC's for the different compartments using the equilibrium partitioning method. [3, 4] Based on this report limit and target values for water, sediment and soil were proposed for several compounds by the Dutch Ministry of Environment. [5] The second project concerns the derivation of integrated environmental quality objectives for several trace metals, volatile compounds and pesticides with a risk for secondary poisoning. For nine trace metals integrated environmental quality objectives have already been derived. [6]

1.2 The project 'Volatile Compounds'

Because most of the compounds evaluated until now were not volatile no integrated environmental quality objectives were derived for the compartment air. It was recognized, however, that transport via air can be an important route for several compounds, e.g. for heavy metals and volatile compounds. It was decided to give attention to this aspect in a project called 'Volatile Compounds' concerned with the derivation of integrated environmental quality objectives for 46 volatile substances. Selected compounds are presented in appendix 2. The the following had to be done:

- derivation MPC's in air, water, sediment and soil based on (eco)toxicological data,
- derivation of partition coefficients in order to apply the equilibrium partitioning method,
- development of a model for harmonization of the MPC's for the different compartments.

The present report contains the results of one of the activities of the project on volatile compounds, i.e. the derivation of preliminary MPC's in air. The derivation of MPC's in water, sediment and soil is described in Van de Plassche et al. (1993). [7] The derivation of partition coefficients and the model for harmonization, called INS-BOX, will be discussed in an integration report of the project 'Volatile Compounds'. Values derived there can be used to set integrated environmental quality objectives (limit and target values).

Within the framework of these activities a workshop was organized on October 8, 1991 at the National Institute of Public Health and Environmental Protection. In this workshop, to which experts from scientific research institutes, governmental institutes and the industry participated, a first approach was discussed. [8] The approach presented in the workshop to derive MPC's in air is used in the present report.

In order to derive MPC's in air it was decided to use a step-wise approach. First *preliminary*

MPC's in air will be derived based on a literature search from reviews only. This can be regarded as the screening stage. These preliminary MPC's in air and the MPC's in water, sediment and soil will be harmonized using the INS-BOX model. If it can be concluded from calculations with INS-BOX that the preliminary MPC in air gives rise to problems in other compartments this preliminary MPC in air will be re-evaluated. This means that only original literature and not reviews will be used for deriving a MPC in air. Also a minimum data-set will have to be present for the derivation of a MPC. This means that e.g. information on mutagenicity, carcinogenicity, reproduction, teratogenicity and at least a 90 day sub-chronic study must be available for each compound.

1.3 Derivation of preliminary Maximum Permissible Concentrations in air

Preliminary MPC's in air are derived for both humans (MPC_{human}) and the ecosystem (MPC_{eco}). Both MPC's will be compared and the lowest one will be selected as the preliminary MPC in air, which will be used in the model INS-BOX.

With respect to the derivation of a preliminary MPC_{human} the selected volatile compounds can be divided into two groups. The first group comprises 34 compounds, for which no limit and/or target values exist yet in The Netherlands. For these compounds toxicological data were collected from reviews, evaluated and extrapolated to a preliminary MPC_{human}. The second group comprises 12 compounds for which limit and/or target values have already been set by the Ministry of Housing, Physical Planning and Environment. The data set for these compounds was only updated, to see if recent studies necessitate a re-evaluation of these values.

For all compounds also ecotoxicological data were collected from reviews. These data were used to calculate a preliminary MPC_{eco}. Only for ethylene a limit value has been set by the Ministry of Housing, Physical Planning and Environment, based only on ecotoxicological data for plants. The data set for this compound was not updated because a recent review by Slooff et al. (1991) was available. [9]

Standards for peak values in air have been set for 3 out of the 46 compounds by the Ministry of Housing, Physical Planning and Environment. An overview of these values is presented in appendix 6. For deriving MPC's in air also accounting for peakconcentrations first of all the ratio between peak (short term) exposure to high concentrations and chronic exposure to the compound in air must be known. In order to determine whether peak concentrations actually occur and to calculate this ratio a substantial amount of monitoring data or actual concentrations and data on emission (diffuse or point sources; height of emission; spread of point sources) are needed. These data are not available for the compounds discussed here. An overview of all measured data in the Netherlands will be presented in the integration report. Only data on effects during (sub)chronic exposure were used for deriving a preliminary MPC_{human}; a strategy for deriving MPC_{human}'s based on effect data including peak exposure has not been developed yet. For these reasons it is decided not to take occurance of possible peak concentrations into account yet.

2. METHODOLOGY

2.1 Literature search for toxicity data

To provide a data set only reviews present at the Toxicology Advisory Centre of the National Institute of Public Health and Environmental Protection were used. In appendix 1 a list of consulted reviews and handbooks is presented. The most reliable studies were selected and in case of doubt experiments were judged by experts. Also studies in humans were searched for.

2.2 Selection of parameters and criteria

Parameters:
To protect humans the full toxicological profile was taken into account, e.g. toxicological parameters like mortality, growth, reproduction, teratogenic effects, organ weight, hematological changes, urinalysis, (histo)pathological and biochemical changes.
For the ecosystem only those parameters were studied that affect species on the level of population. Primarily these parameters are mortality, growth and reproduction. Besides, for plants parameters like yield and photosynthesis are taken into account.

Selection criteria for collected studies for deriving a preliminary MPC_{human}:
The most reliable studies were used for the evaluation of each compound. Studies considered suitable for deriving a MPC_{human} were:

A. Studies in which animals were exposed for 4 w, or longer. Furthermore, the exposure time in these studies must be 4 h/d and 5 d/w, or longer. Studies for which no information was available concerning the exposure time, were excluded.
B. Studies in which more than one exposure concentration was used, so a NOAEL or LOAEL[1] could be derived. This aspect should apply to all studies under A to E.
C. Teratogenicity studies, in which females are exposed during at least that part of pregnancy covering the period of organogenesis. Only teratogenic effects, defined as irreversible, structural effects on the foetuses, have been evaluated.
D. Case-controlled human studies, in which more than one concentration is tested during a known exposure time. Also human studies should result in a NOAEL or LOAEL.
E. Oral studies (≥ 90 days), but only in case no inhalation studies were available meeting the mentioned demands.

Selection criteria for collected studies for deriving a preliminary MPC_{eco}:
Studies on all organisms were colleced, e.g. mammals, birds, insects and plants. For plants, birds and insects no international accepted guidelines exist for exposure via air. 'Expert judgement' was therefore most important in the assessment of the reliability of these studies: studies were assessed on a case by case basis and the OECD guidelines were used as a

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[1] Different criteria are used in several types of studies in toxicology and ecotoxicology, e.g. NOEC, NOEL, NOAEL, NEC, NOLC, LOEC, and LOAEL. For reasons of readability, only the terms NOAEL and LOAEL will be used.

general source for assessing study design.
As stated above studies with mammals are used. This means that the same study can be used for deriving a preliminary MPC_{human} as well as a preliminary MPC_{eco} but for the ecosystem in general only the parameters growth, reproduction and mortality are selected.
To derive a preliminary MPC_{eco} also acute and sub-acute studies using the inhalation route with mammals were taken into account. For acute studies the exposure time had to be 4 h/d or longer, based on the OECD guideline for acute inhalation studies. [10] For sub-acute and (sub)chronic studies the eposure time had to be 4 h/d and 5 d/w or longer.

2.3 Extrapolation methods

Collected data were extrapolated to preliminary MPC_{human}'s and preliminary MPC_{eco}'s in air, according to the extrapolation methods described in this section. For the derivation of preliminary MPC_{human}'s two different kinds of compounds should be distinguished. Extrapolation of preliminary MPC_{human}'s for non-carcinogenic compounds is described in paragraph 2.3.1.1, while the extrapolation method for data on genotoxic carcinogenic compounds is presented in paragraph 2.3.1.2. The extrapolation method of MPC_{eco}'s is identical for all compounds and will be described in paragraph 2.3.2.

2.3.1 The derivation of MPC_{human}'s in air

2.3.1.1 Non-carcinogenic compounds

After the collection of data, the NOAELs/LOAELs from animal and human expèriments are extrapolated to a preliminary MPC_{human}.
For the selection of the NOAEL/LOAEL used for deriving a preliminary MPC_{human} and the derivation of the preliminary MPC_{human} itself, the next procedure was followed:

1. Correction to continuous exposure: All NOAELs and LOAELs are corrected for continuous exposure (24h/d; 7d/w) by multiplication with a factor: N/7 * M/24, in which N is the number of exposure days per week and M the number of hours per day.
2. The lowest corrected NOAEL's and LOAEL's from the data set are selected for further consideration.
3. A study with chronic exposure is preferred to a study with a subchronic exposure time, if it concerns studies with the same species and parameter. This rule is applied even if the corrected NOAEL or LOAEL obtained from the chronic study is higher.
4. Oral studies are only used in case whether no or no reliable inhalation studies are available. The oral MPC_{human}'s, derived from a NOAEL or LOAEL in an oral study by application of uncertainty factors, are converted into MPC_{human}'s for inhalatory exposure using the following formula [11]:

   inhalation preliminary MPC_{human} * IR * t * B_{inh} = oral preliminary MPC_{human} * BW * B_{oral}

   in which:
   IR = inhalation rate (0.83 m^3/h)

t = duration of exposure per day (24 h)
B_{inh} = inhalation bioavailability (set at 75%)
BW = body weight humans (70 kg)
B_{oral} = oral bioavailability (set at 100%)

Preliminary MPC_{human}'s should be expressed in mg/m^3 and mg/kg bw for inhalation and oral exposure, respectively.

The formula mainly consists of constant factors, which makes it possible to simplify the formula to:

inhalation preliminary MPC_{human} = 4.66 * oral preliminary MPC_{human}

5. The lowest NOAELs and LOAELs are used for extrapolation, by applying uncertainty factors[2] for interspecies and intraspecies variation and for extrapolation from sub-chronic to chronic exposure. The uncertainty factors (UF) used are presented in table 2.1. Due to the irreversibility and severity of the effect, NOAELs from teratogenicity tests were extrapolated with an extra factor 10 for teratogenic effects. In this case the UF for exposure time (sub-chronic → chronic) was not applied.
   It should be noted that, because it concerns a first screening of the toxicological information available for these compounds, the UF's are applied rather rigidly: only the duration of the study and the lowest NOAEL/LOAEL are taken into account.
   For the derivation of MPC's after the harmonization procedure (see paragraph 1.2), when the original literature is studied, a more flexible approach is suggested for the application of UF's. Aspects as type of effect (nature, severity and biological significance), duration of the study and extent of the data set of available information will be taken into account.
6. After extrapolation the lowest value is accepted as the preliminary MPC_{human}.

Table 2.1. Uncertainty factors for extrapolation of a chronic NOAEL [12, 13, 14, 15]

Uncertainty caused by:	Uncertainty factor (UF)
Interspecies variability	10
Intraspecies variability	10
Sub-chronic instead of chronic study[1]	10
LOAEL instead of NOAEL[1]	10

[1] If NOAEL or LOAEL is based on teratogenic effects an extra UF of 10 is applied, but the UF for sub-chronic → chronic is not used.

[2] Several terms are used for factors applied in human and environmental effect assessment, e.g. uncertainty, assessment and extrapolation factor. In this report uncertainty factor (UF) is used.

The NOAEL's and LOAEL's from animal experiments expressed as mg/m^3 are directly applied to derive the MPC_{human}'s. Due to the lack of a generally accepted procedure for the conversion of inhalation exposure in animal studies to exposure for humans, no dosimetric correction has been carried out. Because it is expected that this correction will not change the order of magnitude of the derived MPC_{human}'s it is recognized that the use of relatively large uncertainty factors, as applied in the procedure presented here, will sufficiently compensate for this deficiency. Therefore the use of NOEL's and LOAEL's, uncorrected for possible dosimetric differences between various animal species, is considered to be acceptable.

2.3.1.2 Genotoxic carcinogenic compounds

For genotoxic carcinogens a linear "non-threshold" cancer risk model has been used in The Netherlands for deriving MPC_{human}'s for genotoxic, carcinogenic compounds in (integrated) criteriadocuments. The linear extrapolation method will be shortly discussed: tumour incidence schemes from chronic animal studies are consulted and an effect concentration (C_{exp}) is selected for further calculation. The MPC_{human} is calculated then by applying the following formula [16]:

$$MPC_{human} = (I_{human}/I_{exp}) * (t_{exp}/t_{life}) * (t_{expos}/t_{life}) * C_{exp}$$

in which:

MPC_{human}	= maximum permissible concentration in air for humans in mg/m^3
I_{human}	= accepted tumour incidence for humans ($1:10^4$ lifetime[3])
I_{exp}	= experimental tumour incidence at the selected C_{exp}
t_{exp}	= duration of the experiment in days
t_{life}	= lifetime of test animal in days (rat: 1000; mouse: 750)
t_{expos}	= exposure time in days
C_{exp}	= effect concentration selected for extrapolation; in most cases this is the lowest concentration in mg/m^3, causing a significantly increased I_{exp}, corrected for continuous exposure (24 h/d; 7d/w).

2.3.2 The derivation of MPC_{eco}'s in air

In The Netherlands two extrapolation methods are used for deriving environmental quality objectives.

1. For preliminary effect assessment: modified EPA method [17]. This method is applied in case less than 4 chronic NOAEL values for species from different taxonomic groups are available. In the following section this method will be shortly described.
2. For refined effect assessment: Modification 0 of the method of van Straalen and

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3 All limit and target values for carcinogenic compounds are presented according to the risk philosophy of the Ministry of Housing, Physical Planning and Environment based on a risk of 10^{-6} per year as defined in "Premises for Risk Management". [2]

Denneman as developed by Aldenberg and Slob [17, 18]. This statistical method is applied if at least 4 chronic NOAEL values for species from different taxonomic groups are available. This method is not used in this study, due to lack of chronic toxicity data, and will therefore not be described.

The modified EPA method:

In the modified EPA method uncertainty factors (UF's) are applied to toxicity data. Until recently the modified EPA method was used only for deriving MPC_{eco}'s for soil and surface water in The Netherlands. Slooff presented a proposal for air at 'The 3rd US-Dutch expert workshop on comparative risk analysis for air pollution prevention' in Seattle, USA in 1991. [19] He considered mammals, birds, plants/lichens, and insects as representative taxonomic groups for the part of the terrestrial ecosystem exposed to air pollutants. It should be stated that the method only allows to make an indicative judgement of the effects of a compound as the method has no scientific basis. In table 2.3 the method is presented [17, 19].

To calculate a preliminary MPC_{eco} the lowest[4] toxicity value of concern is divided by an uncertainty factor of which the size depends on the number and type of toxicity data available (see table 2.3). If acute data or reliable QSAR[5] estimates for acute toxicity for at least mammals or birds, plants or lichens, and insects are available an uncertainty factor of 100 is used on the lowest L(E)C50 from the data set. If less acute data are present a factor of 1000 is used.

If chronic data or reliable QSAR estimates for chronic toxicity for at least mammals or birds, plants or lichens, and insects are available an uncertainty factor of 10 is used on the lowest NOAEL of the data set. If less than 3 NOAEL values for mammals or birds, plants or lichens, and insects are available, the lowest value obtained after application of the various uncertainty factors on acute as well as chronic data is selected as the preliminary MPC_{eco}.

L(E)C50 and NOAEL values are corrected for continuous exposure according to the formula presented in paragraph 2.3.1.1. NOAEL's as well as LC50 values for mammals were corrected for continuous exposure although corrected LC50 values can be too low in case mortality takes place in the first hours of exposure. In most acute studies however the exposure time is only 4 hours. Results from sub-acute inhalation studies (exposure time less than one month) for birds and mammals are extrapolated to chronic values by applying an extra uncertainty factor of 10 with the exception of studies with exposure during gestation. If a LOAEL is available, a NOAEL is calculated as LOAEL/10. The factor 10 is used in order to be consisting with the uncertainty factor used for deriving a MPC_{human} (see table 2.1).

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4 Because it concerned the derivation of a *preliminary* MPC_{eco} toxicity data were not weighted (calculation of geometric mean value if more values are presented for the same species for the same parameter) as in the method proposed by Slooff [17].

5 It is recognized that at the moment no QSAR's are available to obtain toxicity data for organisms exposed via air. To be consistent with the modified EPA method used for derivation of MPC's for water and soil QSAR estimates have been added however to the scheme presented in table 2.3.

Table 2.3. Modified EPA method for air [17, 19]

available information	uncertainty factor (UF)
lowest acute L(E)C50 value or QSAR estimate for acute toxicity	1000[a]
lowest acute L(E)C50 value or QSAR estimate for acute toxicity for minimal mammals or birds and plants or lichens and insects	100[a]
lowest chronic NOAEL value or QSAR estimate for chronic toxicity	10[a]
lowest chronic NOAEL value or QSAR estimate for chronic toxicity for minimal mammals or birds and plants or lichens and insects	10

[a] extrapolated values based on acute L(E)C50 and chronic NOAEL toxicity data are compared and the lowest one is selected as the preliminary MPC_{eco}.

3. TOXICITY DATA PER COMPOUND

3.1 Introduction

The selected 46 volatile compounds are listed in appendix 2. Toxicity data from reviews for those compounds for which no limit and/or target value is present are given in appendix 4. In appendix 5 toxicity data for compounds for which a limit and/or target values has been set are presented. Toxicity data used for derivation of a preliminary MPC_{human} as well as for a preliminary MPC_{eco} are presented. For both preliminary MPC's studies with mammals were used. For preliminary MPC_{eco}'s also data on species like insects, birds and plants were collected.
For several compounds one or more human studies were mentioned in the searched literature, which were not included however in the data set as presented in appendices 4 and 5. It concerned (occupational) studies in which the effects of only one concentration were studied, so no LOAEL or NOAEL could be derived. In most cases the exact effect concentration was not known. None of the collected human data met the demands described in paragraph 2.2. It was concluded that these data could not be used for the derivation of a preliminary MPC_{human} for any of the compounds.
In paragraphs 3.2.1 and 3.2.2 the available data on the two groups of compounds mentioned above is described with respect to the derivation of a preliminary MPC_{human}. In paragraph 3.3 data used for the derivation of a preliminary MPC_{eco} are discussed.

3.2 Toxicity data for the derivation of a preliminary MPC_{human}

3.2.1 Compounds for which no official MPC_{human} in air is available

In appendix 4 the toxicity data on this group of compounds can be found. In the following paragraphs the available data are described per compound and a motivation is given for the selection of the NOAEL/LOAEL used for deriving a preliminary MPC_{human}. The NOAELs/LOAELs mentioned in this paragraph are the values already corrected for continuous exposure (see paragraph 2.3.1.1.).
In contrast to the other compounds of this group, the chlorobenzenes were evaluated in a recent integrated criteriadocument by Slooff et al. [20]. Because no inhalation MPC_{human}'s could be derived due to lack of reliable toxicity data, the chlorobenzenes were further studied by searching for more recent information.

3.2.1.1. 2-Chloro-1,3-butadiene (or chloroprene)

The variation within the data set was large, but there were no clear differences in sensitivity between the three tested species. Tested parameters were mortality, growth, biochemistry, hematology, organweight, (histo)pathology and reproduction. From inhalation studies with rats sub-chronic LOAELs were obtained varying from 0.08 to 25 mg/m^3. The NOAELs varied from 0.05 mg/m^3 in hamsters to 65 mg/m^3 in rats. The value used for deriving a preliminary MPC_{human} was the lowest LOAEL of 0.08 mg/m^3 on organ weight and biochemistry, obtained

from a 2 month rat study. This LOAEL resulted in the lowest value after extrapolation.

3.2.1.2. 3-Chloropropene (or allylchloride)

From two teratogenicity studies a NOAEL on teratogenicity was observed of 27 mg/m^3. Sub-chronic inhalation studies were performed in rats, guinea pigs, rabbits, cats and dogs. All tested animals were equally sensitive. The lowest NOAEL, on (histo)pathology, is 2 mg/m^3. This value was used for deriving a preliminary MPC_{human}.

3.2.1.3. 1,2-Dichlorobenzene

The parameters (histo)pathology, hematology and biochemistry were tested. Sub-chronic (6.5 months) inhalation studies were performed in rats, mice and guinea pigs. There appeared to be no difference in sensitivity between the tested animals. The NOAEL, on (histo)pathology, hematology and biochemistry, of 60.4 mg/m^3 was used for deriving a preliminary MPC_{human}.

3.2.1.4. 1,3-Dichlorobenzene

No useful data were available for deriving a preliminary MPC_{human}.

3.2.1.5. 1,4-Dichlorobenzene

For 1,4-dichlorobenzene (sub-)chronic inhalation studies were performed in rats, mice, guinea pigs and rabbits. Tested parameters were mortality, growth, (histo)pathology, biochemistry and organweight. There was no large variation in the respons of the different species. The lowest chronic NOAEL of 67 mg/m^3, on (histo)pathology, organ weight and biochemistry, in rats and mice, was used for deriving a preliminary MPC_{human}.

3.2.1.6. 1,1-Dichloroethane (or ethylidene dichloride)

NOAELs/LOAELs were found concerning the parameters mortality, growth, (histo)pathology, hematology, biochemistry, teratogenicity and reproduction. From sub-chronic studies in five test animals, NOAELs were obtained varying from 366 to 854 mg/m^3. NOAELs were for all species within the same range. Exposure during pregnancy resulted in a NOAEL on teratogenicity of 7,805 mg/m^3. For deriving a preliminary MPC_{human}, the lowest NOAEL of 366 mg/m^3, on hematology and biochemistry in cats, was used.

3.2.1.7. 1,1-Dichloroethene (or vinylidene chloride)

Tested parameters were mortality, growth, (histo)pathology, hematology, biochemistry, teratogenicity and reproduction. Chronic and sub-chronic studies were performed in six species showing a similar sensitivity towards the compound. For mice two chronic studies were mentioned, with NOAELs of 4 and 39 mg/m^3. The lowest LOAEL on (histo)pathology in a

chronic rat study was 17 mg/m^3. From sub-chronic studies LOAELs and NOAELs were derived for six species of test animals. Exposure of rats and rabbits during pregnancy resulted in NOAEL's on teratogenicity of 23 and 93 mg/m^3, respectively.
A NOAEL on growth of 20 mg/m^3 from a sub-chronic monkey study, was used for deriving a preliminary MPC_{human}. Apart from the fact that extrapolation of the chronic rat LOAEL of 17 mg/m^3 and the mouse NOAEL of 4 mg/m^3 resulted in comparable preliminary MPC_{human}'s, the monkey study was preferred to these studies because of two reasons. In the first place, monkeys are more closely related to humans than rats and mice are. In the second place, the monkeys were continuously exposed to the compound instead of a few hours a day and a few days a week.

3.2.1.8. 1,2-Dichloroethene (or acetylene dichloride)

Sub-chronic studies were performed in rats, rabbits, guinea pigs and dogs. Tested parameters were mortality, growth, (histo)pathology, organweight, biochemistry and hematology. It should be noted that the relative potencies of the cis- en trans-isomer are not known, because the exact composition of the test substance was not specified. All animals appeared to be equally sensitive. The lowest NOAEL/LOAEL was a LOAEL of 357 mg/m^3 on biochemistry and (histo)pathology in rats. This study was used for deriving a preliminary MPC_{human}.

3.2.1.9. 1,2-Dichloropropane

Sub-chronic studies in three species of experimental animals were mentioned. Tested parameters were mortality, growth, hematology, biochemistry, (histo)pathology and reproduction. There was no large variation in sensitivity of the various species. After correction the NOAEL's varied from 43 to 850 mg/m^3. The LOAEL of 128 mg/m^3, on hematology in rabbits, was used for deriving a preliminary MPC_{human}.

3.2.1.10. 1,3-Dichloropropane

No useful data were available for deriving a preliminary MPC_{human}.

3.2.1.11. 1,3-Dichloropropene

Tested parameters were mortality, growth, (histo)pathology, organweight, biochemistry, hematology, reproduction and teratogenicity. NOAEL values were within the same range, indicating a similar sensitivity of rats, mice and rabbits for the compound. Sub-chronic studies resulted in NOAEL's/LOAEL's varying from 1 to 75 mg/m^3. The same parameters were chronically tested in the same species, which is the reason for preferring the chronic studies for extrapolation. NOAELs and LOAELs obtained from chronic studies varied from 4 to 22 mg/m^3. More critical teratogenicity data were not present. The lowest chronic NOAEL of 4 mg/m^3, on (histo)pathology in rats and mice, was used for deriving a preliminary MPC_{human}. It should be noted that the relative potencies of the cis- and trans-isomer are not known,

because in all studies a mixture of both isomers was used.

3.2.1.12. 2,3-Dichloropropene

No useful data were available for deriving a preliminary MPC_{human}.

3.2.1.13. Ethylbenzene

The parameters growth, biochemistry, hematology, organweight, (histo)pathology and teratogenicity were tested. Sub-chronic studies were performed in mice, rats and guinea pigs and resulted in NOAELs varying from 39 to 1,129 mg/m^3. The lowest sub-chronic NOAEL of 39 mg/m^3, on biochemistry, was obtained from a 16w study with rats, and was used for deriving a preliminary MPC_{human}.

3.2.1.14. Ethylene (or ethene)

No useful toxicity data were available for deriving a preliminary MPC_{human}.

3.2.1.15. Hexachlorobenzene

No inhalation studies on hexachlorobenzene were described. Chronic or sub-chronic oral studies were performed in five species. Tested parameters were mortality, (histo)pathology, organweight, biochemistry and reproduction. There was no large difference in sensitivity between the various species, in case similar parameters were compared. From the most critical oral study an oral MPC_{human} was derived in Slooff et al. (1991). [20] It concerned a 12m rat study with a NOAEL on (histo)pathology of 0.05 mg/kg b.w. For lack of inhalation data, this NOAEL was also used for deriving a preliminary inhalation MPC_{human}.

3.2.1.16. Hexachloroethane

Tested parameters were mortality, growth, (histo)pathology, teratogenicity and reproduction. A NOAEL on teratogenicity of 446 mg/m^3 was found. A NOAEL of 27 mg/m^3, on mortality, growth and (histo)pathology was observed in studies with rats, guinea pigs and dogs. No variation in sensitivity was observed in these species. The mentioned NOAEL of 2 mg/m^3, being the most critical value, was used for deriving a preliminary MPC_{human}.

3.2.1.17. Monochlorobenzene

For monochlorobenzene sub-chronic inhalation studies were performed in three equally sensitive species, resulting in NOAELs varying from 42 to 195 mg/m^3. Tested parameters were hematology, biochemistry, (histo)pathology and organweight. The lowest NOAEL of 42 mg/m^3,

on (histo)pathology in rats, was used for deriving a preliminary MPC_{human}.

3.2.1.18. 2-Monochlorotoluene

In reviews only few toxicity data were found. A 3 week study in rat resulted in a NOAEL on growth and (histo)pathology of 469 mg/m^3. In the methodology section studies shorter than 4 weeks were considered not suitable for extrapolation. A teratogenicity study resulted in a NOAEL on reproduction of 775 mg/m^3. This NOAEL was used for deriving a preliminary MPC_{human}.

3.2.1.19. 3-Monochlorotoluene

No useful toxicity data were available for deriving a preliminary MPC_{human}.

3.2.1.20. 4-Monochlorotoluene

No useful toxicity data were available for deriving a preliminary MPC_{human}.

3.2.1.21. Pentachlorobenzene

For pentachlorobenzene no inhalation studies were found. Sub-chronic oral studies were performed in three species, resulting in NOAELs varying from 1.7 to 12.5 mg/kg bw. Tested parameters were (histo)pathology, organweight and teratogenicity. The lowest NOAEL of 1.7 mg/kg bw, on (histo)pathology and organ weight, was used for deriving a preliminary MPC_{human} in air.

3.2.1.22. Pentachloroethane

No useful toxicity data were available for deriving a preliminary MPC_{human}.

3.2.1.23. Tetrachlorobenzene

For tetrachlorobenzene no reliable inhalation data were available. A 90d oral rat study, resulting in a NOAEL on biochemistry of 0.34 mg/kg b.w., was used for deriving a preliminary MPC_{human}.

3.2.1.24. 1,1,2,2-Tetrachloroethane

Two sub-chronic studies in rats and rabbits were mentioned, resulting in NOAELs varying from 0.2 to 1 mg/m^3. Tested parameters were hematology, biochemistry and (histo)pathology. The

sensitivity of both species were comparable. Both studies, in which the animals were exposed for only 3-4 h/d, did not meet all criteria (exposure ≥4 h/d) described in the methodology section. Due to lack of better information and considering the small difference with the set exposure time-limit, the study was accepted. The lowest NOAEL of 0.2 mg/m^3, on hematology and biochemistry, was used for deriving a preliminary MPC_{human}.

3.2.1.25. Trichlorobenzene

For this compound sub-chronic studies in four species were performed with NOAELs varying from 4 to 155 mg/m^3. Tested parameters were biochemistry, organweight and (histo)pathology. Only small differences in sensitivity were seen between the various species. In rats and rabbits a LOAEL of 46.5 mg/m^3 was found. The lowest NOAEL of 4 mg/m^3, on biochemistry, was used for deriving a preliminary MPC_{human}.

3.2.1.26. 1,1,1-Trichlorethane

For 1,1,1-trichloroethane chronic and sub-chronic studies in seven species of test animals were performed. No remarkable differences in sensitivity were noticed between different species, in case the same parameters were compared. Tested parameters were mortality, growth, (histo)pathology, organweight, biochemistry and reproduction. NOAEL's were obtained varying from 145 to 5,400 mg/m^3. Two LOAEL's of 790 and 380 mg/m^3 were found on biochemistry and organweight. The LOAEL of 380 mg/m_3 in gerbils, after extrapolation resulting in the lowest value, was used for deriving a preliminary MPC_{human}.

3.2.1.27. 1,1,2-Trichloroethane

No chronic or sub-chronic inhalation studies were found from reviews. Several sub-chronic and chronic oral studies were mentioned. Tested parameters were mortality, growth, hematology, biochemistry, (histo)pathology, organweight and reproduction. Tested species, rats and mice, were equally sensitive. The lowest NOAEL of 3.9 mg/kg b.w., on biochemistry, growth and hematology, was obtained from a 90d study in mice. This oral NOAEL was used for deriving a preliminary MPC_{human} as described in paragraph 2.3.

3.2.1.28. 2-Xylene

Sub-chronic studies were performed in four test animals: rat, guinea pig, monkey and dog. Tested parameters were growth, (histo)pathology, hematology and reproduction. The lowest NOAEL of 337 mg/m^3, on growth, (histo)pathology and hematology, was the same for all mentioned animals. This value was used for deriving a preliminary MPC_{human}.

3.2.1.29. 3-Xylene

Only few data were available on 3-xylene. Tested parameters were mortality, hematology, (histo)pathology, biochemistry and reproduction. One sub-chronic mice study with a LOAEL of 829 mg/m^3 on biochemistry was found from reviews. This study was not accepted because only one concentration was used. In a sub-acute rat study a LOAEL of 36 mg/m^3, on biochemistry, was mentioned. This value was not considered reliable either, because it concerned a study shorter than 4 weeks. Besides, biochemical effects can often be observed in the first period of exposure, but disappear in a later stage. A NOAEL on reproduction of 1500 mg/m^3 resulted from the only usable inhalation study. From a teratogenicity study a NOAEL of 1,000 mg/m^3 on teratogenic effects was obtained, which was used for deriving a preliminary MPC_{human}.

3.2.1.30. 4-Xylene

Only few data were available on 4-xylene. A teratogenicity study, in which rabbits were continuously exposed for 14 days, lead to a NOAEL on teratogenicity of 1,000 mg/m^3. This value was used for deriving a preliminary MPC_{human}.

3.2.1.31. Xylene-mixture

Mixed xylene contained all three isomers and 6-15% ethylbenzene. Sub-chronic studies were performed with rats, dogs and gerbils, leading to NOAELs/LOAELs on (histo)pathology, hematology, biochemistry, organ weight and growth varying from 233 to 1,392 mg/m^3. No differences in sensitivity were observed between the various species. Reproduction appeared to be the most sensitive parameter: a LOAEL on reproduction of 65 mg/m^3 was obtained from a 5.5 months rat study. This LOAEL was used for deriving a preliminary MPC_{human}.

3.2.2 Compounds for which a limit and/or target value in air is available

The twelve compounds of this group contained compounds which are regarded as carcinogens in The Netherlands: acrylonitrile, benzene, 1,2-dichloroethane, ethylene oxide and vinylchloride. The MPC_{human}'s for the other, non-carcinogenic, compounds are based on studies using other toxicological parameters. The compounds belonging to this group are dichloromethane, tetrachloroethene, tetrachloromethane, toluene, trichloroethene and trichloromethane and also styrene (considered to be non-carcinogenic at low concentrations).
Toxicity data are given in appendix 5. Studies used for the derivation of the limit and/or target value in air and more recent, not yet evaluated studies are presented. Studies already evaluated in integrated criteriadocuments are not presented. It should be noted that appendix 5 also contains data used for deriving preliminary MPC_{eco}'s.

3.2.2.1. Acrylonitrile

The limit/target value for acrylonitrile in air is based on an effect concentration (C_{exp}) of 44 mg/m^3 on carcinogenicity in rats. For acrylonitrile no recent studies were found. Only a supplementary study of the extrapolated carcinogenicity study was detected.

3.2.2.2. Benzene

The limit/target value of benzene is based on cytotoxic effects of benzene at 3 mg/m^3. [21] More recent data were not found in reviews.

3.2.2.3. 1,2-Dichloroethane (or ethylene dichloride)

The limit/target value was derived from a rat carcinogenicity study. This oral 78 week study resulted in a C_{exp} of 47 mg/kg b.w. More recent carcinogenicity studies were not found.

3.2.2.4. Dichloromethane (or methylene chloride)

The study from which the limit/target value was derived, was a 2 year rat study with a NOAEL on pathology of 173 mg/m^3. This NOAEL was not corrected for continuous exposure. More recent and critical studies were not found in the consulted reviews.

3.2.2.5. Ethylene oxide

The limit/target value was based on a 25 month rat carcinogenicity study with a C_{exp} of 17.8 mg/m^3. Searching recent reviews resulted in two carcinogenicity studies, which were not evaluated yet. For both studies the original publications, containing the incidence schemes, were observed for further details. The first was a 2 year mouse study with a lowest effect concentration of 91.5 mg/m^3. The incidence scheme resulting from this study was disturbed by the outbreak of a *Mycoplasma pulmonis* infection in all groups. The second study with the same duration was performed in rats and resulted in a lowest effect concentration of 60.4 mg/m^3. During this experiment an outbreak of sialodacryoadenitis virus infection occurred. Both studies were considered not suitable for deriving a preliminary MPC_{human}.

3.2.2.6. Styrene

The limit/target value was derived from a long-term human study with a LOAEL on pathology of 84 mg/m^3. From recent reviews the most critical study resulted in a corrected NOAEL on (histo)pathology of 118 mg/m^3. This value was used for deriving a preliminary MPC_{human}.

3.2.2.7. Tetrachloroethene (or PER)

The limit/target value was based on a human study with a NOAEL on the central nervous system of 135 mg/m^3. Up-dating of the data-set yielded a recent 30 day mouse study with a corrected LOAEL on organweight of 62 mg/m^3, used for deriving a preliminary MPC_{human}.

3.2.2.8. Tetrachloromethane (= carbontetrachloride)

For this compound no new studies were found during up-dating the toxicological information. The limit/target value was based on a NOAEL on (histo)pathology of 6.1 mg/m^3, obtained from a 90 day study in which rats were continuously exposed.

3.2.2.9. Toluene

The limit/target value was derived from a 7 hours human study with a NOAEL on pathology of 150 mg/m^3. A recent 14 week sub-chronic mouse study resulted in a corrected NOAEL on mortality of 73 mg/m^3, which was used for deriving a preliminary MPC_{human}.

3.2.2.10. Trichloroethene

The limit/target value is based on a human carcinogenicity study with an effect level of 270 mg/m^3. More recent carcinogenicity studies were not found by up-dating the data-set.

3.2.2.11. Trichloromethane (or chloroform)

The limit/target value for trichloromethane was based on a 6m rat study with a NOAEL on (histo)pathology, hematology and biochemistry of 110 mg/m^3. This value was not corrected for continuous exposure. More recent studies were not found.

3.2.2.12. Vinylchloride

The limit/target value was derived from human carcinogenicity studies. More recent information was not found during up-dating the data set.

3.3 Toxicity data for the derivation of a MPC_{eco}

For almost all compounds toxicity data were available for mammals tested on the parameters survival, growth or reproduction as can be seen in appendix 4 and 5. Useful data for other taxonomic groups appeared to be very scarce. For plants data were available for some compounds, i.e. benzene, 1,1,1-trichloroethane and especially ethylene. For birds only one study with hexachloroethane is present. For insects only data for acrylonitrile were available:

this concerned studies in which the suitability of acrylonitril as a fumigant to control insects was tested. Toxicity data presented in the following paragraphs are the ones corrected for continuous exposure.

3.3.1. Acrylonitrile

Data were available for mammals and insects. The lowest NOAEL for mammals was 8 mg/m^3 for rats for mortality. For insects only acute data were available, the lowest LC50 being 230 mg/m^3 for *Sitophilus granarius*. The LC50 for insects is used for the derivation of a preliminary MPC_{eco}.

3.3.2. Benzene

Useful data were only available for mammals. The lowest LC50 was 5,000 mg/m^3 for mice. The lowest NOAEL is 4.7 mg/m^3 for reproduction for rats, calculated as LOAEL/10. The chronic value is used for the derivation of a preliminary MPC_{eco}. For plants some acute data was present for barley. No LC50 was calculated however because the exposure time was very short, i.e. only 30 min.

3.3.3. 2-Chloro-1,3-butadiene

(Sub-)acute as well as (sub-)chronic toxicity data were only available for mammals. The lowest LC50 was 197 mg/m^3 for mice. The study with rats resulting in a NOAEL for reproduction of 0.05 mg/m^3 is used, however for the derivation of a MPC_{eco}.

3.3.4. 3-Chloropropene

Only some acute and sub-acute data were available for mammals. The LC50 value of 1,113 mg/m^3 for rats and mice is used for the derivation of the MPC_{eco} although using the NOAEL value of 27 mg/m^3 for teratogenic effects from a study with rats and rabbits will result in almost the same MPC_{eco}.

3.3.5. 1,2-Dichlorobenzene

Only acute data for mammals were available, varying from 1890 to 2345 mg/m^3 for mice and rats, respectively. The value of 1890 mg/m^3 is used for the derivation of a MPC_{eco}.

3.3.6. 1,3-Dichlorobenzene

No useful data were available for deriving a MPC_{eco}.

3.3.7. 1,4-Dichlorobenzene

Sub-acute and (semi)chronic data for mammals were available. A sub-acute study with mice resulted in a LOAEL of 301 mg/m^3 for mortality. The chronic studies resulted in a LOAEL of 1,142 mg/m^3 for mortality for rats, guinea pigs and rabbits. The sub-acute LOAEL is used for the derivation of a MPC_{eco}. A NOAEL of 3.01 mg/m^3 is calulated as LOAEL/100 (exposure time < 1 month and a factor 10 because of the LOAEL).

3.3.8. 1,1-Dichloroethane

Acute and semi-chronic data were available for mammals. One LC50 of 23,787 mg/m^3 for rats was present. A NOAEL of 732 mg/m^3 for mortality was present from a semi-chronic study with rats, guinea pigs, rabbits and cats. A NOAEL of 494 mg/m^3 can be calculated from the LOAEL of 4,944 mg/m^3 for growth from a teratogenicity study with rats. The LC50 value is used for the derivation of a MPC_{eco}.

3.3.9. 1,2-Dichloroethane

(Sub-)chronic data were available for mammals. A NOAEL, calculated as LOAEL/10, of 0.2 mg/m^3 for reproduction in a study with rats is used for the derivation of a MPC_{eco}.

3.3.10. 1,1-Dichloroethene

For mammals many toxicity data were available, (sub-)acute as well as (sub-)chronic. It is remarkable that acute and chronic toxicity data for the mouse do not differ much. For the whole data-set the lowest LC50 value is 77 mg/m^3 for male mice, while the lowest NOAEL value is 20 mg/m^3 for growth for the rhesus monkey. Another LC50 of 359 mg/m^3 is preferred however because the exposure time was 22-23h in stead of 4h for the LC50 of 77 mg/m^3. The LC50 value iof 359 mg/m^3 is used for the derivation of a MPC_{eco}.

3.3.11. 1,2-Dichloroethene

Only one acute value was present being a LC50 of 21,020 mg/m^3 for mice. The same NOAEL of 806 mg/m^3 for mortality and growth was available for rats, rabbits, guinea pigs and dogs. The LC50 is used for the derivation of a MPC_{eco}.

3.3.12. Dichloromethane

The lowest NOAEL present is 124 mg/m^3 for mortality and growth for mice, calculated as LOAEL/10. This value is used for the derivation of a MPC_{eco}.

3.3.13. 1,2-Dichloropropane

Only data were available for mammals. The lowest LC50 value was 952 mg/m^3 for mice. The lowest chronic value is a NOAEL of 43 mg/m^3 for growth from a study with rats. The former value is used for the derivation of a MPC_{eco}.

3.3.14. 1,3-Dichloropropane

Only one value is available, a LC50 of 6,000 mg/m^3 for the rat.

3.3.15. 1,3-Dichloropropene

Many (sub-)acute as well as (sub-)chronic data were available for mammals. No data were present for other taxonomic groups. The lowest LC50 is 450 mg/m^3 for the rat. The lowest NOAEL value is 8 mg/m^3 for growth for rats and mice. The LC50 value is used for the derivation of a MPC_{eco}.

3.3.16. 2,3-Dichloropropene

Only a LC50 values for mammals was available, being 378 mg/m^3 for rats.

3.3.17. Ethylbenzene

Toxicity data were present for mice, rats, rabbits and guinea pigs. One LC50 was available, being 2,900 mg/m^3 for rats. The lowest NOAEL was 363 mg/m^3 for growth in a study with guinea pigs. The acute value is used for the derivation of a MPC_{eco}.

3.3.18. Ethylene

Only one acute LC50 was present for mammals while many data, acute as well as chronic were available for plants from a report of Van der Eerden (1987). [22] Based on these data a acceptable concentration of 30 (1 hour average) and 2 μg/m^3 (24 hour average) is calculated by Slooff et al. (1991) in the 'Exploratory report ethylene'. The 24 hour average value is used as the preliminary MPC_{eco}.

3.3.19. Ethylene oxide

The lowest NOAEL present is 1.9 mg/m^3 for reproduction for rhesus monkeys, calculated as LOAEL/10. The lowest LC50 is 250 mg/m^3 for mice. The chronic value is used for the derivation of a MPC_{eco}.

3.3.20 Hexachlorobenzene

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.21. Hexachloroethane

Sub-acute and sub-chronic data were available for mammals while for birds a chronic study was present. The lowest NOAEL of 27 mg/m^3 for mortality for rats, guinea pigs and dogs is used for the derivation of a MPC_{eco}.

3.3.22. Monochlorobenzene

Only acute studies with mammals were available. LC50 values varied from 1854-2206 and 2298-3468 mg/m^3 for mice and rats, respectively. The value of 1854 mg/m^3 is used for the derivation of a MPC_{eco}.

3.3.23. 2-Monochlorotoluene

Only some information for mammals was available. A NOAEL of 46.9 mg/m^3 for growth for rats is used for the derivation of a MPC_{eco}. This value is obtained by dividing the value presented in appendix 5 by 10 because the exposure time was less than 1 month.

3.3.24. 3-Monochlorotoluene

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.25. 4-Monochlorotoluene

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.26. Pentachlorobenzene

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.27. Pentachloroethane

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.28. Styrene

Only data for mammals were available. The lowest LC50 is 1,890 mg/m^3 for rats. The lowest NOAEL is 26.3 mg/m^3 for reproduction for mice calculated as LOAEL/10. The LC50 is used for deriving a preliminary MPC_{eco}.

3.3.29. Tetrachlorobenzene

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.30. 1,1,2,2-Tetrachloroethane

Only acute data for mammals were available. The lowest LC50 of 583 mg/m^3 for rats is used for deriving a preliminary MPC_{eco}.

3.3.31. Tetrachloroethene

Only for mammals data were available. The lowest LC50 was 5,050 mg/m^3 for mice. The lowest NOAEL was 12.3 mg/m^3 for mortality for mice, calculated as LOAEL/10. The NOAEL is used for the derivation of a MPC_{eco}.

3.3.32. Tetrachloromethane

Only for mammals data were available. The lowest LC50 was 11,525 mg/m^3 for female mice. A NOAEL of 6.1 mg/m^3 for mortality for rats and guinea pigs is used for the derivation of a MPC_{eco}.

3.3.33. Toluene

Only for mammals data were available. The lowest LC50 was 5,533 mg/m^3 for rats. The lowest NOAEL was 73 mg/m^3 for mortality for mice. The acute value is used for the derivation of a MPC_{eco}.

3.3.34. Trichlorobenzene

No useful data were available for deriving a preliminary MPC_{eco}.

3.3.35. 1,1,1-Trichloroethane

Data were available for plants and mammals. For mammals only (sub-)chronic data were present: the lowest NOAEL being 145 mg/m^3 for growth for rats. For plants the lowest EC50

was 19,000 mg/m^3 for growth for *Brassica napus*. The NOAEL for rats is used for deriving a preliminary MPC_{eco}.

3.3.36. 1,1,2-Trichloroethane

Only acute data were available for mammals. The lowest LC50 of 397 mg/m^3 for rats is used for deriving a preliminary MPC_{eco}.

3.3.37. Trichloroethene

Only for rats and mice data were available. The lowest LC50 was 7,567 for mice. Only one NOAEL of 189 mg/m^3 for growth for rats was available. The acute value is used for deriving a preliminary MPC_{eco}.

3.3.38. Trichloromethane

Only for mammals data were available. One LC50 was available, being 1,534 mg/m^3 for mice. The lowest NOAEL was 4.3 mg/m^3 for reproduction for rats, calculated as LOAEL/10. The chronic value is used for the derivation of a MPC_{eco}.

3.3.39. Vinylchloride

Only for mammals data were available. The lowest LC50 was 24,479 mg/m^3 for mice. The lowest NOAEL was 6 mg/m^3 for reproduction for rats. The chronic value is used for the derivation of a MPC_{eco}.

3.3.40. 2-Xylene

Only for mammals data were available. The lowest LC50 was 4,567 mg/m^3 for rats. The lowest NOAEL was 337 mg/m^3 for growth for rats, guinea pigs, monkeys and dogs. The acute value is used for deriving a preliminary MPC_{eco}.

3.3.41. 3-Xylene

Some acute data were available for mammals. The lowest LC50 was 5,728 mg/m^3 for mice. The lowest NOAEL was 300 mg/m^3 for mortality for rats calculated as LOAEL/10. The LC50 value is used for deriving a preliminary MPC_{eco}.

3.3.42. 4-Xylene

Only some (sub-)acute data were available for mammals. The lowest LC50 was 3,299 mg/m^3 for rats. The lowest NOAEL was 15 mg/m^3 for reproduction for rats, calculated as LOAEL/10. The LC50 value is used for deriving a preliminary MPC_{eco}.

3.3.43. Xylene-mixture

Only for mammals data were available, acute as well as (sub-)chronic. The lowest LC50 was 3,625 mg/m^3 for rats. The lowest NOAEL was 6.5 mg/m^3 for reproduction for rats, calculated as LOAEL/10. The latter value is used for deriving a preliminary MPC_{eco}.

4. CALCULATION OF PRELIMINARY MAXIMUM PERMISSIBLE CONCENTRATIONS IN AIR FOR HUMANS AND ECOSYSTEMS

4.1 Preliminary MPC_{human}'s for compounds for which no limit and/or target value for humans is available

In this section, preliminary MPC's for humans are derived from the selected corrected NOAELs or LOAELs. A summary of these NOAELs and LOAELs, the used uncertainty factors and the preliminary MPC_{human}'s is presented in table 4.1.
For 10 compounds no preliminary MPC_{human} in air could be calculated for humans due to lack of data: 1,3-dichlorobenzene, 1,3-dichloropropane, 2,3-dichloropropene, ethylene, 3-monochlorotoluene, 4-monochlorotoluene, pentachlorobenzene, pentachloroethane, 1,2,3,4-tetrachlorobenzene and 1,2,3,5-tetrachlorobenzene.

TABEL 4.1: The extrapolation of preliminary MPC's in air for humans: compounds for which no limit/target value in air is available

Compound	NOAEL/LOAEL (mg/m^3)	NOAEL/LOAEL (mg/m^3) corrected for continous exposure	Type of study	Uncertainty factor	Motivation	Preliminary MPC_{human} ($\mu g/m^3$)
2-chloro-1,3-butadiene	0.08	0.08	rat; 2m; $LOAEL_{o,b}$	10,000	int-intra-subchr.-LOAEL	0.008
3-chloropropene	9.3	2	guinea pig, rat, rabbit, dog; 6m; $NOAEL_p$	1,000	int-intra-subchr.	2
1,2-dichlorobenzene	290	60.4	rat, guinea pig, mouse; 6.5m; $NOAEL_p$	1,000	int-intra-subchr.	60
1,4-dichlorobenzene	450	67	rat; 76w, mouse; 57w; $NOAEL_{o,b}$	100	int-intra	670
1,1-dichloroethane	2,050	366	cat; 3m; $NOAEL_{h,b}$	1,000	int-intra- subchr.	366
1,1-dichloroethene	20	20	monkey; 3m; $NOAEL_g$	1,000	int-intra- subchr.	20
1,2-dichloroethene	1,498	357	rat; 4m; $LOAEL_{p,b}$	10,000	int-intra-subchr.-LOAEL	36

Compound	NOAEL/LOAEL (mg/m^3)	NOAEL/LOAEL (mg/m^3) corrected for continous exposure	Type of study	Uncertainty factor	Motivation	Preliminary MPC_{human} ($\mu g/m^3$)
1,2-dichloropropane	714	128	rabbit; 13w; $LOAEL_h$	10,000	int-intra-subchr.-LOAEL	13
1,3-dichloropropene	21	4	rat,mouse; 2y; $NOAEL_p$	100	int-intra	40
ethylbenzene	220	39	rat; 16w; $NOAEL_b$	1,000	int-intra-subchr.	39
hexachlorobenzene	50 μg/kg bw	0.23	rat; 12m; $NOAEL_p$; oral	100	int-intra	2.3
hexachloroethane	150	27	guinea pig, dog, rat; 6w; $NOAEL_{m,g,p}$	1,000	int-intra- subchr.	27
monochlorobenzene	234	42	rat; 10w; $NOAEL_p$	1,000	int-intra-subchr.	42
2-monochlorotoluene	3,100	775	rat; gd6-19 $NOAEL_t$;	1,000	int-intra- terat.	774
pentachlorobenzene	1.7 mg/kg bw	7.9	rat; 13w; $NOAEL_{o,p}$; oral	1,000	int-intra-subchr.	8
1,2,4,5-tetrachlorobenzene	0.34 mg/kg bw	1.6	rat; 90d; $NOAEL_b$; oral	1,000	int-intra-subchr.	1.6

Compound	NOAEL/LOAEL (mg/m^3)	NOAEL/LOAEL (mg/m^3) corrected for continous exposure	Type of study	Uncertainty factor	Motivation	Preliminary MPC_{human} ($\mu g/m^3$)
1,1,2,2-tetrachloroethane	2	0.2	rat,rabbit; 7m; $NOAEL_{h,b}$	1,000	int-intra-subchr.	0.2
trichlorobenzene	22.3	4	rat; 3m; $NOAEL_b$	1,000	int-intra-subchr.	4
1,1,1-trichloroethane	380	380	gerbil; 3m; $LOAEL_b$	10,000	int-intra-subchr.-LOAEL	38
1,1,2-trichloroethane	3.9 mg/kg bw	18.2	mouse; 3m; oral; $NOAEL_{b,g,h}$	1,000	int-intra- subchr.	18.2
2-xylene	337	337	guinea pig, rat, monkey, dog; 3m; $NOAEL_{g,h,p}$	1,000	int-intra- subchr.	337
3-xylene	1,000	1,000	rabbit; gd7-20; NO-AEL_t	1,000	int-intra- terat.	1,000
4-xylene	1,000	1,000	rabbit; gd7-20; $NOAEL_t$	1,000	int-intra- terat.	1,000
xylene-mixture	261	65	rat; 5.5m; $LOAEL_r$	10,000	int-intra-subchr.-LOAEL	6.5

4.2 Limit values and preliminary MPC_{human}'s for compounds for which a limit and or target value for humans has been set

In this section limit values and preliminary MPC_{human}'s based on new information are presented for those compounds for which a limit and or target value in air is available. The limit values and their underlying studies are presented in table 4.2. Values for genotoxic carcinogenic compounds are presented based on a risk of 10^{-6} per year as stated in paragraph 2.3.1.

By searching recent review series, the data set for each compound was updated. In case recent studies were found that could give rise to re-evaluation of a limit value, the most critical NOAEL/LOAEL is presented and a preliminary MPC_{human} is derived and presented also in table 4.2. It should be stressed that preliminary MPC_{human}'s derived for these compounds are not meant to replace existing limit values. Preliminary MPC_{human}'s are presented in orde tc assess whether a re-evaluation of the limit and/or target value may be necessary because new information is present which may lead to different conclusions.

TABLE 4.2: Limit values and derivation of preliminary MPC's in air for humans based on new information for those compounds for which a limit and/or target value has been set.

Compound	NOAEL/LOAEL or C_{exp} (mg/m^3)	NOAEL/LOAEL (mg/m^3) corrected for continuous exposure	Type of study	Uncer-tainty factor	Motivation	Limit value or prelim. MPC_{human} ($\mu g/m^3$)[1]
acrylonitrile	44		rat; 2y; C_{exp}			1 [23]
benzene			cytotoxic effects			10 [24]
1,2-dichloroethane	47 mg/kg bw		rat; 78w; C_{exp}; oral			100[2]
dichloromethane	173	173	rat; 2y $NOAEL_p$	100	int-intra	1,700[2]
ethylene oxide	17.8		rat; 25m; C_{exp}			3[2]
styrene	84		human; $LOAEL_p$	100	min.eff.-intra	800[2]
	565	118	rat; 13w; $NOAEL_p$	1,000	int-intra-subchr.	118 (*)
tetrachloroethene	135	32	$NOAEL_{cns}$	12.5	intra-subac.	2000 [25]
	62	62	mouse; 30d; $LOAEL_o$	10,000	int-intra-subchr.-LOAEL	6.2 (*)
tetrachloromethane	6.1	6.1	rat; 90d; $NOAEL_p$	100	int-intra	60[2]

Compound	NOAEL/LOAEL or C_{exp} (mg/m^3)	NOAEL/LOAEL (mg/m^3) corrected for continuous exposure	Type of study	Uncer-tainty factor	Motivation	Limit value or pre-lim. MPC_{human} ($\mu g/m^3$)[1]
toluene	150		human; 7h; $NOAEL_p$	50	intra-lim.data	300[2]
	376	73	mouse; 14w; $NOAEL_m$	1,000	int-intra-subchr.	73 (*)
trichloroethene	270	64	human epid.; C_{exp}			50 [25]
trichloromethane	110	110	rat; 6m; $NOAEL_{p,h,b}$	1,000	int-intra-subchr.	100[2]
vinylchloride			human epid. carc.			100[2]

[1] preliminary MPC_{human}'s are marked with an asterisk (*). The other values are limit values for which the reference is given.

[2] no limit value has been set for this compound. Value presented derived from Guinée and Blom [26].

4.3 The calculation of preliminary MPC_{eco}'s in air

Preliminary MPC_{eco}'s were calculated according to the modified EPA method as described in paragraph 2.3.2. Only this method could be applied because for all selected compounds less than four chronic NOAEL values from different taxonomic groups were available. In the table 4.4 the preliminary MPC_{eco}'s are presented together with the input data for the modified EPA method.

For tri-, tetra-, penta- and hexachlorobenzene(s), 3-monochlorotoluene, 4-monochlorotoluene, and pentachloroethane no toxicity data were available. No preliminary MPC_{eco} could therefore be derived for these compounds. This means that for 33 compounds a MPC_{eco} could be derived. Only for acrylonitrile and ethylene the preliminary MPC_{eco} was based on data for another taxonomic group than mammals. The preliminary MPC_{eco} for ethylene differs from the other ones. The value is based on toxicity data for plants derived from chronic effect concentrations. Based on these data the method of Aldenberg and Slob, used in refined effects assessment, was applied by Slooff et al (1991). [9]

Ethylene is the only compound for which a limit value is present based on ecotoxicological data for plants. The Health Council of The Netherlands proposed a limit value of 300 (1 hour average, 99.99 percentile) and 30 $\mu g/m^3$ (24 hour average, 99.7 percentile) in 1984. [27] These values were based on effect data for less sensitive plant species (for sensitive plant species these values were 120 and 12 $\mu g/m^3$). The limit values were adopted and published by the ministry of Housing, Physical Planning and Environment in 1985. [28] Van der Eerden proposed revised values based on an update of the literature about effects of ethylene on plants: 300 (1 hour average) and 9 $\mu g/m^3$ (24 hour average), based on effect data for sensitive plants. [22] The method applied by Slooff et al. (1991) resulted in lower values. They state that "although these are not to be considered as recommended new limit values for ethylene (as the NOECs used are highly uncertain) they imply that the present standards may be too high according to the current risk philosophy".

Therefore it is proposed to use the 24 hour average value of 2 $\mu g/m^3$ derived by Slooff et al. (1991) as preliminary MPC_{eco}. It should be stated that this value differs from the other MPC_{eco} values because it is a 24 hour average. This concentration is almost equal to natural background concentrations. Considering the biological role of ethylene (it regulates the process of growth and development and is known as an ageing hormone) it is not surprising that effects can be expected at background concentrations. [9]

In case the preliminary MPC_{eco} was based on toxicity data for mammals, acute data were used 20 out of 31 times. Although in many cases sub-chronic and chronic data were available still acute data had to be used, because the lowest value after extrapolation is selected as the preliminary MPC_{eco}, being a consequence of the modified EPA method.

Table 4.3: Preliminary MPC's in air for ecosystems in mg/m^3

Compound	pre. MPC_{eco} (mg/m^3)	based on:	
		LC50 (mg/m^3)	NOAEL (mg/m^3)
acrylonitrile	0.23	230 (insect)	
benzene	0.47		4.7 (mammal)
2-chloro-1,3-butadiene	0.005		0.05 (mammal)
3-chloropropene	1.1	1,113 (mammal)	
1,2-dichlorobenzene	1.9	1,890 (mammal)	
1,4-dichlorobenzene	0.3		3.0 (mammal)
1,1-dichloroethane	24	23,787 (mammal)	
1,2-dichloroethane	0.02		2 (mammal)
1,1-dichloroethene	0.36	359 (mammal)	
1,2-dichloroethene	21	21,020 (mammal)	
dichloromethane	12		124 (mammal)
1,2-dichloropropane	1.0	952 (mammal)	
1,3-dichloropropane	6	6,000 (mammal)	
1,3-dichloropropene	0.45	450 (mammal)	
2,3-dichloropropene	0.38	378 (mammal)	
ethylbenzene	2.9	2,900 (mammal)	
ethylene	0.002[1] (plants)		
ethyleneoxide	0.19		1.9 (mammal)
hexachloroethane	2.7		27 (mammal)
monochlorobenzene	1.9	1,854 (mammal)	
2-monochlorotoluene	4.7		46.9 (mammal)
styrene	1.9	1,890 (mammal)	
1,1,2,2-tetrachloroethane	0.58	583 (mammal)	
tetrachloroethene	1.2		12.3 (mammal)
tetrachloromethane	0.61		6.1 (mammal)

Compound	pre. MPC_{eco} (mg/m^3)	based on:	
		LC50 (mg/m^3)	NOAEL (mg/m^3)
toluene	5.5	5,533 (mammal)	
1,1,1-trichloroethane	15		145 (mammal)
1,1,2-trichloroethane	0.40	397 (mammal)	
trichloroethene	7.6	7,567 (mammal)	
trichloromethane	0.43		4.3 (mammal)
vinylchloride	0.6		6 (mammal)
2-xylene	4.6	4,567 (mammal)	
3-xylene	5.7	5,728 (mammal)	
4-xylene	3.3	3,299 (mammal)	
xylene mixture	0.65		6.5 (mammal)

[1] = 24 hour average determined by Slooff et al. (1991) [9].

5. DISCUSSION AND CONCLUSIONS

5.1 The derivation of preliminary MPC_{human}'s

As already emphasised in the introduction, a first screening has been performed for a number of volatile compounds based on a literature search in reviews. Therefore preliminary MPC_{human}'s were derived in a conservative manner, resulting in sometimes relatively low preliminary MPC_{human} values due to the use of high uncertainty factors were used.
The use of reviews has several disadvantages. Although excellent reviews exist of course, essential information may not be included. Secondly, a recent review was not always available. And finally, the information presented in reviews has to be accepted as it is. It is often difficult to assess the reliability of the study described, certainly when only the result is given. E.g. if a NOAEL on growth in a mammalian study is given one does often not know whether this was the most sensitive parameter or whether other parameters like (histo)pathology and biochemistry were not studied at all.

Compounds for which no limit and/or target values are available:
For 24 compounds it was possible to derive a preliminary MPC_{human} from available toxicity data in reviews. For 16 compounds a suitable inhalation study was available for extrapolation, but for 8 compounds the preliminary MPC_{human} had to be calculated from an oral study, due to lack of inhalation data. For the remaining compounds no preliminary MPC_{human} could be derived.
In analysing the resulting preliminary MPC_{human}'s, in some cases a difference was observed between isomers:

Dichlorobenzenes: The preliminary MPC_{human} for 1,2-dichlorobenzene was determined at 60 $\mu g/m^3$ and for 1,4-dichlorobenzene at 670 $\mu g/m^3$. For both compounds sufficient data were available, but for the 1,2-isomer it concerned relatively long sub-chronic studies, while for the 1,4-isomer also a few chronic studies were present, which explains the difference of a factor 10. The extrapolated 1,2-isomer study had a duration time of 6.5 months (sub-chronic) and effects on (histo)pathology, biochemistry and hematology were seen that were not expected to accumulate in a more chronic study. This indicates a probable over-estimation of the preliminary MPC_{human} for 1,2-dichlorobenzene. For 1,3-dichlorobenzene no preliminary MPC_{human} could be derived at all.

Dichloroethanes: For 1,1-dichloroethane a preliminary MPC_{human} of 370 $\mu g/m^3$ was determined, while for 1,2-dichloroethane a limit value exists of 1 $\mu g/m^3$. The reason for this is that the limit value for the 1,2-isomer is based on a carcinogenic effect after oral application while the preliminary MPC_{human} for 1,1-dichloroethane, which is considered a non-carcinogen, is based on toxic effects on hematology and biochemistry in a sub-chronic study.

Dichloroethenes: The preliminary MPC_{human} for 1,1-dichloroethene was 20 $\mu g/m^3$ and for 1,2-dichloroethene 36 $\mu g/m^3$, which are comparable values.

Trichloroethanes: The preliminary MPC_{human}'s were 38 $\mu g/m^3$ for 1,1,1-trichloroethane and 14 $\mu g/m^3$ for 1,1,2-trichloroethane, which is within the same range. The preliminary MPC_{human} for the 1,1,1-isomer is derived from an extensive inhalation data set, while the preliminary MPC_{human} for 1,1,2-isomer is based on a small set of oral data. It is not known whether or not it is correct for this compound to convert oral data into inhalation data.

Xylenes: The preliminary MPC_{human}'s for the various xylenes vary from 1,000 $\mu g/m^3$ for 3-xylene and 4-xylene, 337 ug/m^3 for 2-xylene, to 6.5 $\mu g/m^3$ for the xylene mix. There is no good explanation for the fact that the preliminary MPC_{human} for the xylene mix is very low compared to the xylene-isomers. The xylene mix contains all three isomers and 6-15% ethylbenzene. The data sets for the xylene mix and 2-xylene are more complete than for the 3- and 4-isomer. From the xylene-mix data it appeared that reproduction is the most sensitive parameter. For the separate isomers studies on this parameters were lacking, which could be the reason for the relatively high preliminary MPC_{human}'s. It can be concluded that the preliminary MPC_{human}'s for 2-, 3- and 4-xylene are probably too high, because they were derived from studies on less sensitive parameters than reproduction. A re-evaluation of the data and the application of a more flexible extrapolation method might solve this problem in a later stage. For now 6.5 $\mu g/m^3$ is proposed as a preliminary MPC_{human} for the total group of xylenes, although also the preliminary MPC_{human}'s for the individual isomers may be used in the INS-BOX model.

Compounds for which limit and/or target values are available:
For 12 compounds limit and/or target values were available. In addition, for 7 of these compounds preliminary MPC_{human}'s were derived. Based on new information preliminary MPC_{human}'s were derived for styrene, tetrachloroethene and toluene. In all cases the preliminary MPC_{human} was lower than the limit value. The toxicity data used for deriving the limit values for di- and trichloromethane were not corrected for continous exposure.

5.2 The derivation of preliminary MPC_{eco}'s

For almost all compounds a preliminary MPC_{eco} is derived. All preliminary MPC_{eco}'s however are based on toxicity data for mammals, except for acrylonitrile and ethylene. The data for mammals are also used for the derivation of preliminary MPC_{human}'s. It remains uncertain whether the MPC_{eco} is not underestimated if only mammalian toxicity data are present. It is known from literature that plants can be more susceptible for air pollutants than mammals, e.g. fluoride. [29] For plants however almost no data were present. The scarcity of toxicity data for plants is confirmed by Debus et al. (1989), De Jong et al. (1991) and van Dijk (1992). [30, 31, 32] De Jong et al. (1991) carried out literature study on the side-effects of pesticides on fungi and vascular plants while Van Dijk (1992) and Debus et al. (1991) investigated the phytotoxicity of several volatile organic compounds. Stix and Schulze (1990) evaluated the available scientific literature for 16 compounds with respect to potential phytotoxic effects, a.o. ethylene, tri- and tetrachloroethene, di-, tri- and tetrachloroethane, benzene, toluene, and 2-xylene. They concluded that only for ethylene sufficient information was present to establish air quality standards. [33]
Based on the toxicity data for these compounds no conclusions can be drawn with respect to the taxonomic groups considered representative for the compartment air by Slooff for application of the modified EPA method (see 2.3.2).
The modified EPA method uses the lowest L(E)C50 or NOAEL value of the whole data-set of a compound for extrapolation. As a consequence of this approach the preliminary MPC_{eco} was in 20 out of 31 cases based on a LC50 value while for many mammalian species chronic data were available. This can be considered as an unsatisfactory situation. A solution might be to use the refined effects assessment method if for more than 3 mammalian species sub-chronic

or chronic NOAEL values are available. The calculated value with the Aldenberg and Slob method should remain however an indicative MPC because only for one taxonomic group data are available.

5.3 Proposed preliminary MPC's in air

A comparison of the preliminary MPC's in air between ecosystems and humans showed a big difference. The values obtained for the ecosystem were much higher than those for humans. Only for 1,4-dichlorobenzene the preliminary MPC_{eco} was lower than the preliminary MPC_{human}. Because of the great uncertainties in the modified EPA method used for the calculation of the preliminary MPC_{eco}, and because both values differ only a factor 2 the preliminary MPC_{human} is proposed as the preliminary MPC in air. For the other compounds the more conservative preliminary MPC's for humans will be used for the harmonization of the MPC's for air, water and soil using the model INS-BOX. Only for 1,3-dichloropropane, 2,3-dichloropropene and ethylene, the preliminary MPC_{eco}, as presented in table 4.4, will be used as preliminary MPC's in air because no preliminary MPC_{human} could be derived for these compounds. It should be stated that these preliminary MPC's are almost certainly too high because for all compounds the preliminary MPC_{human} was lower than the preliminary MPC_{eco}. An exception may be ethylene because plants are very sensitive for this compound. For 3- and 4-monochlorotoluene and pentachloroethane neither a preliminary MPC_{human} nor a preliminary MPC_{eco} could be derived. An overview of the preliminary MPC's in air is presented in table 5.1. The value for 1,2,4,5-tetrachlorobenzene can also be used for the other isomers.

5.4 Suggestions for further studies

5.4.1. Derivation of MPC_{human}

During this study several difficulties were met, concerning the uncertainty in the ultimate risk estimation due to non-validated extrapolation methods. Further research on the validation of these methodologies is needed to reduce these uncertainties.

<u>The use of uncertainty factors to extrapolate to a preliminary MPC_{human}</u>
The use of uncertainty factors is of course inevitable. Sometimes however, high uncertainty factors of 1,000 to 10,000 were used. There is a general need to validate these factors, especially in cases where high factors are used, e.g. for a study with mammals resulting in a sub-chronic LOAEL.

<u>Extrapolation from oral to inhalation data</u>
In case no inhalation data were available, data from oral studies were used for the derivation of a preliminary MPC_{human} in air. This conversion from oral to inhalation values has not been validated however. Apart from this, there are also differences and uncertainties in bioavailability of the compound following administration by these routes. A special case is the difference in effects between both routes: some compounds can be carcinogenic when applied orally and not after inhalation. Further (experimental) research into this area is therefore necessary.

Table 5.1: Overview of preliminary MPC's in air, limit and target values in $\mu g/m^3$.

Compound	limit value[5] ($\mu g/m^3$)	target value[5] ($\mu g/m^3$)	preliminary MPC[1] ($\mu g/m^3$)	
			MPC_{human}	MPC_{eco}
acrylonitrile[2]	1 [23]	0.1 [23]		230
benzene[2]	10 [24]	1 [34]		470
2-chloro-1,3-butadiene			**0.008**	5
3-chloropropene			**2**	1,100
1,2-dichlorobenzene			**60**	1,900
1,3-dichlorobenzene			-	-
1,4-dichlorobenzene			**670**	300
1,1-dichloroethane			**366**	24,000
1,2-dichloroethane[2]	100 [26]	1 [35]		**20**
1,1-dichloroethene			**20**	360
1,2-dichloroethene			**36**	21,000
dichloromethane			**300**	12,000
1,2-dichloropropane			**13**	1,000
1,3-dichloropropane			-	**6,000**
1,3-dichloropropene			**40**	450
2,3-dichloropropene			-	**380**
ethylbenzene			**39**	2,900
ethylene	300; 30[4]		-	**2**[3]
ethylene oxide[2]	3 [26]	0.03 [34]		**190**
hexachlorobenzene			**2.3**	-
hexachloroethane			**27**	2,700
monochlorobenzene			**42**	1,900
2-monochlorotoluene			**775**	4,700
3-monochlorotoluene			-	-
4-monochlorotoluene			-	-

Compound	limit value[5] ($\mu g/m^3$)	target value[5] ($\mu g/m^3$)	preliminary MPC[1] ($\mu g/m^3$)	
			MPC_{human}	MPC_{eco}
pentachlorobenzene			**8**	-
pentachloroethane			-	-
styrene	800 [26]	8 [35]	**120**	1,900
1,2,4,5-tetrachlorobenzene			**1.6**	-
1,1,2,2-tetrachloroethane			**0.2**	580
tetrachloroethene	2,000 [25]	25 [25]	**62**	1,200
tetrachloromethane	60 [26]	1 [35]	**6**	610
toluene	300 [26]	3 [26]	**73**	5,500
trichlorobenzene			**4**	-
1,1,1-trichloroethane			**38**	15,000
1,1,2-trichloroethane			**18.2**	400
trichloroethene	50 [25]	50 [25]	**190**	7,600
trichloromethane	100 [26]	1 [35]	**13**	430
vinylchloride[2]	100 [26]	1 [23]	-	**600**
2-xylene			**340**	4,600
3-xylene			**1,000**	5,700
4-xylene			**1,000**	3,300
xylene mixture			**6.5**	650

[1] preliminary MPC's are printed bold

[2] presented MPC values for carcinogenic compounds are based on an accepted cancer risk of 10^{-6} per year

[3] 24 hour average

[4] 300 $\mu g/m^3$ (1 hour average; 99.99 percentile) and 30 $\mu g/m^3$ (24 hour average; 99.7 percentile) [36]

[5] reference for limit and target value is given

- : from available data no preliminary MPC could be derived

Extrapolation to continuous exposure

Toxicity values from studies with short exposure time and duration were corrected for continuous exposure (24h/d and 7d/w) by linear extrapolation. It is not known to what extent the effects are under- or overestimated by applying linear extrapolation. With respect to this aspect the type of effect caused by the compound is also important. Further studies on the validation of this method are required.

Extrapolation of sub-acute data

Only inhalation studies longer than 4 weeks were used for deriving a preliminary MPC_{human}. For some compounds only sub-acute inhalation studies were available. If this was the case sub-chronic oral studies were searched for. It might be argued however that sub-acute inhalation studies can also be used for deriving a preliminary MPC_{human}. Due to a lack of knowledge of the relationship between sub-acute and (sub)chronic effects, research migh be warranted. In the first place to demonstrate which studies should be preferred for deriving reliable inhalation MPC_{human}'s, and secondly to determine how extrapolation from sub-acute to (sub)chronic effects should be performed.

Dosimetric conversion

At present no generally accepted procedure for the extrapolation of local as well as systemic effects in animals following inhalatory exposure to a dosimetrically corrected value for human beings is available. Research in this area is necessary to facilitate a more reliable comparison of effects occuring in different species, exposed through the inhalatory route.

5.4.1. Derivation of MPC_{eco}

Toxicity data were almost only available for mammals. It is necessary to obtain more data for other taxonomic groups than mammals. This implies also the development of test methods, e.g. for insects and birds. If data for other taxonomic groups than mammals will become available this can also lead to more well-founded MPC values.

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APPENDIX 1. Literature searched for toxicity data

The following review series and toxicological handbooks are consulted:

1. ATSDR (Agency for Toxic Substances and Disease Registry) Toxicological profiles.
2. ACGIH (American Conference of Governmental Industrial Hygienists) Documentation of the threshold limit values and biological exposure indices. Fifth edition, Cincinnati.
3. Berlin, A. et al. (1989) The toxicology of chemicals; Carcinogenicity: summary reviews of the scientific evidence. Directorate General for Employment, Social Affairs and Education - Health and Safety Directorate.
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31. WHO (World Health Organization) (1987) Air Quality Guidelines for Europe. Copenhagen.

APPENDIX 2. List of volatile compounds and conversion factors

Compound:	Conversion factor: (1 ppm = .. mg/m^3)
acrylonitrile	2.2
benzene	3.2
2-chloro-1,3-butadiene	3.6
3-chloropropene	3.1
dichlorobenzene (3 isomers)	6.01
dichloroethane (2 isomers)	4.1
1,1-dichloroethene	4
1,2-dichloroethene	3.9
dichloromethane	3.6
1,2-dichloropropane	4.8
1,3-dichloropropane	4.6*
1,3-dichloropropene	4.5
2,3-dichloropropene	4.5
ethylbenzene	4.4
ethylene	1.2
ethylene oxide	1.8
hexachlorobenzene	1.7
hexachloroethane	9.8
monochlorobenzene	4.6
monochlorotoluene (3 isomers)	5.3
pentachlorobenzene	10.2*
pentachloroethane	8.3*
styrene	4.3
tetrachlorobenzene (3 isomers)	8.8*
1,1,2,2-tetrachloroethane	6.9
tetrachloroethene	6.9
tetrachloromethane	6.5
toluene	3.8
trichlorobenzene (3 isomers)	7.5
1,1,1-trichloroethane	5.4
1,1,2-trichloroethane	5.5*
trichloroethene	5.4
trichloromethane	4.9
vinylchloride	2.6
xylene (3 isomers)	4.4
xylene-mixture	4.4

*: conversion factor (CF) for this compound was not mentioned in consulted literature; these CF's were calculated from the molecular gas volume and the molecular weights obtained from handbooks (temperature set at 0°C, air pressure at 1 atm.)

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1. ATSDR (Agency for Toxic Substances and Disease Registry) Toxicological profile for...
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APPENDIX 3. Abbreviations and Latin names

B	=	bioavailability (after inhalation or oral intake)
BW	=	body weight
C_{exp}	=	concentration causing a carcinogenic effect and selected for extrapolation
Corr.conc.	=	concentration after extrapolation to continuous exposure (NOAEL or LOAEL to 24h/d and 7d/w; LC50 to 24h/d)
EPA	=	U.S. Environmental Protection Agency
Gd	=	gestation day
HC	=	Dutch Health Council
I	=	tumor incidence
IR	=	inhalation rate (in m^3/h)
LC50	=	concentration which is lethal for 50% of the test animals
LOAEL	=	lowest observed adverse effect level
MPC	=	maximum permissible concentration in air
NOAEL	=	no observed adverse effect level
Prelim.MPC	=	preliminary maximum permissible concentration in air (in mg/m^3 or ug/m^3)
QSAR	=	quantitative structure-activity relation
RIVM	=	National Institute of Public Health and Environmental Protection
t_{exp}	=	duration of the experiment (in days)
t_{expos}	=	exposure time (in days)
t_{life}	=	lifetime of test animal (in days)
TAC	=	Toxicology Advisory Centre
UF	=	uncertainty factor
VROM	=	Dutch Ministry of Housing, Physical Planning and Environment

parameters:

b	=	biochemistry (incl. immunology, neurochemistry and urinalysis)
c	=	carcinogenicity
g	=	growth
h	=	hematology
m	=	mortality
o	=	organweight
p	=	(histo)pathology
r	=	reproduction
t	=	teratology

test animals:

AP	=	Alderley Park
B	=	Beagle
CR	=	Charles River
F	=	Fischer 344
H	=	Harley
NZ	=	New Zealand White
S	=	Swiss
SD	=	Sprague Dawley

W	=	Wistar
f	=	female
m	=	male

exposure time:

h	=	hour
d	=	day
w	=	week
m	=	month
y	=	year
gd	=	gestation days

Latin names for test animals:

canis domesticus	= dog
cavia aperea	= guinea pig
coturnix coturnix	= japanese quail
cricetus cricetus	= hamster
felis domesticis	= cat
gallus domesticus	= chicken
macaca fascienularis	= monkey
macaca mulatta	= rhesus monkey
mus musculus	= mouse
oryctolagus cuniculus	= rabbit
rattus norvegicus	= norvegian (laboratory) rat
sus scrofa domesticus	= pig

APPENDIX 4. Toxicity data for compounds for which no limit and/or target value is available

CONTENTS:

2-CHLORO-1,3-BUTADIENE (= CHLOROPRENE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	8h	8h	LC50	591	197	1
rattus norvegicus	4h	4h	LC50	8,072	1,345	1
rattus norvegicus (CR,m)	4h	4h	LC50	8,200	1,367	2,4
rattus norvegicus (CR,m)	2w	4h/d	$NOAEL_m$	6,118	1,020	1
rattus norvegicus	5d	5d;6h/d	$NOAEL_r$	362	65	3
rattus norvegicus	20d	20d;4h/d	$NOAEL_r$	0.6	0.1	3
rattus norvegicus (m)	22d	22d;4h/d	$NOAEL_r$	91	9	3
mammals: sub-chronic/chronic data:						
rattus norvegicus	4w	5d/w;6h/d	$LOAEL_g$	140	25	2
rattus norvegicus (W)	4w	5d/w;6h/d	$LOAEL_{g,b,o}$	141	25	1
rattus norvegicus	2m	7d/w;24h/d	$LOAEL_{o,b}$	0.08	0.08	5
rattus norvegicus	4.5m	7d/w;24h/d	$NOAEL_r$	0.05	0.05	1
rattus norvegicus (m)	5m	7d/w;8h/d	$NOAEL_{m,h,g}$	195	65	1,5
rattus norvegicus (f)	6m	6d/w;5h/d	$LOAEL_r$	30	5	1
cricetus cricetus	4w	5d/w;6h/d	$NOAEL_{g,p}$	140	25	2
cricetus cricetus	4w	5d/w;6h/d	$NOAEL_{o,g}$	141	25	1
cricetus cricetus	18m	5d/w;6h/d	$NOAEL_p$	36.2	6	5

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3-CHLOROPROPENE (= ALLYLCHLORIDE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	4h	4h	LC50	6,678	1,113	2
rattus norvegicus	4h	4h	LC50	6,678	1,113	2
mammals: sub-chronic/chronic data:						
rattus norvegicus	6m	5d/w;7h/d	$NOAEL_p$	9.3	2	3
cavia aperea	6m	5d/w;7h/d	$NOAEL_p$	9.3	2	3
oryctolagus cuniculus	3m	6d/w;6h/d	$NOAEL_p$	17.5	4	3
oryctolagus cuniculus	6m	5d/w;7h/d	$NOAEL_p$	9.3	2	3
felis domesticus	3m	6d/w;6h/d	$NOAEL_p$	17.5	4	3
canis domesticus	6m	5d/w;7h/d	$NOAEL_p$	9.3	2	3
teratogenicity studies:						
rattus norvegicus (SD)		gd 6-15;7h/d	$NOAEL_t$	93	27	3
oryctolagus cuniculus (NZ)		gd 6-18;7h/d	$NOAEL_t$	93	27	3

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1. NIOSH (1976) National Institute for Occupational Safety and Health, Criteria for a recommended standard occupational exposure to Allyl Chloride.
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1,2-DICHLOROBENZENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus	6h		LC50	9,380	2,345	2
mus musculus	6h		LC50	7,560	1,890	2
mammals: sub-chronic/chronic data:						
rattus norvegicus	6.5m	5d/w;7h/d	$NOAEL_{p,h,b}$	290	60.4	1,2
mus musculus	6.5m	5d/w;7h/d	$NOAEL_{p,h,b}$	290	60.4	1,2
cavia aperea	6.5m	5d/w;7h/d	$NOAEL_{p,h,b}$	290	60.4	1,2

References:

1. Hesse, J.M., G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated Criteria Document Chlorobenzenes; effects. Appendix to Report no. 710401015, RIVM.
2. Gesellschaft Deutscher Chemiker (1990) Beratergremium für umweltrelevante Altstoffe (BUA): o-Dichlorbenzol, BUA-Stoffbericht 53.

1,4-DICHLOROBENZENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	2w	7d/w;8h/d	$LOAEL_{m,p}$	902	301	2
mammals: sub-chronic/chronic data:						
rattus norvegicus	13w	5d/w;8h/d	$LOAEL_{m,p,g}$	4,796	1,142	2
rattus norvegicus	6-7m	5d/w;7h/d	$NOAEL_{p,b,o}$	589	123	2
rattus norvegicus	76w	5d/w;5h/d	$NOAEL_{p,b,o}$	450	67	1,2
mus musculus	5-7m	5d/w;7h/d	$NOAEL_{p,b,o}$	950	198	2
mus musculus	57w	5d/w;5h/d	$NOAEL_{p,b,o}$	450	67	2
cavia aperea	5w	5d/w;8h/d	$LOAEL_{m,p,g}$	4,796	1,142	2
cavia aperea	6-7m	5d/w;7h/d	$NOAEL_{p,b,o}$	589	123	2
oryctolagus cuniculus	3m	5d/w;8h/d	$LOAEL_{m,p,g}$	4,796	1,142	2
oryctolagus cuniculus	5-7m	5d/w;7h/d	$NOAEL_{p,b,o}$	950	198	2

References:

1. Hesse, J.M., G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated Criteria Document Chlorobenzenes; effects. Appendix to Report no. 710401015, RIVM.
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1,1-DICHLOROETHANE (= ETHYLIDENE-DICHLORIDE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus		8h	LC50	71,360	23,787	1,2
mammals: sub-chronic/chronic data:						
rattus norvegicus *	26w	5d/w;6h/d	$NOAEL_{h,b,m,p,g}$	4,100	732	3,4,5,6
rattus norvegicus *	6m	5d/w;7h/d	$NOAEL_{p,b}$	4,100	854	2,3,4,5
cavia aperea *	26w	5d/w;6h/d	$NOAEL_{h,b,m,p,g}$	4,100	732	3,4,5,6
cavia aperea	6m	5d/w;7h/d	$NOAEL_{p,b}$	4,100	854	2,3,4,5
oryctolagus cuniculus *	26w	5d/w;6h/d	$NOAEL_{h,b,m,p,g}$	4,100	732	3,4,5,6
oryctolagus cuniculus	6m	5d/w;7h/d	$NOAEL_{p,b}$	4,100	854	2,3,4,5
felis domesticus	13w	5d/w;6h/d	$NOAEL_{h,b,g}$	2,050	366	3,4,5
canis domesticus	6m	5d/w;7h/d	$NOAEL_{p,b}$	4,100	854	2,3,4,5
teratogenicity studies:						
rattus norvegicus (m)	20d	gd 6-15;7h/d	$NOAEL_t$	26,760	7,805	3,4,5
			$LOAEL_g$	16,950	4,944	3,4,5

*: first 13 weeks the animals were exposed to 2,050 mg/m^3

References

1. ACT (1984) Toxicological Advisory Centre, Ethylenedichloride, review DGMH.
2. American Conference of Governmental Industrial Hygienists (1986) Documentation of the threshold limit values and biological exposure indices. Fifth edition, Cincinnati.
3. Clayton, G.D. and F.E. Clayton (eds) (1981) Patty's industrial hygiene and toxicology. Third revised edition, volume IIb.
4. Fawell, J.K. and S. Hunt (1988) Environmental toxicology; organic pollutants. Ellis Horwood Limited, Chichester.
5. Directoraat-Generaal van de Arbeid (1987) Rapport inzake grenswaarde 1,1-Dichloorethaan. RA 8/87
6. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for 1,1-dichloroethane. U.S. Public Health Service in collaboration with Environmental Protection Agency (EPA).

1,1-DICHLOROETHENE (= VINYLIDENE CHLORIDE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus (m)	14d	4h	LC50	460	77	1,3,5
mus musculus (f)			LC50	820	137	1,3,5
mus musculus (m)	1d	22-23h	LC50	392	359	1,3,6
mus musculus (f)			LC50	420	385	1,3
mus musculus	5d	6h/d	$NOAEL_r$	200	50	1
rattus norvegicus	4h	4h	LC50	12,800	2,133	5
rattus norvegicus	4h	4h	LC50	40,000	6,667	1
rattus norvegicus	14d	4h	LC50	32,000	5,333	3
rattus norvegicus (SD)	14d	4h	LC50	34,400	5,733	1,5
rattus norvegicus (m)	14d	4h	LC50	28,400	4,733	1,3,5
rattus norvegicus (f)	14d	4h	LC50	41,200	6,867	1,3,5
rattus norvegicus (AP)	3w	5d/w;6h/d	$LOAEL_{g,o}$	2,000	500	1,3
			$LOAEL_p$	800	200	1,3
cricetus cricetus (m)	14d	4h	LC50	6,640	1,107	1,3
cricetus cricetus (f)			LC50	11,780	1,963	1,3
mammals: sub-chronic/chronic data:						
mus musculus	1y	5d/w;6h/d	$NOAEL_h$	220	39	1
			$LOAEL_p$	220	39	1
mus musculus (S)	52w	4-5d/w;4h/d	$NOAEL_p$	40	4	3,4
rattus norvegicus	5w	5d/w;6h/d	$LOAEL_{p,b}$	400	71	1
rattus norvegicus	11w	5d/w;6h/d	$NOAEL_r$	220	39	1
rattus norvegicus	90d	24h/d	$NOAEL_p$	60	60	1
rattus norvegicus	6m	5d/w;6h/d	$NOAEL_{p,h}$	264	47	1
rattus norvegicus	18m	5d/w;6h/d	$NOAEL_h$	288	51	1
			$LOAEL_p$	96	17	1
cavia aperea	6w	5d/w;8h/d	$NOAEL_{p,h}$	400	95	1
cavia aperea	90d	4h/d	$NOAEL_p$	192	32	1
oryctolagus cuniculus	6w	5d/w;8h/d	$LOAEL_g$	400	95	1
oryctolagus cuniculus	90d	24h/d	$LOAEL_g$	100	100	1

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
canis domesticus	6w	5d/w;8h/d	$NOAEL_{p,h}$	400	95	1
canis domesticus	90d	24h/d	$NOAEL_p$	100	100	1
macaca mulatta	6w	5d/w;8h/d	$NOAEL_p$	400	95	1
			$LOAEL_g$	400	95	1
macaca mulatta	90d	24h/d	$NOAEL_m$	60	60	1
macaca mulatta	90d	24h/d	$NOAEL_g$	20	20	1
teratogenicity studies:						
rattus norvegicus		gd 6-15;7h/d	$NOAEL_t$	80	23	1
oryctolagus cuniculus		gd 6-18;7h/d	$NOAEL_t$	320	93	1

References:

1. ATSDR (1989) Agency for Toxic Substances and Disease Registry, Toxicological Profile for 1,1-dichloroethene. U.S Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
2. RECT (1988) Reviews of Environmental Contamination and Toxicology, vol.106. Springer-Verlag New York.
3. IPCS (1990) Environmental Health Criteria 100, Vinylidene Chloride. WHO, Geneva.
4. Gesellschaft Deutscher Chemiker (1988) Beratergremium für umweltrelevante Altstoffen (BUA): 1,1-Dichlorethen, BUA-Stoffbericht 33.
5. ECETOC (1985), Joint Assessment of Commodity Chemicals, no.5: Vinylidene Chloride.
6. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.

CIS-1,2-DICHLOROETHENE AND TRANS-1,2-DICHLOROETHENE (= ACETYLENE DICHLORIDE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc.	Reference (mg/m^3)
mammals: acute/sub-acute data:						
mus musculus	1d	6h/d;trans	LC50	84,070	21,020	1
rattus norvegicus	2w	5d/w;8h/d	$LOAEL_b$	1,498	357	1
mammals: sub-chronic/chronic data:						
rattus norvegicus	16w	5d/w;8h/d trans	$LOAEL_{p,b}$	1,498	357	1
rattus norvegicus	6m	5d/w;7h/d	$NOAEL_{g,m,o,h,b}$	3,870	806	3
oryctolagus cuniculus	6m	5d/w;7h/d	$NOAEL_{g,m,o,h,b}$	3,870	806	3
cavia aperea	6m	5d/w;7h/d	$NOAEL_{g,m,o,h,b}$	3,870	806	3
canis domesticus	6m	5d/w;7h/d	$NOAEL_{g,m,o,h,b}$	3,870	806	3

References:

1. ATSDR (1989), Agency for Toxic Substances and Disease Registry, Toxicological Profile for cis-1,2-dichloroethene, trans-1,2-dichloroethene and 1,2-dichloroethene. U.S Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
2. Ware, G.W. (ed.) (1988) Reviews of Environmental Contamination and Toxicology, vol.106, pag 81-93. Springer-Verlag, New York.
3. ACGIH (1986) American Conference of Governmental Industrial Hygienists inc. Documentation of the threshold limit values and biological exposure indices, 5th edition, p.185.

1,2-DICHLOROPROPANE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc.	Reference (mg/m^3)
mammals: acute/sub-acute data:						
mus musculus		10h	LC50	2,285	952	2
mus musculus		10h	LC50	3,325	1,385	4
mus musculus	5d	7h/d	$LOAEL_m$	4,400	1,283	1
mus musculus	2w	4-5d/w;6h/d	$NOAEL_p$	143	20	2
rattus norvegicus		8h	LC50	9,520	3,173	2,3,5
rattus norvegicus		8h	LC50	14,420	4,807	2,6
rattus norvegicus	5d	7h/d	$LOAEL_m$	4,400	1,283	1
rattus norvegicus	2w	4-5d/w;6h/d	$NOAEL_p$	4760	680	2
oryctolagus cuniculus	5d	7h/d	$NOAEL_m$	10,400	3,033	1
oryctolagus cuniculus	2w	4-5d/w;6h/d	$NOAEL_p$	1,430	204	2
cavia aperea	5d	7h/d	$NOAEL_m$	4,400	1,283	1
mammals: sub-chronic/chronic data:						
mus musculus	13w	5d/w;6h/d	$NOAEL_{p,h,m,g,r}$	714	128	2
rattus norvegicus	13w	5d/w;6h/d	$NOAEL_{p,h}$	714	128	2
			$NOAEL_g$	238	43	2
oryctolagus cuniculus	13w	5d/w;6h/d	$NOAEL_{p,m,r}$	4,760	850	2
oryctolagus cuniculus	13w	5d/w;6h/d	$LOAEL_h$	714	128	2

References:

1. Commissie voor phytopharmacie (1956), report ACT (Toxicological Advisory Center).
2. ATSDR (1989) Agency for Toxic substances and disease registry, Toxicological profile for 1,2-dichloropropane. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
3. Ware, G.W. (ed.) (1988) Reviews of environmental contamination and toxicology. Volume 104, pag 93-103. Springer-Verlag, New York.
4. World Health Organization (1986) IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans. Volume 41, Lyon, France.
5. ACT (1984) Toxicological Advisory Center, review DGMH.
6. ACGIH (1986) American Conference of Governmental Industrial Hygienists inc., Documentation of the threshold limit values and biological exposure indices, 5th edition.

1,3-DICHLOROPROPANE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus (W)	14d	4h	LC50	36,000	6,000	1

References:

1. Tunstall laboratories (1986), The toxicology of fine chemicals: the acute 4-hour inhalation LC50 of 1,3-dichloropropane in rats with cover letter dated 042586. EPA/OTS, Doc #878216428.

CIS-1,3-DICHLOROPROPENE AND TRANS-1,3-DICHLOROPROPENE *

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus (W)	14d	4h	LC50	3,310	552	1
rattus norvegicus		4h	LC50	3,270	545	3
rattus norvegicus		4h	LC50	2,700	450	3
mammals: sub-chronic/chronic data:						
mus musculus (CD1)	28d	5d/w;6h/d	$NOAEL_g$	45.4	8	3
			$NOAEL_{m,o,p}$	133	24	3
mus musculus (CD1,f)	90d	5d/w;6h/d	$NOAEL_m$	419	75	3
			$NOAEL_{g,p}$	145	26	3
mus musculus (B6C3F1)	13w	5d/w;6h/d	$NOAEL_{g,o,b}$	136	24	1
mus musculus (B6C3F1)	2y	5d/w;6h/d	$NOAEL_{g,h}$	90.8	16	3
			$NOAEL_{b,o}$	90.8	16	3
			$NOAEL_p$	22.7	4	3
mus musculus (B6C3F1)	2y	5d/w;6h/d	$NOAEL_p$	83.5	15	4
mus musculus (B6C3F1)	2y	5d/w;6h/d	$NOAEL_p$	124	22	4
rattus norvegicus (F)	28d	5d/w;6h/d	$NOAEL_{g,m}$	133	24	3
			$NOAEL_{o,p}$	133	24	3
rattus norvegicus (F)	90d	5d/w;6h/d	$NOAEL_m$	419	75	3,4
rattus norvegicus (F)			$NOAEL_g$	145	26	3
rattus norvegicus (F,f)			$NOAEL_p$	53.9	10	3
rattus norvegicus (F,m)			$NOAEL_p$	145	26	3
rattus norvegicus (F,f)	10-12w	5d/w;6h/d	$NOAEL_r$	373	67	4
rattus norvegicus (F,f)	10-12w	5d/w;6h/d	$NOAEL_{g,p}$	42	8	4
rattus norvegicus	13w	5d/w;7h/d	$NOAEL_g$	145	30	2
rattus norvegicus (F)	13w	5d/w;6h/d	$NOAEL_g$	136	24	1,3
rattus norvegicus (F)			$NOAEL_p$	45.4	8	1,3
rattus norvegicus (F,m)	13w	5d/w;6h/d	$NOAEL_p$	42	8	4
rattus norvegicus (F,f)	13w	5d/w;6h/d	$NOAEL_p$	124	22	4
rattus norvegicus	6m	5d/w;7h/d	$NOAEL_p$	4.54	1	1,2,5
rattus norvegicus (F,f)	1y	5d/w;6h/d	$NOAEL_{g,b}$	90.8	16	3
rattus norvegicus (F,f)	2y	5d/w;6h/d	$NOAEL_{g,b}$	90.8	16	3
rattus norvegicus (F,f)	2y	5d/w;6h/d	$NOAEL_p$	21	4	4
rattus norvegicus (F)	2 generations	5-7d/w;6h/d	$NOAEL_{o,p,g}$	136	24	1,3
teratogenicity studies:						
rattus norvegicus (F)		gd 6-15;6h/d	$NOAEL_t$	545	136	1,3
			$LOAEL_g$	91	23	1,3
oryctolagus cuniculus (NZW)		gd 6-18;6h/d	$NOAEL_t$	545	136	1,3
			$NOAEL_g$	91	23	1,3

*: 1,3-Dichloropropene used in studies contained 46-51% cis- and 42-53% trans-isomer and had a purity varying from

90-97%.

References:

1. IPCS (1990) International Programme on Chemical Safety, Environmental Health Criteria for 1,3-dichloropropene, 1,2-dichloropropane, DD. 1st Draft.
2. IARC (1986) International Agency for Research on Cancer, IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans, Some Halogenated Hydrocarbons and Pesticide Exposures, vol.41.
3. ACT (1989) Toxicological Advisory Center, 1,3-Dichloorpropeen, review.
4. IRIS-report 1,3-dichloropropene (last revised 01-01-91).
5. Clayton, G.D. and F.E. Clayton (eds) (1981) Patty's industrial hygiene and toxicology. Third revised edition, volume IIb.

2,3-DICHLOROPROPENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus	4h	4h	LC50	2,270	378	1

ORAL

Species	Observation	Exposure time	Criterion	Conc. (mg/kg b.w.)	Reference
mammals: acute/sub-acute data:					
rattus norvegicus			LD50	320	1,2

References:

1. ESF (1984) European Science Foundation, Assessment of the impact of the emission of certain organochlorine compounds: chlorophenols, chloropropenes and epichlorohydrin on the aquatic environment.
2. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.

ETHYLBENZENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus	4h	4h	LC50	17,400	2,900	1,2
mammals: sub-chronic/chronic data:						
mus musculus	4w	5d/w;6h/d	$NOAEL_{b,h,p}$	3,402	608	3
mus musculus (B6C3F1)	13w	5d/w;6h/d	$NOAEL_{o}$	1,075	192	5
rattus norvegicus	4w	5d/w;6h/d	$NOAEL_{h}$	1,672	299	3
rattus norvegicus (F344)	13w	5d/w;6h/d	$NOAEL_{o}$	1,075	192	5
rattus norvegicus	16w	5d/w;6h/d	$NOAEL_{p}$	2,610	466	3
rattus norvegicus (W)	16w	5d/w;6h/d	$NOAEL_{b}$	220	39	1
			$NOAEL_{p}$	1,290	230	1
rattus norvegicus	5-7m	5d/w;7h/d	$NOAEL_{g,p}$	5,420	1,129	1,2
			$NOAEL_{o}$	1,760	363	1,2
oryctolagus cuniculus	4w	5d/w;6h/d	$NOAEL_{b,h,p}$	7,004	1,251	3
cavia aperea	5-7m	5d/w;7h/d	$NOAEL_{g,p,o}$	1,740	363	1,2
teratogenicity studies:						
rattus norvegicus (CFY)		gd 7-15;24h/d	$LOAEL_{g}$	600	600	1,3,5
			$NOAEL_{t}$	2,430	2,430	1,3,5
rattus norvegicus (SD)		gd 1-19;7h/d	$NOAEL_{t}$	4,300	1,254	1,3,5
oryctolagus cuniculus (NZW)		gd 1-24;7hr/d	$NOAEL_{t}$	4,300	1,254	1,3,5

References:

1. ECETOC (1986) European Chemical Industry, Ecology & Toxicology Centre. Ethylbenzene. Joint Assessment of Commodity Chemicals (JACC).
2. ACT (1987) Toxicology Advisory Center, Ethylbenzene, review.
3. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for Ethylbenzene. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
4. ACGIH (1986) American Conference of Governmental Industrial Hygienist inc., Documentation of the threshold limit values and biological exposure indices, 5th edition.
5. Dutch expert committee for occupational standards (1992) Health-based recommended occupational exposure limit for ethylbenzene. CIP-gegevens Koninklijke Bibliotheek, Den Haag.

ETHYLENE (= ETHENE)

INHALATION

Species	Exposure time	Criterion	Conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:				
mus musculus	unspecified	LC50	$1.1x10^6$	2
plants acute/sub-acute data:				
acacia farnesiana	6h	epinasty	2,500	1
african violet	1-2d	withering of flowers	115	1
antirrhinum sp.	1h	accelerated aging of flowers	575	1
arachis hypogaea	2h	less photosynthesis (33%)	290	1
arachis hypogaea	2h	no effect	115	1
arachis hypogaea	5h	inhibition of photosynthesis	40	1
camellia japonica	1d	shedding of leaves	1,150	1
capsicum annuum l.	2d	epinasty	575	1
cattleya sp.	1h	damaging of parts of the flower	345	1
cattleya sp.	24h	accelerated aging of flowers	12	1
citron plants	2d	shedding of leaves	1,850	1
coton	5d	shedding of leaves	575	1
cucumber	5d	yellowing of fruits	345	1
dianthus caryophyllus	6h	closing of the flowerbud	115	1
dianthus caryophyllus	6h	accelerated aging of flowers	115	1
dianthus caryophyllus	16h	curling of the leaves	115-230	1
dianthus caryophyllus	2d	accelerated aging of flowers	58	1
dianthus cariophyllus	5d	20% of lifetime of the flower	20	1
fragoria var. gorella	1d	curling of leaves	1,150	1
fragoria var. gorella	14d	growth inhibition	575	1
fragoria var. gorella	21d	growth inhibition	115	1
fraxinus pennsylvanica	5h	inhibition of photosynthesis	20	1
lemon plants	1d	shedding of leaves	1,725	1
lepidium var groka	14d	growth inhibition	575	1
lepidium var groka	21d	growth inhibition (30%)	115	1

Species	Exposure time	Criterion	Conc. (mg/m^3)	Reference
lycopersicum esculentum	4h	changing in habitus	1,150	1
lycopersicum esculentum	20h	epinasty	115	1
lycopersicum esculentum	2d	epinasty	115	1
narcissus	3d	growth inhibition	4,600	1
narcissus	3d	growth inhibition	2,300	1
phaseolus vulgaris	4h	growth inhibition	115	1
phaseolus vulgaris	12h	chlorose of the eldest leaves	115	1
phaseolus vulgaris	14d	growth inhibition (30%)	115	1
pisum sativum	12h	growth inhibition (20%)	290	1
pisum sativum	48h	growth inhibition	12	1
pisum sativum	14d	growth reduction and epinasty	60	1
pisum sativum	14d	growth inhibition and epinasty	115	1
rhaphanus sativus radicula	14d	growth inhibition (30%)	115	1
rose	5d	epinasty and shedding of leaves	380	1
solanum tuberosum	16-20h	epinasty	60	1
tabacco	5h	inhibition of photosynthesis	550	1
tagetus sp.	1d	epinasty	575	1
tulipa gesneriana	8.5d	disorder in flowering	460	1
tulipa gesneriana	1h	accelerated aging of flowers	460	1
xanthium pennsylvanicum	14d	growth inhibition of the flower	1,150	1
plants: sub-chronic/chronic data:				
avena sativa L. cv Random	100d	20% less flowers per vegetable	8	1
brassica campestris	87d	reduction of number of seeds and seed-weight	150	1
lycopersicum esculentum	28d	harvest reduction	50	1
phaseolus vulgaris	75d	harvest reduction	30	1
solanum tuberosum	28d	growth reduction	27	1
solanum tuberosum	28d	growth inhibition	2,300	1
solanum tuberosum	98d	harvest reduction	20	1
symphonicarpus albus	103d	flower- and fruitabortion	50	1
triticum var nainari	90d	growth inhibition	575	1
triticum var nainari	90d	growth inhibition	115	1

References:

1. Van der Eerden L.J. (1987) Grenswaarden voor effecten van etheen op planten. Instituut voor Plantenziektenkundig Onderzoek - Dienst Landbouwkundig Onderzoek.
2. Slooff W. et al. (1991) Exploratory report Ethylene. Report no. 71041010; RIVM, Bilthoven.
3. Health Council (1984) Advies inzake gasvormige koolwaterstoffen; Advieswaarde voor de kwaliteit van de buitenlucht. Reportno.3.

HEXACHLOROBENZENE

ORAL

Species	Observation	Exposure time	Criterion	Conc. (mg/kg bw)	Reference
mammals: sub-chronic/chronic data:					
mus musculus	120w		$LOAEL_m$	6	2,3
			$LOAEL_p$	12	2,3
rattus norvegicus	19w		$NOAEL_o$	0.08	2
rattus norvegicus	12m		$NOAEL_p$	0.05	1
rattus norvegicus	15w		$NOAEL_b$	0.1	2
rattus norvegicus	15w		$NOAEL_p$	0.5	2,3
			$LOAEL_b$	0.5	2,3
rattus norvegicus	2y, 4 generations		$LOAEL_m$	8	2,3
			$LOAEL_{o,b}$	2	2,3
			$NOAEL_r$	1	2,3
rattus norvegicus	90w		$LOAEL_{m,p}$	6	2
rattus norvegicus	130w, F1 generation		$LOAEL_r$	2	2,3
			$NOAEL_p$	0.08	
rattus norvegicus	103w		$LOAEL_p$	2	2
cricetus cricetus	>1y		$NOAEL_m$	8	2,3
			$LOAEL_p$	4	2,3
sus scrofa domesticus	90d		$NOAEL_{b,p}$	0.05	2,3
macaca mulatta	60d		$LOAEL_m$	64	2

References:

1. Hesse, J.M., G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated Criteria Document Chlorobenzenes; effects. Appendix to Report no. 710401015, RIVM.
2. Agency for Toxic Substances and Disease Registry (1990) Toxicological profile for Hexachlorobenzene.
3. Directorate-General of Labour (1990) Health-based recommended occupational exposure limit for hexachlorobenzene. Dutch expert committee for occupational standards.

HEXACHLOROETHANE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus (SD)	14d	2x8h	$NOAEL_{m,p,g}$	2,500	1,667	2
mammals: sub-chronic/chronic data:						
rattus norvegicus (SD)	6w	5d/w;6h/d	$NOAEL_{m,g,p}$	150	27	2
cavia aperea (H)	6w	5d/w;6h/d	$NOAEL_{m,g,p}$	150	27	2
canis domesticus (B)	6w	5d/w;6h/d	$NOAEL_{m,g,p}$	150	27	2
teratogenicity studies:						
rattus norvegicus (SD)	9d	gd 6-16	$NOAEL_t$	2,500	456	2
		5d/w;6h/d	$NOAEL_g$	470	84	2
birds: sub-chronic/chronic data:						
coturnix coturnix	6w	5d/w;6h/d	$NOAEL_{g,p,m}$	2,500	446	4

References:

1. IARC (1979) Internationale Agency for Research on Cancer, IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans, vol.20: Some Halogenated Hydrocarbons.
2. Gesellschaft Deutscher Chemiker (1988), Beratergremium für umweltrelevante Altstoffen (BUA): Hexachlorethanen, BUA-Stoffbericht 34.
3. CEC (1990) Commission of the European Communities, Scientific Advisory Committee to examine the toxicity and ecotoxicity of chemical compounds: Environment and quality of life. Report EUR 12964 EN.
4. Weeks, M.H., R.A. Angerhofer, R. Bishop, J. Thomasino, and C.R. Pope (1979). The toxicity of hexachloroethane in laboratory animals. Am. Ind. Hyg. Assoc. **40**, (3), 187-199.

MONOCHLOROBENZENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus (f)	6h	6h	LC50	8,822	2,206	2,3
mus musculus (f)	6h	6h	LC50	7,416	1,854	3
rattus norvegicus (m)	6h	6h	LC50	13,870	3,468	2,3
rattus norvegicus (m)	6h	6h	LC50	9,192	2,298	3
mammals: sub-chronic/chronic data:						
rattus norvegicus	44d	5d/w;7h/d	$NOAEL_{p,h,b}$	936	195	2
rattus norvegicus (SD)	10w	5d/w;6h/d	$NOAEL_{p}$	234	42	1,2
rattus norvegicus (SD)	24w	5d/w;6h/d	$NOAEL_{o,h}$	351	63	2
oryctolagus cuniculus	44d	5d/w;7h/d	$NOAEL_{p,h,b}$	936	195	2
oryctolagus cuniculus	24w	5d/w;7h/d	$NOAEL_{o,h}$	351	73	2
cavia aperea	44d	5d/w;7h/d	$NOAEL_{p,h,b}$	936	195	2

References:

1. Hesse, J.M, G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated criteria document chlorobenzenes; effects. Appendix to report no. 710401015, RIVM.
2. Gesellschaft Deutscher Chemiker (1990) Beratergremium für umweltrelevante Altstoffen (BUA): Chlorbenzol. BUA-Stoffbericht 54.
3. IPCS/WHO (1991) Environmental Health Criteria 128: Chlorobenzenes other than hexachlorobenzene, Geneva.

2-MONOCHLOROTOLUENE(=o)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus	3w	5d/w;6h/d	$NOAEL_{g,p}$	2,628	469	1
teratogenicity studies:						
rattus norvegicus		gd 6-19;6h/d	$NOAEL_t$	3,100	775	1
			$NOAEL_g$	1,100	275	1

References:

1. Gesellschaft Deutscher Chemiker (1989). Beratergremium für umweltrelevante Altstoffen (BUA): Chlortoluole (Methylchlorbenzole), BUA-Stoffbericht 38.
2. IRIS-document on 2-Chlorotoluene, last revised on 02-01-90.

3-MONOCHLOROTOLUENE(=m)

No data are available concerning the toxicology and carcinogenicity of 3-monochlorotoluene. It occurs mainly as an impurity (ref.1).

References:

1. Gesellschaft Deutscher Chemiker (1989), Beratergremium für umweltrelevante Altstoffen (BUA): Chlortoluole (Methylchlorbenzole), BUA-Stoffbericht 38.

4-MONOCHLOROTOLUENE(=p)

For monochlorotoluene no suitable inhalation or oral data were found.

References:

1. Gesellschaft Deutscher Chemiker (1989), Beratergremium für umweltrelevante Altstoffen (BUA): Chlortoluole (Methylchlorbenzole), BUA-Stoffbericht 38.
2. IRPTC (1984) International Register of Potentially Toxic Chemicals, Scientific reviews of Soviet literature on toxicity and hazards of chemicals 62: Toluenes, halogenated. UNEP/IRPTC, Moscow.
3. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.

PENTACHLOROBENZENE

ORAL

Species	Observation Exposure time	Criterion	Conc. (mg/kg bw)	Reference
mammals: sub-chronic/chronic data:				
mus musculus (B6C3F1)	13w	$NOAEL_{o,p}$	5	2
rattus norvegicus	180d	$NOAEL_{r}$	6.3	1,2
		$NOAEL_{o,p}$	12.5	1,2
rattus norvegicus (F)	13w	$NOAEL_{o,p}$	1.7	2

References:

1. Hesse, J.M, G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated criteria document chlorobenzenes; effects. Appendix to report no. 710401015, RIVM.
2. IPCS/WHO (1991) Environmental Health Criteria 128: Chlorobenzenes other than hexachlorobenzene. Geneva.

PENTACHLOROETHANE

For pentachloroethane no suitable inhalation or oral data were found.

References:

1. IARC (1986) International Agency for Research on Cancer, IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans, vol.41: Some Halogenated Hydrocarbons and Pesticide Exposures.

TETRACHLOROBENZENE

ORAL

Species	Observation Exposure time	Criterion	Conc. (mg/kg bw)	Reference
mammals: sub-chronic/chronic data:				
rattus norvegicus	90d 1,2,4,5-isomer	$NOAEL_b$	0.34	1

References:

1. Hesse, J.M, G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated criteria document chlorobenzenes; effects. Appendix to report no. 710401015, RIVM.

1,1,2,2-TETRACHLOROETHANE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	8h	8h	LC50	4,550	1,517	2,6
rattus norvegicus	4h	4h	LC50	7,000	1,167	2,6
rattus norvegicus	4h	4h	LC50	3,500	583	4
rattus norvegicus	6h	6h	$LOAEL_m$	7,000	1,750	3
mammals: sub-chronic/chronic data:						
rattus norvegicus	7-11m	5d/w;3-4h/d	$NOAEL_{h,b}$	2	0.2	2
oryctolagus cuniculus	7-11m	5d/w;3-4h/d	$NOAEL_p$	10	1	2
			$NOAEL_{h,b}$	2	0.2	2

References:

1. IARC (1979) International Agency for Research on Cancer, IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, vol.20: Some Halogenated Hydrocarbons.
2. Gesellschaft Deutscher Chemiker (1989) Beratergremium für umweltrelevante Altstoffe (BUA), BUA-Stoffbericht 29: 1,1,2,2-Tetrachlorethan.
3. ATSDR (1989) Agency for Toxic Substances and Disease Registry, Toxicological Profile for 1,1,2,2-Tetrachloroethane. U.S. Public Health Service in collaboration with U.S Environmental Protection Agency (EPA).
4. Shell (1987) Toxicological data sheets, vol.21.
5. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.
6. Henschler, D. (1986) Toxikologisch-arbeitsmedizinische Begründungen von MAK-Werte. Weinheim, Deutsche Forschungsgemeinschaft.

TRICHLOROBENZENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: sub-chronic/chronic data:						
rattus norvegicus	6w	5d/w;7h/d	$LOAEL_b$	223	46.5	1,2,4
			$NOAEL_o$	223	46.5	1,2,4
rattus norvegicus (CD)	13w	5d/w;6h/d	$NOAEL_p$	100	17.9	1,2,3
rattus norvegicus (SD)	3m	5d/w;6h/d	$NOAEL_b$	22.3	4	2,4
rattus norvegicus (SD)	26w	5d/w;7h/d	$NOAEL_p$	742	155	1,2,4
oryctolagus cuniculus (NZ)	6w	5d/w;7h/d	$LOAEL_o$	223	46.5	1,2,4
oryctolagus cuniculus (NZ)	26w	5d/w;7h/d	$NOAEL_p$	742	155	1,2,4
macaca fascienularis	26w	5d/w;7h/d	$NOAEL_p$	742	155	1,2,4
canis domesticus (B)	6w	5d/w;7h/d	$NOAEL_o$	223	46.5	1,2,4

References:

1. Hesse, J.M, G.J.A. Speyers and R.D.F.M. Taalman (1991) Integrated criteria document chlorobenzenes; effects. Appendix to report no. 710401015, RIVM.
2. IPCS/WHO (1991) Environmental Health Criteria 128: Chlorobenzenes other than hexachlorobenzene. Geneva.
3. Gesellschaft Deutscher Chemiker (1988) Beratergremium für umweltrelevante Altstoffe: 1,3,5-Trichlorbenzol. BUA-Stoffbericht 16.
4. Gesellschaft Deutscher Chemiker (1987) Beratergremium für umweltrelevante Altstoffe: 1,2,4-Trichlorbenzol. BUA-Stoffbericht 17.

1,1,1-TRICHLOROETHANE

In the exploratory report on 1,1,1-trichloroethane no MPC is derived.

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
plants: acute/sub-acute data:						
Sorghum bicolor	14d	14d	$EC50_g$	48,000	48,000	6
Brassica napus	14d	14d	$EC50_g$	19,000	19,000	6
mammals: sub-chronic/chronic data:						
mus musculus	3m	5d/w;6h/d	$NOAEL_p$	5,400	967	5
			$NOAEL_m$	10,800	1,929	5
mus musculus	2y	5d/w;6h/d	$NOAEL_{p,g}$	2,700	482	3
mus musculus	2y	5d/w;6h/d	$NOAEL_m$	8,100	1,446	5
rattus norvegicus	4w	5d/w;6h/d	$LOAEL_{o,b}$	4,428	790	5
rattus norvegicus	100d	7d/w;24h/d	$NOAEL_o$	1,350	1,350	1,5
rattus norvegicus	3m	5d/w;6h/d	$NOAEL_p$	5,400	967	5
rattus norvegicus	3m	7d/w;24h/d	$NOAEL_{o,g,p,b}$	2,060	2,060	1,5
rattus norvegicus	2y	5d/w;6h/d	$NOAEL_{p,g}$	2,700	482	3,5
rattus norvegicus(f)	2y	5d/w;6h/d	$NOAEL_g$	810	145	5
			$NOAEL_m$	8,100	1,446	5
gerbil	3m	7d/w;24h/d	$NOAEL_{g,m}$	5,400	5,400	5
			$NOAEL_b$	1,134	1,134	5
gerbil	3m	7d/w;24h/d	$LOAEL_b$	380	380	1,5
oryctolagus cuniculus	3m	7d/w;24h/d	$NOAEL_{o,p,b}$	2,060	2,060	1,5
			$NOAEL_g$	750	750	1,5
oryctolagus cuniculus	6m	5d/w;7h/d	$NOAEL_{g,r}$	2,700	563	1,5
cavia aperea	3m	7d/w;24h/d	$NOAEL_{o,g,p,b}$	2,060	2,060	1,5
canis domesticus	3m	7d/w;24h/d	$NOAEL_{o,p,b}$	2,060	2,060	1,5
canis domesticus	3m	7d/w;24h/d	$NOAEL_g$	750	750	1,5
macaca mulatta	3m	7d/w;24h/d	$NOAEL_{o,g,p,b}$	2,060	2,060	1,5

References:

1. Slooff, W., P.F.H. Bont, J.A. Janus and C.H.A. Quarles van Ufford (1991) Exploratory report 1,1,1-trichloroethane, RIVM, Bilthoven.
2. WHO (1989) International Programme on Chemical Safety (IPCS) Environmental Health Criteria for 1,1,1-trichloroethane, restricted draft. Geneva, Switzerland.

3. RIVM (1991) Toxicological evaluation of 1,1,1-trichloroethane prepared by the RIVM- Toxicology Advisory Centre for the EEC-Scientific Committee on Cosmetology (unpublished). RIVM, Bilthoven, The Netherlands.
4. Nationale MAC-commissie, werkgroep van deskundigen (1981) Rapport inzake grenswaarde 1,1,1-trichloorethaan. Voorburg, The Netherlands.
5. ATSDR (1990) Agency of Toxic Substances and Disease Registry, Toxicological profile for 1,1,1-Trichloroethane. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
6. Thompson, R.S., and N.G. Carmichael (1989). 1,1,1-Trichloroethane: medium-term toxicity to carp, daphnids, and higher plants. Ecotox. Environ. Saf. 17, 172-182.

1,1,2-TRICHLOROETHANE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	6h	6h	LC50	1,980	495	2
rattus norvegicus	14d	4h	LC50	2,380	397	3
rattus norvegicus	6h	6h	LC50	7,873	1,968	2
rattus norvegicus	8h	8h	LC50	4,755	1,585	2

ORAL

Species	Observation	Exposure time	Criterion	Conc. (mg/kg b.w.)	Reference
mammals: sub-chronic/chronic data:					
mus musculus (m)	90d	drinking water	$NOAEL_{o,h}$	305	2
mus musculus (m)	90d	drinking water	$NOAEL_{b}$	4.4	2,4
mus musculus (f)	90d	drinking water	$NOAEL_{b,g,h}$	3.9	2,4
mus musculus (m)	78w		$NOAEL_{m,p}$	195	2
rattus norvegicus	90d	drinking water	NOAEL	39	4
rattus norvegicus	78w		$NOAEL_{m,p}$	92	2
			$NOAEL_{b,o}$	92	2

References:

1. IARC (1979) International Agency for Research on Cancer, IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans, vol.20.
2. ATSDR (1989) Agency for Toxic Substances and Disease Registry, Toxicological Profile for 1,1,2-Trichlorethane. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
3. Henschler, D. (1986) Toxikologisch-arbeitsmedizinische Begründungen von MAK-Werte. Weinheim, Deutsche Forschungsgemeinschaft.
4. IRIS-report 1,1,2-trichloroethane (last revised 08-01-90)

2-XYLENE (=o)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus (f)	1d	6h/d	LC50	19,988	4,997	3,4,6
rattus norvegicus		4h	LC50	27,400	4,567	7
rattus norvegicus		6h	LC50	18,835	4,709	6
mammals: sub-chronic/chronic data:						
rattus norvegicus	6w	7d/w;8h/d	$NOAEL_p$	15,225	5,075	6
rattus norvegicus	90d	7d/w;24h/d	$NOAEL_{g,h,p}$	337	337	1
cavia aperea	90d	7d/w;24h/d	$NOAEL_{g,h,p}$	337	337	1
macaca mulatta	90d	7d/w;24h/d	$NOAEL_{g,h,p}$	337	337	1
canis domesticus	90d	7d/w;24h/d	$NOAEL_{g,h,p}$	337	337	1
teratogenicity studies:						
rattus norvegicus		gd 7-14;24h/d	$NOAEL_t$	3,000	3,000	1
			$NOAEL_g$	1,500	1,500	1
oryctolagus cuniculus		gd 7-20;24h/d	$NOAEL_{t,g}$	1,000	1,000	1

References:

1. IARC (1989) International Agency for Research on Cancer, IARC monographs on the evaluation of carcinogenic risks to humans, vol.47: Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufacture and painting.
2. ACT (1990) Toxicological Advisory Centre, Xylene, review.
3. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for total Xylenes. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
4. ECETOC (1986) Joint Assessment of Commodity Chemicals, no.6: Xylenes.
5. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.
6. Directorate-General of Labour (1990) Health-based recommended occupational exposure limit for Xylene. Concept, Voorburg.
7. ACT (1987) Commission of the European Communities; Working group "dangerous substances".

3-XYLENE (=m)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	1d	6h	LC50	22,912	5,728	2,3,5
rattus norvegicus		6h	LC50	26,035	6,509	5
rattus norvegicus	2w	5d/w;6h/d	$LOAEL_b$	200	36	1
mammals: sub-chronic/chronic data:						
mus musculus	7w	5d/w;4h/d	$LOAEL_b$	6,960	829	2
teratogenicity studies:						
rattus norvegicus		gd 7-14;24h/d	$NOAEL_t$	3,000	3,000	1
			$NOAEL_{m,g}$	1,500	1,500	1
oryctolagus cuniculus		gd 7-20;24h/d	$NOAEL_{t,g}$	1,000	1,000	1

References:

1. IARC (1989) International Agency for Research on Cancer, IARC monographs on the evaluation of carcinogenic risks to humans, vol.47: Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufacture and painting.
2. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for total Xylenes. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
3. ECETOC (1986) Joint Assessment of Commodity Chemicals, no.6: Xylenes.
4. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.
5. Directorate-General of Labour (1990) Health-based recommended occupational exposure limit for Xylene. Concept, Voorburg.

4-XYLENE (=p)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus	1d	6h	LC50	16,996	4,249	2,3,5
rattus norvegicus		4h	LC50	19,793	3,299	4
rattus norvegicus	1d	4h/d	LC50	20,619	3,437	2
rattus norvegicus		6h	LC50	19,960	4,990	5
rattus norvegicus	1.5w	5d/w;6h/d	$LOAEL_b$	3,480	621	2
teratogenicity studies:						
rattus norvegicus		gd 7-16;6h/d	$NOAEL_g$	3,500	875	1,2
rattus norvegicus		gd 7-14;24h/d	$NOAEL_g$	1,500	1,500	1
			$NOAEL_t$	3,000	3,000	1
oryctolagus cuniculus		gd 7-20;24h/d	$NOAEL_{g,m}$	500	500	1
			$NOAEL_t$	1,000	1,000	1

References:

1. IARC (1989) International Agency for Research on Cancer, IARC monographs on the evaluation of carcinogenic risks to humans, vol.47: Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufacture and painting.
2. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for total Xylenes. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
3. ECETOC (1986) Joint Assessment of Commodity Chemicals, no.6: Xylenes.
4. Sax, I and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.
5. Directorate-General of Labour (1990) Health-based recommended occupational exposure limit for Xylene. Concept, Voorburg.
6. ACT (1984) Toxicological Advisory Centre, DGMH Review on p-xylene.

XYLENE-MIXTURE*

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus (f)	1d	6h/d	LC50	16,960	4,240	1,2
rattus norvegicus		4h	LC50	21,750	3,625	6
rattus norvegicus (m)	1d	4h	LC50	29,145	4,858	1,2,3,4,5
rattus norvegicus		4h	LC50	47,635	7,939	7
			$NOAEL_m$	2,523	421	1,3
rattus norvegicus	1d	4h/d	LC50	27,622	4,604	3
mammals: sub-chronic/chronic data:						
rattus norvegicus	30d	30d;24h/d	$NOAEL_o$	1,390	1,390	7
			$LOAEL_b$	1,390	1,390	7
rattus norvegicus	4w	5d/w;6h/d	$LOAEL_p$	2,610	466	3
rattus norvegicus	4w	5d/w;6h/d	$LOAEL_p$	1,001	179	3
rattus norvegicus	66d	5d/w;6h/d	$NOAEL_{p,b,h}$	≥3,500	625	2
rattus norvegicus	13w	5d/w;6h/d	$NOAEL_{p,b,h}$	3,524	629	3,7
rattus norvegicus	90d	24h/d	$NOAEL_p$	1,392	1,392	3
rattus norvegicus	110-130d	6d/w;8h/d	$LOAEL_{g,h}$	3,000	857	1
			$LOAEL_{b,p}$	3,000	857	1
rattus norvegicus	18w	5d/w;6h/d	$NOAEL_{p,b}$	1,305	233	3
rattus norvegicus	5.5m	7d/w;6h/d	$LOAEL_r$	261	65	3
canis domesticus	13w	5d/w;6h/d	$NOAEL_{p,b,h}$	3,524	629	3,4,7
gerbil	3m	30d/m;24h/d	$NOAEL_b$	696	696	3,7

*: Mixed xylene contains all three isomers and 6-15% ethylbenzene.

References:

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3. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for total Xylenes. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
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5. ACGIH (1986) American Conference of Governmental Industrial Hygienist inc., Documentation of the threshold limit values and biological exposure indices, 5th edition.
6. Sax, I. and R.J. Lewis (1989) Dangerous properties of industrial materials, 7th edition. Van Nostrand Reinhold, New York.

APPENDIX 5. Toxicity data on compounds for which a limit and/or target value is available

CONTENTS:

ACRYLONITRILE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus			LC50	300		1
rattus norvegicus			LC50	930		1
cavia aperea			LC50	990		1
mammals: sub-chronic/chronic data:						
rattus norvegicus	13w	5d/w;6h/d	$LOAEL_g$	240	43	1
rattus norvegicus	2y	5d/w;6h/d	C_{exp}	44	7.9	1
rattus norvegicus	2y	5d/w;7h/d	$LOAEL_c$	132	27.5	3
rattus norvegicus (f)	2y	5d/w;6h/d	$NOAEL_m$	44	8	3
canis domesticus	13w	5d/w;6h/d	$LOAEL_g$	240	43	1
insects: acute/sub-acute data:						
Callosobruchus chinensis		24h	LC50	435	435	6
Oryzaephilus surinamensis		24h	LC50	755	755	6
Rhizopertha dominica		24h	LC50	692	692	6
Sitophilus oryzae		24h	LC50	404	404	6
Tribolium castaneum		24h	LC50	1,054	1,054	6
Sitophilus granarius		8h	LC50	700	230	7,8
Tribolium confusum (4^{th} instar)		8h	LC50	1,900	630	7,8
Tenebroides mauretanicus		8h	LC50	2,800	930	7,8

References:

1. Ministerie van VROM, directie Lucht (1984) Criteriadocument over acrylonitril. Publicatiereeks lucht nr. 29.
2. Gezondheidsraad (1985) Advies inzake acrylonitril in de buitenlucht. Den Haag.
3. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological profile for Acrylonitrile. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
4. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.
5. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
6. Rajendran, S., and M. Muthu (1976). Toxicity of acrylonitrile to the adults of five species of stored products insects. Bulletin of Grain Technology 14, (3), 179-181.
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BENZENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus		4h	LC50	43,700	7,283	1
rattus norvegicus		7h	LC50	31,950	9,319	1
mus musculus		8h	LC50	15,000	5,000	1
plants: acute/sub-acute data:						
barley	24h	30min.	LC100	50,000		1
			LC85	25,000		1
			LC25	17,000		1
mammals: sub-chronic/chronic data:						
mus musculus	70w	5d/w;6h/d	$NOAEL_m$	960	171	1
teratogenicity studies:						
rattus norvegicus	10d	gd 6-15;7h/d	$LOAEL_r$	160	47	1
rattus norvegicus	10d	gd 6-15;6h/d	$LOAEL_r$	320	80	1
oryctolagus cuniculus	14d	gd 7-20;24h/d	$NOAEL_r$	1,000	1,000	2

References:

1. Slooff W. (ed) (1988) Integrated criteriadocument benzene. Report no. 758476003, RIVM.
2. ATSDR (1991) Agency for Toxic Substances and Disease Registry, Update of Toxicological profile for benzene. Draft version. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
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5. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
6. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.

1,2-DICHLOROETHANE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus		6h	LC50	5,100	1,275	1
rattus norvegicus		6h	LC50	6,666	1,667	1
mus musculus		6h	LC50	1,061	265	1
mammals: sub-chronic/chronic data:						
rattus norvegicus	78w	oral	C_{exp}	47 mg/kg bw		1
rattus norvegicus	4m	5d/w;7h/d	$NOAEL_g$	420	88	1,4
rattus norvegicus (f)	4m	6d/w;4h/d	$LOAEL_r$	15	2	1,4
rattus norvegicus	176d	5(-7)d/w;6h/d	$NOAEL_r$	101	18	1,4
rattus norvegicus (f)	9m	6d/w;4h/d	$LOAEL_r$	57	8	1,4
cavia aperea	4m	5d/w;7h/d	$LOAEL_m$	420	88	1,4

References:

1. Ministerie van VROM, directie Lucht (1984) Criteriadocument over 1,2-dichloorethaan. Publicatiereeks lucht nr. 30.
2. Gezondheidsraad (1985) 1,2-dichloorethaan; toetsing van een criteriadocument. Den Haag.
3. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.
4. IPCS/WHO (1987) Environmental Health Criteria 62: 1,2-dichloroethane, Geneva.
5. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.

DICHLOROMETHANE (= METHYLENE CHLORIDE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: sub-chronic/chronic data:						
rattus norvegicus	2y	5d/w;6h/d	$NOAEL_p$	173	31	1,6
rattus norvegicus	2y	5d/w;6h/d	$NOAEL_p$	714	128	5
rattus norvegicus	2y	5d/w;6h/d	$LOAEL_m$	12,495	2,231	5
mus musculus	102w	5d/w;6h/d	$LOAEL_{g,m}$	6,940	1,239	1
gerbil	3m	7d/w;24h/d	$LOAEL_b$	750	750	5
gerbil	3m	7d/w:24h/d	$LOAEL_p$	750	750	5
canis domesticus	14w	7d/w;24h/d	$LOAEL_m$	3,570	3,570	5

References:

1. Slooff W. and J.P.M. Ros (eds) (1990) Basisdocument dichloormethaan (en advies Gezondheidsraad). Rapport nr.3: serie basisdocumenten; Publicatiereeks milieubeheer. RIVM, Bilthoven.
2. Van Apeldoorn M.E. et al. (1988) Integrated criteria document dichloromethane - effects. Appendix to Report nr 758473009. RIVM, Bilthoven.
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4. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.
5. ATSDR (1991) Agency for Toxic Substances and Disease Registry, Toxicological profile for methylene chloride, draft version. U.S. Public Health Service in collaboration with U.S Environmental Protection Agency (EPA).
6. Fawell J.F. et al. (1991) Organochlorine compounds in drinking water: their origin and maximum admissible concentrations. ER contract No. B6612/90/007751.

ETHYLENE OXIDE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus muscuslus		4h	LC50	1,500	250	1
canis domesticus		4h	LC50	1,730	288	1
rattus norvegicus		4h	LC50	2,630	438	1
mammals: sub-chronic/chronic data:						
mus musculus	26w	5d/w;6h/d	$NOAEL_{m,g}$	180	32.1	1
mus musculus	2y	5d/w;6h/d	$LOAEL_c$	91.5		4,5,6
mus musculus	2y	5d/w;6h/d	$NOAEL_m$	183	33	4
rattus norvegicus	26w	5d/w;7h/d	$NOAEL_{m,g}$	90	18.8	1
rattus norvegicus	26w	5d/w;6h/d	$NOAEL_{m,g}$	180	32.1	1
rattus norvegicus F	2y	5d/w;6h/d	$LOAEL_c$	60.4		7
rattus norvegicus F344	25m	5d/w;6h/d	C_{exp}	17.8		1
cavia aperea	25-32w	5d/w;7h/d	$NOAEL_{m,g}$	200	41.7	1
oryctolagus cuniculus	25-32w	5d/w;7h/d	$NOAEL_{m,g}$	200	41.7	1
macaca mulatta	25-32w	5d/w;7h/d	$NOAEL_{m,g}$	200	41.7	1
macaca mulatta	2y	5d/w;7h/d	$NOAEL_m$	183	38	4
macaca mulatta	2y	5d/w;7h/d	$LOAEL_r$	92	19	4

References:

1. Ministerie van VROM, directie Lucht (1984) Criteriadocument over ethyleenoxide. Publicatiereeks lucht nr. 55.
2. Gezondheidsraad (1986) Ethyleenoxide en styreen; toetsing van criteriadocumenten.
3. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
4. ATSDR (1990) Agency for Toxic Substances and Disease Registry, Toxicological Profile for Ethylene oxide. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA)
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STYRENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus		4	LC50	11,340	1,890	1
rattus norvegicus		4	LC50	11,800	1,967	1
rattus norvegicus		6	LC50	19,396	4,849	1
humans: sub-chronic/chronic data:						
humans	long-term	5d/w;8h/d	$LOAEL_p$	84	20	1
mammals: sub-chronic/chronic data:						
rattus norvegicus	7w	5d/w;8h/d	$NOAEL_g$	2,440	581	1
rattus norvegicus	13w	5d/w;7h/d	$NOAEL_p$	565	118	5
rattus norvegicus	6m	5d/w;8h/d	$LOAEL_g$	6,000	1,429	1
cavia aperea	6m	5d/w;8h/d	$LOAEL_{m,g}$	6,000	1,429	1
cavia aperea	27w	5d/w;7h/d	$NOAEL_{m,g}$	3,000	625	1
teratogenicity studies:						
rattus norvegicus	11d	gd 6-16;7h/d	$LOAEL_r$	1,260	368	1
cricetus cricetus	11d	gd 6-16;6h/d	$NOAEL_r$	3,150	788	1
oryctolagus cuniculus	13d	gd 6-18;7h/d	$NOAEL_r$	1,260	368	1
mus musculus	11d	gd 6-16;6h/d	$LOAEL_r$	2,100	525	1
mus musculus	11d	gd 6-16;6h/d	$LOAEL_r$	1,050	263	1

References:

1. Ministerie van VROM, directie Lucht (1986) Criteriadocument over styreen. Publicatiereeks lucht nr. 57.
2. Gezondheidsraad (1986) Ethyleenoxide en styreen; toetsing van criteriadocumenten.
3. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
4. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.
5. Gesellschaft Deutscher Chemiker (1990) Beratergremium für umweltrelevant Altstoffe; Styrol. BAU-Stoffbericht 48. VCH, Weinheim.
6. The Styrene Information and Research Center (1990) Thesirc Review; a critical review of the reproductive and developmental data on styrene. vol.1, no.2.

TETRACHLOROETHENE (= PER)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
humans: acute/sub-acute data:						
humans	4d	8h/d	$NOAEL_{cns*}$	135	32	1
mammals: acute/sub-acute data:						
mus musculus		4h	LC50	35,000	5,833	1
mus musculus		6h	LC50	20,200	5,050	1
mus musculus		12h	LC50	25,100	12,550	1
mus musculus	14d	5d/w;6h/d	$NOAEL_p$	2,933	524	5
mus musculus	14d	6h/d	$NOAEL_p$	2,760	690	5
mus musculus	14d	5d/w;6h/d	$NOAEL_b$	6,038	1,078	5
mus musculus	21d	6h/d	$LOAEL_p$	2,760	690	5
rattus norvegicus		6h	LC50	27,800	6,950	1
rattus norvegicus	14d	5d/w;6h/d	$NOAEL_b$	6,038	1,078	5
rattus norvegicus	14d	6h/d	$NOAEL_p$	2,760	690	5
rattus norvegicus	21d	6h/d	$NOAEL_p$	2,760	690	5
mammals: sub-chronic/chronic data:						
mus musculus	28d	6h/d	$NOAEL_p$	2,760	690	5
mus musculus	30d	24h/d	$LOAEL_o$	62	62	5
mus musculus	13w	5d/w;6h/d	$NOAEL_p$	690	123	5
mus musculus	13w	5d/w;6h/d	$NOAEL_m$	5,520	986	5
mus musculus	103w	5d/w;6h/d	$LOAEL_{m,p}$	690	123	5
rattus norvegicus	28d	6h/d	$NOAEL_p$	2,760	690	5
rattus norvegicus	4w	7d/w;6h/d	$NOAEL_p$	2,760	690	5
rattus norvegicus	13w	5d/w;6h/d	$NOAEL_m$	5,520	986	5
rattus norvegicus	13w	5d/w;6h/d	$LOAEL_p$	1,380	246	5
rattus norvegicus	103w	5d/w;6h/d	$LOAEL_m$	1,380	246	5
gerbil	3m	24h/d	$LOAEL_b$	414	414	5

*: central nerve system

References:

1. Ministerie van VROM, directie Lucht (1984) Criteriadocument over tetrachlooretheen. Publicatiereeks lucht nr. 32.
2. Gezondheidsraad (1985) Advies inzake trichlooretheen en tetrachlooretheen in de buitenlucht op basis van criteriadocumenten over deze stoffen. Den Haag.
3. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
4. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.
5. ATSDR (1991) Agency for Toxic Substances and Disease Registry, Update of the toxicological profile for tetrachloroethylene, Draft version. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).

TETRACHLOROMETHANE (= CARBONTETRACHLORIDE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus (f)		6h	LC50	46,099	11,525	1
mus musculus		7h	LC50	50,000	14,583	1
mammals: sub-chronic/chronic data:						
rattus norvegicus	90d	7d/w;24h/d	$NOAEL_{p,m}$	6.1	6.1	1
cavia aperea	90d	7d/w;24h/d	$NOAEL_{p,m}$	6.1	6.1	1,4

References:

1. Ministerie van VROM, directie Lucht (1986) Criteriadocument over tetrachloormethaan. Publicatiereeks lucht nr. 58.
2. Gezondheidsraad (1987) Chloroform en tetrachloormethaan toetsing van een criteriadocument. Den Haag.
3. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
4. ATSDR (1989) Agency for Toxic Substances and Disease Registry, Toxicological Profile for Carbon Tetrachloride. U.S. Public Health Service in collaboration with U.S Environmental Protection Agency (EPA).

TOLUENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus		4h	LC50	33,200	5,533	2
mus musculus		6h	LC50	26,100	6,525	2
mus musculus		7h	LC50	46,000	13,417	2
mus musculus	20d	7d/w;6h/d	$NOAEL_g$	≥3,800	≥950	2
humans: sub-chronic/chronic data:						
human		7h	$NOAEL_p$	150		1,2,3,4,5
mammals: sub-chronic/chronic data:						
rattus norvegicus	2y	5d/w;6h/d	$NOAEL_{p,r}$	1,128	201	2,7
mus musculus	14w	5d/w;6.5h/d	$NOAEL_m$	376	73	7

References:

1. Slooff, W and P.J. Blokzijl (ed.) (1988) Integrated Criteria Document Toluene. RIVM, Bilthoven.
2. Slooff, W and P.J. Blokzijl (ed.) (1987) Integrated Criteria Document Toluene, effects. RIVM, Bilthoven.
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TRICHLOROETHENE

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus		4h	LC50	45,400	7,567	1
mus musculus		6h	LC50	31,627	7,907	1
rattus norvegicus		6h	LC50	31,957	7,989	1
mammals: sub-chronic/chronic data:						
rattus norvgicus	90d	7d/w;24h/d	$NOAEL_g$	189	189	1
rattus norvegicus (f)	104w	5d/w;7h/d	$NOAEL_p$	540	113	5
teratogenicity studies:						
mus musculus	10d	gd 6-15;7h/d	$NOAEL_r$	≥1,620	≥473	1
rattus norvegicus	21d	gd 0-20;6h/d	$NOAEL_r$	≥2,700	≥675	1

References:

1. Ministerie van VROM, directie Lucht (1984) Criteriadocument over trichlooretheen. Publicatiereeks lucht nr. 33.
2. Gezondheidsraad (1985) Advies inzake trichlooretheen en tetrachlooretheen in de buitenlucht op basis van criteriadocumenten over deze stoffen. Den Haag.
3. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
4. World Health Organization (1987) Air Quality Guidelines for Europe. Copenhagen.
5. ATSDR (1991) Agency for Toxic Substances and Disease Registry, Update of toxicological profile for trichloroethylene, Draft version. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).

TRICHLOROMETHANE (= CHLOROFORM)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
mus musculus		6h	LC50	6,150	1,534	1
mammals: sub-chronic/chronic data:						
rattus norvegicus	6m	5d/w;4h/d	$NOAEL_{p,h,b}$	110	13	1
rattus norvegicus	6m	5d/w;7h/d	$NOAEL_{m}$	220	46	1
canis domesticus	6m	5d/w;7h/d	$NOAEL_{p,m}$	122	25	4
teratogenicity studies:						
rattus norvegicus	10d	gd 7-16;7d/w	$LOAEL_{r}$	147	147	4
rattus norvegicus	10d	gd 6-15;7h/d	$LOAEL_{r}$	146	43	1

References:

1. Ministerie van VROM, directie Lucht (1986) Criteriadocument over chloroform. Publicatiereeks lucht nr. 54.
2. Gezondheidsraad (1987) Chloroform en tetrachloormethaan, toetsing van een criteriadocument. Den Haag.
3. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.
4. ATSDR (1991) Agency for Toxic Sunstances and Disease Registry, Update for toxicological profile for chloroform, Draft version. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).

VINYLCHLORIDE (= CHLOROETHENE)

INHALATION

Species	Observation	Exposure time	Criterion	Conc. (mg/m^3)	Corr.conc. (mg/m^3)	Reference
mammals: acute/sub-acute data:						
rattus norvegicus		2h	LC50	390,000	32,500	1
mus musculus		2h	LC50	293,750	24,479	1
cavia aperea		2h	LC50	595,000	49,583	1
oryctolagus cuniculus		2h	LC50	595,000	49,583	1
mammals: sub-chronic/chronic data:						
rattus norvegicus	52w	5d/w;4h/d	$LOAEL_c$	26		1
rattus norvegicus	6m	6d/w;6h/d	$NOAEL_r$	26	6	4
mus musculus	6m	5d/w;6h/d	$LOAEL_m$	130	23	4
mus musculus	6m	5d/w;6h/d	$NOAEL_m$	520	93	4
teratogenicity studies:						
rattus norvegicus		gd 6-15; 7h/d	$NOAEL_r$	6,500	1,899	1
mus musculus		gd 6-15; 7h/d	$NOAEL_r$	1,300	379	1
oryctolagus cuniculus		gd 6-18; 7h/d	$NOAEL_r$	6,500	1,899	1

References:

1. Ministerie van VROM, directie Lucht (1984) Criteriadocument over vinylchloride. Publicatiereeks lucht nr. 34.
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4. ATSDR (1991) Agency for Toxic Substances and Disease Registry, Update of toxicological profile for Vinylchloride, Draft version for public comment. U.S. Public Health Service in collaboration with U.S. Environmental Protection Agency (EPA).
5. World Health Organization, International Agency for Research on Cancer (1987) IARC monographs on the evaluation of carcinogenic risks to humans. Supplement 7, Lijon.

APPENDIX 6. Peak values for volatile compounds

compound	peak value ($\mu g/m^3$) limit value	remark
ethylene	300	1 hour average, 99.99 percentile
	30	24 hour average, 99.7 percentile
trichloroethene	300	1 hour average, 98 percentile
tetrachloroethene	8,300	1 hour average, 98 percentile

Reference:
J. de Bruijn (1991) Stoffen en normen: overzicht van belangrijke stoffen en normen in het milieubeleid 1991-1992. Ministerie van VROM (in Dutch).