FROM TOXIC RELEASES TO DAMAGES ON HUMAN HEALTH: A METHOD FOR LIFE CYCLE IMPACT ASSESSMENT, WITH A CASE STUDY ON DOMESTIC RAINWATER USE

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ABSTRACT

Life Cycle Assessment (LCA) is a tool developed to evaluate the environmental impact of a product or a system. After a decade of research in the LCA field, significant progress has been achieved but methodologies for the assessment of toxicological impacts on human health are still in the development phase. This dissertation contributes to the research required in this field. More specifically, its main **objective** is to develop a Life Cycle Impact Assessment (LCIA) procedure for human health respecting the guidance developed under the umbrella of the Society of Environmental Toxicology and Chemistry (SETAC). This means that we aim to implement an original procedure to quantify the potential carcinogenic and noncarcinogenic effects of toxic releases on human health (chapters 2 and 3), and to develop a new method describing the fate of atmospheric releases and the resulting exposure on humans (chapter 4). A framework summarized in figure 5.1 is also proposed to combine the effect assessment with the fate and exposure assessment, in order to derive a so-called human damage factor (chapter 5). A set of heavy metals (cadmium, chromium(VI), chromium(III), copper, methylmercury, beryllium, lead and inorganic arsenic) and of criteria air pollutants (CO, SO_2, NO_X and fine particles) is chosen for a full application of the procedure developed in this dissertation. The use of this procedure to the Cycleaupe case study is also part of the objectives of this research. This study aims to determine whether systems using rainwater or reducing water consumption are "friendlier" from an environmental perspective than conventional toilet flushing (chapter 6).

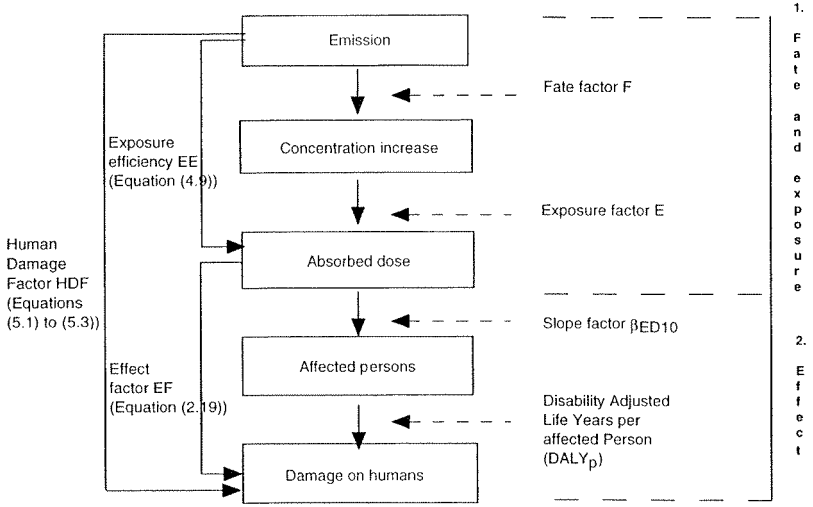

Figure 5.1 Overview of the framework proposed in this thesis for assessing the damage induced on human health by a toxic released into air.

In **chapters 2 and 3**, a new paradigm based on the effect dose ED_{10h} is derived from the Risk Assessment concept of benchmark dose. It is proposed and explored for the first time in LCIA. The ED_{10h} is defined as the best estimate of the dose which induces a 10% added risk over background for humans. Carcinogenic and noncarcinogenic risks towards humans are characterized by drawing a straight line from the ED_{10h} down to the origin of the dose-response function. The slope of this straight line is called the slope factor and is denoted βED_{10}. The linear dose-response function without threshold, which is assumed in this ED_{10}-approach, is discussed. The ED_{10h} is calculated for chemicals with bioassay data available in the Integrated Risk Information Service (IRIS) database provided by the US Environmental Protection Agency (US EPA). New correlations between the ED_{10h} and the more widely available tumor dose TD_{50a} (for carcinogenic effects) and the No Observable Adverse Effect Level NOAEL (for noncarcinogenic effects) are determined. They are applied to quantify the slope factor of more than 900 chemicals.
A weighting of the different health outcomes associated with chemicals is proposed, based upon the Disability Adjusted Life Years per affected person ($DALY_p$) concept. For carcinogenic endpoints, the $DALY_p$ is calculated for different types of tumors, using data reported in the literature. This shows that all cancers have more or less the same severity and an average $DALY_p$ of 11.1 years of life lost per affected person is derived. For noncarcinogenic effects, a simplified classification of the adverse effects into three categories is chosen and a $DALY_p$ of 11.1, 1.1 and 0.11 years of life lost per affected person is respectively assigned to each of the three categories.
Finally, the slope factor βED_{10} and the $DALY_p$ for each substance are combined together in an original way to derive its effect factor. This effect factor is expressed in years of life lost per absorbed mass. Appendix 1.1 summarizes the effect factors calculated for more than 900 toxic releases. Effect factors for carcinogenic outcomes range from $1.3 \cdot 10^{-9}$ for cinnamyl anthranilate up to $3.4 \cdot 10^{-1}$ [yr lost / mg absorbed] for 2,3,7,8-tetrachlorodibenzo-p-dioxin. Effect factors for noncarcinogenic endpoints range from $4.2 \cdot 10^{-12}$ for 1-Chloro-1,1-difluoroethane to $1.4 \cdot 10^{-3}$ [yr lost / mg absorbed] for beryllium.

In **chapter 4**, a semi-empirical approach is developed to evaluate the fate and exposure for atmospheric releases of metals, carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_X) and fine particles. For that purpose, we apply for the first time in LCA the concept of exposure efficiency, which is defined as the ratio between the dose absorbed by the population and the emission inducing that absorption. Three types of exposure efficiency are defined for a world release into air of a given compound. A specific exposure efficiency is directly based on the rural and urban concentrations inhaled by humans. A continental exposure efficiency is defined by considering an uniform world continental concentration over urban and rural inhabited regions (marine and desert regions are excluded). A global exposure efficiency is similarly defined from the global world concentration of a substance.
Exposure efficiencies are calculated for fine particles, CO, NO_X and SO_2. The specific

exposure efficiency ranges from $3.9 \cdot 10^{-6}$ to $2.4 \cdot 10^{-5}$ [mg absorbed / mg emitted], demonstrating that only a very small fraction of an air release is inhaled by humans. The exposure efficiency for metals after inhalation is assumed to be equal to the exposure efficiency for fine particles, since airborne metals are attached to particulate matter. If atmospheric deposition on an agricultural soil occurs, humans can be exposed through a transfer into food products. A first evaluation of this transfer indicates that it can increase the exposure efficiency of metals released into air by a factor 5 up to 70. Specific exposure efficiencies are selected in this thesis to describe the fate and exposure of atmospheric releases. We show for the first time that specific exposure efficiencies are higher by a factor 3 than continental exposure efficiencies, indicating that the use of one-box continental models tend to underestimate the exposure efficiency that can be expected in the real world. This is due to the fact that higher emissions occur in highly populated regions. As a first approximation, the factor 3 could be used as a corrective factor to derive the specific exposure efficiency from the exposure efficiency predicted by one-box continental models.

In **chapter 5**, exposure efficiencies presented in chapter 4 and effect factors presented in chapters 2 and 3 are multiplied to derive the so-called Human Damage Factors (HDF). The damage factors are expressed in years of life lost per emitted mass. Using that factor, the emission of a substance can be converted into its potential damage induced on humans.
The damage factors are calculated for NO_X, SO_2, CO and fine particles, as well as for the selected set of metals released into air or into agricultural soils (see appendix 1.2 for the summarized results). When the transfer into food products is not accounted for, the damage factors for the studied metals range from $1.7 \cdot 10^{-11}$ for chromium(VI) up to $1.3 \cdot 10^{-8}$ [yr lost / mg emitted] for beryllium. Lead has the highest damage factor ($1.9 \cdot 10^{-8}$ [yr lost / mg emitted]) if transfer into food products is considered. Damage factors ranging from $2.7 \cdot 10^{-10}$ to $6.6 \cdot 10^{-10}$ [yr lost / mg emitted] are found for NO_X, SO_2 and fine particles, while carbon monoxide is characterized by a damage factor 10^3-folds lower. Per emitted mass, metals inhaled by humans induce damages of the same order of magnitude than NO_X, SO_2 and fine particles; when atmospheric deposition on agricultural soils and its subsequent transfer into food are accounted for, metals present higher damage factors. An indirect validation of the damage factors is presented for SO_2, NO_X, CO, fine particles and some metals, by applying their damage factors to their total emissions over Switzerland and Europe. The evaluated damages are plausible and in accordance with results reported in other studies.

In **chapter 6**, a Life Cycle Analysis is performed to compare five scenarios for toilets flushing. This LCA is the first one carried out on the whole water cycle, including both the water supply and the wastewater treatment. The drinking water supply system, the rainwater recuperation system and the wastewater treatment system are included in the system

boundaries. Results demonstrate that economic toilets (3.5 [l/flushing]) lead to a significant reduction of the energy requirements compared to conventional toilets (9 [l/flushing]). A conventional water supply and a rainwater recuperation with a storage tank of 10 m^3 are characterized by similar energy consumption. A rainwater storage tank of 20 m^3, designed to be completely independent of the conventional water supply system, is energetically disadvantageous. Calorific losses, linked to the temperature increase of flushing water within the house, have a significant contribution to the energy requirement. The advantage of economic toilets is confirmed when looking at the inventory emissions. An initial LCIA was performed using the critical surface-time CST95 method of Jolliet and Crettaz [1997]. It showed that the conventional scenario using economic toilets (CONVeco) is the most advantageous for all impact classes. When applying the human damage factors developed in this thesis (see chapter 5), the conventional scenario (CONVeco) is still characterized by lower impacts on humans than the recuperation scenario (REC10eco). However, the substances having the major effect on human health differ from those found with the CST95 method; reasons for that change are discussed.

Key worlds:

Life Cycle Impact Assessment, human health, toxic releases, fate and exposure, exposure efficiency, carcinogenic and noncarcinogenic effects, slope factor, human damage factor, water management, rainwater recuperation.

RESUME

L'Analyse de Cycle de Vie (ACV) permet d'évaluer l'impact environnemental d'un produit ou d'un système. Après plusieurs années de recherche dans le domaine des ACV, des progrès significatifs ont été réalisés. Cependant, les méthodologies d'évaluation de l'impact toxicologique des substances toxiques sur la santé humaine sont toujours en phase de développement. La présente thèse contribue à la recherche supplémentaire requise dans ce domaine. Plus spécifiquement, son objectif principal est de développer une méthode d'évaluation de l'impact environnemental pour la santé humaine. Ladite méthode doit respecter la structure développée par la société européenne de toxicologie et de chimie (SETAC). Cette thèse vise donc à mettre en place une procédure permettant de quantifier les effets cancérigènes et non cancérigènes des substances chimiques sur la santé humaine (chapitres 2 et 3). Une méthode décrivant le devenir des substances émises dans l'air et l'exposition en résultant sur les humains est également proposée (chapitre 4). Un cadre d'analyse (voir figure 5.1 ci-dessus) est proposé afin de combiner l'évaluation de l'effet toxique, avec l'évaluation du devenir des substances. Un facteur de dommage sur l'homme peut alors être déduit (chapitre 5). Un ensemble de métaux lourds (cadmium, chrome(VI), chrome(III), cuivre, méthyle-mercure, béryllium, plomb et arsenic inorganique) et de polluants atmosphériques (CO, SO_2, NO_X et particules fines) est choisi pour une application complète de la méthode développée dans cette thèse. La méthode est testée à l'étude dénommée "Cycleaupe". Cette étude vise à déterminer si les systèmes utilisant l'eau pluviale ou réduisant la consommation d'eau induisent une charge environnementale moindre qu'un rinçage conventionnel des toilettes (chapitre 6).

Dans les **chapitres 2 et 3**, une nouvelle approche, basée sur la dose d'effet notée ED_{10h}, est dérivée du concept de "benchmark dose" développé en Evaluation du Risque. Elle est proposée et explorée pour la première fois en ACV dans cette thèse. L'ED_{10h} est définie comme la meilleure estimation de la dose induisant un risque pour les hommes de 10% par rapport au niveau de base. Le risque cancérigène et non cancérigène pour les hommes se caractérise en traçant une ligne droite à partir de ED_{10h} vers l'origine de la fonction "dose-réponse". La pente de cette droite est appelée le facteur de pente et est dénoté $\beta ED10$. La fonction "dose-réponse" linéaire et sans seuil, qui est supposée dans l'approche proposée, est discutée. L'ED_{10h} est calculée pour des substances toxiques ayant des données d'essai sur animaux disponibles dans la base de données IRIS (Integrated Risk Information Service database) de l'Agence Américaine de l'Environnement (US EPA). Les corrélations entre l'ED_{10h} et les paramètres plus largement disponibles comme la dose de tumeur TD_{50a} (pour des effets cancérigènes) et la dose non associée à un effet nocif notable NOAEL (pour des effets non cancérigènes) sont déterminées. Elles sont appliquées afin de quantifier le facteur de pente de plus de 900 substances.
Une pondération des différents types d'effets nocifs sur la santé humaine est proposée en se

basant sur le concept des années de vie perdue par personne affectée ($DALY_p$). Pour les effets cancérigènes, les $DALY_p$ sont calculés pour différents types de tumeur, en utilisant des données rapportées en littérature. Il ressort que tous les cancers ont plus ou moins la même sévérité et une valeur moyenne de 11.1 ans de vie perdue par personne affectée est dérivée. Pour les effets non cancérigènes, une classification simplifiée en trois catégories est proposée et une $DALY_p$ de 11.1, 1,1 et 0,11 ans de vie perdue par personne affectée est respectivement attribuée à chacune des trois catégories.
Finalement, le facteur de pente β_{ED10} et la $DALY_p$ pour une substance donnée sont combinés afin de dériver son facteur d'effet. Ce facteur d'effet est exprimé en années de vie perdue par masse absorbée. L'annexe 1.1 résume les facteurs d'effets calculés pour plus de 900 substances toxiques. Les facteurs d'effets pour les effets cancérigènes vont de $1.3 \cdot 10^{-9}$ pour l'anthranilate cinnamylique à $3.4 \cdot 10^{-1}$ [année perdue / mg absorbé] pour la 2,3,7,8-tetrachlorodibenzo-p-dioxine. Les facteurs d'effets pour les effets non cancérigènes vont de $4.2 \cdot 10^{-12}$ pour le 1-Chloro-1,1-difluoroethane à $1.4 \cdot 10^{-3}$ [année perdue / mg absorbé] pour le béryllium.

En **chapitre 4**, une approche semi-empirique est développée afin d'évaluer le devenir et l'exposition pour des émissions atmosphériques de métaux lourds, de monoxyde de carbone (CO), de dioxyde de souffre (SO_2), d'oxyde d'azote (NO_X) et de particules fines. Pour ce faire, le concept d'efficacité d'exposition est utilisé. L'efficacité d'exposition est définie comme le rapport entre la dose absorbée par la population et l'émission induisant cette absorption. Trois types d'efficacité d'exposition sont définis pour une émission atmosphérique mondiale d'une substance donnée. Une efficacité spécifique d'exposition, directement basée sur les concentrations rurales et urbaines inhalées par les hommes, est définie. Une efficacité d'exposition continentale est également définie, en considérant la concentration continentale mondiale pour les régions habitées (les régions marines et désertiques sont exclues). Une efficacité d'exposition globale est définie de façon similaire à partir de la concentration globale mondiale d'une substance. L'efficacité d'exposition est calculée pour les particules fines, le CO, NO_X et SO_2. L'efficacité d'exposition spécifique présente des valeurs allant de $3.9 \cdot 10^{-6}$ à $2.4 \cdot 10^{-5}$ [mg absorbé /mg émis], indiquant que seulement une très petite fraction d'une émission atmosphérique est inhalée par les humains. L'efficacité d'exposition pour les métaux après inhalation est supposée égale à l'efficacité d'exposition des particules fines, étant donné que les métaux dans l'air sont liés aux particules. Si une déposition atmosphérique sur un sol agricole a lieu, les hommes peuvent être exposés suite à un transfert dans des produits alimentaires. Une première évaluation de ce transfert indique qu'il peut augmenter l'efficacité d'exposition des métaux émis dans l'air d'un facteur 5 à 70. L'efficacité d'exposition spécifique est choisie dans cette thèse pour décrire le devenir et l'exposition des émissions atmosphériques. Elle est supérieure d'un facteur 3 à l'efficacité d'exposition continentale, indiquant que l'utilisation de modèles continentaux à un compartiment tend à sous-estimer l'efficacité d'exposition qui peut avoir lieu dans la réalité. Ceci est dû au fait que des émissions plus élevées ont lieu dans les régions les plus peuplées. Comme première approximation, le facteur 3 pourrait être utilisé

comme facteur correctif, afin de dériver l'efficacité d'exposition spécifique à partir de l'efficacité prédite par les modèles continentaux à un compartiment.

Dans le **chapitre 5**, l'efficacité d'exposition déterminée au chapitre 4 et les facteurs d'effet déterminés aux chapitres 2 et 3 sont multipliés afin de déduire les facteurs de dommage sur l'homme (HDF). Ces facteurs de dommage sont exprimés en années de vie perdue par masse émise. En utilisant ces facteurs, l'émission d'une substance peut être convertie en dommage potentiel qu'elle induit sur les humains.
Les facteurs de dommage sont calculés pour NO_X, SO_2, CO et les particules fines, ainsi que pour les métaux émis dans l'air ou dans un sol agricole (voir annexe 1.2 pour le résumé des résultats). Lorsque le transfert dans les produits alimentaires n'est pas considéré, les facteurs de dommage pour les métaux étudiés présentent des valeurs allant de $1.7 \cdot 10^{-11}$ pour chromium(VI) à $1.3 \cdot 10^{-8}$ [année perdue / mg émis] pour le béryllium. Le plomb a le facteur de dommage le plus élevé ($1.9 \cdot 10^{-8}$ [année perdue / mg émis]) si le transfert dans des produits alimentaires est considéré. Des facteurs de dommage allant de $2.7 \cdot 10^{-10}$ à $6.6 \cdot 10^{-10}$ [année perdue / mg émis] sont obtenus pour NO_X, SO_2 et les particules fines, alors que le monoxyde de carbone est caractérisé par un facteur de dommage 10^3 inférieur. Par masse émise, les métaux inhalés par les hommes induisent des dommages du même ordre de grandeur que le NO_X, SO_2 et les particules fines; quand la déposition atmosphérique sur les sols agricoles et le transfert ultérieur dans la nourriture sont considérés, les métaux présentent des facteurs plus élevés. Une validation indirecte des facteurs de dommage est présentée pour le SO_2, NO_X, CO, les particules fines et quelques métaux, en appliquant leur facteur de dommage à leurs émissions totales ayant lieu en Suisse et en Europe. Les dommages évalués sont plausibles et en accord avec ceux rapportés dans d'autres études.

Dans le **chapitre 6**, une Analyse de Cycle de Vie est entreprise pour comparer cinq scénarios de rinçage des toilettes. Le système d'approvisionnement en eau potable, le système de récupération d'eau pluviale et le système de traitement des eaux usées sont inclus dans les limites de système. Les résultats démontrent que des toilettes économiques (3,5 [l/rinçage]) permettent une réduction significative des besoins en énergie, comparativement à des toilettes conventionnelles (9 [l/ rinçage]). Un approvisionnement conventionnel en eau et une récupération de l'eau pluviale à l'aide d'une citerne de 10 m^3 ont des besoins en énergie similaires. Une citerne de stockage de l'eau pluviale de 20 m^3, conçue afin d'être complètement indépendant du système d'approvisionnement conventionnel d'eau, est désavantageuse d'un point de vue énergétique. Les pertes calorifiques, liées au réchauffement de l'eau de rinçage dans la maison, ont une contribution significative au besoin en énergie. Les avantages des toilettes économiques sont confirmés en considérant les émissions de l'inventaire. Une première évaluation de l'impact a été exécutée en utilisant la méthode des surface-temps critique (CST95) développée par Jolliet et Crettaz [1997]. Elle

indique que le scénario conventionnel utilisant des toilettes économiques (CONVeco) est le plus avantageux, pour toutes les classes d'impact. En appliquant les facteurs de dommage sur l'homme développés dans cette thèse (voir chapitre 5), le scénario conventionnel (CONVeco) a toujours un impact inférieur sur la toxicité humaine comparativement au scénario de récupération (REC10eco). Cependant, les substances ayant l'effet principal sur la santé humaine diffèrent de celles trouvées avec la méthode CST95; les raisons de ce changement sont discutées.

Mots clefs:

Analyse de cycle de vie, santé humaine, émissions toxiques, devenir des substances, efficacité d'exposition, effets cancérigènes et non cancérigènes, facteur de pente, facteur de dommage humain, gestion de l'eau, eau pluviale.

1. INTRODUCTION

Life Cycle Assessment (LCA) is a tool developed for evaluating the environmental impact of a product or a system. Within this tool, the impact of toxic releases on human health must be evaluated. After a decade of intensive research in the LCA field, the methodology for the assessment of toxicological impacts on human health is still in the development phase. Although many methods have been developed, none is accepted by the international community. This dissertation contributes to the effort, at two levels. Firstly, the proposals in this thesis represent an improvement to the 1995 Critical Surface-Time method presented in Jolliet and Crettaz [1997], whose new version should be released by the end of 2000. Secondly, this thesis provides a contribution at the international consensus-building level to the second Society of Environmental Toxicology and Chemistry (SETAC) working-group on impact assessment chaired by Udo de Haes et al. [1999]. This SETAC working group aims to contribute to the establishment of best available practices regarding impact categories.

This introduction presents different basic concepts required to understand the objectives of this dissertation. Section 1.1 outlines the methodology of Life Cycle Assessment, its stages and the impact assessment within LCA. Section 1.2 provides a description of aspects relevant to human health, the focus of this dissertation. The framework proposed by the SETAC to characterize human health within LCA is described. Potentials and drawbacks of existing impact assessment methods are reviewed. The need for research in the context of human health impact assessment is expressed. The objectives and structure of this dissertation in response to these research needs are then presented in section 1.3.

1.1 LIFE CYCLE ASSESSMENT

1.1.1 Definition

Life Cycle Assessment (LCA) is a tool developed for evaluating the environmental impact of a product, system or activity required to achieve a specific function. It provides input into sustainable development decision-making and has to account for all relevant environmental aspects. On the contrary, economic and social aspects are not within the scope of the analysis. One specific characteristic of LCA and a key distinction from risk assessment is that the whole life cycle of a product or system must be investigated, at least theoretically, from cradle to grave (extraction of raw materials, production, use and final disposal).

The first attempt to look at product systems was in the late 1960s. With the oil shortages in the early 1970s, attention was primarily focused on the energy requirements of different

product life cycles. In the 1980s, studies mainly examined packaging systems. It is in the 1990s that LCA has received significant attention. Life cycle thinking now plays an important quantitative role in the development of public and industrial policy. In most studies, LCA is used to compare competitive products that perform the same function and to demonstrate that one option is more environmentally preferable to another. LCA is also used to identify the main environmental burdens associated with a product and to determine whether modifications can make it "friendlier" from an environmental perspective [Curran, 1996].

1.1.2 Stages

The Society of Environmental Toxicology and Chemistry (SETAC) presented a consensus to define LCA as a phased approach composed of four stages [Consoli et al., 1993]. Recently, these four stages (see figure 1.1) have been described as part of the International Standards Organization's 14000 standards on Environmental Management Systems [ISO, 1997]. They are:

- Goal definition and scooping: The goal and scope definition describes the aim of the study, the product investigated by the study as well as the function and functional unit of the product.
- Life cycle inventory: The Life Cycle Inventory (LCI) quantifies the energy requirements, the resources consumption and the toxic releases into air, water and soil throughout the entire life cycle of a product, from cradle to grave. The system boundaries are defined.
- Life cycle impact assessment: The Life Cycle Impact Assessment (LCIA) provides a basis to quantify the impact or burden on human and ecological health of the inputs and outputs quantified in the inventory.
- Interpretation: In the interpretation, results are discussed and sensitivity analyses are presented. Improvement assessment can be part of the interpretation, when a reduction of the environmental burden is sought.

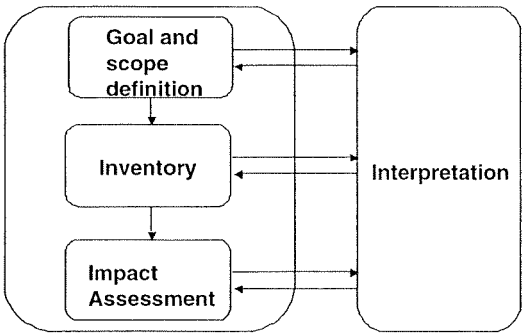

Figure 1.1 The four components of the Life Cycle Assessment [ISO, 1997].

1.1.3 Life Cycle Assessment and Risk Assessment

LCA is one of the many environmental analysis tool available to support decision-making. Other tools include Environmental Impact Assessment, Environmental Audit, Substance Flow Analysis, Risk Assessment, etc [Udo de Haes and Huppes, 1994]. Risk Assessment (RA) is of particular interest for our study, since both LCA and RA involve an exposure analysis and an effect analysis. We demonstrate in chapters 2 to 4 that many principles used within Life Cycle Impact Assessment are based upon developments carried out in Risk Assessment. The definition of Risk Assessment and differences between RA and LCA are presented below.

Risk Assessment is the characterization of potential adverse health effects resulting from human exposure to hazardous situations or chemicals [NRC, 1983]. The National Research Council proposed to organize Risk Assessment in four main steps. In the hazard identification step, diseases that may be induced by a chemical are identified. In the dose-response assessment step, the relationship between the dose and the extent of injury or disease is described. The exposure assessment step describes the size and composition of the population exposed to a substance, as well as the frequency, duration and route of the exposure. Finally, in the risk characterization step, results from the three previous steps are integrated to characterize the risk that humans may experience adverse effects [NRC, 1983]. RA and LCA have been developed with different motivations and therefore significantly differ. One characteristic specific to LCA is that emissions are reported in a LCA per functional unit, where the functional unit is the unit representing the function of the studied product or system. For instance, the functional unit for paint is a square meter of painted area that has a certain life span. Furthermore, the potential impact or burden of a product (or system) is assessed in LCA, by looking at the whole life cycle and at all the relevant environmental classes at a global or regional scale. In comparison, Risk Assessment helps to estimate the potential impact of a substance or a hazardous situation, by looking at a specific part of the life cycle, in terms of human toxicity and ecotoxicity, at a local scale. LCA and RA therefore differ in their objectives, their spatial scale as well as the environmental aspects and the chain of processes that they address. Last, but not least, LCA is used in most cases to compare competitive products performing the same function. In order not to bias the comparison, a best estimate of the potential risk of the toxic releases associated with each products is required. On the contrary, conservative values are commonly assumed in Risk Assessment to be consistent with prudent health policy.

1.1.4 Impact assessment within Life Cycle Assessment

a) Arguments for conducting an impact assessment

Many life cycle studies have been restricted to a Life Cycle Inventory. Conclusions are then drawn from the emissions and energy results, rather than from the effects on human health and the ecosystem. However, an inventory can commonly consist of a list of 50 or more chemicals. When product A has lower emissions than product B for all substances, it can be concluded that product A is "friendlier" from an environmental perspective.

However, product A usually has fewer releases of some substances but more of others. The relative importance of these toxic compounds in terms of impacts can vary significantly. It is therefore not straightforward to conclude which product is better and which are the most important substances in the inventory. This shows that the relationship between the releases and their environmental impacts must be established. Impact assessment is therefore an essential step of most LCAs and its improvement through research is of paramount importance.

b) Nature of the impact assessment within LCA

Life Cycle Impact Assessment (LCIA) provides a basis for interpretation of the data available in the inventory of a product life cycle. Consequently, LCIA is tied to the characteristics of the life cycle inventory. Commonly, inventories do not specify the sites of emissions, and the background concentration of substances at these sites is usually unknown. Furthermore, the releases of a toxic compound in each stage of the life cycle of a product are added and reported as a single emission value, without spatial and temporal information. The lack of spatial and temporal information in the inventory makes it difficult to estimate the actual effects on humans in an LCIA [Burke et al., 1996].

c) Stages of the impact assessment

LCA practitioners adapted a three-stage procedure for the impact assessment. These stages are [ISO, 2000]:

- **Classification:** Classification is the assignment of the Life Cycle Inventory inputs and outputs into impact classes or categories. The SETAC identified significant impact classes to address within an LCA. These impact classes include human toxicity, ecotoxicity, global warming, depletion of stratospheric ozone, photo-oxidant formation, acidification, eutrophication, etc [Consoli et al., 1993].
- **Characterization:** Characterization is the process of weighting within an impact category the releases assigned to that category. An impact score for each impact class, expressing all emissions in term of an equivalent emission of a reference substance, is calculated. For instance, the emissions of methane, dinitrogen oxide and chlorofluorocarbons can be transformed into an equivalent emission of carbon dioxide in the impact class of "global warming", by multiplying them by the commonly adopted characterization factors "global warming potentials" or GWPs. The CO_2 equivalents can then be added to determine the total contribution or burden in the context of "global warming".

Characterization coefficients are available in the literature for global warming [Houghton et al., 1991], depletion of stratospheric ozone [WMO, 1989], photo-oxidant formation [UNECE, 1990], eutrophication and acidification [Heijungs et al., 1992]. In contrast, a list of characterization coefficients accepted by the international community is still lacking for toxicological impacts to human health. Further research is needed to help achieve an international consensus. This dissertation contributes to this research, hence human toxicity is described in greater detail in section 1.2.

- **Weighting across impact categories**: The weighting across impact classes is the assignment of relative values to the different classes, in order to compare their impact score.

Although it can be a desirable stage, the assignment of relative weights to the impact categories is value-laden and was considered by ISO to be an optional step. The weighting across impact categories is not studied in this thesis.

1.2 HUMAN HEALTH WITHIN LCIA

In this section, the guideline developed under the guidance of the SETAC for the impact assessment of human health is presented. A classification of the most widely used impact assessment methods is presented, together with a discussion of their potential benefits and drawbacks.

1.2.1 Characterization of human toxicity within LCIA

a) SETAC's framework

The working group on Life Cycle Impact Assessment of SETAC-Europe [Jolliet et al., 1996] proposed a framework for the characterization of toxic releases. According to this framework, the effect score of a substance i released in a medium m is expressed as the product of its effect factor and its fate and exposure factor, as stated in equation (1.1). The effect factor characterizes the implicit toxicity of the substance, while the fate and exposure factor integrates the fate behavior of the toxic release and the resulting exposure to humans. Equation (1.1) could easily be generalized to account for intermedia transfer.

$$S_i^m = E_i^m \cdot F_i^m \cdot M_i^m \qquad \text{Equation (1.1)}$$

where:

S_i^m: Effect score of substance i, emitted in medium m (air, water, soil or food chain)

M_i^m: Emission from substance i into medium m.

E_i^m: Effect factor of substance i in medium m.

F_i^m: Fate and exposure factor of substance i in medium m.

b) Human Toxicity Potential

Global warming potential, acidification potentials, etc are available in the literature to weight substances contributing to global warming, acidification, etc. Similarly, Guinée and Heijungs [1993] introduced the Human Toxicity Potential (HTP) to weight toxic releases. With this factor, the emission of a substance i released into medium m can be expressed as an equivalent emission of a reference substance released into a reference medium. According to the SETAC's framework, the human toxicity potential has to integrate the effect, the fate and the exposure of a compound. The Human Toxicity Potential of a substance i can therefore be derived by calculating its fate factor and effect factor, and normalizing this value by the fate factor and effect factor of the reference substance (see equation (1.2)).

$$HTP_i^m = \frac{E_i^m \cdot F_i^m}{E_{ref\text{-}s}^{ref\text{-}m} \cdot F_{ref\text{-}s}^{ref\text{-}m}} \qquad \text{Equation (1.2)}$$

where

HTP_i^m : Human Toxicity Potential of substance i, released in medium m [kg ref-s / kg substance i].

$E_{ref\text{-}s}^{ref\text{-}m}$: Effect factor of the reference substance (ref-s) emitted in the reference medium (ref-m).

$F_{ref\text{-}s}^{ref\text{-}m}$: Fate and exposure factor of the reference substance (ref-s) emitted in the reference medium (ref-m).

1.2.2 Review of Life Cycle Impact Assessment methodologies

Many impact assessment procedures have been developed in the last decade. Based upon the SETAC's framework presented in section 1.2.1, some of the most widely used impact assessment procedures can be classified in four levels of sophistication [Fava et al., 1993; Jolliet et al., 1996]. Their potential and drawbacks are discussed here; for a more comprehensive discussion, refer to sections 2.1.3, 3.1.2 and 4.1.2.

- **Methods without fate and effect analysis (level 1)**

These methods simply sum the emissions listed in a Life Cycle Inventory, without accounting for the toxic effect and the fate and exposure behaviour. They are clearly inadequate, since the compounds' fate, exposure and toxicity characteristics are excluded.

- **Methods with effect analysis, without fate and exposure assessment (level 2)**

These procedures are limited to the consideration of the substance's toxicity. They compare the emission to a maximal critical concentration or to a No Effect Concentration. Some of these concentrations are based on national regulatory standards, which can incorporate considerations of technical feasibility, cost, public policy, societal values, etc., that have no relation to the toxicological impact of a compound. In addition, fate and exposure are ignored. For example, a compounds' persistence is not accounted for, while it is known that residence times in air and soil can vary from a few days to many years. This minimizes the impact of chemicals with a long residence time. Examples of such methods are the critical-volume method [BUS, 1984], the Ecological Scarcity method "Okofaktoren 1997" [BUWAL, 1998] and the "CML-92" method of Heijungs et al. [1992].

- **Methods with a partial fate analysis (level 3)**

These methods partially take into account fate and exposure of chemicals by integrating their persistence and bioaccumulation. In the Environmental Design of Industrial Products method, Hauschild [1994] applied a bioconcentration factor and a biodegradation factor. However, chemical degradation and intermedia transport were excluded.

• Generic methods, with a full fate and exposure analysis (level 4)

These methods consider the fate and exposure as well as the toxic effect of substances in a generic way. The fate analysis is generally based on Mackay multimedia models using generic information to assess the fate of emissions in the environment. While such multimedia models have the advantage of taking the intermedia transfer directly into account, there is no general agreement about their accuracy and reliability. Moreover, they require the knowledge of a large number of parameters and their validity is limited to some types of chemicals [Guinée and Heijungs, 1993]. As an alternative, Jolliet and Crettaz [1997] suggested a semi-empirical approach called the Critical Surface-Time method (CST95).

The effect assessment is generally based on factors like the Reference Dose (for noncancer effects) or the 95% upper confidence limit $q1^*$ (for cancer effects) developed in Risk Assessment. The conservative assumptions behind these factors reflect policy-based decisions for risk assessment and may bias the comparison of toxic releases in LCIA. Further limitations of this kind of effect assessment are presented in the introduction of chapters 2 and 3. Examples of such methods are the Eco-Indicator 99 [Goedkoop and Spreinsma, 1999] and the approaches developed by Hertwich [1999], Guinée et al. [1996] and Huijbregts [1999].

• Site-specific methods, with a full fate and exposure analysis (level 5)

These methods try to estimate actual impacts on humans, by integrating site-specific (e.g. background, geographical) and temporal-specific information. Potting et al. [1999] and Sparado and Rabl [1999] proposed approaches to account for local conditions at the release site. A site-specific appreciation of the effect factor and of the fate and exposure factors is difficult due to the characteristics of the Life Cycle Inventory. Thus, no complete site-specific method is available at the present time.

We showed in this section that a framework for assessing the impact of toxic releases on human health is available and internationally accepted. However, none of the existing LCIA methods has been widely accepted by the scientific community, indicating that methodologies for the impact assessment are still in the development phase. Further research is therefore required, both on the effect side and in the assessment of fate and exposure.

1.3 OBJECTIVES AND STRUCTURE OF THE THESIS

1.3.1 Main objectives

Our review of existing LCIA methods indicates that further research is required in the context of toxicological impacts to human health. Udo de Haes et al. [1996] and Jolliet et al. [1996] identified the inclusion of fate and exposure as one of the major issues to be addressed. Chapter 4 of this thesis explores some new concepts for that fate and exposure assessment, for the air compartment.
However, the main focus of this dissertation is the effect evaluation. Indeed, most of the international research effort has focused on the fate and exposure assessment, while less attention has been paid to the effect component of the analysis. However, this topic is extremely relevant for the comparison of substances. An expert panel of the International Life Science Institute (ILSI) evaluated the human health component of LCIA and concluded that a clear need exists for developments adapted to the specific aims of LCA [Burke et al., 1996]. The panel recommended further research in order to develop valid procedures for the relative impact assessment of human health. We therefore decided to put the emphasis on the effect component of LCIA (chapters 2 and 3) and on its consistent combination with the fate and exposure assessment (chapter 5). Another reason for focusing on the effect evaluation for LCIA is the fruitful collaboration with the Harvard School of Public Health, Boston, where I carried out research in 1998.

Detailed objectives are presented in the introduction of each chapter. In summary, the following objectives are addressed in this dissertation:

1) Describe and implement an improved procedure for quantifying the potential carcinogenic and noncarcinogenic effects of toxic releases on human health, for an application in LCA (chapters 2 and 3). Although chronic noncarcinogenic and carcinogenic effects are discussed in two different chapters, we aim to develop a procedure applicable to both types of effects, so that they can be compared and eventually aggregated.
2) Develop a method for describing the fate of atmospheric releases and the resulting exposure on humans (chapter 4).
3) Propose a framework for combining the effect assessment with the fate and exposure assessment, in order to derive a so-called human damage factor. Apply this framework to selected chemicals, including several heavy metals and key air pollutants (chapter 5).
4) Apply and test the impact assessment methodology developed in this dissertation to the Cycleaupe case study, whose specific goals are to determine whether systems using rainwater or reducing water consumption are "friendlier" from an environmental perspective than conventional toilet flushing and to determine the key pollutants associated with each system (chapter 6).

This dissertation therefore contributes to the research on the impacts caused on humans by toxic substances in Life Cycle Impact Assessment. It complements studies on other effect mechanisms on human health, such as the study of Goedkoop and Spriensma [1999] on

damages associated with ozone formation, climate change, ionizing radiation and stratospheric ozone depletion. Emissions of waterborne chemicals are not considered, but would fit into the methodology developed for this dissertation.

1.3.2 Selected substances

There are thousands of substances released into the environment and we have to focus our study on an important subset. As indicated in the third objective listed in section 1.3.1, several heavy metals were chosen for a full application of the procedure developed in this dissertation, that is for the fate and exposure assessment as well as for the effect analysis. Reasons for putting the emphasis on metals are numerous. In the Cycleaupe case study presented in chapter 6, the releases of some fifty chemicals are quantified in the Life Cycle Inventory. Lead, cadmium, chromium, copper and arsenic appeared to play by far the most important role in the context of human toxicity, according to the CST95 impact assessment methodology. In the European concerted action for agriculture, we similarly concluded that metals have the highest contribution to human health for a wheat production [Audsley et al., 1997]. Furthermore, arsenic (rank 1), lead (rank 2), mercury (rank 3), cadmium (rank 7) and chromium(VI) (rank 16) are among the top 20 hazardous substances for humans at hazardous waste sites, among the 275 studied by the Agency for Toxic Substances and Disease Registry [ATSDR, 1999]. These reasons justify that we focus in this thesis on the following heavy metals: cadmium, chromium(VI), chromium(III), copper, methylmercury, beryllium, lead and inorganic arsenic.
Full application of the procedure developed in this research is also presented for some criteria air pollutants: carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_X) and fine particles (particles with a diameter lower than 1µm, as defined by the Intergovernmental Panel on Climate Change [IPCC, 1995]). Damages induced on human health by these air pollutants will be compared to those of metals.

In addition to the full fate, exposure and effect assessment carried out for the mentioned metals and air pollutants, a more focused evaluation of the effect component for many more chemicals is part of the objective of this dissertation.

1.3.3 Structure of the thesis

The third objective reported in section 1.3.1 relates to the development of a framework combining the effect assessment with the fate and exposure evaluation. The key steps of this framework are presented here, since they reflect the structure of this thesis. Based on the developments presented in chapters 2 to 4, this framework is expended in greater detail in chapter 5.
The proposed framework starts with the emission of a toxic compound and finishes with the quantification of the damage on human health (see figure 1.2). The two stages required for assessing this damage are the fate and exposure analysis, followed by the effect analysis, in

accordance with the SETAC-Europe framework for human toxicity presented in section 1.2.1.

In the fate and exposure analysis (first step), the release of a substance is linked to the resulting concentration increase in each medium of the environment and the dose absorbed by humans is then derived by taking into account the exposure. The absorbed dose can be directly deduced from the emission, by combing the fate and exposure analysis. Chapter 4 focuses on this fate and exposure analysis for carbon monoxide, sulfur dioxide, nitrogen oxides, fine particles and atmospheric releases of metals.

In the effect analysis (second step), the absorbed dose is linked to the affected persons, using results from the dose-response analysis. The severity of the disease is taken into account to derive the damage on humans. This damage can be directly assessed from the absorbed dose, as explained in chapters 2 and 3.

By combining the fate and exposure analysis with the effect assessment, the damage induced on humans by an emission can be estimated (see chapter 5).

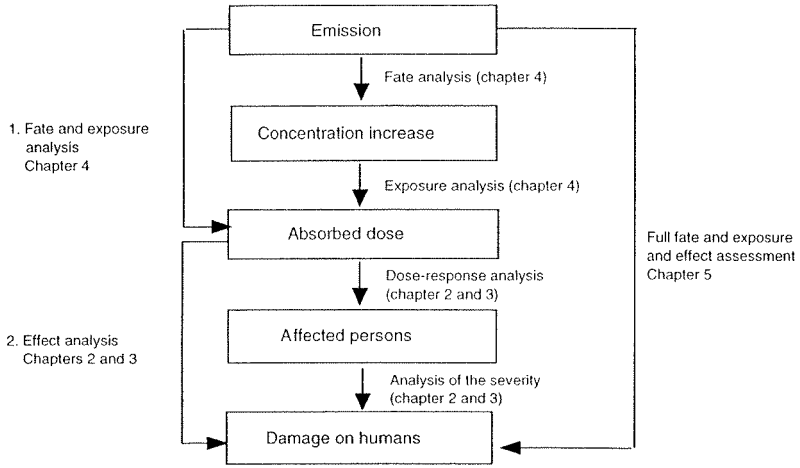

Figure 1.2 Schematic overview of the framework proposed in this dissertation for assessing the damage induced on human health by the release of a compound (corresponding chapters are indicated).

2. EFFECT FACTOR FOR CARCINOGENIC EFFECTS

ABSTRACT

This chapter aims to quantify the carcinogenic risk resulting from a chronic exposure to a large number of toxic releases, and to derive their effect factors for an application in Life Cycle Impact Assessment (LCIA). A description of the carcinogenesis is presented first. Concepts developed in Risk Assessment by the US Environmental Protection Agency (EPA), as well as the potentials and shortcomings of methods currently applied in LCIA to characterize carcinogenic effects, are discussed.

Derived from the Risk Assessment concept of benchmark dose, the ED_{10}-approach based on the effect dose ED_{10h} is proposed and explored for the first time in LCIA. The ED_{10h} is defined as the best estimate of the dose inducing a 10% added risk over background for humans. Cancer risk towards humans is characterized by drawing a straight line from the ED_{10h} down to the origin of the dose-response function. The slope of this straight line is called the slope factor and is denoted βED_{10}. In a first stage, we calculated the ED_{10h} for 44 substances, using their bioassay data available in the US EPA's Integrated Risk Information Service database (IRIS). Slope factors ranging from $7 \cdot 10^{-4}$ for di(2-ethylhexyl)adipate up to 8 [risk of cancer / mg/kg-day] for aldrin are found. In a second stage, the correlation between the ED_{10h} and the more widely available tumor dose observed in animals TD_{50a} is determined in order to derive the slope factor for a large number of compounds. It is applied to more than 600 toxic releases, leading to slope factors ranging from 10^{-4} up to 10^{4} [risk of cancer / mg/kg-day]. Slope factors are specifically determined for the heavy metals selected in section 1.3.2. An extrapolation of the ED_{10h} from the lethal dose LD_{50a} for data-poor substances is tested. Since these two parameters are badly correlated (R^2=0.14; n=41), an extrapolation of the carcinogenic effect from the lethal dose is not applied in this chapter.

The Disability Adjusted Life Years per affected Person ($DALY_p$) is calculated for different types of tumors, in order to weight the carcinogenic endpoint associated with each compound. It shows that all cancers have more or less the same severity and an average $DALY_p$ of 11.1 [yr/pers] is derived. The slope factor βED_{10} and the $DALY_p$ for a given substance can finally be combined to derive its effect factor. The effect factor is expressed in years of life lost per absorbed mass. Effects factors ranging from $1.3 \cdot 10^{-9}$ for cinnamyl anthranilate up to $3.4 \cdot 10^{-1}$ [yr lost / mg absorbed] for 2,3,7,8-tetrachlorodibenzo-p-dioxin are found, reflecting that the range in the carcinogenic effect is very large. For the selected metals, effect factors vary from $3.4 \cdot 10^{-7}$ for an oral exposure to lead to $1.1 \cdot 10^{-4}$ [yr lost /

mg absorbed] for inhalation of chromium(VI), showing a factor 320 between the lowest and the highest effect factor.

The linear dose-response function without threshold, which is assumed in the ED_{10}-approach, is discussed. The linearity or nonlinearity at low doses can not be addressed on the basis of empirical data. When available, information on the mechanism of action can rather be considered to flag chemicals whose mutagenic mode of carcinogenicity provides support to linearity. The comparison between the 95% upper confidence limit q_1^* commonly used in different LCIA methodologies and the slope factor β_{ED10} indicates that the ED_{10}-approach provides a risk estimate lower only by a factor 2 than q_1^*. Thus, it should not be concluded that the ED_{10}-approach provides a fundamentally less biased estimate of low-dose risks than does the upper-bound q_1^*; using the ED_{10h} as a point of departure is likely to overestimate the risk in many cases for dose-response curves that are truly less than linear at low doses. However, the ED_{10}-approach has the advantage to be based on a simple linear extrapolation, and not on mathematical models that have little biological justifications and only give the appearance of specific knowledge. It also makes explicit the assumption of linearity and can be applied to characterize both carcinogenic (chapter 2) and noncarcinogenic effects (chapter 3) of toxic releases. However, it is clear that ED_{10}-approach does not consider the specific mode of action of chemicals. The application of biologically based models could be used in the future as a substitute for well-know substances.

As explained in chapter 1 and summarized on figure 1.2, the damage induced by toxic releases on human health can be assessed by combining their fate and exposure with their harmful potential. This chapter deals with the evaluation of carcinogenic outcomes, while chapter 3 will focus on noncarcinogenic effects. Carcinogenic and noncarcinogenic effects are discussed in two different chapters, since different parameters and procedures are conventionally available for their characterization. Thus, there is a fundamental difference in the conventional EPA's Risk Assessment of carcinogenic and noncarcinogenic effects. While carcinogenic risk is quantified using a non-threshold mechanism, a threshold is rather assumed for noncarcinogenic risk to compare the exposure dose to the threshold. A reason for not quantifying noncarcinogenic effects is that noncarcinogenic Risk Assessment was developed to establish permitted doses in air, water and food. Since exposures to chemicals at doses above the permitted level were not allowed, risk resulting from doses above that dose did not have to be assessed [Price et al., 1997]. Although carcinogenic and noncarcinogenic effects are discussed in two different chapters, we aim to develop a procedure applicable to both types of effects, so that they can be compared and eventually be aggregated.

2.1 INTRODUCTION

Most of the methods applied in Life Cycle Impact Assessment (LCIA) for characterizing carcinogenic effects are based upon the principles developed in Risk Assessment. These principles and their application in Life Cycle Assessment (LCA) are presented in this introduction. This enables discussing the drawbacks of existing LCIA methods and to present the objectives of this chapter. Before that, basic notions of toxicology are presented, together with a discussion on the contribution of environmental factors to the major causes of deaths. The carcinogenesis process is also described, in order to better capture the mechanism of action leading to the incidence of neoplasm. This will help to discuss the procedure adopted in this chapter.

2.1.1 Basic notions of human health

a) Toxicology

A toxic substance is a substance producing an adverse effect in organisms. Toxicology is the study of toxic substances and their injurious effects on living organisms. While descriptive toxicology refers to toxicity testing, mechanistic toxicology is concerned with understanding the mechanism by which chemicals exert their toxic effects. Finally, regulatory toxicology indicates whether a chemical poses a sufficient low risk to be marketed, using data provided by descriptive and mechanistic toxicologists [Eaton and Klaassen, 1996]. Descriptive toxicity and mechanistic toxicity provide the basis data for the evaluation of the effects of toxic releases within LCIA.

Major factors determining the degree of severity induced by the exposure to a chemical include the chemical form of the substance and the dose, duration and route of exposure. The other chemicals to which persons are exposed should also be considered, as well as the age, sex, diet, genetic makeup, lifestyle and state of health [ATSDR, 1999]. Concerning the duration of exposure, four exposure periods are commonly distinguished for animals, acute (less than 1 day), subacute (less than one month), subchronic (1 to 3 months) and chronic (more than 3 months) [Eaton and Klaassen, 1996]. Both chapters 2 and 3 focus on the chronic effects of chemicals. For the route of administration, an approximate descending order of effectiveness would be intravenous, inhalation, intraperitonal, oral and dermal route of exposure [Eaton and Klaassen, 1996]. We pay special attention to specify the route of exposure in chapters 2 and 3.

b) Causes of death

Figure 2.1 shows that the most common causes of deaths in Western Europe are cardiovascular diseases, cancers, respiratory diseases and injuries [EEA, 1996]. In developing regions, diarrhoeal disease and tuberculosis are among the leading causes of deaths and cancer does not belong to the 10 leading causes [Murray and Lopez, 1996(a)]. All together, 50.5 million deaths were reported worldwide in 1990, that is about 1% of the world population. Cancer accounted for 6 million of deaths worldwide (see table 2.3 for the contribution of the different types of cancer) and killed more than 500000 people in the European Union and in the United States [Murray and Lopez, 1996(a)].

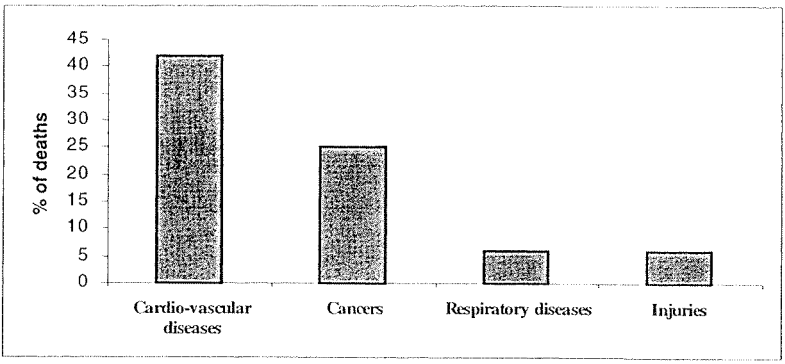

Figure 2.1 Leading causes of death in the European Union [EEA, 1996].

The extent of public ill-health determined by environmental factors is difficult to quantify. Environmental stresses for which there are reasonably good exposure and effect data are estimated to be a major factor in 5% of the diseases for a developed country like the Netherlands, according to a preliminary report prepared for the World Health Organization (WHO) on the basis of Dutch data [EEA, 1999]. A WHO global estimate indicated that it can be as much as 23% worldwide [EEA, 1999].

The contribution of environmental factors to the main causes of death in Europe has been discussed by the European Environmental Agency [EEA, 1996]. While the dominant risk

factors are related to behavioural factors such as smoking or unhealthy diet and to various host characteristics such as genetic predisposition, a number of environmental factors also contribute to these health problems. They are discussed here for the three main causes of death in the European Union:

- The main recognized risk factors for cardiovascular diseases are hypertension, high blood cholesterol and smoking. The role of environmental factors is not yet clear. Exposure to elevated carbon monoxide levels with the formation of carboxyhaemoglobin may impair the oxygen-carrying capacity of the blood, resulting in an aggravation of cardiovascular diseases. Lead and particles may also play a role in cardiovascular diseases.
- Factors increasing the risk of cancer include lifestyle (e.g. smoking) and genetic factors. Environmental aspects also play a role. The relative contribution of carcinogenic contaminants in food to the overall impact of diet is not known.
- Chronic airway diseases such as bronchitis and asthma are important respiratory diseases. While smoking is the main risk factor, air pollution also significantly contributes. Air pollution induces lower respiratory tract illness, chronic obstructive lung disease, allergic disease, etc. It is estimated that 40000 to 150000 extra deaths of respiratory diseases per year are associated to pollution by air particles in Europe [EEA, 1999].

2.1.2 Insights into the carcinogenesis process

• Generality

A human carcinogen is a substance that leads to a statistically significant increased incidence of cancer in humans, as compared with the incidence in unexposed humans [Pitot and Dragan, 1996]. A mass of cancer cells is called a malignant tumor. Malignant tumors can grow rapidly, invade and destroy nearby tissues. They can eventually metastasize by spreading to other parts of the body [Compton, 1999]. Although commonly referred to as a single disease, cancer is a group of more than 100 diseases [Compton, 1999]. Cancer can indeed occur in any part of the body where cells grow and divide. The proportion of human cancer caused by a variety of environmental agents indicates that diet (35%) and tobacco (30%) are the main contributors, while pollution and occupation account for only 2% and 4% of cancer deaths respectively [Doll and Peto, 1981]. Other estimates for the industrialized world confirm that the proportion of cancers due to environmental pollution is below 5% [Hofstetter, 1998].

• Mechanism of action

The mechanism of carcinogenesis is not yet fully understood and is still a topic of research. However, it is now broadly accepted that the transformation of a normal cell into a cancer cell is a multistage process involving the initiation, promotion and progression of the normal cell into a neoplastic cell. The initial step is the initiation of a mutation by a chemical that binds to the deoxyribonucleic acid (DNA). A mutation is the alteration of the genetic material in the nucleus of cells. The initiation is generally understood to be an irreversible event. Many genotoxic substances are considered to cause the initiation. The promotion stage is characterized by an expansion of the initiated cells. Promoting compounds act by different mechanisms to increase rates of cell proliferation or decrease rates of cell death.

An important feature of this stage is its reversibility and in some cases the existence of a threshold. In the progression, cells in the stage of the promotion are converted into malignant cells. Progression is understood to require a second genetic mutation [Beck et al., 1994].
Chemicals can act at one or more of these stages and can act directly or indirectly. A complete carcinogen is a chemical possessing properties of initiating, promoting and progressor chemicals. On the contrary, an initiating substance is a chemical capable only of initiating cells and a promoting chemical is a compound capable of causing the expansion of initiated cells [Pitot and Dragan, 1996]. Many chemicals directly interact with DNA. However, not all carcinogenic action is mediated by direct genotoxic effects and some chemicals can increase the incidence of neoplasm through indirect effects. Indirect effects include changes in the efficiency of immune surveillance in destroying incipient tumors at early stages, changes in the efficiency of DNA repair or enhancement of cell replication leaving less time for repair, saturation of detoxification processes, changes in metabolic processing, growth alteration by hormones and growth factors, etc [Rees and Hattis, 1994].

2.1.3 Methods in Life Cycle Impact Assessment

The characterizion of the carcinogenic potency of chemicals by some of the most frequently used LCIA methods is presented here. We propose a classification of methods among two levels of sophistication.

a) Linear methods, based on acceptable levels (level 1)

These methods characterize both carcinogenic and noncarcinogenic effects by using parameters like the Acceptable Daily Intake (ADI), the Reference Dose (RfD) or the Tolerable Daily Intake (TDI). These parameters are defined as the daily human exposure to a hazardous substance that is likely to be without an appreciable risk of adverse health effects over a specified route, for a lifetime exposure [Taylor et al., 1999]. For carcinogenic compounds, ADIs and RfDs can be derived from the slope of the dose-response curve at low doses. These methods implicitly assume a linear dose-response curve without threshold (doubling the emission results in doubling the effect) and do not quantify the damage on human health. They are therefore referred to as linear and not damage-oriented methods.

As an example, Guinée et al. [1996] characterized the carcinogenic effects of toxic releases with a No Effect Level for humans. This so-called virtually safe level has been derived by Jager et al. [1994] of the Dutch National Institute of Public Health and Environmental Protection (RIVM). It corresponds to the dose at which 1 in 10000 people die of cancer, taken over a life-time. This risk of 1 in 10000 is set to be the maximum accepted risk for carcinogenic chemicals in the Netherlands. Huijbregts [1999] also used the daily intake corresponding to a life-time risk of 1 in 10000 as the Human Limit Value (HLV) for carcinogenic substances. In earlier work [Jolliet and Crettaz, 1997], we adopted similar values in the Critical Surface-Time approach CST95.

b) Linear methods, using the upper-bound $q1^*$ (level 2)

These methods also assume the linearity of the dose-response function. However, they use the 95% upper confidence limit $q1^*$ defined by the US Environmental Protection Agency (EPA) for carcinogen Risk Assessment (see section 2.1.4). Since the risk is quantified, these methods are referred to as linear and damage-oriented approaches.
The Eco-Indicator 99 method developed by Goedkoop and Spriensma [1999] is a good illustration of a damage-oriented approach. Hofstetter [1998] contributed to Eco-Indicator 99 by developing damage factors linking emissions with the damage they cause on humans for more than 100 carcinogens. He used unit risks estimates derived from the q1* and reported by the EPA and by the World Health Organization (WHO). In his dissertation, Hertwich [1999] from UC Berkley also characterized cancer risk with $q1^*$ values reported in the database of the Environmental Defence Fund [EDF, 1998].

Since methods used in LCIA are based on principles developed for Risk Assessment, these principles are presented below. This will help to understand the shortcomings of existing LCIA methods and the need for new developments in this field.

2.1.4 Risk Assessment by the US EPA (1986 Guideline)

The four main steps of Risk Assessment as defined by the National Research Council [NRC, 1983] have been presented in section 1.1.3. In this section, some concepts of the 1986 EPA's Guideline for Carcinogen Risk Assessment are described. It is not intended to be a comprehensive review, but rather focuses on the parts relevant for our application to LCIA.

a) Hazard Identification

Hazard identification aims to determine whether a chemical poses a carcinogenic hazard in exposed humans. A weight-of-evidence approach is used by the EPA to classify a compound into one of the five categories presented in table 2.1 [EPA, 1986]. These categories are used in section 2.6 to classify metals with respect to their carcinogenic potential. The second step of the RA, the dose-response assessment, is the most relevant for our analysis of the effect in LCIA. It is therefore discussed below in more details.

Group	Description
A	Human carcinogen
B	Probable human carcinogen
	B1: Limited human evidence
	B2: Sufficient evidence in animals
	Inadequate or no human evidence
C	Possible human carcinogen
D	Not classifiable as to human carcinogen
E	Evidence of noncarcinogenicity for humans

Table 2.1 Categories proposed by the EPA to classify carcinogenic chemicals [EPA, 1986].

b) Dose-response relationship

The dose-response relationship is one of the most fundamental concept of toxicology. As explained by Eaton and Klaassen [1996], two types of dose-response relationships can be distinguished for noncancer toxicity. The individual dose-response curve describes the response of an individual to varying doses of a chemical. It is characterized by a dose-related increase in the severity of the response. In the dose-response relationship for a population of individuals, a specific endpoint is identified and the dose required to produce that endpoint in the population is determined. This curve reflects the differences in the susceptibility to chemicals among individuals. Only a few individuals are hypersusceptible (resistant) and respond to the lowest (highest) dose, while the larger number of individuals respond to intermediate doses. In this dissertation, the dose-response relationship for a population will provide the basis for the evaluation.

c) Extrapolation toward low doses and curve fitting models

The two main categories of data for the evaluation of chemicals (drugs are not discussed here) are epidemiological studies and animal toxicology. Since epidemiological studies generally are not available, results from experiments on animals are frequently used for estimating the dose-response relationship. Using animal data poses different problems. One must evaluate whether the animal data is relevant to humans and determine an equivalent dose scale with which to extrapolate from the animal data to humans (see part e). The extrapolation from high to low doses is also required [Rees and Hattis, 1994]; it is discussed here.

The number of animals is limited during a bioassay (typically 50 to 60 animals per group), mainly for practical considerations. Obtaining statistically valid results from such small groups of animals requires to use relatively large doses so that the effect will occur frequently enough to be detected. At best, a risk in the range of 10^{-2} (1/100) can be detected in animal experiments. Human health risks, ranging from 10^{-4} to 10^{-6}, are consequently clearly out of the experimental field [Kodell and Park, 1995]. Models have therefore been developed for extrapolating the risk from high to low doses [Olin et al., 1995]. The extrapolation is carried out by fitting a model to the observed data and extending the model from the observed range of doses towards the lower doses.

Statistical models can be distinguished from mechanistic models [Faustman and Omenn, 1996]. Statistical models are tolerance-distribution models in which it is assumed that each individual has a tolerance level. The distribution of these tolerances for the entire population is described in terms of a probability distribution. In the log-probit model, a normal probability distribution is chosen [Rees and Hattis, 1994]. The logistic model and the Weibull model are other statistical models that we will use later in this chapter and in chapter 3.

Mechanistic models describe the dose-response relationship with a mathematical equation that is consistent with postulated biological mechanism of response. For instance, hit models have been developed, where a hit is defined as a cellular event inducing cancer. The one-hit model, in which only one hit is required for a cell to be altered, is the simplest mechanistic model. As theories of carcinogenesis have grown in complexity, multi-hit models assuming that more than one hit is required for the development of neoplasm have been developed

[Faustman and Omenn, 1996]. The Linearized Multistage Model (LMS) is another example of a mechanistic model. Since it is the default model used in the 1986 EPA's guideline for carcinogen Risk Assessment [EPA, 1986], it is described in more details below.

d) Linearized Multistage Model

Armitage and Doll [1957] developed a multistage model which is based on the hypothesis that a serie of ordered stages is required to form a tumor. This model was generalized by Crump [1980]. The multistage model assumes that all carcinogens act by the same non-threshold mechanism and that many stages occur before a tumor appears [Armitage, 1985; Kodell and Park, 1995].

Observed data often present a nonlinear relationship in the experimental region. The linearized multistage model integrates this nonlinearity at high doses and assumes a linear curve for low doses. It is characterized by an exponential polynomial form, as indicated in equation (2.1), where q_0 is determined by the background incidence, q_1 defines the linear component of the tumor risk and the higher order terms define the degree of high-dose nonlinearity [Rees and Hattis, 1994]. At low doses, the higher order polynomial terms become very small and the probability of tumors is dominated by the linear term. Thus, equation (2.1) simplifies to equation (2.2) for low doses, where q_1 is the slope of the linear dose-response curve at low exposure levels.

$$R(d) = 1 - \exp[-(q_0 + q_1 \cdot d + \ldots + q_k \cdot d^k)] \qquad \text{Equation (2.1)}$$

where:

R(d): Response at dose d [Risk]
qi: Non-negative constant of the model
d: Dose [mg/kg-day]
k: Number of groups of animals considered in the bioassay minus one

$$R(d) = q_1 \cdot d \qquad \text{Equation (2.2)}$$

where:

q_1: Low-dose slope $[\frac{\text{Risk}}{\text{mg/kg-day}}]$

The Maximum Likelihood Estimate (MLE) is the value of the linear term for which the likelihood of the data is maximized [Crump, 1984]. It is denoted q_1. It is sensitive to modifications in bioassay data and small changes in the tumor incidence in the lowest experimental group can result in cases where q_1 is changed by many orders of magnitude [Rees and Hattis, 1994]. The usual approach to address this problem is to determine the 95% upper confidence limit q_1^* on the q_1 term [Crump, 1984]. The US EPA uses the upper confidence limit q_1^* for Risk Assessment, on the basis of its biological plausibility (non-threshold) and its conservatism.

e) Animal to human data

In addition to requiring an extrapolation from high to low doses, using animal data poses the challenge to derive human equivalent doses or concentrations from animal tests.

For an oral exposure, the adjustment should use toxicokinetic information on the substance when adequate data are available. However, in most cases, there are insufficient data for such an adjustment [EPA, 1996(a)]. As a default, the human equivalent dose is estimated according to the "surface" scaling. This scaling is based upon the assumption that different species are equally sensitive to a substance if they absorb the same dose per unit of body surface. The human equivalent dose is then smaller than the animal dose on a body weight basis, reflecting that humans are more vulnerable on a body weight basis. The body surface scaling factor is equal to 6 for rats and 13 for mice [EPA, 1998]. For completeness, it should be mentioned that the US EPA now favors the ¾-power of body mass as a basis for the adjustment. This leads to somewhat lower human equivalent doses. Also, some risk assessment agencies assume "body weight" equivalence, that is doses in [mg/kg/day] as equally carcinogenic [Rhomberg, 2000].

For an exposure by inhalation, the default method is a toxicokinetic approach described by the EPA [1994]. Dosimetric adjustments are carried out to account for differences between rodents and humans in physiology, ventilatory parameters, metabolic processes, etc. The dosimetric adjustment depends on the type of substance (particle or gas) and the location of the observed effect (respiratory or extra respiratory) [Rees and Hattis, 1994]. The lung deposition of inhaled particles and gases is estimated, as well as the internal doses of gases with different absorption characteristics [EPA, 1994].

f) Other Risk Assessment procedures

To conclude this review of Risk Assessment, we want to emphasize that many Risk Assessment procedures exist. Moolenaar [1994] summarized some of the methodologies used by different countries. The approach of the EPA in estimating the upper bound to human risk is unique. The European Union, the United Kingdom, Denmark and the Netherlands divide carcinogens into genotoxic and nongenotoxic chemicals and use different extrapolation procedures for each class. They treat nongenotoxic carcinogens as threshold toxicants and derive an Acceptable Daily Intake for these compounds [Moolenaar, 1994]. Also, several classification schemes exist for the hazard identification. For instance, the International Agency for Research on Cancer (IRAC) classifies compounds into group 1 (the substance is carcinogenic to humans), group 2A or 2B (the substance is probably or possibly carcinogenic), group 3 (unclassifiable as to carcinogenicity) and group 4 (probably not carcinogenic) [IARC, 1982].

2.1.5 Drawbacks of existing LCIA methods

Leading LCIA methods have been classified in section 2.1.3 into two categories. In the first category, approaches are based on the application of an Acceptable Daily Intake or another similar parameter. These methods allow to weight carcinogenic compounds and to transform their releases into the equivalent emission of a reference substance. However, they are not

explicitly damage-oriented, since they do not quantify the damage on human health. Furthermore, they do not distinguish the severity of carcinogenic and other health outcomes. The setting of an acceptable risk at 1 death over 10000 people, as proposed by Guinée et al. [1996], is also highly subjective. A stricter acceptable level (for instance 1 death over 1 million people) could instead be set, changing the acceptable level by a factor 100.

Approaches of the second category have the advantage to explicitly quantify the damage induced by carcinogenic compounds and a method like the Eco-Indicator 99 differentiates between the severity of carcinogenic effects and other toxic effects. However, their application in LCIA has some drawbacks:

- The risk at low doses is extrapolated using the linearized multistage model as a default model. While different models properly fit the observed data, they may lead to large differences in the estimated risk at low doses, since none of these models correctly represents the mechanism of carcinogenesis [NRC, 1983; Gray, 1998]. The application of the linearized multistage model only gives the impression of specific knowledge unwarranted for a default procedure like the multistage model. No discussion on the mechanism of action is provided.
- The upper confidence limit q_1^* is unlikely to underestimate risk at low exposure levels, which is consistent with prudent health policy [Beck et al., 1994]. This conservative approach is acceptable for Risk Assessment, where an upper bound of the human cancer potency is sought. However, it is not adequate for LCIA where it might bias the comparison of compounds. Best estimates rather than conservative estimates must be evaluated in LCIA, since the impact assessment aims to compare toxic releases. LCIA methods using q_1^* do not indicate that this factor may overestimate the risk and that q_1^* should therefore be applied with extreme caution, particularly for substances for which there is no evidence to support a linear mode of action.
- Specific comments concerning the Eco-Indicator 99 could be made. For instance, when the unit risk is known for only one exposure pathway, the risk for other routes is extrapolated using data on inhalation rate, food or water consumption. The toxicokinetic differences for different routes of exposure are not taken into account [Goedkoop and Spriensma, 1999]. This can be misleading, as we will show in section 2.6 for metals.

2.1.6 Objectives

The main procedures available in LCIA to characterize carcinogenic effects and their drawbacks have been discussed. This chapter aims to propose a new paradigm responding to some of the limitations encountered in the impact assessment step of LCA. More precisely, this chapter has the following objectives:

1) To quantify the risk of cancer resulting from a chronic exposure (damage-oriented approach), using recent developments in health risk assessment of the US EPA and adapting them to the specific requirements of LCIA, for instance by avoiding conservatism as much as possible.

A quantification applicable to both carcinogenic and noncarcinogenic effects would be beneficial to compare these effects and eventually aggregate them into a single score for human health.
2) To develop a procedure for quantifying the cancer risk for compounds with a tumor dose available in the literature.
3) To test whether acute toxicity data is a good predictor of cancer potency for data-poor substances.
4) To discuss high to low dose extrapolation.
5) To weight carcinogenic effects by assessing their severity.
6) To combine the risk quantification with the evaluation of the cancer severity to derive the effect factor for a large number of chemicals and the set of metals selected in section 1.3.2. This effect factor must be expressed in a unit compatible with the result of the fate and exposure assessment.

A new paradigm is proposed in section 2.2 for quantifying the cancer risk in Life Cycle Impact Analysis. It is applied to more than forty substances in section 2.3 and to the set of selected metals in section 2.6. A comparison with impact assessment methods using the upper confidence limit q_1^*, a discussion on linearity and threshold as well as sensitivity analyses are also presented in section 2.3. A procedure for quantifying the risk from the tumor dose is implemented in section 2.4 and demonstrated on more than 600 toxic releases. The use of the lethal dose as a predictor of cancer potency for incompletely tested chemicals is investigated in section 2.5 and the severity of the different types of tumor is discussed in section 2.7. Effect factors are finally derived in section 2.8, by combining the risk quantification (sections 2.3 to 2.6) with the severity of the tumor types (section 2.7), as illustrated in figure 2.2. Conclusions are drawn in section 2.9.

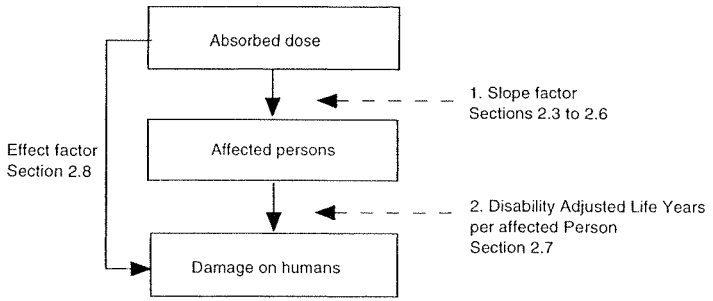

Figure 2.2 Overview of the stages followed in this chapter to assess the effect factor of carcinogenic chemicals.

2.2 THE ED10-APPROACH: A NEW PARADIGM FOR LCIA

This section describes the ED_{10}-approach that we propose to quantify the carcinogenic risk in LCIA. Since it is related to recent developments in the Risk Assessment strategy of the US EPA, these developments are briefly discussed.

2.2.1 Recent developments in the EPA's Risk Assessment

The US EPA recently proposed a guideline for carcinogen Risk Assessment [EPA, 1996], in order to replace the 1986 guideline described in section 2.1.4. The chemical's mode of action, investigated in the hazard identification, becomes a central element of the evaluation. When detailed information on the mechanism of action is available, it is recommended to use a biologically based model or a case-specific model. However, data are generally insufficient to support these types of models [EPA, 1996].

• Benchmark dose BMD_{10}

The proposed default procedure is to use a curve-fitting model for the observed data and to identify the benchmark dose. The benchmark dose BMD_{10} is defined as the 95% lower confidence limit to the dose producing a 10% risk over background [Crump, 1984] (see figure 2.3). Since 50 subjects are a typical sample size for experiments on rodents, there may not be sufficient power to detect response changes much below 10%, justifying the selection of a 10% response level [Rees and Hattis, 1994]. The benchmark concentration BMC_{10} could be similarly defined.

• Extrapolation down to low doses

For the extrapolation down to low doses, the BMD_{10} is used as a point of departure for extrapolating in a linear manner the relationship towards low doses if the evidence supports a linear mode of action. If there is sufficient evidence to support a nonlinear mode of action, a risk quantification by fitting a model to the response data and extrapolating towards low doses is rejected, because different models can lead to a wide range of results and there is currently no general basis to choose among models. Instead, a margin of exposure is derived by comparing the benchmark dose to the environmental exposure [EPA, 1996].

2.2.2 The slope factor β_{ED10}

For the first time in LCIA, we introduce in this section the ED_{10}-approach. We define the effect dose ED_{10} as the best estimate or the maximum likelihood estimate of the dose corresponding with a 10% added risk over background incidence (see figure 2.3). The ED_{10} for humans and animals is denoted ED_{10h} and ED_{10a}, respectively. The ED_{10h} is derived by modeling the dose-response data with the multistage model. This model is then only used for fitting the data in the range of the observations. Sensitivity analyses will show in section 2.3.3 that the choice of the model has little influence on the ED_{10h}.

The key principle of the ED_{10}-approach is the application of the ED_{10h} as a point of departure to extrapolate the risk down to low doses. Cancer risk towards humans is then characterized by drawing a straight line from the ED_{10h} down to the origin of the dose-response function (if the background tumor incidence is zero), as illustrated in figure 2.3. The slope of this straight line is called the slope factor and is denoted β_{ED10} (see equation (2.3) and figure 2.3). The slope factor can be interpreted by saying that "the steeper the slope, the higher the risk".

$$\beta_{ED10} = \frac{0.1}{ED_{10h}} \qquad \text{Equation (2.3)}$$

where:

β_{ED10}: Slope factor $[\frac{\text{Risk}}{\text{mg/kg-day}}]$

ED_{10h}: Best estimate of the effect dose inducing an added risk of 10% over background incidence for humans [mg/kg-day]

0.1: Response level corresponding to the dose ED_{10h} [Risk]

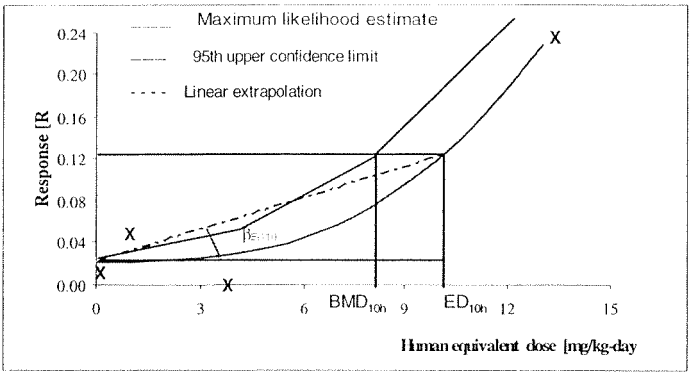

Figure 2.3 Dose-response function for acephate (insecticide) predicted by fitting the multistage model written by Crouch [1985] to the data (denoted X on the figure) observed in a mice bioassay, and reported in the Integrated Risk Information Service database [EPA, 1998].
95th upper confidence limit predicted by the BMDS software [EPA, 1999].
BMD_{10h}: Benchmark dose for humans.
ED_{10h}: Effect dose for humans.
β_{ED10}: Slope factor based on the ED_{10h}.

The slope factor β_{ED10} is expressed in terms of a lifetime risk of cancer per daily dose. Risk is defined as the probability of an adverse outcome under given conditions. The risk expected to occur for a lifetime exposure (70 years for humans) is deduced, since the effect dose is based upon chronic data or subchronic data adjusted to account for a lifetime exposure. As an example, a slope factor β_{ED10} of 10^{-4} [Risk of cancer / mg/kg-day] for a

substance i means that a lifetime exposure to 1 mg of substance i per kilogram of body weight and per day would result in 1 additional case of cancer in a population of 10000 people. In other words, the potential risk for a person to develop a cancer, when that person absorbs 1 mg of substance i per day and per kilogram of body weight during its entire lifetime, is 0.01%.

Finally, while the ED_{10}-approach is based upon the 1996 US EPA's proposed guideline for cancer Risk Assessment, adaptations at two levels were required for an application in LCIA:
- The ED_{10h} is considered instead of the BMD_{10h} as a point of departure. LCIA aims avoid the use of a conservative estimate that may bias the comparison of chemicals. Using the ED_{10h} instead of the BMD_{10h} is necessary to account for the different objectives and requirements of Life Cycle Assessment and Risk Assessment.
- A straight line is drawn from the ED_{10h} down to the origin of the dose-response curve for all compounds, while the EPA is restricting the linear extrapolation to chemicals with sufficient evidence for a linear mode of action. Restricting the analysis to these chemicals would mean to attribute a risk of zero to potentially nonlinear substances; this is not acceptable for comparing chemicals in LCIA. Furthermore, comparing the BMD_{10h} to the exposure level of humans implicitly assumes an extrapolation. We prefer an explicit extrapolation that can be discussed; the linearity and the non-threshold hypotheses are discussed in sections 2.3.5 and 2.3.6.

2.3 SLOPE FACTORS DIRECTLY QUANTIFIED FROM BIOASSAYS

The ED_{10}-procedure has been presented in the previous section. Its application to LCIA is explored in this section for 44 compounds with bioassay results available in the Integrated Risk Information Service (IRIS) database. It will also be applied in section 2.4 to a larger number of chemicals and in section 2.6 to metals selected in the introduction (see 1.3.2). In the present section, slope factors are compared with upper bounds q_1^* and sensitivity analyses are performed to test different models. The linearity and non-threshold hypothesis is also discussed.

2.3.1 Slope factors for 44 compounds

Bioassay results available in the US EPA's Integrated Risk Information Service database [EPA, 1998] have been considered for 44 chemicals. These compounds are listed in appendix 2.1.2, with indications on their production volume. More than 50% of these compounds are High Production Volume Chemicals (HPVC), that is chemicals with a production or imported quantity exceeding 1000 tonnes in at least one OECD country [OECD, 1997]. Their bioassay data for an oral exposure are listed in appendix 2.1.1, with information on the target organ where the tumor is expected to develop. From these bioassay data, we were able to plot the dose-response curve for each substance, and thus to assess the ED_{10h} and derive the slope factor for each compound. Since doses administrated to animals are adjusted in the IRIS database to human equivalent doses for carcinogens, effect doses for humans (ED_{10h}) are gained from the analysis. They are presented for each substance in appendix 2.1.2, together with indications on the route(s) of exposure for which they are valid. The computer program written by Crouch [1985] to carry out the calculations of the multistage model has been selected for modeling the data in the range of the observation and to assess the ED_{10h}. The application of other models is discussed in sensitivity analyses (section 2.3.3).
Figure 2.4 summarizes the slope factors derived for the studied chemicals. They range from $7.2 \cdot 10^{-4}$ for di(2-ethylhexyl)adipate up to 8.5 [Risk of cancer / mg/kg-day] for aldrin. A factor 10^4 is thus observed between the lowest and the highest cancer risk.

As an example of calculations, the multistage model provides the following dose-response curve for acephate: $R(d)=1-[\exp-(0.022 + 0.00011 \cdot d^3)]$. An ED_{10h} of 10 [mg/kg-day] and a slope factor β_{ED10} of 10^{-2} [Risk of cancer / mg/kg-day] are derived (also see figure 2.3). This means that a lifetime exposure to 1 [mg/kg-day] of acephate (or 70 [mg/pers-day]) would result in 1 additional case of cancer in a population of 100 people.

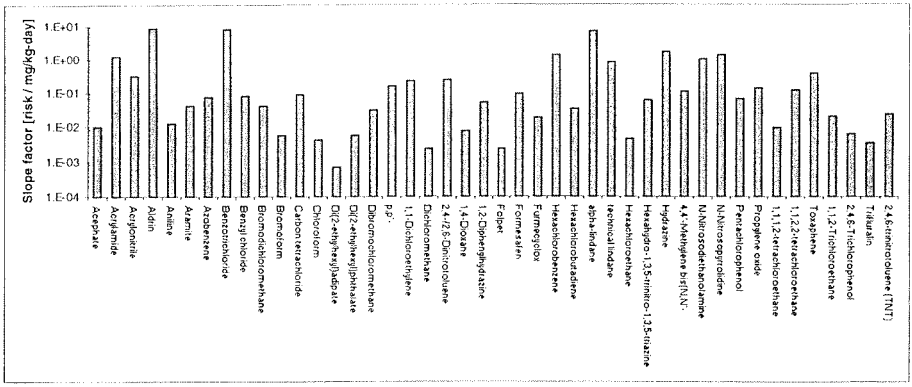

Figure 2.4 Slope factor βED10 for the 44 chemicals listed in appendix 2.1.2.

2.3.2 Effect dose versus benchmark dose

The program written by Crouch [1985] has been used in section 2.3.1 for assessing the ED_{10h}. This program does not provide the BMD_{10h} as a main result. On the contrary, the Benchmark Dose Software (BMDS) recently released by the US EPA [EPA, 1999] provides both the benchmark dose and the effect dose as outputs. It is applied here to compare these two doses. Benchmark doses and effect doses predicted by the multistage model are plotted in figure 2.5 (see appendix 2.1.2 for detailed values). A regression analysis, carried out on the logarithmic values of the parameters, leads to the following correlation (see figure 2.5, log-log scale):

$$BMD_{10h} = x \cdot (ED_{10h})^{y} \qquad \text{Equation (2.4)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 0.59$, $0.56<x<0.67$; $y = 1.0 \pm 0.038$; $R^2=0.98$, 33 measurements, mean square=0.0109.

Equation (2.4) shows that the ED_{10h} and the BMD_{10h} are well correlated ($R^2=0.98$). On average, the ED_{10h} is higher by a factor 1.7 than the BMD_{10h}. This factor indicates the implication of using the ED_{10h} rather than the BMD_{10h} in LCIA.
While the difference between the BMD_{10h} and the ED_{10h} is low, appendix 2.1.4 indicates that the ratio q_1^*/q_1 ranges from 4 up to infinite for 40% of the chemicals, reflecting the large difference between the conservative (q_1^*) and the most likelihood (q_1) estimate of the slope at low doses. At a higher response level, the difference between the conservative (BMD_{10h}) and the most likelihood (ED_{10h}) estimate is much smaller, mainly because these doses are closer to the observed values and are thus much less uncertain.

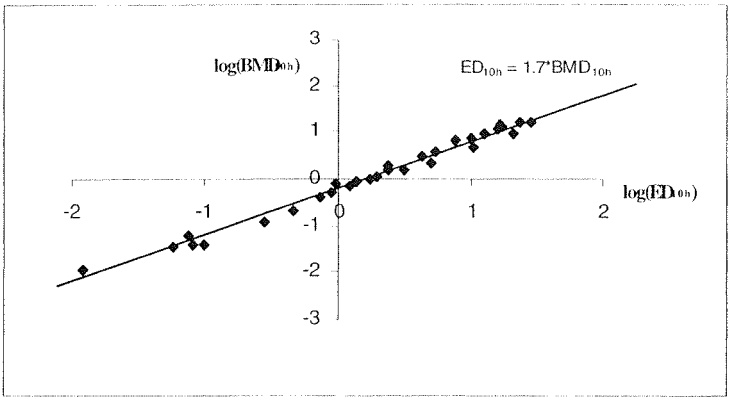

Figure 2.5 Comparison of the ED_{10h} and the BMD_{10h}, for 33 chemicals listed in appendix 2.1.2 (n=33, R^2=0.98). These doses are derived from the multistage model provided in the EPA's Benchmark Dose Software [EPA, 1999].

2.3.3 Sensitivity analyses

Slope factors presented in section 2.3.1 have been calculated using the ED_{10h} as a point of departure and the multistage model as a curve-fitting model. Other models and other points of departure could be considered for assessing the risk of cancer. Sensitivity analyses are carried out in this section to test the choice of the point of departure and of the model. We propose to test five points of departure (ED_{10h}, ED_{1h}, $ED_{0.1h}$, $ED_{0.01h}$, $ED_{0.001h}$) and five models: the Weibull model, the logistic model, the multistage model, quantal linear model and the quantal quadratic model. These quantal models are provided in the EPA's Benchmark Dose Software [EPA, 1999].

Effect doses gained from the different models and from the different points of departure are presented in table 2.2 and figure 2.6 for acephate. The ED_{10h} varies from one model to another one by a factor 1.6, whereas the $ED_{0.001h}$ varies by a factor 3200. Thus, the lower the response level, the higher the difference between the effect doses predicted by the different models. The reason is that the effect dose is less dependent on the model if its response level is close to the experimental data corresponding to high exposure dose. This indicates that the extrapolation towards low doses is highly uncertain, as reported in the literature [NRC, 1983; Gray, 1998]. The ED_{10h} is the smallest reliable dose which is fairly independent from the model. The choice of the multistage in section 2.3.1 for assessing the ED_{10h} has therefore a limited impact, as any model predicts about the same ED_{10h}.

The point of departure also influences the risk quantification. For acephate, the ratio of the slope factors $\beta ED10/\ \beta ED0.001$ varies from 1 to 1850 (see table 2.2), depending on the shape of the dose-response curve given by the model. A high ratio indicates that the model is predicting a strongly sublinear curve (e.g. the Weibull model), while a ratio close to 1 means that a linear curve is predicted by the model (e.g. the quantal linear model). The

rationale for keeping the ED_{10h} as the point of departure is that it is the smallest dose fairly independent from the model.

Results of the sensitivity analysis for other compounds than acephate are presented in appendix 2.1.3. They confirm that the ED_{10h} is fairly independent from the model, while the $ED_{0.001h}$ strongly varies from one model to another (up to a factor $7 \cdot 10^4$ for alpha-lindane).

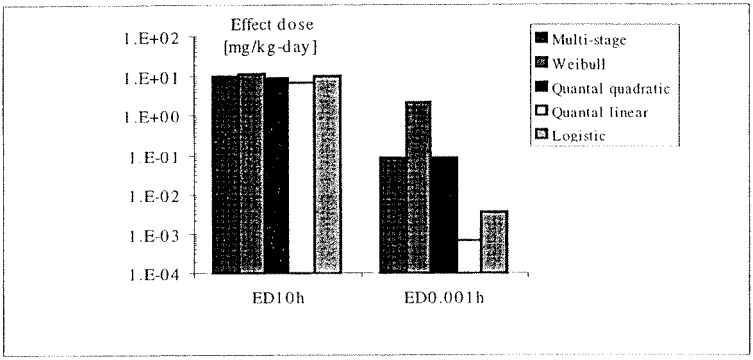

Figure 2.6 Effect doses ED_{10h} and $ED_{0.001h}$, calculated for acephate using different models reported in the Benchmark Dose Software [EPA, 1999].

Model	ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/ kg-day]	ED_{1h} [mg/ kg-day]	$ED_{0.1h}$ [mg/ kg-day]	$ED_{0.01h}$ [mg/ kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/ kg-day]	β_{ED10} / β
Multi-stage	10.0	1.0E-02	2.8	0.87	0.27	8.7E-02	1.1E-04	87
Weibull	11.4	8.8E-03	7.4	4.9	3.3	2.1E+00	4.8E-06	184
Quantal quadratic	9.0	1.1E-02	2.8	0.87	0.28	8.8E-02	1.1E-04	98
Quantal linear	6.9	1.4E-02	0.7	0.065	0.0065	6.6E-04	1.5E-02	1
Logistic	9.6	1.0E-02	2.5	0.31	0.035	3.5E-03	2.9E-03	3.6
Max./Min. value	1.6		11.3	75	508	3182		

Table 2.2 Effect doses and slope factors for different points of departure and different models, calculated for acephate using the Benchmark Dose Software [EPA, 1999].
ED_{Xh}: Best estimate of the effect dose inducing an added risk over background of X% for humans.

2.3.4 Comparison with LCIA methods applying q1*

The slope factor β_{ED10} can be compared with the upper confidence limit $q1^*$s applied in LCIA by Goedkoop and Spriensma [1999] and Hertwich [1999]. Both factors have been assessed for the same 44 chemicals (refer to appendix 2.1.2 for detailed values). A regression analysis, carried out on the logarithmic values of the β_{ED10} and $q1^*$ parameters, leads to the following correlation (see figure 2.7, log-log scale):

$$\beta_{ED10} = x \cdot (q1^*)^y \qquad \text{Equation (2.5)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 0.5$, $0.42<x<0.59$; $y = 0.95 \pm 0.058$; $R^2=0.96$, 44 measurements, mean square=0.0401

As the power is not significantly different from one, equation (2.5) simplifies to:

$$\beta_{ED10} = 0.5 \cdot q1^* \qquad R^2=0.94 \qquad \text{Equation (2.6)}$$

Figure 2.7 shows that the slope factors β_{ED10}s and $q1^*$s are strongly correlated ($R^2=0.94$), confirming similar conclusions presented by Shoaf et al. [1995]. On average, the upper bound $q1^*$ is higher by a factor 2 than the slope gained from the ED_{10}h. Figure 2.7 shows that the slope factors β_{ED10} is higher than $q1^*$ only for five compounds: acephate, aniline, aramite, alpha-lindane, 4,4'-methylene bis(n,n'-dimethyl)aniline. The reason is that the multistage model predicts for these 5 substances a strongly sublinear curve.

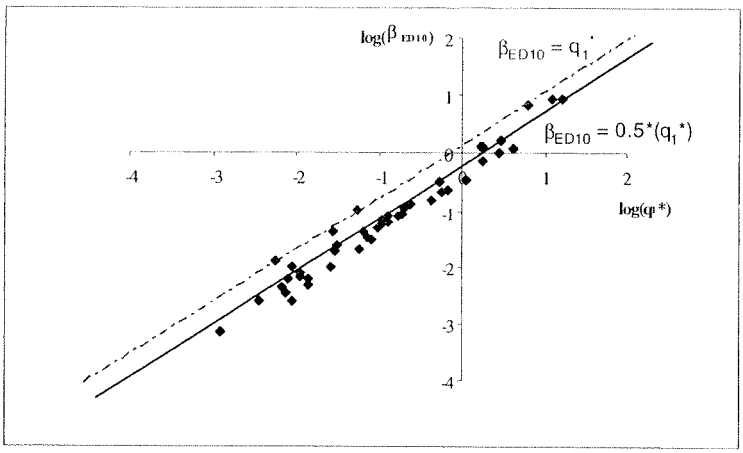

Figure 2.7 Comparison of the upper confidence limit $q1^*$ and the slope factor β_{ED10}, for the 44 chemicals listed in appendix 2.1.2 ($R^2=0.94$, n=44).

2.3.5 Discussion on the threshold

The ED_{10h} is associated with a response level of 10%. This level is orders of magnitude above the typical environmental levels to which humans are exposed. However, we use the ED_{10h} as a point of departure to assess the carcinogenicity at low human exposure range, assuming a linear dose-response function without threshold. The threshold assumption is discussed here, while the linearity hypothesis is discussed in section 2.3.6.

There is a relative agreement that carcinogenesis is likely to be a non-threshold phenomenon for genotoxic carcinogens, since it is believed that just one molecule of these substances can induce cancer by damaging the DNA. However, there is much debate over whether carcinogenesis is a threshold phenomenon for nongenotoxic substances [Beck et al., 1994]. Nongenotoxic carcinogens do not damage DNA, but become active in the proliferation of cancer through secondary mechanisms. They may therefore have thresholds. As an example, the mechanism of action of saccharin provides strong evidence that saccharin causes bladder tumors in rats only at doses high enough to cause precipitation of silicate in urine [Beck et al., 1994].
Divergence exists between regulatory agencies to classify carcinogens into threshold and non-threshold substances. The European Union considers genotoxic and non-genotoxic carcinogens as non-threshold and threshold chemicals, respectively [Gray, 1998; Faustman and Ommen, 1996]. On the contrary, the US EPA conventionally handles all carcinogens as non-threshold substances [EPA, 1986]. The absence of detectable threshold for radiation-induced carcinogenesis has been used to support this hypothesis [Pitot and Dragan, 1996]. Dioxin is a good illustration of divergence between agencies. While the US EPA provides an upper bound q_1^* for dioxin (TCDD), countries like Canada consider dioxin as a non-genotoxic substance characterized by an Acceptable Daily Intake [Beck et al., 1994]. These assessments are based on policy decisions rather than on biologic modeling of low-dose effects, since there is generally insufficient information to decide about the presence or absence of a threshold.
The ED_{10}-procedure is based on a non-threshold; a threshold is not integrated, in particular because it is extremely delicate in LCIA to evaluate whether the exposure occurs above or below the presumed threshold (refer to section 3.3.3 for a more comprehensive discussion on the threshold).

2.3.6 Discussion on linearity

a) Shape of the dose-response curve

There is an extensive debate on whether risk is linearly proportional to the exposure for low doses or whether nonlinearity must be accounted for.One could think of estimating the linearity hypothesis by looking at the shape of the dose-response curve predicted by a curve-fitting model. As an example, the dose-response curves for acephate and chloroform are plotted in figures 2.3 and 2.8. Based on the general shape of these curves predicted by the

multistage model, acephate and chloroform could respectively be classified as "sublinear" and "linear" chemicals. However, inspection of figure 2.3 indicates that there is no significant difference in the response for the first three groups of animals and that a minimal variability in the response of 0.05 is to be expected. Taking into account that variability, a linear extrapolation from the highest observed value (dose=13 mg/kg-day; response=0.24) down to the origin of the dose-response function would be as equally compatible with the bioassay data as the sublinear curve gained from the multistage model. Conversely, the linear dose-response function plotted in figure 2.8 for chloroform could turn into a sublinear curve if the third and fourth group of animals were excluded from the analysis. It is interesting to note that the US EPA has gone through a comprehensive analysis that showed chloroform to be a nonlinear carcinogen, on biological grounds [Rhomberg, 2000]. Similar comments could be made for other chemicals, looking at their dose-response curve and values observed in bioassays. The general conclusion is that there is little evidence concerning the general shape of the dose-response curve that can be obtained from rodent bioassays. There is even less evidence that can be obtained about the linearity at low level of exposure, since the risk at that level is not measurable by animal experiments.

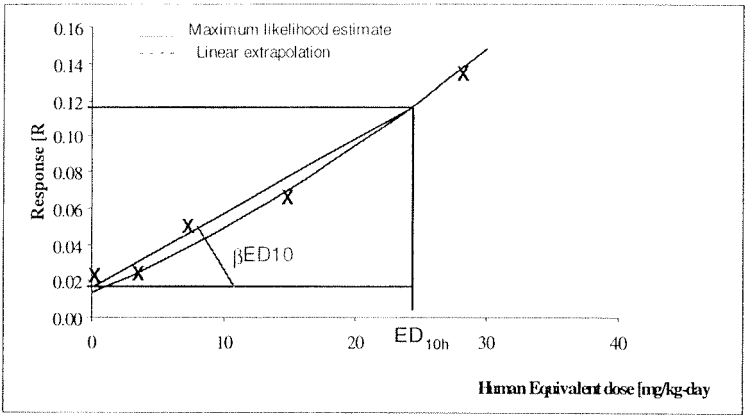

Figure 2.8 Dose-response curve for chloroform, predicted by fitting the multistage model written by Crouch [1985] to the data (denoted X on the figure) observed in a rats bioassay and reported in the IRIS database [EPA, 1998].

b) Mode of action

We have shown that the linearity or nonlinearity can not be addressed on the basis of empirical data. Information on the mechanism of action, gathered during the hazard identification, could instead be considered [EPA, 1996(a)]. Input data for assessing the mode of action are tests for mutagenicity, the stage(s) during the carcinogenic process at which the compound is active, tumor data in humans and animals, structure activity relationships (SARs), etc [EPA, 1996(a)].

Complete information on the mode of action is still lacking for most compounds. However, a simplified classification can be carried out with the following rationale. If a compound is carcinogenic in animals and is observed to cause mutations, the inference that its mode of

action is through mutagenicity is strong [EPA, 1996(a)] and the assumption of a linear mechanism of carcinogenesis has some mechanistically-based justifications. As an example, available data for alkene oxide and brominated alkane support a mutagenic mode of action and therefore support the linearity of their dose-response relationship [EPA, 1996(a)]. On the contrary, if a compound is carcinogenic in animals but not mutagenic (for instance it induces cancer by promotion of cell growth), it probably induces cancer by an indirect mechanism and can therefore be potentially nonlinear. This simplified classification is applied in section 2.4.4, using the genotoxicity database of Gold and Zeiger [1997].
The rationale for that scheme is that a single molecule of a DNA-reactive chemical has a small but nonzero chance of setting in motion a chain of events leading to carcinogenesis. In addition, the transformation processes that lead to DNA damage depend on the number of collision between molecules of the chemical and cellular reactants. At low doses, the number of available cellular-reactant molecules does not change as a function of the concentration of the chemical. Thus, there is linearity in the relationship between exposure of the chemical and the number of DNA adducts produced [Rees and Hattis, 1994].

c) Biologically based dose-response models
In the long term, the development of biologically based dose-response models could help to reflect the biological characteristics of carcinogenesis as accurately as possible and thus offer a better mechanism-based projection of the risk at low doses. The best known of these models is the MVK model (Moolgavkar-Venson-Knudson) which reproduces quite well the multistage characteristics of neoplastic development, with the consideration of the rate at which normal cells are converted to initiated cells and the rate at which the initiated cells are converted to neoplastic cells [Pitot and Dragan, 1996]. That model has not been yet widely applied, but this may change in the next years.
Biologically based models could represent a new strategy for the evaluation of the risk. Conventional assessment relies on curve-fitting models with minimal biological basis to analyze the biological "black box" between the exposure (input) and the effect (output). With biological models, critical events along the pathway between exposure and effect could be described for well-known chemicals, by including information on pharmacokinetic and pharmacodynamic. The identification of changes in the kinetics over a dose range, over different routes and over species would enable a better mechanism-based projection of risk beyond the range of possible observations in terms of dose, route of exposure and species [Beck et al., 1994].

d) Impact of the linearity assumption
The ED_{10}-procedure assumes linearity for all chemicals. For substances that would indeed be sublinear, the application of the ED10h as a point of departure would lead to a maximal value of the slope factor. A scheme can be proposed to face that issue. Linear chemicals can be flagged, based on the mechanism of action (see above, part b). The contribution of the other chemicals is to discuss individually. If the substance does not play a role in a given case study, the eventual overestimation of the risk has no incidence. On the contrary, if the substance plays a significant role, more information would be required to improve the evaluation of its effect. A departure from the ED_{10} approach could then be made if new

information improves the understanding of the mechanism of action so that the low dose-response curve can be assessed from this understanding.
In conclusion, using the ED_{10} as a point of departure does not avoid all the bias and the "true" risk is overestimated for sublinear compounds. For a screening analysis, using a maximal value of the slope factor can be justified as a way to determine if the risk induced by a substance is low enough that it can be eliminated from further consideration.

2.4 SLOPE FACTORS ESTIMATED FROM THE TUMOR DOSE

Slope factors have been determined in the previous section for 44 substances, using their bioassay results found in the IRIS database. Since results are only available for a limited number of chemicals in this database, it is investigated in this section whether the ED_{10h} can be estimated from a more widely available carcinogenic parameter: the tumor dose. The tumor dose TD_{50a} is defined as the dose inducing tumors in half of the tested animals at the end of their standard lifespan [Peto et al., 1984]. It is often reported in the literature as a measure of the carcinogenicity. Krewski et al. [1993] found that the TD_{50a} is correlated to the upper bound q_1^*. We have shown in section 2.3.4 that q_1^* is correlated to the ED_{10h}. This suggests a correlation between the TD_{50a} and the ED_{10h}. A confirmation of this correlation is provided in this section and applied to more than 600 substances to derive their slope factors.

2.4.1 Correlation TD_{50a}-ED_{10h}

A theoretical correlation between the tumor dose and the effect dose is represented in equation (2.7). It is based on the assumption of a linear dose-response curve between the TD_{50a} and the ED_{10a} [Rhomberg, 2000]. Equation (2.8) is derived by introducing the human equivalent dose ED_{10h} into equation (2.7). The human dose can be derived from the animal dose, applying the conversion factor from animal-to-human. Based on the "surface" scaling procedure explained in section 2.1.4.e)), this factor is equal to 6 for rats and 13 for mice. Equation (2.9) is derived by applying an average animal-to-human conversion factor of 10.

$$ED_{10a} = \frac{TD_{50a}}{6.6} \qquad \text{Equation (2.7)}$$

$$ED_{10h} = \frac{TD_{50a}}{6.6 \cdot CF_{a->h}} \qquad \text{Equation (2.8)}$$

$$ED_{10h} = \frac{TD_{50a}}{66} \qquad \text{Equation (2.9)}$$

where:

TD_{50a}: Dose inducing tumors in half of the tested animals [mg/kg-day]

ED_{10a}: Dose inducing a cancer risk of 10% over background for animals [mg/kg-day]

ED_{10h}: Dose inducing a cancer risk of 10% over background for humans [mg/kg-day]

$CF_{a->h}$: Animal-to-human conversion factor [-]

2.4.2 Validation

The theoretical correlation TD_{50a}-ED_{10h} given in equation (2.9) needs to be validated. For that purpose, the tumor dose of the 44 chemicals listed in appendix 2.1.2 has been searched in the Carcinogenic Potency Database published by Gold and Zeiger [1997]. TD_{50a} have been found for 37 substances and are reported in appendix 2.1.2. The TD_{50a}-ED_{10h} correlation for these chemicals is plotted in figure 2.9. A regression analysis, carried out on the logarithmic values of the parameters, leads to the following correlation:

$$ED_{10h} = x \cdot (TD_{50a})^y \qquad \text{Equation (2.10)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 0.04$, $0.019 < x < 0.085$; $y = 0.96 \pm 0.18$; $R^2 = 0.77$, 37 measurements, mean square=0.26

As the power is not significantly different from 1, equation (2.10) simplifies to:

$$ED_{10h} = 0.04 \cdot TD_{50a} = TD_{50a}/25; \quad R^2 = 0.75 \qquad \text{Equation (2.11)}$$

Equation (2.11) confirms the theoretical relationship given in equation (2.9). It is statistically significant (R^2=0.75) and indicates that the higher the tumor dose, the higher the effect dose and the less carcinogenic a chemical.

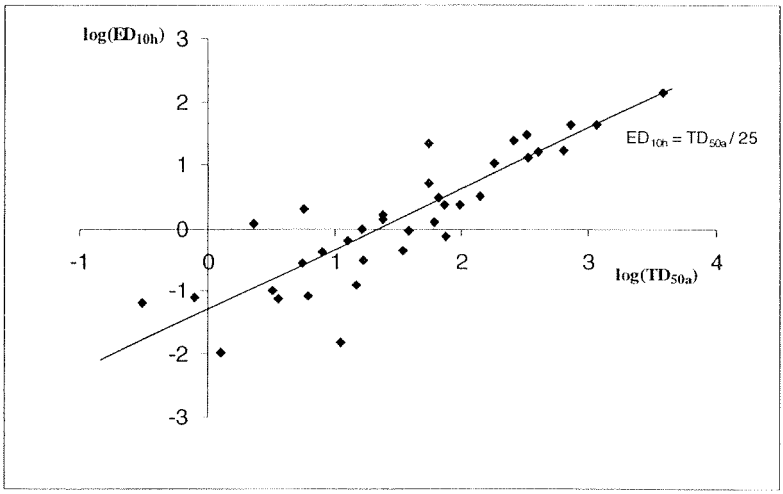

Figure 2.9 Correlation between the tumor dose TD_{50a} and the effect dose ED_{10h}, for 37 substances listed in appendix 2.1.2 (n=37, R^2=0.75).
TD_{50a}s are provided in the Carcinogenic Potency Database [Gold and Zeiger, 1997] and ED_{10h}s are derived from the IRIS database in section 2.3.1.

Two different databases, that is the Integrated Risk Information Service for the ED_{10h} and the Carcinogenic Potency Database for the TD_{50a}, have been considered to derive the TD_{50a}-ED_{10h} correlation presented in figure 2.9. Therefore, part of the variance in this correlation is due to the consideration of different bioassay results. A second TD_{50a}-ED_{10h} correlation has been determined in order to evaluate the uncertainty induced by using different bioassay results. It is plotted in figure 2.10, where both the TD_{50a} and the ED_{10h} are calculated by fitting the multistage model to the bioassay data reported in the IRIS system. A regression analysis, carried out on the logarithmic values, leads to the correlation:

$$ED_{10h} = x \cdot (TD_{50a})^y \qquad \text{Equation (2.12)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 0.045$, $0.034 < x < 0.06$; $y = 0.98 \pm 0.064$; $R^2 = 0.95$, 44 measurements, mean square=0.046.

As the power is not significantly different from 1, equation (2.12) simplifies to:

$$ED_{10h} = 0.045 \cdot TD_{50a} = TD_{50a}/22; \quad R^2 = 0.94 \qquad \text{Equation (2.13)}$$

A higher regression coefficient R^2 is obtained when the same bioassay results are used (R^2=0.94 versus R^2=0.75), indicating that the variance in the TD_{50a}-ED_{10h} relationship reported in figure 2.9 is mainly due to the consideration of different data for deriving the effect dose and the tumor dose. The mean square on the log-value is of 0.046 when the same bioassay results are considered, instead of 0.26 when two different database are used. This indicates that about 4/5 of the mean square is induced by the use of different bioassay data.

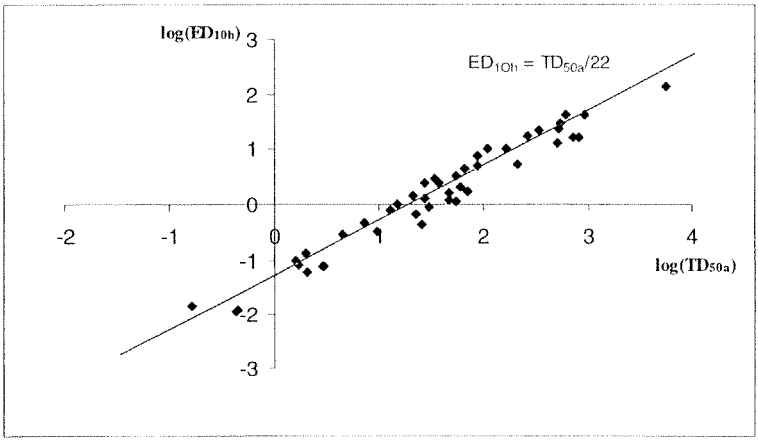

Figure 2.10 Correlation between the tumor dose TD_{50a} and the effect dose ED_{10h}, for the 44 chemicals reported in appendix 2.1.2 (n=44, R^2=0.94). Both doses are derived using bioassays reported in the IRIS database.

2.4.3 Extrapolated slope factor $\beta_{ED10\text{-extr.}}$

As the validation step has confirmed the correlation between the tumor dose and the effect dose, we can use the tumor dose to derive the ED_{10h}. A quick evaluation of the slope factor is consequently feasible from a compound's tumor dose. The TD_{50a}-ED_{10h} correlation determined in the validation process (equation (2.11)) is chosen, since it is based on experimental values. The extrapolated slope factor is denoted $\beta_{ED10\text{-extr.}}$ and is given by equation (2.14), by combining equations (2.3) and (2.11).

$$\beta_{ED10\text{-extr.}} = \frac{0.1}{ED_{10h}} = \frac{0.1}{TD_{50a}} \cdot 25 = \frac{2.5}{TD_{50a}} \qquad \text{Equation (2.14)}$$

where:

$\beta_{ED10\text{-extr.}}$: Slope factor extrapolated from the tumor dose $[\frac{\text{Risk}}{\text{mg/kg-day}}]$

Two comments about that extrapolation should be mentioned. Firstly, Gold and Zeiger [1997] reported the tumor doses without indication of their relevance toward humans. The application of the TD_{50a} to derive human cancer risk assumes that chemicals inducing tumors in rodent cancer tests are potential human carcinogens. This assumption may be debatable for some substances. For instance, while there is sufficient animal evidence about lead carcinogenicity, the available human evidence is considered by the EPA to be inadequate to refute or demonstrate any carcinogenicity for humans from lead exposure [EPA, 1998].

Secondly, Gold and Zeiger [1997] reported in their handbook the bioassay results used for determining the tumor dose. Consequently, the ED_{10h} could be directly derived from these data. This has not been undertaken, since the validation step shows that the TD_{50a}-ED_{10h} correlation is good enough for a first screening of the cancer risk in LCIA. A re-calculation for chemicals of particular interest is always possible if required.

2.4.4 Application

a) Selection of chemicals

Substances are selected based on data availability and relevance. The Carcinogenic Potency Database [Gold and Zeiger, 1997] contains results of 5152 long-term cancer tests on 1298 chemicals. Different tumor doses are frequently derived from one test, since various exposure paths and sites of tumor can be studied during a test. An experiment is classified as positive if the author of the study reports that the chemical is carcinogenic or presents some evidence of carcinogenic activity. If there is only one positive test on a chemical, then the tumor dose for the most potent site of tumor is reported. Otherwise, the harmonic mean of the most potent tumor dose from each positive test is calculated by Gold and Zeiger [1997]. When an experiment is terminated before the standard lifespan, the data are corrected by a duration adjustment factor [Gold and Zeiger, 1997].

b) Results

For chemicals without positive results, there is not enough evidence for a judgement about the carcinogenicity and the slope factor can not be estimated (n.e.). On the contrary, the procedure summarized in section 2.4.3 can be applied to 671 substances with a positive result in at least one test. For these compounds, the tumor dose provided in the Carcinogenic Potency Database is listed in appendix 2.2, as well as the slope factor derived from the TD_{50a}. Information on the main route of exposure, on the target organ where the tumor is expected to develop and on the production volume is also provided in this appendix. More than 20% of the compounds are high production volume chemicals.

Figure 2.11 presents the frequency histogram of the slope factors derived from the TD_{50a}. Slope factors range from 10^{-4} for cinnamyl anthranilate up to 10^{4} [risk of cancer / mg/kg-day] for 2,3,7,8-tetrachlorodibenzo-p-dioxin, reflecting that the range of the cancer risk can be 100 million-fold (see appendix 2.2 for detailed values). Most chemicals are characterized by a risk ranging from 10^{-3} to 10^{1} [Risk of cancer / mg/kg-day].

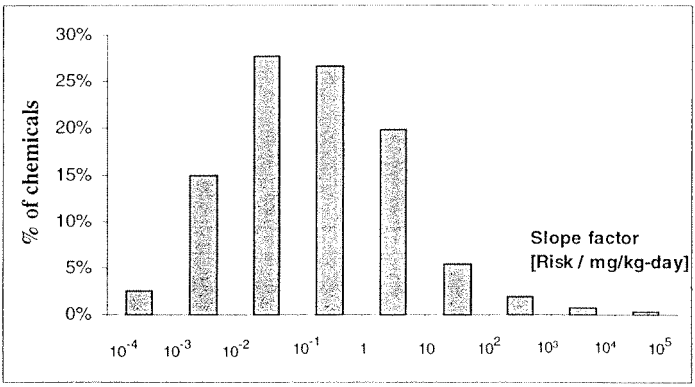

Figure 2.11 Frequency histogram for the slope factors derived from the TD_{50a} for 671 substances (see appendix 2.2 for detailed values).

Appendix 2.2 also indicates the results of the *Salmonella* mutagenicity test (Ames test) reported in the genotoxicity database of Gold and Zeiger [1997]. As explained in section 2.3.6, we can use this information for a first evaluation of the linearity of the dose-response curve of a substance. The rationale consists to assume that a chemical which is carcinogenic in animals and causes mutation has a linear mode of action. Among the 220 chemicals with non-equivocal results in the genotoxicity database, 49% have positive results in the Ames mutagenicity test and 51% have negative results (see appendix 2.2). Chemicals with positive results, that is chemicals whose mutagenic mode of carcinogenicity provides evidence of linearity, can be flagged.

2.5 SLOPE FACTORS FOR INCOMPLETELY TESTED CHEMICALS

Slope factors have been assessed in the previous section for more than 600 chemicals, using tumor doses reported in the Carcinogenic Potency Database. However, these substances are only a small share of all the chemicals that act as initiators, promotors or progressors of cancer. How can we deal with the other 100000 substances registered in the European Inventory of Existing Commercial Chemical Substances [EEA, 1998]? Only for a small fraction of these compounds results of long-term bioassays are available and the carcinogenicity of many chemicals to which humans are exposed will never be investigated, mainly because animal bioassays take many years to be completed and are expensive. Data required to deem carcinogenic potencies such as the ED_{10h} or the TD_{50a} are consequently often lacking and the approaches presented in sections 2.3 and 2.4 are thus not applicable for a majority of chemicals.
The tendency is to neglect the carcinogenic effect of incompletely tested compounds [Gray et al., 1997], which is debatable as about half of the chemicals reported by Gold and Zeiger [1997] have been found to be carcinogenic. Some authors [Zeise et al., 1984 and 1986; Metzger et al., 1989; Gold and Zeiger, 1997] support that readily available lethal doses could be used to approximate the carcinogenic risk of compounds. This proposal is examined in this section.

2.5.1 Extrapolation from the LD_{50a}

The lethal dose LD_{50a} is defined as the dosage of a chemical needed to produce death in 50% of the treated animals [Eaton and Klaassen, 1996]. The LD_{50a} of 41 of the 44 chemicals listed in appendix 2.1.2 has been found in the Registry of Toxic Effects of Chemical Substances (RTECS) [NIOSH, 1998]. The LD_{50a}-ED_{10h} correlation for these chemicals is plotted in figure 2.12. A regression analysis, carried out on the logarithmic values of the parameters, leads to the following correlation:

$$ED_{10h} = x \cdot (LD_{50a})^y \qquad \text{Equation (2.15)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 0.042$, $0.0027 < x < 0.63$; $y = 0.52 \pm 0.4$; $R^2 = 0.14$; 41 measurements, mean square=0.94.

The regression coefficient $R^2=0.14$ indicates that the lethal dose and the effect dose are poorly correlated. Substances with a similar lethal dose can differ by a factor up to 10^4 in their ED_{10h} (see figure 2.12). Different reasons explain the poor correlation between the effect dose and the lethal dose. First, the ED_{10h} is associated with chronic and carcinogenic effects while the lethal dose corresponds to acute lethality. Causality is unlikely between toxicity and carcinogenicity, since they entail different mechanisms. In addition, the lethal

effect after a single exposure clearly differs from carcinogenic effects produced by repeated chronic exposure. Second, only the lowest lethal dose found in the literature for a given species and route of exposure is presented in the RTECS database, regardless of reliability and statistical significance [NIOSH, 1998].
The use of acute data for comparing chemicals in a long-term exposure context would result in extremely high levels of uncertainty (see figure 2.12). Consequently, the lethal dose has not been applied in this chapter to quantify the risk of cancer induced by incompletely tested chemicals, not even for a first screening. We instead set the slope factor of incompletely tested chemicals as "not estimated". Clues about how to manage this situation are discussed below.

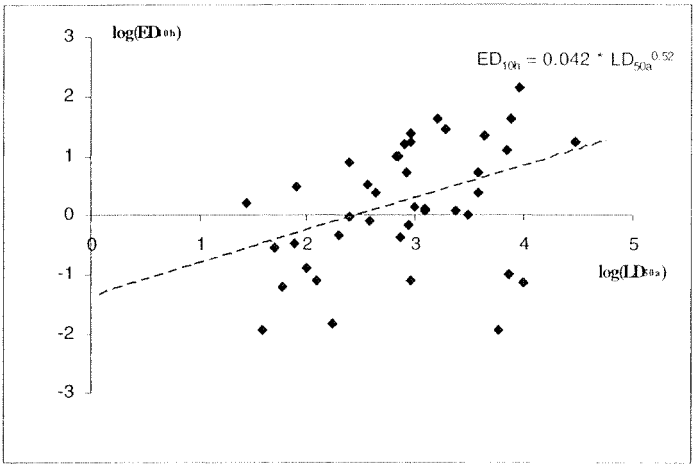

Figure 2.12 Correlation between the lethal dose LD_{50a} and the effect dose ED_{10h}, for 41 of the 44 chemicals listed in appendix 2.1.2 (n=41; R^2=0.14).

2.5.2 Discussion

Structure Activity Relationships (SARs) have been used to assess the relative carcinogenicity of chemically related compounds [Pitot and Dragan, 1996]. Mutagenicity tests have also been developed to screen for potential carcinogens, with the rationale that the initiation event of carcinogenesis is a mutagenic event. The *Salmonella* test developed by Ames et al. [1973] has received the widest attention. While the SARs and the mutagenicity tests are useful for screening substances and hazard identification, they do not permit to quantify the risk of cancer in the impact assessment of LCA.
A proper carcinogenicity testing of a substance, involving an assessment of the ED_{10h} or of the TD_{50a} by a long-term bioassay, therefore appears to be required to quantify its cancer risk estimate. It would be economically unrealistic to test all chemicals, since a comprehensive toxicity testing of one substance can cost up to $5 million [EEA, 1998;

Eaton and Klaassen, 1996]. However, among the thousand of existing substances, priority could be put on the 1500 more widely used chemicals that account for 95% of the global production [Keating, 1993] and have thus the potential for creating the largest exposure to humans. In that perspective, the Organization for Economic Cooperation and Development (OECD) has launched a program for determining whether High Production Volume Chemicals (HPVC) are adequately managed under existing controls. The OECD proposed to screen HPVC chemicals for potential risk, so that resources can be concentrated on undertaking further work on chemicals of concern [OECD, 1998]. By 1998, 86 HPVC were classified in list 1 (low priority for further work, since the risk is low), 13 were classified in list 2 (further testing beyond the initial assessment is required to more precisely evaluate the risk) and 10 were classified in list 3 (further risk management might be necessary). Results from the OECD may be integrated in our procedure, if quantitative values are provided in the future.

2.6 SLOPE FACTORS FOR METALS

As explained in section 1.3.2, metals are chosen in this dissertation as an example of application of the proposed impact assessment method. In this section, their slope factors is assessed by distinguishing between the oral and the inhalation routes of exposure. Since atmospheric metals are attached to particulate matter, their health effect by inhalation is linked to particles. The size of particles is the key determinant of their absorption in the lung. Particles greater than 10 μm in diameter are deposited in the upper airway (phyrynx, trachea), while particles characterized by a diameter lower than 2.5 μm ($PM_{2.5}$) penetrate deep in the lungs, reach the alveoli, can penetrate in blood to be distributed into the body and accumulate in the kidneys, bones, teeth, etc. [Künzli et al., 1997].
To be consistent with what has been done so far for other chemicals, we based in priority our judgment on the IRIS database [EPA, 1998]. The EPA used epidemiological studies for cadmium, chromium(VI), beryllium and inorganic arsenic. Data reported in the IRIS system for these studies are not transparent and comprehensive enough to make it possible to derive the effect dose by plotting the dose-response curve. Therefore, the relationship between β_{ED10} and q_1^* presented in equation (2.6) is applied below to derive the slope factors β_{ED10} of these metals. For lead and methylmercury, no quantification of the risk is provided by the EPA. An evaluation of the cancer risk from the TD_{50a} is therefore proposed. Table 2.4 summarizes the slope factors calculated for the different metals, while their evaluation is presented below for each metal.

2.6.1 Cadmium

• Exposure by inhalation
There is limited evidence of cadmium carcinogenicity from occupational epidemiological studies, because of the variety of confounding factors that occur in situations of human exposure. On the contrary, sufficient evidence of carcinogenicity in rats and mice by inhalation exist. The EPA therefore classifies cadmium as a probable human carcinogen (class B1).
In the IRIS database [EPA, 1998], the reference study is a group of 602 workers who had been employed in a cadmium smelter for a minimum of 6 months during the years 1940-1969. The tumor type associated with the exposure is lung tumor. Thun et al. [1985] were able to ascertain that the increased lung cancer risk observed in workers was not due to the presence of arsenic or to smoking. We use the q_1^* estimate of 3.5 [Risk of cancer / mg/m^3] reported in the IRIS database to derive a slope factor of 1.75 [Risk of cancer / mg/m^3], applying equation (2.6). In terms of dose, this corresponds to a slope factor β_{ED10} equal to 6.1 [Risk of cancer / mg/kg-day] and an ED_{10h} of 0.0165 [mg/kg-day].

The form of cadmium that is of most interest for the inhalation exposure is cadmium oxide (main form of airborne cadmium). The primary form of cadmium in studies is therefore cadmium oxide. Experimental studies in laboratory animals have also used other forms such as cadmium chloride, cadmium sulfide and cadmium sulfate. In general, these forms of cadmium have similar toxicological effects [Taylor et al., 1999].

• **Oral exposure**

Cadmium has not been shown to be carcinogenic following oral exposure in humans [Taylor et al., 1999] and no risk evaluation is provided in the IRIS system for the oral exposure. However, evidence of non-carcinogenicity for humans has not been demonstrated and we should therefore not conclude that its cancer potency is zero. We therefore determine that the cancer risk after oral ingestion of cadmium can not be estimated (n.e.).

Route-to-route extrapolation is often practiced when the data for one route of exposure are missing. However, inhalation data should not be used to derive the oral risk when chemicals are expected to have different carcinogenicity by inhalation than by oral uptake. Since metals belong to that kind of chemicals [EPA, 1994], we do not propose to derive the slope factor after an oral exposure to cadmium from its inhalation slope factor. For the same rationale, route-to-route extrapolation is also not applied for the other metals.

2.6.2 Chromium(VI)

• **Exposure by inhalation**

Chromium(VI) is classified as a known human carcinogen by the inhalation route of exposure (class A). Long term exposure to chromium has been associated with lung cancer in workers of chromium-related industries. These workers are exposed to levels in air that are 100 to 1000 times higher than those found in the natural environment. The reference study used in the IRIS database [EPA, 1998] is a cohort of 332 workers employed from 1931-1951 in a chromate industry in Ohio. Lung cancer death rates increased by gradient of exposure to total chromium [Mancuso, 1975]. The cancer mortality was assumed to be due to chromium(VI). We use the corresponding q_1^* estimate of 12 [Risk / mg/m^3] reported in the IRIS database to derive a slope factor of 6 [Risk of cancer / mg/m^3], applying equation (2.6). In terms of dose, this corresponds to a slope factor β_{ED10} equal to $2.1 \cdot 10^1$ [Risk of cancer / mg/kg-day] and an ED_{10h} of 0.0048 [mg/kg-day].

The mechanism of chromium(VI) carcinogenicity is believed to result from the formation of mutagenic DNA lesions following intracellular reduction of Cr(VI) to Cr(III). Chromium(VI) readily passes through cell membranes and is rapidly reduced intracellularly to generate Cr(V) and Cr(IV) intermediates [EPA, 1998].

• **Oral exposure**

There are no data in the literature suggesting that chromium(VI) is carcinogenic by the oral route of exposure [EPA, 1998; Wilbur and Voytek, 1999]. Carcinogenicity of chromium(VI) by this route can therefore not be determined (class D) and we determine that the cancer risk of chromium(VI) after oral exposure can not be estimated.

2.6.3 Chromium(III)

Occupational exposure to trivalent chromium by inhalation has been studied in the chromate manufacturing and ferrochromium industries. However, exposures to both Cr(III) and Cr(VI) were encountered. Hexavalent chromium(VI) has been assumed as the likely agent of excess cancer risk in chromium workers. Indeed, animal studies reveal that chromium (VI) is carcinogenic, whereas the data from exposure of animals to trivalent chromium do not support evidence of its carcinogenicity [EPA, 1998]. Data are therefore inadequate to determine the potential carcinogenicity of trivalent chromium which is not classified as to its human carcinogenicity (class D) in the IRIS database [EPA, 1998]. However, the classification of hexavalent chromium as a known human carcinogen raises a concern for the carcinogenic potential of trivalent chromium. We therefore determine that the cancer risk of chromium(III) can not be estimated with the present level of knowledge.

2.6.4 Copper

The IRIS database [EPA, 1998] reports that there are no human data and inadequate animal data for copper compounds. Similar conclusions are reported in the ATSDR's toxicological profile on copper [ATSDR, 1990]. Therefore, copper is not classified as to its human carcinogenicity (class D) in the IRIS database. We therefore determine that the cancer risk of copper can not be estimated. Corrections of this assessment may occur in the future if new studies provide evidence of some carcinogenic effects.

2.6.5 Methylmercury

• Exposure by inhalation

Carcinogenicity of methylmercury by inhalation can not be determined. We therefore determine that the cancer risk of methylmercury can not be estimated for that exposure pathway.

• Oral exposure

The IRIS database reports that there are inadequate data in humans and limited evidence of carcinogenicity in animals for methylmercury. Methylmercury is consequently classified as a possible human carcinogen (class C) in the IRIS database [EPA, 1998] which does not provide a quantitative estimate of the risk.

Gold and Zeiger [1997] reported a TD_{50a} of 3.12 and 1.91 [mg/kg-day] for rats orally exposed to mercuric chloride (CASN 7487-94-7) and mercurymethyl chloride (CASN 115-09-3) respectively. In appendix 2.2, we derive a slope factor $\beta ED10$ of 0.8 and 1.3 [Risk of cancer/ mg/kg-day] for these 2 forms of mercury respectively. The slope factor of 1.3 [Risk of cancer/ mg/kg-day] is selected for a first screening of methylmercury. Since this slope factor is only based on evidence in rodents for mercurymethyl chloride and that inadequate

data is reported on humans for methylmercury, its uncertainty is higher than slope factors derived from the upper bound q_1^*.

2.6.6 Beryllium

• Exposure by inhalation

Based on the limited evidence of carcinogenicity in humans exposed to airborne beryllium and sufficient evidence of carcinogenicity in animals, beryllium is classified as a probable human carcinogen (class B1) for the inhalation route of exposure. Wagoner et al. [1980] conducted an epidemiology study on the appearance of lung cancer after exposure to beryllium oxide. This study is reported in the IRIS database [EPA, 1998] and we use it as the reference study. The lifetime cancer risk for an exposure to beryllium oxide is evaluated at 2.4 [Risk of cancer/ mg/m^3]. We use that q_1^* estimate to derive a slope factor of 1.2 [Risk of cancer / mg/m^3], applying equation (2.6). In terms of dose, this corresponds to a slope factor $\beta ED10$ equal to 4.2 [Risk of cancer / mg/kg-day] and an $ED10_h$ of 0.024 [mg/kg-day].

• Oral exposure

Carcinogenicity of beryllium by the oral route of exposure can not be determined (class D). We therefore determine that the cancer risk of beryllium can not be estimated for that exposure pathway.

2.6.7 Lead

• Exposure by inhalation

Carcinogenicity of lead by inhalation can not be determined. We therefore determine that the cancer risk of lead can not be estimated for that exposure pathway.

• Oral exposure

There is sufficient animal evidence about lead carcinogenicity. However, all the available epidemiological studies lack quantitative exposure information. Thus, the available human evidence is considered to be inadequate to refute or demonstrate any potential carcinogenicity from lead exposure [EPA, 1998]. Therefore, lead is classified as a probable human carcinogen (class B2) by the EPA. The EPA determined that it is not appropriate to quantify the carcinogenic risk of lead, because known toxicokinetic differences between humans and animals can not be taken into account in the standard methods for quantifying risks [Ennever, 1994].

Gold and Zeiger [1997] reported a $TD50_a$ of 46.6 and 181 [mg/kg-day] for kidney tumor, in rats orally exposed to lead acetate (CASN 301-04-2) and lead subacetate (CASN 1335-32-6) respectively. In appendix 2.2, we derive a slope factor $\beta ED10$ of $5.4 \cdot 10^{-2}$ and $1.4 \cdot 10^{-2}$ [Risk of cancer / mg/kg-day] for these two forms of lead respectively. The risk of $5.4 \cdot 10^{-2}$ [Risk of cancer / mg/kg-day] is selected for a first screening of the carcinogenicity of lead. Since

this risk estimate is only based on evidence in rodents for lead subacetate and since no evidence is reported on humans for lead, its uncertainty may be higher than slope factors derived from the upper bound q_1^*.

2.6.8 Inorganic arsenic

Organic arsenic is usually less harmful than inorganic arsenic and the following assessment focuses on inorganic arsenic. Inorganic arsenic is classified as a human carcinogen in the IRIS database [EPA, 1998], based on sufficient evidence from human data (class A). On the contrary, carcinogenicity has not been demonstrated in animals [IARC, 1980], indicating that rodents may not be a good model for testing arsenic carcinogenicity.

- **Exposure by inhalation**

For the inhalation exposure, two epidemiological studies on smelter workers are reported in the IRIS database [EPA, 1998]. The associated tumor type is lung cancer. We use the q_1^* estimate of 4.3 [Risk / mg/m^3] reported by the EPA to derive a slope factor of 2.15 [Risk of cancer / mg/m^3], applying (2.6). In terms of dose, this corresponds to a slope factor β_{ED10} equal to 7.5 [Risk of cancer / mg/kg-day] and an ED_{10h} of 0.013 [mg/kg-day].

- **Oral exposure**

Tseng et al. [1968] and Tseng [1977] provided data on skin cancer prevalence rates associated with ingestion of inorganic arsenic. They studied some 40000 Taiwanese persons exposed to arsenic in drinking water and 7500 relatively unexposed controls. The results are used in the IRIS database [EPA, 1998] to develop dose-response data. We use the q_1^* estimate of 1.5 [Risk / mg/kg-day] reported by the EPA to derive a slope factor β_{ED10} of $7.5 \cdot 10^{-1}$ [Risk of cancer / mg/kg-day], applying equation (2.6).

2.7 SEVERITY OF THE TUMORS

Slope factors have been calculated in sections 2.3, 2.4 and 2.6 for more than 600 chemicals. The indication on the organ where the tumor is expected to develop has been provided in appendices 2.1.1 and 2.2, as well as under the discussion of each metal in section 2.6 (see also table 2.4 for a summary). A weighting of the different cancers is required, since their severity can differ depending on the organ affected. The Disability Adjusted Life Years (DALY) concept is proposed for this weighting.

2.7.1 The DALY approach

Murray and Lopez [1996(a);(b)] published a comprehensive health statistic for the World Health Organization and the World Bank. The burden of disease on human populations is provided in this study. In their analysis, Murray and Lopez [1996(a);(b)] distinguished between mortality and morbidity outcomes.

- They introduced the concept of Years of Life Lost (YLL) due to premature death to evaluate how long people would have lived if they had not been affected by a disease. The actual YLL for an individual can never be known and it must be assumed that the individual conforms to a reference population. We calculated the Years of Life Lost per affected person (YLL_p) due to a given tumor, using equation (2.16). We did not weight differently the importance of one year of life lost depending on the age at which death occurs and did not discount future damages compared to the present ones, which would not be compatible with the LCA's philosophy.

$$YLL_p = \frac{L}{N} \qquad \text{Equation (2.16)}$$

where:

YLL_p: Years of Life Lost per affected Person [yr/pers]

L: Total expected Years of Life Lost [yr]

N: Total Number of deaths [pers]

- The Years of Life lived with a Disability (YLD) are also introduced by Murray and Lopez [1996(a)] to account for a decrease in quality of life due to a disease. We calculated the Years of Life lived with a Disability per affected person (YLD_p) for a given tumor, using equation (2.17). A zero disability weight W represents perfect health and a unit disability weight corresponds to death.

$$YLD_p = D \cdot W \qquad \text{Equation (2.17)}$$

where:

YLD_p: Years of Life lived with a Disability per affected Person [yr/pers]

D: Duration of the disability [yr/pers]

W: Disability weight, describing the severity of the disability [-]

- The Disability Adjusted Life Years per affected Person ($DALY_p$) can be derived by summing up the YLL_p and YLD_p, as stated in equation (2.18). Thus, the $DALY_p$ makes it possible to account for both the years of life lived with a disease and the years of life lost due to premature death.

$$DALY_p = YLL_p + YLD_p \qquad \text{Equation (2.18)}$$

where:

$DALY_p$: Disability Adjusted Life Years per affected Person [yr/pers]

2.7.2 $DALY_p$ for different tumors

We calculated the $DALY_p$ for 16 types of tumors, using equation (2.18) and data provided by Murray and Lopez [1996(b)] at a world level. Disability weights have been fixed by a panel of experts made up of health providers. Hospital registers have been considered to assess the duration of the disability, the number of deaths and the total years of life lost for the 16 tumors.

Table 2.3 indicates that the contribution of the years of life lived with the disability (YLD_p) to the $DALY_p$ is small. The role of premature death is consequently crucial and the value choice concerning the disability weight of the cancer has little influence. It is also interesting to compare the severity of the various tumors. Table 2.3 shows that the different types of cancer have more or less the same severity: the prostate cancer has the lowest $DALY_p = 5.9$ [yr/pers], and leukemia has the highest $DALY_p = 19.9$ [yr/pers]. An average $DALY_p$ of 11.1 [yr/pers] can be derived, by weighting each $DALY_p$ according to the prevalence of its associated cancer. This average $DALY_p$ is applied as a default value in section 2.8, in order to derive the effect factor of the carcinogenic substances studied in the previous chapters. This is acceptable since the $DALY_p$ is characterized by a small range of values. If required, a specific $DALY_p$ can be applied by looking at the site of tumor reported for a given experiment. This is carried out in section 2.8 only for the selected metals.

Type of cancer	Disability W [-]	D [yr disab./pers]	YLD_p = W · D [yr lost/pers]	Death L [yr lost]	N [pers]	YLL_p = L/N [yr lost/pers]	Disability + Death $DALY_p$ = YLD_p + YLL_p [yr lost/pers]
Cancers preterminal							
Mouth and oropharynx	0.145	4.3	0.62	3.2E+06	2.9E+05	11.4	12.0
Oesophagus	0.217	1.7	0.37	3.4E+06	3.6E+05	9.4	9.8
Stomach	0.217	2.9	0.63	7.0E+06	7.5E+05	9.3	9.9
Colon and rectum	0.217	3.7	0.80	3.9E+06	4.7E+05	8.3	9.1
Liver	0.239	1.6	0.38	6.3E+06	5.0E+05	12.6	13.0
Pancreas	0.301	1.2	0.37	1.5E+06	1.8E+05	8.1	8.5
Trachea, bronchus, lung	0.146	1.8	0.26	8.3E+06	9.5E+05	8.8	9.0
Melanoma	0.045	4.2	0.19	5.1E+05	4.8E+04	10.6	10.8
Breast	0.069	4.2	0.29	3.8E+06	3.2E+05	11.8	12.0
Cervix uteri	0.066	3.8	0.25	2.7E+06	2.0E+05	13.3	13.6
Corpus uteri	0.066	4.5	0.30	5.8E+05	6.4E+04	9.0	9.3
Ovary	0.081	3.4	0.28	1.3E+06	1.1E+05	12.2	12.5
Prostate	0.113	4.2	0.47	1.1E+06	1.9E+05	5.5	5.9
Bladder	0.085	4.2	0.36	9.8E+05	1.3E+05	7.5	7.8
Lymphomas and myeloma	0.089	3.5	0.31	3.0E+06	2.1E+05	13.8	14.1
Leukemia	0.112	3.1	0.35	4.4E+06	2.3E+05	19.6	19.9
Cancers terminal	0.809	n.a.		1.3E+07	1.0E+06	12.7	12.7
					6.0E+06		11.1

Table 2.3 Disability Adjusted Life Years per affected Person ($DALY_p$) for various sites of tumor, using data reported by Murray and Lopez [1996(a);(b)].

W: Disability weight [-]

D: Duration of the disability [yr/pers]

L: Total expected Years of Life Lost, worldwide [yr]

N: Total Number of deaths, worldwide [pers]

YLD_p: Years of Life lived with a Disability per affected Person [yr/pers]

YLL_p: Years of Life Lost per affected Person [yr/pers]

2.8 EFFECT FACTORS

The ultimate objective of this chapter is to derive the effect factor for a large number of chemicals and for the metals selected in section 1.3.2. The determination of these effect factors is presented here and results are discussed. Effect factors are summarized in appendix 1.1.

2.8.1 Definition

The slope factor β_{ED10} and the Disability Adjusted Life Years per affected Person ($DALY_p$) have been presented and calculated in the previous sections. We combine them together to derive the effect factor, as indicated in equation (2.19). In this equation, the conversion factor $1/(BW \cdot LT_h \cdot N_{365})$ is applied to express the slope factor in units compatible with the $DALY_p$, that is in persons affected by a cancer per absorbed mass. The effect factor is expressed in years of life lost per absorbed mass.

$$EF_i = \left[\beta_{ED10-i} \cdot \frac{1}{BW} \cdot \frac{1}{LT_h} \cdot \frac{1}{N_{365}}\right] \cdot DALY_p \qquad \text{Equation (2.19)}$$

where:

EF_i: Effect factor of substance i [yr lost / $mg_{absorbed}$]

β_{ED10-i}: Slope factor of substance i $[\frac{Risk}{mg/kg\text{-}day}]$

BW: Body weight [kg/pers]

LT_h: Lifetime of humans [yr]

N_{365}: Number of days per year [days/yr]

$DALY_p$: Disability Adjusted Life Years per affected Person, for the cancer associated with substance i [yr /pers]

2.8.2 Results

a) Effect factors for metals

The derivation of the effect factors for the selected metals is summarized in table 2.4. The effect factors of metals vary from $3.4 \cdot 10^{-7}$ for lead to $1.1 \cdot 10^{-4}$ [yr lost/mg absorbed] for chromium(VI), showing a factor 320 between the lowest and the highest effect factor. Estimates of the effect factor for lead and methylmercury are presented in italic in table 2.4. They are indeed derived from the tumor dose TD_{50a} for lead acetate and mercurymethyl

chloride (see sections 2.6.5 and 2.6.7), while the EPA judged that it is not appropriate to quantify the carcinogenic risk for lead and methylmercury [EPA, 1998].
For cadmium, chromium(VI) and beryllium, the effect factor is determined only for an exposure by inhalation, while the effect factor is provided for lead and methylmercury only for the oral route of exposure. The absence of adequate data for one route of exposure has been discussed in section 2.6, as well as the reasons for not extrapolating from one route to another route for metals. It should not be interpreted that the risk is equal to zero for a route with inadequate data and the abbreviation "n.e." in table 2.4 means that the risk can not be evaluated. In the interpretation of the LCIA results, it must be kept in mind that the oral (inhalation) pathway has not been included for cadmium, chromium(VI) and beryllium (lead and methylmercury).

	Metal	CAS RN	Route of exposure	Data type	Cancer category	Type of cancer	β_{ED10} [Risk / mg/kg-day]	$DALY_p$ [yr lost/pers]	EF [yr lost / m absorbed
1	Cadmium	7440-43-9	Oral		D		n.e.		n.e.
			Inhalation	Human	B1	Lung	6.1E+00	9	3.1E-05
2	Chromium(VI)	18540-29-9	Oral		D		n.e.		n.e.
			Inhalation	Human	A	Lung	2.1E+01	9	1.1E-04
3	Chromium(III)	16065-83-1	Oral / inhalation		D		n.e.		n.e.
4	Copper	7440-50-8	Oral / inhalation		D		n.e.		n.e.
5	Methylmercury	22967-92-6	Oral	Rats	C	Kidney	1.3E+00	11.1	*8.1E-06*
			Inhalation				n.e.		n.e.
6	Beryllium	7440-41-7	Oral		D		n.e.		n.e.
			Inhalation	Human	B1	Lung	4.2E+00	9	2.1E-05
7	Lead	7439-92-1	Oral	Rats	B2	Kidney	5.4E-02	11.1	*3.4E-07*
			Inhalation				n.e.		n.e.
8	Inorganic arsenic	7440-38-2	Oral	Human	A	Skin	7.5E-01	10.8	4.5E-06
			Inhalation	Human	A	Lung	7.5E+00	9	3.8E-05

Table 2.4 Evaluation of the effect factor EF from the slope factor β_{ED10} and the Disability Adjusted Life Years per affected Person ($DALY_p$), for the studied metals.
n.e. = not estimated.

b) Effect factors for the other chemicals studied in this chapter

The effect factors for the more than 600 chemicals studied in sections 2.3 and 2.4 are summarized in appendix 1.1. Their calculations are presented in appendices 2.1.2 and 2.2. These appendices indicate that the effect factor varies from $1.3 \cdot 10^{-9}$ for cinnamyl anthranilate to $3.4 \cdot 10^{-1}$ [yr lost / mg absorbed] for 2,3,7,8-tetrachlorodibenzo-p-dioxin.

2.9 Conclusions

Effect factors have been calculated in this chapter for more than 700 substances, by combining their slope factors β_{ED10} with their Disability Adjusted Life Years per affected Person $DALY_p$. Metals have been studied with specific attention. A factor larger than 100 million-folds has been found between the lowest and the highest effect factors, indicating that the range in the carcinogenic potency is very large. Most of the variation of the effect factors among toxic releases is due to differences in the slope factors, since all cancer effects have similar $DALY_p$. We also found that the lethal dose LD_{50a} should not be used to extrapolate in a reliable way the effect factor for data-poor substances.

In the ED_{10}-approach, the effect dose ED_{10h} has been used as a point of departure to derive the slope factors. From the previous sections, it can be concluded that this approach has the following advantages:
- It can be applied to characterize both carcinogenic (this chapter) and noncarcinogenic (chapter 3) effects of chemicals. Adopting a similar approach for both types of health outcomes is not a requirement in LCIA, but permits to compare these effects on a common framework and to distinguish their severity. The final benefit is that these effects can eventually be aggregated into a single final score for human health.
- It exploits the correlation between the ED_{10h} and the tumor dose TD_{50a}, and thus enables deriving slope factors for more than 700 substances, compared to about 200 values reported in previous studies.
- It is based on a simple linear extrapolation, and not on mathematical models that give the appearance of specific knowledge while they have little biological justifications. It makes the assumption of linearity explicit, and this assumption can be tested by looking at the mechanisms of action.
- It follows recent developments in the Risk Assessment strategy of the Environmental Protection Agency and adapts them to the specific requirements of LCIA, for instance by choosing the maximum likelihood estimate ED_{10h} rather than the lower confidence limit BMD_{10h} as a point of departure.
- The severity of carcinogenic endpoints is integrated in the analysis, using the Disability Adjusted Life Years per affected Person concept. Thus, the effect factor can quantify the damage in years of life lost per absorbed mass (damage-oriented approach) and can easily be combined with the fate and exposure assessment studied in chapter 4 (see section 5.1).

However, effect factors determined in this chapter are characterized by different uncertainty sources (see section 5.4.1). In particular, limitations of the ED_{10}-approach due to the linearity and non-threshold assumption can be mentioned:
- Using the ED_{10h} as a point of departure is likely to overestimate the risk for chemicals with a sublinear dose-response curve. The comparison with the upper confidence limit q_1^* indicated that the ED_{10}-approach provides a risk estimate lower only by a factor 2 than q_1^*.

Thus, it should not be concluded that the ED_{10}-approach gives a fundamentally less biased estimate of low-dose risks than does the upper-bound q_1^*. For a screening analysis, using a maximal value of the slope factor can be justified as a way to determine if the risk induced by a substance is low enough that it can be eliminated from further consideration. If the substance has a significant contribution, its mechanism of action should be studied in order to determine the implication of the linear hypothesis.

- The same linear and non-threshold mechanism of action is assumed for all chemicals. This is a simplified representation of the carcinogenesis, since carcinogenic substances can actually be involved in different stages of carinogenesis. The flagging of genotoxic carcinogens, using information provided by mutagenicity tests, is a first proposal to account for differences in action between substances.
- The ED_{10h} indicates the risk at high exposure levels and two compounds having the same ED_{10h} can have different slopes at low exposure levels.

As an answer to these limitations, some reviewers could recommend to use the ED_{10h} only for ranking toxic releases, and not for quantifying their risk on humans. An implicit extrapolation would then be carried out, since the ED_{10h} would be used to weight the effects of chemicals at low exposure levels. We prefer to perform an explicit extrapolation which can be discussed. In that sense, the ED_{10}-approach can be understood as a default screening procedure. Departure from this procedure can, and should be made if new information improves the understanding of the mechanism of action to the point that the low dose-response curve can be more precisely assessed from this understanding.

3. EFFECT FACTOR FOR NONCARCINOGENIC EFFECTS

ABSTRACT

This chapter aims to quantify the noncarcinogenic risk resulting from a chronic exposure to a large number of toxic releases, and to derive their effect factors for an application in Life Cycle Impact Assessment (LCIA). A description of different types of noncarcinogenic health outcomes is first provided. Concepts developed in Risk Assessment by the US Environmental Protection Agency (EPA), as well as the potentials and shortcomings of methods currently applied in LCIA to characterize noncarcinogenic effects, are discussed.

The ED_{10}-approach introduced in chapter 2 is applied in this chapter to noncarcinogenic effects. The linear dose-response function without threshold, which is assumed in the ED10-approach, is discussed. The non-threshold assumption is justified by the growing recognition that "no evidence" does not necessarily mean "no effects" and by recent epidemiological studies suggesting that there are no safe level for some compounds.
In a first stage, we calculated the ED_{10h} for beryllium, methyl methacrylate and methylene diphenyl diisocyanate, using their bioassay data reported in the US EPA's Integrated Risk Information Service database (IRIS). For eight other substances, the ED_{10h} (best estimate of the dose inducing a 10% added risk over background for humans) was directly found in the IRIS database or was extrapolated from the benchmark dose. Slope factors ranging from $2.4 \cdot 10^{-5}$ for 1,1,1,2 tetrafluoroethane up to $3 \cdot 10^{1}$ [risk of a critical endpoint / mg/kg-day] for methylmercury are found. In a second stage, the correlation between the effect dose for animals (ED_{10a}) and the more widely available No Observed Adverse Effect Level in animals ($NOAEL_a$) is determined in order to derive the slope factor for a large number of compounds. The human equivalent dose ED_{10h} for a lifetime exposure is derived from the ED_{10a}, using animal-to-human and subchronic-to-chronic conversion factors adapted to LCIA. The ED_{10h} is thus derived from the $NOAEL_a$ for more than 300 substances, leading to slope factors ranging from 10^{-6} up to 10^{3} [risk of a critical endpoint / mg/kg-day]. Slope factors are specifically determined for the set of metals selected in section 1.3.2. Like for carcinogenic effects, an extrapolation of the noncarcinogenic outcomes from the lethal dose LD_{50a} is not applied in this chapter, since the lethal dose LD_{50a} and the ED_{10h} are poorly correlated (R^2=0.26; n=9).

The critical endpoints associated with each substance are characterized by different severity and therefore need to be weighted. A simplified classification of the critical adverse effects into three categories is chosen. To make it compatible with the Disability Adjusted Life Years per affected Person ($DALY_p$) approach selected in chapter 2 to weight carcinogenic

effects, a $DALY_p$ of 11.1, 1.1 and 0.11 years of life lost per person is respectively assigned to the three categories, corresponding to high, medium and low severity. Special attention is paid to classify metals and substances with epidemiological data into the most appropriate category, whereas category 2 is used as the default category for the other substances. The slope factor β_{ED10} and the $DALY_p$ are finally combined together to derive the effect factor (see figure 3.1), which is expressed in years of life lost per absorbed mass. Effects factors ranging from $4.2 \cdot 10^{-12}$ for 1-Chloro-1,1-difluoroethane to $1.3 \cdot 10^{-3}$ [yr lost / mg absorbed] for beryllium are found, reflecting the very large range in the noncarcinogenic effect. The effect factors for the selected metals vary from $9.2 \cdot 10^{-8}$ for chromium(VI) up to $1.3 \cdot 10^{-3}$ [yr lost / mg absorbed] for inhalation of beryllium, showing a factor 10^4 between the lowest and the highest effect factor. The effect factor for the respiratory effects of fine particles, sulfur dioxide, nitrogen oxide and carbon monoxide are also presented, using values calculated by Hofstetter [1998].

The procedure developed in this chapter is discussed and compared to other LCIA methodologies. The ED_{10}-approach has the advantage to quantify the risk of noncarcinogenic adverse effects for a relatively large number of chemicals. Since the ED_{10h} is defined as the dose producing a fixed added risk over background of 10%, it makes it possible to compare chemicals on a similar basis. The conservative values of the animal-to-human and subchronic-to-chronic uncertainty factors, which are incorporated in parameters like the reference dose, are furthermore excluded from the ED_{10h}; the human-to-human uncertainty factor, which is inappropriate for an application in LCIA, is not included. Limitations of the ED_{10}-approach are finally discussed.

3.1. INTRODUCTION

While chapter 2 has evaluated the carcinogenic effects of toxic releases, this chapter focuses on their noncarcinogenic effects. Some major noncancer effects such as kidney toxicity, respiratory diseases, neurotoxicity, etc. are first defined in this introduction. Most of the methods applied in Life Cycle Assessment (LCA) for characterizing toxic effects are based upon the principles developed in Risk Assessment. These principles and their application in LCA are then discussed. The drawbacks of existing Life Cycle Impact Assessment (LCIA) methods and the objectives of the chapter are finally presented.

3.1.1 Classes of noncarcinogenic effects

Toxic compounds can be categorized by looking at the part of the body upon which they exert their toxic effect. Although most toxic substances affect many organs, injury or death is usually the result of damage to a single organ or system. Table 3.1 distinguishes eleven classes of noncarcinogenic effects, depending on the affected organ [EDF, 1998]. We completed this table with examples of substances contributing to the different health effect.
Toxicity to the cardiovascular system occurs when substances affect the heartbeat, the blood pressure or the blood's ability to coagulate. Blood toxicity is induced by substances altering the bone marrow's ability to produce the blood cells or by chemicals preventing red blood cells from carrying oxygen (e.g. carbon monoxide). Developmental toxicity is often considered to be a subcategory of reproductive toxicity. Teratogenic effects are defined as defects induced during development between conception and birth [Eaton and Klaassen, 1996].

Health effect	Definition [EDF, 1998]	Examples [EEA, 1996] and [EDF, 1998]
1 Cardiovascular and blood toxicity	Effect on the cardiovascular or hematopoietic system	Carbon monoxide, lead, particles
2 Neurotoxicity	Effect on the nervous system	Lead, methylmercury, PCB, aluminium
3 Respiratory toxicity	Effect on the respiratory system	SO2, NOx, particles
4 Reproductive toxicity	Effect on the reproductive system	Cadmium, DDT, PCB, phthalate
5 Development toxicity	Effect on the developing child	Cadmium, lead, mercury, some pesticides
6 Endocrine toxicity	Effect on the endocrine system	Endocrine disruptors
7 Gastrointestinal or liver toxicity	Effect on the gastrointestinal tract or liver	Acephate, cobalt, DDT
8 Kidney toxicity	Effect on the kidney or bladder	Arsenic, cadmium, 1-4 dioxane
9 Immunotoxicity	Effect on the immune system	Some pesticides
10 Musculoskeletal toxicity	Effect on the muscles, bones and joints	Atenolol, dapsone, mephenytion
11 Skin or sense organ toxicity	Effect on skin or sense organs	Aniline, benzene, fluorine

Table 3.1 Classification of noncarcinogenic health effects [EDF, 1998].

3.1.2 Methods for Life Cycle Impact Assessment

The characterization of the noncarcinogenic potency of toxic releases by some of the most frequently used LCIA methods is presented here. We propose a classification of methods among 4 levels of sophistication.

a) Linear methods, based on acceptable levels (level 1)

These methods apply acceptable levels such as the Reference Dose (RfD), the Acceptable Daily Intake (ADI) or the Tolerable Daily Intake (TDI) to characterize chemicals. They implicitly assume a linear dose-response curve without threshold and do not quantify the risk of noncancer health effects. These methods are therefore referred to as linear and not damage-oriented methods.

Most of the methods currently applied in LCIA proceed in this way. For instance, the Critical Volume method [BUS, 1984] and the Ökofaktoren 97 [BUWAL, 1998] both consider the Swiss guidelines for air and water quality to fix the limit value or the critical flow of chemicals. Guinée et al. [1996] characterized the adverse effect of 94 substances using Acceptable Daily Intakes (ADIs) defined by the World Health Organization and Tolerable Daily Intakes (TDIs) similarly defined by the Dutch National Institute of Public Health (RIVM). The same position is adopted by Huijbregts [1999] for 182 substances. Similarly, the reference dose RfD is used by Hertwich [1999]; in the Critical Surface-Time method 95 (CST95) [Jolliet and Crettaz, 1997], we also used the RfD.

b) Linear methods, based on exposure-response slopes (level 2)

These methods also assume the linearity of the dose-response function, without consideration of any threshold. However, they provide a quantification of the risk based on exposure-response slopes. These methods are therefore damage-oriented.
In the Eco-Indicator 99 method of Goedkoop and Spriensma [1999], Hofstetter [1998] based his assessment on the epidemiological data for the respiratory effects of air pollutants. This epidemiological information is derived from Pilkington et al. [1997] who summarized in the ExternE study the epidemiological data for 7 air pollutants: particulate matter (PM_{10} and $PM_{2.5}$), nitrate, sulfate, sulfur dioxide, nitrogen dioxide, carbon monoxide and ozone. These pollutants cause different respiratory effects such as cough, asthma, bronchitis, lower respiratory symptom, etc. Hofstetter [1998] applied the Disability Adjusted Life Years scale developed by Murray and Lopez [1996(a);(b)] to weight the different respiratory disabilities. His results are presented in appendix 3.1 and are used in this chapter for deriving the effect factors of fine particles, sulfur dioxide, nitrogen dioxide and carbon monoxide (see section 3.8).

c) "Only above threshold" methods, not damage-oriented (level 3)

Linear methods can not discriminate between processes causing concentrations below a postulated threshold and processes inducing concentrations above that threshold. A suggestion to improve this point is the "only above threshold" approach, which was put

forward by White et al. [1995]. In this method, processes with the largest share of emissions in a product's life cycle are identified. Information about the actual location of these processes is gathered. This site-specific information is used to predict surpassing of a presumed threshold. An emission has an effect only if the threshold concentration where it occurs is exceeded. The effect on human health is thus concentration dependent and the impact assessment depends on the emission site: the higher the background concentration, the more significant the impact on human health.

The Threshold Inventory Interpretation Methodology (TIIM) developed by Hogan et al. [1996] is based upon the "only above threshold" concept. A Threshold Emission Factor is defined as the proportion of an emission that effectively contributes to an effect on human health. This factor amounts to 100% if the substance is emitted in a location where the standard is surpassed and to 0% otherwise. Owens and Rhodes [1995] suggested a similar approach.

d) Nonlinear methods, damage-oriented (level 4)

Damage-oriented methods, using a nonlinear dose-response curve, represent the highest level of sophistication in the proposed scheme. They aim to quantify the damage on humans, without assuming a linear dose-response function. None of the methods presently available in Life Cycle Impact Assessment fulfill these requirements. A framework for developing such methods is presented in appendix 3.5 to identify how human health effects could theoretically be quantified.

Since methods used in LCIA are based on principles developed for Risk Assessment, these principles are presented below. This will help to understand the shortcomings of existing LCIA methods and the need for new developments in this field.

3.1.3 Conventional Risk Assessment by the US EPA

The four main steps of Risk Assessment as defined by the National Research Council [NRC, 1983] have been presented in section 1.1.3. In this section, some key features of the noncancer Risk Assessment conventionally followed by the US Environmental Protection Agency (EPA) are presented. This section is not intended to be a comprehensive review, but instead focuses on the notions relevant for our application to LCIA.

• No Observable Adverse Effect Level

The No Observable Adverse Effect Level (NOAEL) is defined as the highest dose at which it is judged that there is no biologically significant increase in the incidence of any adverse effects between the exposed population and the control. If an effect is not identified as adverse, we refer to a No Observable Effect Level (NOEL) rather than to a NOAEL [Faustman and Omenn, 1996]. The NOAEL is not necessarily associated with a zero effect and can correspond to different incidence levels depending on the design of the experiment. Some studies have shown that the response of NOAELs averages 5% risk for continuous

data and can be greater than 10% risk for quantal endpoints [Faustman et al., 1994; Allen et al., 1994(a);(b)].

• **Reference Dose**

The Reference Dose (RfD) is defined as the daily exposure dose to the human population, including sensitive subgroups, that is likely to be without an appreciable risk of adverse effects during a lifetime exposure [Rees and Hattis, 1994]. However, it should not be concluded that all doses below (above) the reference dose are acceptable (unacceptable) [EPA, 1998].

As indicated in equation (3.1), the reference dose is derived from the NOAEL or LOAEL (Lowest Observable Adverse Effect Level) by applying uncertainty factors and a modifying factor. The NOAEL is preferred to the LOAEL, to ensure that the dose is near the threshold and thereby to avoid the introduction of an additional uncertainty. The uncertainty factors account for the uncertainty in the intraspecies and interspecies variation, and in the extrapolation from short-exposure–duration studies to chronic situations. Although 10 represents the default value for the uncertainty factors (see table 3.2), values less than 10 may be used if sufficient data are available. The modifying factor can be used to account for uncertainties not addressed in the uncertainty factors. For instance, the use of a large number of animals in a study may enhance certainty in the NOAEL, resulting in the use of a modifying factor lower than 1 but greater than 0 [Beck et al., 1994].

Different NOAELs for substances inducing more than one toxic effect can be obtained. These NOAELs generally differ. The critical endpoint is defined as the effect exhibiting the lowest NOAEL of relevance for humans [EPA, 1998]. The NOAEL chosen to derive the reference dose corresponds to this critical endpoint. The reference dose is therefore based on the most sensitive substance-induced endpoint considered to be of relevance for humans.

$$RfD = \frac{\text{NOAEL or LOAEL}}{UF_H \cdot UF_A \cdot UF_S \cdot UF_L \cdot MF} \qquad \text{Equation (3.1)}$$

where:

RfD:	Reference Dose [mg/kg-day]
NOAEL:	No Observable Adverse Effect Level [mg/kg-day]
LOAEL:	Lowest Observable Adverse Effect Level [mg/kg-day]
UF:	Uncertainty factor (see table 3.2) [-]
MF:	Modifying Factor [-]

Factor	Default Value	Meaning
UF_H	10	Variation in sensibility in humans (intraspecies variation)
UF_A	10	Extrapolation from animal to human data (interspecies variation)
UF_S	10	Extrapolation from a subchronic to a chronic exposure
UF_L	10	Consideration of a LOAEL instead of a NOAEL
MF	0<MF<10	Uncertainty of the study

Table 3.2 Uncertainty factors conventionally applied for deriving the reference dose from the No Observable Adverse Effect Level [Beck et al., 1998].

3.1.4 Drawbacks of existing LCIA methods

Leading LCIA methods have been classified in section 3.1.2 in different categories. Their drawbacks are discussed here.

a) Linear methods, not damage-oriented (level 1)

These methods allow to weight noncarcinogenic compounds and to transform them into an equivalent emission of a reference substance. We indicated in chapter 2 that they proceed in the same way for carcinogenic effects. These methods are not explicitly damage-oriented, since they do not quantify the damage on human health. Furthermore, carcinogenic and noncarcinogenic effects are considered to be of equal importance and no distinction is made in terms of severity between noncarcinogenic endpoints like neurotoxicity, respiratory diseases, developmental toxicity, etc.

In addition, these LCIA methods are based on the application of the Reference Dose RfD (or a similar parameter), which has been developed for Risk Assessment and not for a relative comparison of compounds. The RfD and NOAEL have been criticized by different authors [Crump, 1984; Allen et al., 1994(a); Kimmel, 1990]. Comparing toxic releases on the basis of their RfD can bias the comparison that is required in LCIA, for the following reasons:
- The response level associated with the NOAEL can significantly change from one compound to another one (e.g. 0% for a substance i and 4% for a substance j). Consequently, the reference dose does not correspond to a well-known region of the dose-response function.
- The RfD does not adequately characterize the dose-response function, since it is derived from a single datapoint. Once the NOAEL is identified, the rest of the curve is ignored.
- By definition, the NOAEL must be one of the experimental doses tested. Therefore, the RfD is strongly dependant on the experimental design (e.g. tested levels, dose spacing)
- A dose defined as a NOAEL in one experiment could turn out to be a LOAEL if more experimental animals had been used. This approach rewards poor experiments, since a study using fewer animals may result in a larger NOAEL (and thus a higher RfD) than a study using a higher number of animals [Crump, 1984].

- Subjectivity is involved in the process. For instance, it must be judged whether a 2% decrease in weight is a NOAEL or a LOAEL.

Two additional objections for an application of the RfD within LCIA can be mentioned:
- The uncertainty factors applied to derive the reference dose from the NOAEL are conservative and thus incorporate worst case scenarios. For instance, Lewis et al. [1990] observed that for 18 chemicals, the ratio of the subchronic-to-chronic NOAEL was 3.5 or less for 14 chemicals and only one substance had a ratio greater than 10. If the chemical with a ratio greater than 10 were excluded from the analysis, the mean subchronic-to-chronic NOAEL ratio was 3.3. A conservative approach is consistent with the objectives of Risk Assessment. However, it is not appropriate for LCIA, since it may bias the comparison of toxic releases. A procedure based upon best estimates, rather than on conservative values, should be chosen for LCIA.
- The adjustments carried out by the animal-to-human and the subchronic-to-chronic uncertainty factors are also required in LCIA, since the evaluation of the long term effect on humans is sought in the impact assessment. However, it is inappropriate to apply the intraspecies uncertainty factor. This factor is relevant for Risk Assessment where a protective level for the whole population is evaluated. It is therefore important in RA to know which groups of individuals are at high risk. The implementation of a human-to-human uncertainty factor addresses that issue. In LCIA, the objective is not to offer a protective level for the all population, but instead to know what is the most probable risk. The risk for the general population is therefore to be assessed. This illustrates that RA coefficients should not be used without consideration in LCIA and that adaptations are required for an application into LCIA.

b) Linear methods, damage-oriented (level 2)

An approach like the Eco-indicator 99 has the advantage of including all the main endpoints associated with criteria air pollutants and of quantifying their damage on humans. However, this approach is too sophisticated to be extended to a large number of compounds and provides damage factors only for the respiratory effects of some criteria air pollutants (particulate matter, nitrate, sulfate, sulfur dioxide, nitrogen dioxide, carbon monoxide) and photo-oxidant substances. Other chemicals and other health outcomes are not accounted for. For instance, noncarcinogenic effects of metals such as damages to the liver, kidney, nervous system etc., are not modeled.

c) "Only above threshold" methods, not damage-oriented (level 3)

Methods applying the "only above threshold" principle should receive credit for trying to integrate the threshold concept. They have the theoretical advantage of enhancing the prediction of the impact on humans, since spatial differentiation and presumed thresholds are taken into account. However, these methods present some strong limitations:
- The existence of thresholds is more and more debated and there is a growing recognition that "no evidence" does not necessarily mean "no effects" (see discussion in section 3.3.3).

- Disregarding an emission if it takes place at a concentration lower than the threshold does not take into account its role to the environmental carrying capacity. This makes an application in Life Cycle Assessment difficult, since LCA is a tool for pollution prevention.
- The requirement for additional data is high, since the localization of all major processes of the inventory needs to be known in order to determine whether the postulated threshold is surpassed or not. This limits the application within regular LCA.
- The assessment of processes that will take place in the future or which are not sufficiently specified in terms of location is not allowed.
- Transfer from a site where the threshold is not reached towards a region where it is exceeded, or vice-versa, should be accounted for.

3.1.5 Objectives

The main LCIA procedures available to characterize noncarcinogenic effects and their drawbacks have been discussed. This chapter has objectives which are similar to those of chapter 2, that is it aims:

1) To quantify the risk of noncancer health outcomes resulting from a chronic exposure to toxic releases (damage-oriented), using recent developments in health Risk Assessment of the US EPA and adapting them to the specific requirements of LCIA.
2) To develop a procedure for quantifying the noncarcinogenic risk for compounds with a No Observable Adverse Effect Level available in the literature .
3) To test whether acute toxicity data is a good predictor of the chronic toxicity for data-poor substances.
4) To discuss high to low dose extrapolation, and the inclusion of the background concentration and of the nonlinearity of the dose-response curve.
5) To evaluate whether the concept of Disability Adjusted Life Years is applicable to weight noncarcinogenic effects and assess their severity.
6) To combine the risk quantification with the evaluation of the severity of noncarcinogenic endpoints, in order to derive the effect factor for a large number of chemicals and for the metals selected in section 1.3.2.

While we present the carcinogenic and noncarcinogenic effects of compounds in two different chapters for reasons cited at the beginning of chapter 2, we aim to characterize these effects in similar ways so that they can eventually be aggregated into a single score. This explains why the above objectives and the structure of chapter 3 are similar to those of chapter 2. The ED_{10}-approach introduced in section 2.2 is proposed in section 3.2 for quantifying the noncancer risk in LCIA. It is applied for 11 substances in section 3.3 and to the selected metals in section 3.6. A discussion on linearity and non-thresholds, as well as sensitivity analyses, are also presented in section 3.3. A procedure for quantifying the risk from the No Observable Adverse Effect Level is implemented in section 3.4 and demonstrated on more than 300 toxic releases. The use of the lethal dose as a predictor of the chronic toxic potency is investigated in section 3.5 and the severity of the different

noncarcinogenic endpoints is discussed in section 3.7. Effect factors are derived in section 3.8, by combining the risk quantification (sections 3.2 to 3.6) with the severity of the adverse effects (see section 3.7), as illustrated in figure 3.1. The ED_{10}-approach is compared to other LCIA methods in section 3.9. Conclusions are finally drawn in section 3.10.

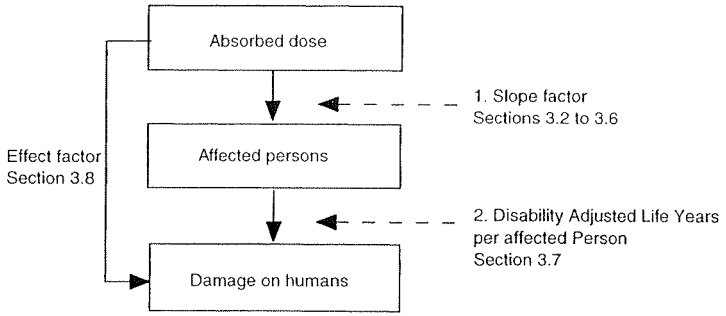

Figure 3.1 Overview of the stages followed in this chapter to assess the effect factor of noncarcinogenic chemicals.

3.2 THE ED_{10}-APPROACH: A NEW PARADIGM FOR LCIA

In this section, the ED_{10}-approach introduced in section 2.2 is proposed for quantifying the noncancer risk of toxic releases in LCIA. Since it is related to recent developments in the Risk Assessment strategy of the US EPA, these latter are briefly discussed.

3.2.1 Recent development in the US EPA's Risk Assessment

The benchmark dose method has been proposed by Crump [1984] as an alternative to the NOAEL approach and extended by Kimmel and Gaylor [1988]. This alternative is supported in the EPA's Benchmark Dose Technical Guidance [EPA, 1996(b); EPA, 1995], where the EPA proposes to use the benchmark dose as a point of departure to derive the reference dose, as stated in equation (3.2). The values for the uncertainty factors and the modifying factor can range from the same values applied to the NOAEL to lower values because of an increased confidence in the response level and the use of a lower confidence limit on the dose [Barnes et al., 1995]. A definition and a description of the benchmark dose have already been provided in section 2.2.1. The main advantages of the benchmark dose with respect to the NOAEL is that it takes into account the full dose-response curve and corresponds to a fixed benchmark response level for all compounds.

$$RfD = \frac{BMD_{10}}{UF \cdot MF} \qquad \text{Equation (3.2)}$$

where:

RfD: Reference Dose [mg/kg-day]

BMD_{10}: Benchmark dose inducing an extra risk of 10% [mg/kg-day]

UF: Uncertainty factor [-]

MF: Modifying Factor [-]

3.2.2 Slope factor β_{ED10}

The ED_{10}-approach has been presented in section 2.2 and applied in chapter 2 to quantify cancer risk of toxic releases. It is also proposed in this chapter for an application to noncarcinogenic health outcomes associated with compounds. For a description of the ED_{10}-approach, refer to section 2.2. Only equation (2.3) presenting the slope factor β_{ED10} gained from the ED_{10}-approach is repeated here.

$$\beta_{ED10} = \frac{0.1}{ED_{10h}} \qquad \text{Equation (2.3)}$$

where:

β_{ED10}: Slope factor $[\frac{\text{Risk}}{\text{mg/kg-day}}]$

ED_{10h}: Best estimate of the effect dose inducing an added risk of 10% over background incidence for humans [mg/kg-day]

0.1: Response level corresponding to the dose ED_{10h} [Risk]

The ED_{10}-approach differs from the EPA's application of the BMD_{10} as described in the Benchmark Dose Technical Guidance at two levels:

- The ED_{10h} is considered instead of the BMD_{10h} as a point of departure, in order to obtain the best estimate of the risk instead of an upper bound of the risk.
- While the EPA proposes to use the benchmark dose to derive the reference dose, we instead use the ED_{10h} as a point of departure to quantify the risk of toxic effects, assuming a linear dose-response curve without threshold. This is a radical difference in the use of the point of departure. Comparing the BMD_{10} (via the RfD) to the exposure level implicitly assumes an extrapolation toward low doses. We prefer an explicit extrapolation which can be discussed; the linearity and the non-threshold hypotheses are discussed in section 3.3.3.

3.3 SLOPE FACTORS DIRECTLY QUANTIFIED FROM BIOASSAYS

The ED_{10}-procedure is applied in this section to quantify the noncarcinogenic endpoint of 11 compounds with bioassay results available in the US EPA's Integrated Risk Information Service (IRIS) database. Sensitivity analyses are performed, and the linearity and non-threshold hypotheses are discussed. The ED_{10}-procedure will also be applied to a larger number of chemicals in section 3.4 and in section 3.6 to the metals selected in section 1.3.2.

3.3.1 Slope factors for 11 chemicals

The effect dose for humans ED_{10h}, the associated slope factor $\beta ED10$ derived from equation (2.3) and the critical endpoint associated with each compound are presented in table 3.3 for 11 substances with bioassay results available in the IRIS database [EPA, 1998]. Appendix 3.2.2 presents the detailed calculations and indications of the production volume of each compound. Eight of them are high production chemicals, that is chemicals with a production or imported quantity exceeding 1000 tonnes in at least one OECD country [OECD, 1997]. While the ED_{10h} has been directly calculated from bioassay data for substances 1 to 6 in table 3.3, the ED_{10h} has been derived from the BMD_{10h} provided in the IRIS database for the other substances, using the ED_{10h}-BMD_{10h} relationship demonstrated below (see equation (3.4)).
Slope factors are summarized in figure 3.2. This figure shows that the variation of the slope factor for these substances is 1 million fold: it ranges from $2.4 \cdot 10^{-5}$ for 1,1,1,2 tetrafluoroethane up to $3.0 \cdot 10^{1}$ [Risk of the critical endpoint / mg/kg-day] for methylmercury.

Insights into the calculations carried out to derive table 3.3 are presented below.

	Chemical	CAS RN	Route of exposure	Data type	Critical endpoint	ED_{10h} (*) [mg/kg-day]	β_{ED10} [Risk / mg/kg-d
Direct calculation of the ED_{10h}							
1	Beryllium	7440-41-7	oral	Dogs, 3.3 year	Small intestinal lesions	8.5E-01	1.2E-01
2	Methyl methacrylate	80-62-6	inh.	Rat, 2 years	Degeneration of the epithelium	2.5E+00	3.9E-02
3	MDI	101-68-8	inh.	Rat, 2 years	Hyperplasia of the epithelium	2.7E-02	3.7E+00
4	Naphtalene	91-20-3	oral	Rat, 3 months	Decrease in body weight	6.1E+00	1.7E-02
5	Phosphoric acid	7664-38-2	inh.	Rat, 3 months	Bronchiolar fibrosis	4.4E-01	2.3E-01
6	Chromium(VI)	18540-29-9	inh.	Rat, 1 to 3 months	LDH in bronchioalveolar lavage fluid	3.4E-03	2.9E+01
ED_{10h} derived from the BMD_{10h} (Equation 3.4)							
7	Antimony trioxide	1309-64-4	inh.	Rats, 1 year	Interstitial Inflammation	1.9E-02	5.3E+00
8	Carbon disulfide	75-15-0	inh.	Epidem. study-12 yrs	Nervous system disfunction	3.1E+00	3.3E-02
9	Methylmercury	22967-92-6	oral	Epidem. study-2 yrs	Neurological abnormalities	6.6E-04	3.0E+01
10	1,1,1,2 Tetrafluoroethane	811-97-2	inh.	Rat, 2 years	Leydig cell hyperplasia	4.2E+03	2.4E-05
11	Tributyltin oxide	56-35-9	oral	Rat, 2 years	Immunosuppression	9.0E-03	1.1E+01

Table 3.3 Derivation of the slope factor $\beta ED10$ from the ED_{10h}, using equation (2.3), for 11 chemicals reported in the IRIS database [EPA, 1998]; the associated critical endpoint and route of exposure are also provided.
MDI (Methylene Diphenyl Diisocyanate)
*: Dose for a lifetime exposure.

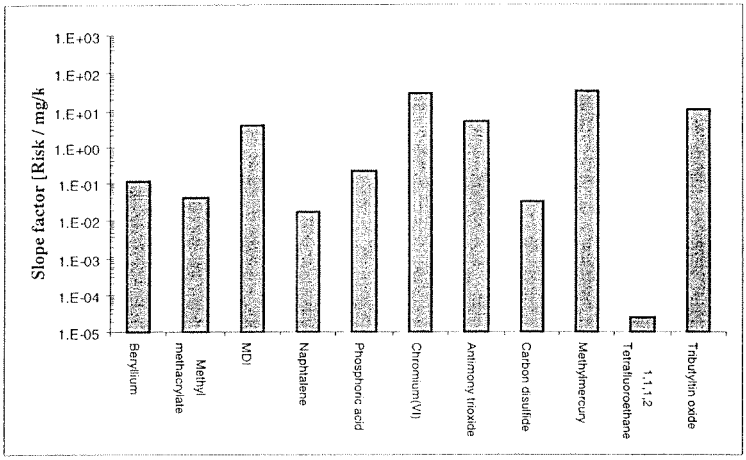

Figure 3.2 Slope factor β_{ED10} for the 11 chemicals listed in table 3.3 (the endpoint and route of exposure associated for each substance is listed in table 3.3).

a) Direct calculation of the ED_{10h}

Bioassay results are available in toxicological reviews supporting the Integrated Risk Information Service (IRIS) database for beryllium, methyl methacrylate and MDI (Methylene Diphenyl Diisocyanate) [EPA (a);(b);(c), 1998]. They are summarized in appendix 3.2.1. From these bioassay data, we were able to plot the dose-response curve for each compound and thus to assess its ED_{10h} and derive its slope factor. The computer program written by Crouch [1985] to carry out the calculations of the multistage model has been selected to model data in the range of the observation and to assess the ED_{10h}. The application of other models is considered in sensitivity analyses (section 3.3.2). Doses or concentrations administrated to animals have been adjusted into human equivalent doses or concentrations, using the EPA's "surface" scaling procedure presented in section 2.1.4.e) and the dosimetric adjustment calculated in the IRIS database (see also section 3.4.3.a) for more explanations). No adjustment for assessing the lifetime risk was required, since chronic experiments are used for these compounds.

As an example of calculations, the multistage model provides the following dose-response curve for the endpoint "degeneration of the olfactory epithelium" associated with methyl methacrylate: $R(d)=1-[\exp-(1.8 \cdot 10^{-8} \cdot d^3)]$. From the effect concentration for animals EC_{10a} of 178 [mg/m^3], a human equivalent concentration EC_{10h} of 8.9 [mg/m^3] is derived after an adjustment for a continuous exposure (6hr/24hr and 5days/7days) and a dosimetric adjustment. The EC_{10h} can be expressed in terms of a human dose ED_{10h} of 2.54 [mg/kg-day], using the inhalation rate and body weight of humans (respectively 20 [m^3/pers-day] and 70 [kg/pers]). A slope factor β_{ED10} of $3.9 \cdot 10^{-2}$ [Risk of degeneration of the olfactory epithelium / mg/kg-day] is finally derived (see table 3.3). This risk means that a lifetime

exposure to 1 [mg/kg-day] of methyl methacrylate would result in 39 additional cases of degeneration of the epithelium in a population of 1000 people. In other words, the potential risk for a person to present a degeneration of the olfactory epithelium, if that person absorbs 1 mg of methyl methacrylate per day and per kilogram of body weight during its entire lifetime, is 3.9%.

For naphtalene, phosphoric acid and chromium(VI), the ED_{10h} is provided in the IRIS database. Since the information required for plotting their dose-response curves is not comprehensive and transparent enough in the IRIS database, we directly used the ED_{10h} provided in the IRIS database to derive the slope factor. An adjustment to derive the lifetime risk is required for these 3 substances, since they were tested in subchronic experiments (see table 3.3). The mean subchronic-to-chronic NOAEL ratio of 3.3 empirically observed by Lewis et al. [1990] is used (see sections 3.1.4.a) and 3.4.3.a) for more explanations).

b) Derivation of the ED_{10h} from the BMD_{10h}

Both the ED_{10h} and the BMD_{10h} are provided in the IRIS system [EPA, 1998] for beryllium, methyl methacrylate, MDI, naphtalene, phosphoric acid and chromium(VI). These effect doses and benchmark doses are listed in appendix 3.2.2 and plotted in figure 3.3. A regression analysis, carried out on the logarithmic values of the parameters, leads to the following correlation:

$$BMD_{10h} = x \cdot (ED_{10h})^y \qquad \text{Equation (3.3)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 0.54$, $0.44 < x < 0.66$; $y = 1.08 \pm 0.095$; $R^2 = 0.99$, 6 measurements, mean square=0.0106.

As the power is not significantly different from 1, equation (3.3) simplifies to:

$$BMD_{10h} = 0.54 \cdot ED_{10h} \qquad R^2 = 0.97 \qquad \text{Equation (3.4)}$$

Figure 3.3 shows that the ED_{10h} is only slightly higher than BMD_{10h}, by an average factor of 1.85. Only 6 chemicals have been considered for that analysis. However, a similar relationship was observed in section 2.3.2 for a larger number of carcinogenic compounds, confirming equation (3.4).

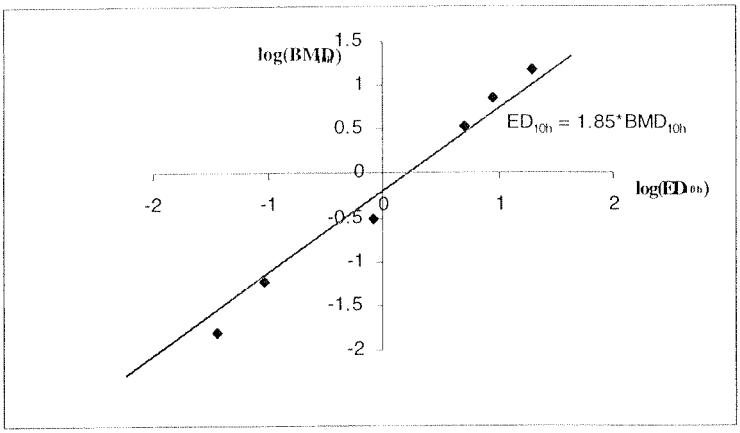

Figure 3.3 Comparison of the ED_{10h} and the BMD_{10h}, for chemicals 1 to 6 listed in table 3.3 and appendix 3.2.2 (n=6; R^2=0.97).

Equation (3.4) has been applied to derive the ED_{10h} for antimony trioxide, carbon disulfide, methylmercury, 1,1,1,2 tetrafluoroethane and tributyltin oxide (substances 7 to 11 in table 3.3). Indeed, the IRIS database [EPA, 1998] only provides the BMD_{10h} for these chemicals. Corresponding slope factors are listed in table 3.3. For methylmercury, the critical endpoint is: neurologic abnormalities in infants. We therefore adjusted the slope factor by a factor 0.2 to account for the share of infants in the population (infants represent 20% of the population, according to Pilkington et al. [1997]).

3.3.2 Sensitivity analyses

Slope factors for beryllium, methyl metacrylate and MDI have been derived above by using the ED_{10h} as a point of departure and the multistage model as a curve-fitting model. Other models and other points of departure could be considered for assessing the slope factor. Sensitivity analyses are carried out in this section to test the choice of the point of departure and of the model. As in chapter 2, we propose to test five points of departure (ED_{10h}, ED_{1h}, $ED_{0.1h}$, $ED_{0.01h}$, $ED_{0.001h}$) and five models provided in the Benchmark Dose Software [EPA, 1999]: the Weibull model, the logistic model, the multistage model, the quantal linear and the quantal quadratic model.

Effect doses ED_{10h} and $ED_{0.001h}$, gained from the different models, are presented in figure 3.4 for methyl methacrylate. The ED_{10h} varies from one model to another one by a factor 8, whereas the $ED_{0.001h}$ varies by a factor 50200. As already concluded in section 2.3.3, the lower the response level, the higher the differences between the effect doses predicted by the different models. Results of the sensitivity analyses for beryllium and MDI

are presented in appendix 3.2.3. They confirm that the ED_{10h} is fairly independent from the model.

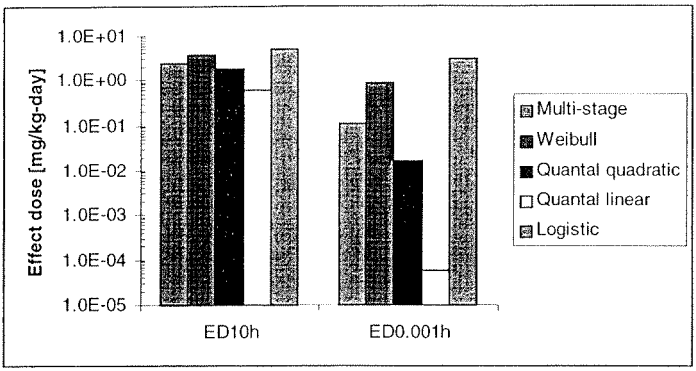

Figure 3.4 Effect dose ED_{10h} and $ED_{0.001h}$ calculated for methyl methacrylate, using different models reported in the Benchmark Dose Software [EPA, 1999].

3.3.3 Discussion on linearity and threshold

The application of the ED_{10h} as a point of departure assumes a linear dose-response function, without threshold. These hypotheses are discussed below.

a) Threshold

There is an extensive debate on the existence of a threshold for noncarcinogenic substances. It is usually supposed that compensating and adaptive mechanisms exist and that they must be overcome before a toxic endpoint is manifested [Faustman and Omenn, 1996]. For instance, there could be a large number of cells performing the same function whose population must be significantly depleted before an adverse effect is seen. While it is impossible to experimentally prove the absence or existence of a threshold [Eaton and Klaassen, 1996; Beck et al., 1994], justifications for the non-threshold assumption made in the ED_{10}-procedure are put forward here.

Firstly, whereas the existence of thresholds was once taken for granted for noncarcinogenic effects, there is nowadays a growing recognition that "no evidence" does not necessarily mean "no effects" and that some substances may have adverse effects below their assumed threshold. For instance, the guideline for occupational exposure to benzene has decreased by two orders of magnitude from 100 ppm in 1927 to the current Occupational Safety and Health Administration's standard of 1 ppm [Beck et al., 1994]. Similarly, the level of lead and cadmium exposure considered as safe has declined many times over the years, as indications about toxicity among workers was replaced by more subtle signs of toxicity in the general population [Ennever, 1994]. There now appears to be no threshold in children for the neurobehavioural effects after an exposure to low levels of lead [EEA, 1999].

Similarly, there is a growing body of epidemiological studies showing small, yet definitive increases in impact associated with air pollutants such as ozone and particulate matter [ExternE, 1995]. Wilson and Spengler [1996] reported that the relationship between mortality and particle exposures is linear, with no hint of a threshold. Pilkington et al. [1997] recommended that the quantification of all respiratory effects should be made on a non-threshold basis, since recent epidemiological studies suggest that there is no safe level of air pollution. In Switzerland, the SCARPOL and SAPALDIA epidemiological studies also concluded that there are no critical thresholds for air pollution [OFS(a), 1999].
Secondly, even if good arguments exist to support the threshold, its evaluation is uncertain and subjective, since it is based upon a choice of what is acceptable and upon the limited capacity to measure subtle signs of toxicity.
Thirdly, even if good arguments would exist to support the threshold for a given substance and if this threshold could be accurately assessed, the slope factor β_{ED10} would not significantly be affected. Equation (2.3) can indeed be rewritten as equation (3.5) to account for the presumed threshold. Since the threshold value is expected to be much lower than the ED_{10h}, the slope factor would not be significantly changed when considering the threshold (see equation (3.5)). The question would rather be to know whether the exposure occurs above or below the threshold. Due to the specific characteristic of the Life Cycle Inventory (emissions occur at unknown places, no temporal information, aggregation of the releases of a given substance), it is extremely delicate to evaluate whether the exposure occurs above or below the threshold.

$$\beta_{ED10} = \frac{0.1}{ED_{10h} - Thr} \simeq \frac{0.1}{ED_{10h}} \qquad \text{Equation (3.5)}$$

where:
Thr: Threshold level [mg/kg-day]

b) Linearity
There is also a debate on whether risk is linearly proportional to the exposure for low doses or whether nonlinearity must be accounted for. We assumed linearity in this chapter for each chemical. As already explained in section 2.3.6, the linearity or nonlinearity can not be addressed on the basis of experimental data. Information on the mechanism of action should rather be considered. For instance, cell cycle kinetics and enzyme activity are being explored in developmental toxicity [Faustman and Omenn, 1994]. However, such information is presently not widely available for noncarcinogenic effects and we therefore could not apply it in this chapter.

3.4 SLOPE FACTORS Estimated FROM THE $NOAEL_A$

Slope factors have been calculated in the previous section for 11 substances, using bioassay results or benchmark doses available in the Integrated Risk Information System. Such results are presently reported in this system only for this limited number of chemicals. Results should become more available in the future, since the EPA intends to use the benchmark dose as a substitute for the NOAEL. In the meantime, we propose in this section a procedure for estimating the ED_{10h} from the more widely available No Observable Adverse Effect Level. We apply it to more than 300 substances to estimate their slope factors and discuss the limitations of this estimation linked to the characteristics of the NOAEL.

3.4.1 Correlation $NOAEL_a$-ED_{10a}

The No Observable Adverse Effect Levels for animals ($NOAEL_a$) of the substances listed in table 3.3 have been searched in the IRIS database [EPA, 1998]. They have been found for 8 substances and are based on the same bioassay data as those used to derive the effect dose. These $NOAEL_a$ are listed in appendix 3.2.2, together with the ED_{10a}. A regression analysis, carried out on the logarithmic values of the parameters, leads to the following correlation (see figure 3.5, log-log scale):

$$ED_{10a} = x \cdot (NOAEL_a)^y \qquad \text{Equation (3.6)}$$

with the following adjusted coefficients and 95% confidence interval:
$x = 1.6$; $0.63<x<4.0$; $y = 0.89 \pm 0.2$; $R^2=0.93$; 8 measurements, mean square=0.2606

As the power is not significantly different from 1, equation (3.6) simplifies to:

$$ED_{10a} = 1.6 \cdot NOAEL_a \qquad R^2=0.91 \qquad \text{Equation (3.7)}$$

This correlation is statistically significant ($R^2=0.91$) and indicates that "the higher the $NOAEL_a$, the higher the ED_{10a} and the less toxic a chemical". Assuming a linear dose-response function between the $NOAEL_a$ and the ED_{10a}, equation (3.7) indicates that the response level associated with the $NOAEL_a$ is of 6%. This is in accordance with Faustman et al. [1994] and Allen et al. [1994(a)] who reported that the $NOAEL_a$ in most study protocols is about the same as the BMD_{10a} for quantal endpoints (i.e. is about the same as $0.54 \cdot ED_{10a}$, according to equation (3.4)).

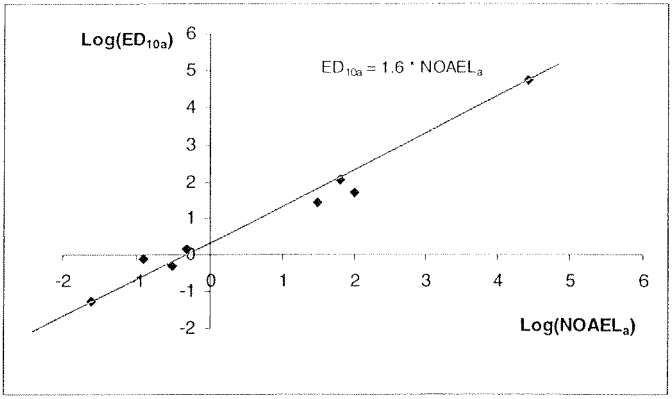

Figure 3.5 Correlation between the No Observable Adverse Effect Level $NOAEL_a$ and the effect dose ED_{10a}, for 8 of the 11 substances listed in Appendix 3.2.2 (n=8, R^2=0.91).

3.4.2 Extrapolated slope factor $\beta_{ED10\text{-}extr}$

The human equivalent effect dose ED_{10h} for a lifetime exposure can be derived from the animal dose ED_{10a}, by adjusting the animal dose (concentration) and by adjusting for a lifetime exposure (see equation (3.8)). An animal-to-human and a subchronic-to-chronic conversion factor are introduced for that purpose.
Combining equations (2.3), (3.7) and (3.8), an evaluation of the slope factor is feasible from a compound's $NOAEL_a$, as indicated in equation (3.9). Extrapolated slope factors are denoted $\beta_{ED10\text{-}extr}$.

$$ED_{10h} = \frac{ED_{10a}}{CF_{a->h} \cdot CF_{sub->chr}} \qquad \text{Equation (3.8)}$$

$$\beta_{ED10\text{-}Extr} = \frac{0.1}{ED_{10h}} = \frac{0.1}{\frac{ED_{10a}}{CF_{a->h} \cdot CF_{sub->chr}}} = 0.062 \cdot \frac{CF_{a->h} \cdot CF_{sub->chr}}{NOAEL_a} \qquad \text{Equation (3.9)}$$

where:

$\beta_{ED10\text{-}extr.}$: Slope factor extrapolated from the $NOAEL_a$ $[\frac{Risk}{mg/kg\text{-}day}]$

$CF_{a->h}$: Animal-to-human conversion factor [-]

$CF_{sub->chr}$: Subchronic-to-chronic conversion factor [-]

3.4.3 Application

a) Calculations

Substances have been selected based on data availability and relevance. The extrapolation procedure summarized in equation (3.9) has been applied to 314 substances with a $NOAEL_a$ available in the IRIS database [EPA, 1998]. These chemicals are listed in appendix 3.3, together with their slope factors derived from the $NOAEL_a$, their associated critical endpoint and their production volume. 45% of the compounds are high production volume chemicals, that is are characterized by a production or imported quantity exceeding 1000 tones in at least one OECD country [OECD, 1997]. When only the $NOEL_a$ (No Observable Effect Level) is available, the extrapolation is based on this value.

Conversion factors are also listed in appendix 3.3. An adjustment to derive the risk for a lifetime exposure is carried out when this adjustment is made in the IRIS database. The subchronic-to-chronic conversion factor (CFsub->chr) is set at 3.3, using the mean subchronic-to-chronic NOAEL ratio of 3.3 empirically observed by Lewis et al. [1990] (see section 3.1.4). This enables the use of a lower value than the conservative default factor of 10 applied by the EPA in the IRIS database.

For the animal-to-human conversion factor ($CF_{a->h}$), the "surface" scaling approach presented in section 2.1.4.e) is used for an oral exposure. Thus, animal-to-human conversion factors of 1.6 for dogs, 6 for rats, 13 for mice, etc. are applied in appendix 3.3. By comparison, a conservative default uncertainty factor of 10 is applied in the IRIS database for most substances. For inhalation exposures, we apply in appendix 3.3 the dosimetric adjustment calculated for each compound in the IRIS database [EPA, 1998]. This adjustment accounts for differences between animals and humans in physiology, ventilatory parameters, metabolic processes, etc. The additional uncertainty factor of 3, used by the EPA to account for additional differences between animals and humans, is not included since it is judged to add conservatism. For a few chemicals, the $NOAEL_h$ for humans is directly obtained from epidemiological studies. The ED_{10h} is then directly derived from the $NOAEL_h$ and the conversion factor $CF_{a->h}$ is set as 1.

b) Results

Figure 3.6 presents the frequency histogram for the slope factors derived from the $NOAEL_a$ for more than 300 substances. Slope factors range from 10^{-6} for 1-Chloro-1,1-difluoroethane up to 10^{3} for beryllium, reflecting that the range of the noncarcinogenic risk can be 1 billion-fold (see appendix 3.3 for detailed values). Most chemicals are characterized by a slope factor ranging from 10^{-3} to 10^{1} [Risk of the critical endpoint / mg/kg-day]. Since only 5% of the extrapolated slope factors are higher than 10 [Risk of the critical endpoint / mg/kg-day], the range of values appearing in figure 3.6 is coherent with the one reported in section 3.3.1, where values ranging from 10^{-5} to 10^{1} [Risk of the critical endpoint / mg/kg-day] were reported.

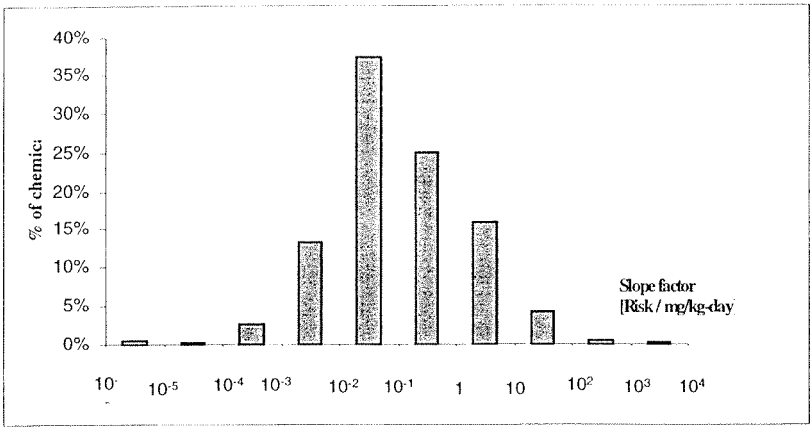

Figure 3.6 Frequency histogram for the slope factors derived from the $NOAEL_a$ for 314 substances (see appendix 3.3 for detailed values).

3.4.4 Limitations

The extrapolation of the slope factor from the $NOAEL_a$ has some limitations related to the characteristics of the $NOAEL_a$. While the incidence level associated with the $NOAEL_a$ can change from one chemical to another one, we assumed that the $NOAEL_a$ corresponds to a fixed response level of 6%, whatever the chemical. This simplification can lead to a misleading evaluation of the slope factor. Thus, if the NOAEL is actually associated with a lower response level, this simplification induces an overestimation of the risk. Secondly, when the bioassay data used to determine the $NOAEL_a$ are limited, there is uncertainty as to whether the identified $NOAEL_a$ may be significantly lower if more comprehensive studies were performed [Gaylor, 1992]. In that sense, the $NOAEL_a$ can be understood as an upper bound of the level with no observable adverse effects. This induces an underestimation of the slope factor derived from the $NOAEL_a$. Other limitations of the $NOAEL_a$, discussed in the introduction (section 3.1.4), enhance the uncertainty of the extrapolated slope factor.
In conclusion, the $NOAEL_a$ is used in this section only to obtain a first order of magnitude of the slope factor for a large number of chemicals. For a more reliable estimate of this factor, it is essential to evaluate the ED_{10h} from fitting a model at the observed range of data.

3.5 SLOPE FACTORS fOR INCOMPLETELY TESTED CHEMICALS

Slope factors have been assessed in the previous section for more than 300 chemicals, using their $NOAEL_a$ reported in the IRIS database. However, these substances are only a small share of all the toxic chemicals. How can we deal with the other 100000 substances registered in the European Inventory of Existing Commercial Chemical Substances [EEA, 1998]? Only a small fraction of these compounds has results of long-term bioassays and the chronic toxicity of many chemicals will never be investigated. Data required to assess chronic toxic potencies such as the ED_{10h} or the $NOAEL_a$ are consequently often lacking and the approaches presented in sections 3.3 and 3.4 are not applicable for a majority of chemicals. The tendency is to neglect the toxic endpoint of incompletely tested compounds [Gray et al., 1997]. Some authors [Venman and Flaga, 1985; Layton et al., 1987] suggest that readily available lethal doses could be used to extrapolate the toxic potency. This proposal is discussed here.

The lethal dose LD_{50a} of 9 of the 11 chemicals listed in table 3.3 has been found in the Registry of Toxic Effects of Chemical Substances database [NIOSH, 1998] (values are given in appendix 3.2.2). The LD_{50a}-ED_{10h} correlation for these chemicals is plotted in figure 3.7. A regression analysis, carried out on the logarithmic values of the parameters, leads to the following correlation:

$$ED_{10h} = x \cdot (LD_{50a})^y \qquad \text{Equation (3.10)}$$

with the following adjusted coefficients and 95% confidence interval:

$x= 0.017$, $0.0001<x<3$; $y= 0.5\pm0.62$; $R^2=0.26$; 9 measurements, mean square=2.48

The regression coefficient $R^2=0.26$ indicates that the lethal dose and the effect dose are poorly correlated. The same statement was made for carcinogenic chemicals in section 2.5 ($R^2=0.14$; $n=41$). Substances with a similar lethal dose, for instance MDI and carbon disulfide, can differ by a factor 100 with respect to their ED_{10h}.

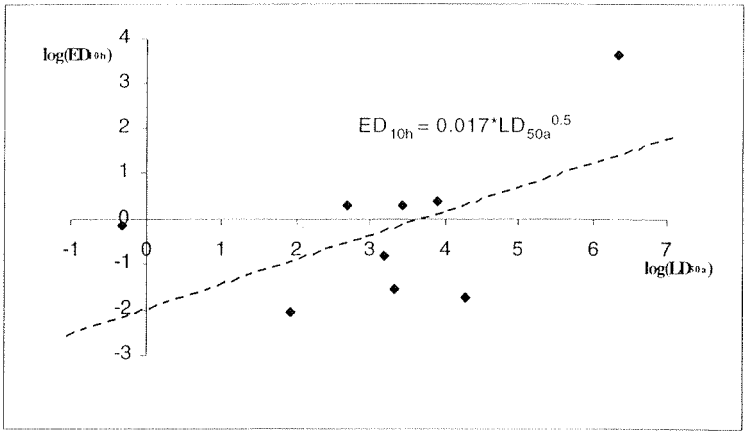

Figure 3.7 Correlation between the effect dose ED_{10h} and the lethal dose LD_{50a}, for 9 of the 11 chemicals listed in appendix 3.2.2 (R^2=0.26; n=9).

The application of the LD_{50a} for comparing chemicals in a long-term exposure context would result in extremely high levels of uncertainty. Consequently, the lethal dose has not been applied in this chapter to quantify the slope factor of incompletely tested chemicals, not even for a first screening. As in chapter 2, we instead define their slope factors as "not estimated". We already discussed in section 2.5 the meaning and implication of defining the risk as "not estimated".

3.6 SLOPE FACTORS FOR METALS

Carcinogenic effects of the metals selected in section 1.3.2 have been studied in section 2.6. This section focuses on their noncarcinogenic outcomes. Table 3.4 summarizes their recognized and suspected adverse effects, according to the Environmental Defense Fund [EDF, 1998] and for the classification of adverse effects presented in section 3.1.1. It indicates that metals like lead and arsenic are toxic to a large range of organs.

Chemical	CAS RN	Cardio-vascular toxicity	Neuro-toxicity	Respi-ratory toxicity	Repro-ductive toxicity	Develop-mental Toxicity	Endocrine toxicity	Gastro-intestinal toxicity	Kidney toxicity	Skin toxicity	Immuno toxicity
1 Arsenic	7440-38-2	S	S	S	S	R	S	S	S	**S**	
2 Beryllium	7440-41-7	S		**S**				**S**	S	S	S
3 Cadmium	7440-43-9	S	S	S	R	R	S		**R**		S
4 Chromium(III)	16065-83-1										
5 Chromium(VI)	18540-29-9			**S**							
6 Copper	7440-50-8	S		S	S	S		S			
7 Lead	7439-92-1	**S**	S	S	R	R	S	S	S	S	S
8 Methylmercury	22967-92-6		**S**			R					S

Table 3.4 Recognized (R) and suspected (S) noncarcinogenic effects generated by the metals studied in this dissertation, according to the Environmental Defense Fund [EDF, 1998].
In bold: critical endpoints reported in the IRIS system [EPA, 1998] (see sections 3.6.1 to 3.6.8).

To be consistent with what has been done so far for other chemicals, we have based our judgment in priority on the IRIS database [EPA, 1998]. Additional information provided in the toxicological profiles of the Agency of Toxic Substances and Disease Register (ATSDR) have also been considered, since they provide a very detailed insight into the toxicological properties of metals. The ATSRD profiles are prepared in accordance with guidelines developed by the ATSDR and the EPA, and a peer review panel is assembled for each chemical [ATSDR, 1999].
The slope factors for the inhalation of beryllium, and for an oral exposure to chromium(VI), chromium(III), lead and inorganic arsenic, are derived from their $NOAEL_a$. For the other metals, the slope factor is evaluated after plotting the dose-response curve at the level of the observed data. Table 3.7 summarizes the slope factors calculated for the different metals, while their evaluation is presented below for each metal.

3.6.1 Cadmium

• Oral exposure

While cadmium is toxic to a wide range of organs, numerous studies in humans and animals indicate that kidney is the main target organ of cadmium toxicity. Changes in the kidney due to cadmium have been well established [Taylor et al., 1999]. The first manifestation is a decreased absorption of low-molecular-weight proteins, indicating damage to the renal tubules (tubular proteinurea). At very high levels of exposure, increased excretion of high-molecular-weight proteins occurs, indicating either severe tubular damage or glomerular damage. Elevated incidences of tubular proteinuria have been found in many epidemiological studies. Nogawa et al. [1989] investigated in Japan the renal effects of total cadmium exposure, using the average cadmium concentration in rice as the measure of cadmium intake and urinary β2-microglobulinuria as the index of renal damage. Crump [1998] used the data reported in Nogawa's study to calculate a BMD_{10h} of $1.3 \cdot 10^{-3}$ [mg/kg-day].

From this benchmark dose, we can derive an ED_{10h} of $2.4 \cdot 10^{-3}$ [mg/kg-day], applying equation (3.4). A slope factor $\beta ED10$ of 41.5 [Risk / mg/kg-day] is derived with equation (2.3). By comparison, a slope factor of 6.3 [Risk / mg/kg-day] can also be estimated from the NOAEL reported for preteinurea in the IRIS database [EPA, 1998] (see appendix 3.3.a)). The slope factor of 41.5 [Risk / mg/kg-day] has been retained, since it is based on a benchmark dose rather than a NOAEL.

The amount of cadmium needed to cause a toxic effect depends on its chemical form. Taylor et al. [1999] underlined that, in general, cadmium compounds that dissolve easily in water (e.g. cadmium chloride $CdCl_2$) and those that can be dissolved in the body (e.g. cadmium oxide CdO) are more toxic than compounds that are very hard to dissolve (e.g. cadmium sulfide CdS), since a high water solubility results in high concentrations of cadmium delivered to target sites.

• Inhalation exposure

Only the oral route of exposure is evaluated in the IRIS database [EPA, 1998] and by the Agency for Toxic Substances and Disease Registry [Taylor et al., 1999]. Sufficient and reliable information is lacking to assess the toxic risk towards cadmium by inhalation. An EPA workgroup is undertaking further investigation to evaluate the toxic risk by inhalation.

When the data for assessing the toxicity by inhalation are not adequate, route-to-route extrapolation is often practiced. Data from the oral route of exposure can be used to derive the risk via inhalation only when respiratory tract effects and/or "first-pass" effects are excluded. "First-pass" effects are effects taking place in the portral-of-entry tissue, prior to entry into the systemic circulation [EPA, 1994]. Oral data should not be used when chemicals are expected to have different toxicity by inhalation and after an oral exposure. Since this is true for metals [EPA, 1994], we did not derive the slope factor after inhalation of cadmium from its oral slope factor. We rather determine that the noncancer risk after inhalation of cadmium can not be estimated (n.e.). For the same rationale, route-to-route extrapolation is also not applied for the other metals.

3.6.2 Chromium(VI)

• Oral exposure

MacKenzie et al. [1958] investigated the effects of chromium(VI) exposure on three groups of 12 male and 9 female rats. This study is selected in the IRIS database [EPA, 1998] and we use it as the reference study. No significant adverse effects were found and there were no pathologic changes in any treatment group. The group of rats receiving 25 [mg Cr(VI)/l] as K_2CrO_4 showed an approximate 20% reduction in water consumption. Based on the body weight of rats (0.35 kg) and their water consumption (0.035 l/day), the concentration of 25 [mg/l] can be converted into an adjusted $NOAEL_a$ of 2.5 [mg Cr(VI)/kg-day] as K_2CrO_4. From this $NOAEL_a$, we can derive an ED_{10h} of 0.67 [mg/kg-day], applying equations (3.7) and (3.8). A slope factor β_{ED10} of 0.15 [Risk / mg/kg-day] is obtained with equation (2.3) (see also appendix 3.3.a)). This factor should only be applied to soluble salts of hexavalent chromium such as potassium dichromate ($K_2Cr_2O_7$), sodium dichromate ($Na_2Cr_2O_7$), potassium chromate (K_2CrO_4) and sodium chromate (Na_2CrO_4) [MacKenzie et al., 1958].

• Inhalation exposure

The slope factor after inhalation of chromium(VI) has already been calculated in table 3.3. We describe here the data considered for this evaluation. Malsch et al. [1994] used the data of Glaser et al. [1990] to study the lower respiratory effects following inhalation of chromium(VI) particulate in rats. The critical endpoint was lactate dehydrogenate (LDH) in bronchioalveolar lavage fluid. This study is selected in the IRIS database and we use it for our assessment. Malsch et al. [1994] calculated a human effect concentration EC_{10h} of $3.6 \cdot 10^{-2}$ [mg/m^3], which is equivalent to a human dose of $1 \cdot 10^{-2}$ [mg/kg-day]. The ED_{10h} of $3.4 \cdot 10^{-3}$ [mg/kg-day] reported in table 3.3 is derived after applying a conversion factor of 3 to account for a less than a lifetime exposure.

3.6.3 Chromium(III)

• Oral exposure

Ivankovic and Preussmann [1975] studied groups of 60 rats fed with chromic oxide (Cr_2O_3) for 2 years. This study is selected in the IRIS database [EPA, 1998] and we use it for our assessment. The total amount of ingested Cr_2O_3 were 360, 720 and 1800 [g/kg] for the three treatment groups. All major organs were examined histologically. No effects due to Cr_2O_3 treatment were observed at any dose level and the dose of 1800 [g Cr_2O_3/kg] was chosen as the $NOAEL_a$. It can be converted into 1468 [mgCr(III)/kg-day]. This $NOAEL_a$ is limited to chromium(III) of insoluble salts, such as chromic oxide (Cr_2O_3) and chromium sulfate ($Cr_2[SO_4]_3$) [EPA, 1998].

From this $NOAEL_a$, we can derive an ED_{10h} of 391 [mg/kg-day], applying equations (3.7) and (3.8). A slope factor β_{ED10} of $2.6 \cdot 10^{-4}$ [Risk / mg/kg-day] is derived with equation (2.3) (see also appendix 3.3.a)).

Deriving a slope factor for chromium(III) could be misleading, since the factor β_{ED10} indicates that there is a risk of an adverse effect at any exposure levels. This is untrue for chromium(III), which it is an essential element required to promote the action of insulin so that glucose can be used in the body [Wilbur et al., 1999]. Wilbur et al. [1999] indicated that the typical daily ingestion of chromium from food is of 60 [ug Cr/pers-day]. Since the National Research Council [NRC, 1989] estimates that 50-200 [ug Cr(III)/pers-day] is an adequate daily intake for chromium to provide its biological function in adults, typical daily intakes of chromium are in the range than the adequate daily intake. We therefore propose to use a risk equal to zero for an oral exposure to chromium(III). The risk estimate of $2.6 \cdot 10^{-4}$ [Risk / mg/kg-day] should only be viewed as a maximal indicative value. We advocate its use only for exposures to very high levels of chromium(III), since it is only under such exposures that an adverse effect is expected to occur. Potential for high exposure exist for workers in industries, people living near major sources of atmospheric release of chromium and people consuming tap water or food products with very high levels of chromium [Wilbur et al, 1999].

- **Inhalation exposure**

The same rationale can be used to determine that the risk by inhalation of chromium(III) is equal to zero. The risk to very high levels of chromium(III) can not be evaluated, since the toxicity of chromium(III) by inhalation is not determined in the IRIS database. We therefore conclude that the toxic risk for an exposure to very high levels of chromium(III) can not be estimated.

3.6.4 Copper

Copper is an essential element for humans, which is incorporated into many enzymes and proteins. Deriving a slope factor for copper may therefore be misleading, for the same arguments than those advanced for chromium(III). As indicated in the ATSDR's toxicological profile of copper [ATSDR, 1990], the typical daily ingestion of copper ranges from 1 to 2 [mg Cu/pers-day]. Since the National Academy of Science [NAS, 1980] reports that 2-3 [mg Cu/pers-day] is an adequate daily intake, typical daily intakes of copper are in the range or lower than the adequate daily intake. We therefore propose to use a risk equal to zero for a typical exposure level to copper.

It is only for people exposed to extremely high levels of copper that an adverse effect might occur. Reliable data are missing for assessing that risk. Thus, no studies on chronic effect for an inhalation exposure to copper are reported in the ATSDR's toxicological profile of copper [ATSDR, 1990]. This profile reports only two studies on long-term effect of copper for an oral exposure, which is insufficient to draw any conclusions. Similarly, the EPA does not provide in the IRIS database an evaluation of the toxic effects of copper compounds (CAS N: 7440-50-8). Only a $NOAEL_a$ is reported for copper cyanide (CAS N: 544-92-3) in

the IRIS database [EPA, 1998]. In appendix 3.3.a), we derived from this $NOAEL_a$ a slope factor β_{ED10} of $2.5 \cdot 10^{-1}$ [Risk / mg/kg-day]. This value is provided only as an indicative value.

3.6.5 Methylmercury

• Oral exposure

The slope factor for an oral exposure to methylmercury has already been calculated in table 3.3. We describe here the data considered for this evaluation. Marsh et al. [1987] investigated the effects of methylmercury exposure, using the exposure in Iraq of 81 mother and child pairs to MeHg-treated seed grain that was mistakenly used in bread. Infants born to mothers who ate contaminated bread during gestation were the most sensitive group and often infants exhibited neurologic abnormalities while their mothers showed no signs of toxicity. The data reported in Marsh et al. [1987] can be placed in five dose groups [Seafood Safety, 1991] and incidence rates can be provided for different abnormalities in neurological development. Using this data set, the EPA calculated a BMD_{10h} of $1.1 \cdot 10^{-3}$ [mg/kg-day], from which we derived an ED_{10h} of $2.2 10^{-3}$ [mg/kg-day] with equation (3.4). The ED_{10h} of $6.6 \cdot 10^{-4}$ [mg/kg-day] reported in table 3.3 is derived after applying a conversion factor of 3 to account for less than a lifetime of exposure.

• Inhalation exposure

The toxicity of methylmercury by inhalation is not determined in the IRIS database. We therefore determine that the toxic risk of methylmercury can not be estimated for that exposure pathway.

3.6.6 Beryllium

• Oral exposure

The slope factor for an oral exposure to beryllium has already been calculated in table 3.3. We describe here the data used for this evaluation. Morgareidge et al. [1976] conducted a long-term study with 5 groups of 10 dogs exposed for 3 years. Bioassay data are reported in appendix 3.2.1. We fitted the multistage model proposed by Crouch [1985] to these observed data and derived an ED_{10a} of 1.4 [mg/kg-day] for dogs. An equivalent human ED_{10h} of 0.85 is obtained, using the animal-to-human conversion factor of 1.6 for dogs (see section 3.4.3.a)).

• Inhalation exposure

Eisenbud et al. [1949] studied the chronic beryllium disease in community residents living near a beryllium plant. This study is selected in the IRIS database [EPA, 1998] and we use it for our assessment. Chronic beryllium disease is a chronic inflammatory lung lesion. In the Eisenbud's study, the beryllium was emitted primarily in the form of beryllium oxide,

although beryllium fluoride was also present. The exposure concentration was estimated to be 10^{-4} [mg/m^3]. A NOAEL for humans of 10^{-4} [mg/m^3] was suggested for the development of chronic beryllium disease, that is $2.8 \cdot 10^{-5}$ [mg/kg-day].
From this NOAEL, we can derive an ED_{10h} of $4.6 \cdot 10^{-5}$ [mg/kg-day] by applying equations (3.7) and (3.8). A slope factor β_{ED10} of $2.2 \cdot 10^{3}$ [Risk / mg/kg-day] is derived with equation (2.3) (see also appendix 3.3.b)).

3.6.7 Lead

• Oral exposure
Lead is probably the metal that has been the most exhaustively studied for years. It is the illustration of a chemical with abundant toxicity data in both animals and humans, but with no commonly accepted NOAEL. Some of the effects induced by lead, particularly changes in the levels of certain blood enzymes and in children's neurobehavioral development, may occur at blood lead levels so low as to be without a threshold [EPA, 1998]. As there does not appear to be a discernible threshold for the neurotoxicity of lead, the EPA has not developed a reference dose RfD for lead.
While the Agency of Toxic Substances and Disease Register (ATSDR) also provides no reference dose for lead, it reviews many toxicological data in the toxicological profile on lead [Abadin and Lados, 1997]. The most sensitive effect is reported by Perry et al. [1988] who studied rats administrated with lead acetate (CAS N: 301-04-2) in drinking water. They reported a $LOAEL_a$ of 0.014 [mg/kg-day] for the increase in blood pressure. Burke et al. [1996] proposed to derive a $NOAEL_a$ of 0.0014 [mg/kg-day] by dividing the $LOAEL_a$ by 10.
From this $NOAEL_a$, we derive an ED_{10h} of $3.7 \cdot 10^{-4}$ [mg/kg-day], applying equations (3.7) and (3.8) and the animal-to-human conversion factor of 6 for rats (see section 3.4.3.a)). A slope factor β_{ED10} of 270 [Risk / mg/kg-day] is obtained with equation (2.3). Since this slope factor is extrapolated from the $NOAEL_a$, its confidence is lower than slope factors evaluated after plotting the dose-response curve near the observed bioassay data. Furthermore, it must be emphasized that no consensus regarding a NOAEL exists for lead in the literature, which increases the uncertainty in the estimated slope factor. The slope factor of lead should therefore only be understood and used as a value for screening the potential damage of lead. Table 3.7 shows that the slope factor for lead is of the same order of magnitude than the slope factor of arsenic. These two metals also rank similarly (number 1 and 2) among the top 20 hazardous substances for humans at hazardous waste sites [ATSDR, 1999].
• Inhalation exposure
The toxicity of lead by inhalation can be estimated neither from the IRIS database or the ATSDR toxicological profile. We therefore determine that the toxic risk of lead can not be estimated for that exposure pathway.

3.6.8 Inorganic arsenic

• **Oral exposure**

Tseng et al. [1968] showed an increased incidence of hyperpigmentation and keratosis (skin lesions) after oral exposure to arsenic by humans. This study is selected in the IRIS database [EPA, 1998] and we use it for our assessment. The control group contains 2552 individuals and shows no evidence of skin lesions [EPA, 1998]. This group is considered as the NOAEL group. The arsenic concentration in the wells used by the individuals of the NOAEL group is 9 [ug/l], which is converted to $8 \cdot 10^{-4}$ [mg/kg-day].

From this NOAEL, we can derive an ED_{10h} of $1.3 \cdot 10^{-3}$ [mg/kg-day], applying equations (3.7) and (3.8). A slope factor β_{ED10} of $7.8 \cdot 10^{1}$ [Risk / mg/kg-day] is obtained with equation (2.3) (see also appendix 3.3.a)).

• **Inhalation exposure**

The toxicity of arsenic by the inhalation route of exposure is not determined in the IRIS database. We therefore determine that the slope factor of arsenic can not be estimated for that exposure pathway.

3.7 SEVERITY OF THE CRITICAL ENDPOINTS

Slope factors have been calculated in sections 3.3, 3.4 and 3.6 for more than 300 chemicals. Their critical endpoints are reported in table 3.3 and appendix 3.3, as well as in table 3.7 for each studied metal. The critical endpoint associated with toxicants can be characterized by large differences in severity, since the spectrum of health effects can range from impairment of wellbeing to irreversible and life-threatening disease (see table 3.5). The weighting of the critical endpoint associated with each compound should therefore be carried out. Some approaches available for aggregating the health outcomes are presented in this section and a proposal for a simple weighting method is presented.

Not too serious (reversible, not life-threatening)				Very serious (irreversible, life-threatening)	
←					→
Headache	Dizziness	Asthma	Miscarriages	Cancer	
Cough, throat irritation		Chronic bronchitis	Kidney damage	Birth defects	
Skin rash	Nausea		Liver damage	Nervous system damage	

Table 3.5 Range of typical human disabilities [EDF, 1998].

3.7.1 The Disability Adjusted Life Years per affected Person concept

The concept of Disability Adjusted Life Years has been presented in section 2.7 to weight carcinogenic effects. For that purpose, the $DALY_p$ was calculated for 16 types of tumors. These calculations are extended here to more than 200 diseases reported by Murray and Lopez [1996(a);(b)] and results are presented in appendix 3.4.

We investigated the possibility to weight the different critical endpoints with the Disability Adjusted Life Years per affected Person ($DALY_p$) reported in appendix 3.4. It appears that this weighting is not feasible at the present time, for two reasons:

• The DALY approach provides coefficients to weight human disabilities, but not to judge about the severity of diseases reported in animal tests. A $DALY_p$ can therefore not be directly applied to the critical endpoints associated with compounds studied in the previous sections, since most of these endpoints refer to health outcomes measured on animals.

Hofstetter [1998] summarized this point by saying that the premise for the application in LCIA of the DALY approach is that the evaluation of the impact on human health uses epidemiological studies. We could attempt to link the endpoints reported in animals with human disabilities. This would require further research to be carried out with toxicologists, for instance with the Swiss Association of Physicians promoting the Environment Protection or the International Society of Doctors for the Environment. This is out of the scope of the present work.

- For the few chemicals with epidemiological studies, the reported health outcomes are not in the $DALY_p$ list which focuses on major human disabilities.For instance, the renal damage induced after a chronic exposure to cadmium is not reported in appendix 3.4.

3.7.2 Classification into 3 categories

a) Categories defined by the International Life Science Institute

Since the DALY approach is inapplicable as such to our analysis, we decided to look at a simpler weighting of the endpoints. An experts panel of the International Life Science Institute proposed a generic list of human health impacts divided into three subcategories: life-threatening and irreversible diseases (category 1), effects that can be irreversible and life-shortening (category 2) and reversible and not life-shortening effects (category 3) [Burke et al., 1996]. The sub-categories are subjectively separated by the panel by a factor 10, i.e. category 1 has a severity factor of 100, category 2 has a factor 10 and category 3 has a factor 1.

Category 1 Irreversible/ life-shortening effects Severity factor = 100	Category 2 May be irreversible/ life-shortening effects Severity factor = 10	Category 3 Reversible / not life-shortening effects Severity factor = 1
Cancer Mutagenicity Teratogenic effects Reproductive effects	Immunotoxicity Neurotoxicity (*) Kidney damage Liver damage Heart disease Pulmonary disease	Irritation Sensitization

Table 3.6 Classification of human health outcomes, by Burke et al. [1996].
(*) Neurotoxicity may also be ranked in category 1.

b) Proposal

For this study, we decided to use the 3 categories proposed by Burke et al. [1996]. To make this simplified classification compatible with the DALY approach used in chapter 2 for

carcinogens, a $DALY_p$ of 11.1 [yr/pers] is proposed as representative for category 1. This value is the average $DALY_p$ for tumors (see section 2.7.2). For categories 2 and 3, a $DALY_p$ of 1.1 and 0.11 [yr/pers] is respectively proposed. These $DALY_p$s are a factor 10 and 100 lower than the $DALY_p$ of category 1, in accordance with Burke's proposal.
The severity factors of 100, 10 and 1 are subjective, since it is inherently impossible to make a pure scientific aggregation of different toxicity impacts. This aggregation required value-laden choices and is equivalent to comparing the impacts of acidification and global warming [Burke et al., 1996]. The severity factors of 100, 10 and 1 must therefore be understood as indicative values. The factor describing the difference of severity between categories 1 and 3 may be higher than 100. For instance, a factor higher than 10^4 can be derived from appendix 3.1, where $DALY_p$s reported by Hofstetter [1998] range from 10^{-4} to 10 [yr lost/pers] for respiratory diseases.

c) Application for substances listed appendix 3.3 and table 3.3
For the substances reported in appendix 3.3 and table 3.3, we propose to use category 2 as a default category; a $DALY_p$ of 1.1 [yr/pers] is therefore applied to all these chemicals. Choosing category 2 as the default category is a "bad case" estimate, since we can legitimately think that most of the critical endpoints reported in appendix 3.3 and table 3.3 are not as severe as health outcomes reported in category 2. For a screening analysis, the "bad" case estimate enables determining if the effect of a chemical is low enough that the substance can be eliminated from further considerations.
Departure from this procedure can be made if the understanding of the severity of the effect is improved. A closer examination of the adverse endpoint of a compound, and its classification into another category as the default one, could and even should be undertaken if that chemical plays an important role in a LCA case study. For this examination, a collaboration with toxicologists is required. For compounds with epidemiological data, a departure from the default approach has already been made. Indeed, these substances are associated with human disabilities, which simplifies their classification into one of the 3 categories listed in table 3.6.

d) Application for metals
Special attention has been paid to classify the endpoint associated with metals into category 1, 2 or 3. The default category has been applied only if no information was available for a specific classification.

- **Cadmium**

Deaths from renal failure due to cadmium exposure are rare [Taylor et al., 1999]. The increased excretion of low-molecular-weight proteins is not adverse in itself, and some debate has arisen concerning whether it should be considered as acceptable or toxic [Ennever, 1994]. But many studies have indicated that increased excretion of other solutes such as calcium also occurs at approximately the same level as proteinuria. This is definitely an adverse effect if it leads to increased calcium wasting [Taylor et al., 1999].

No $DALY_p$ for proteinurea is provided by Murray and Lopez [1996(a)], since it is unlikely that it would be substantial [Lopez, 1999]. In table 3.6, a kidney damage is part of category 2. However, since proteinurea is not adverse in itself, we classify this damage in category 3 and apply a $DALY_p$ of 0.11 [yr/pers] for cadmium.

• **Chromium(VI) and chromium(III)**

For the oral exposure to chromium(VI), the $NOAEL_a$ reported by MacKenzie et al. [1958] is simply based on the non appearance of effects. Since no effects were observed, we apply the default $DALY_p$ of 1.1 [yr lost/pers] for an oral exposure to chromium(VI). The same rationale is used for the oral exposure to chromium(III) for which Ivankovic et al. [1975] reported no effects.

For the inhalation exposure to chromium(VI), no $DALY_p$ for the presence of lactate dehydrogenate (LDH) in bronchioalveolar lavage fluid is provided by Murray and Lopez [1996(a)], since it is unlikely that it would be substantial. When a cellular damage occurs, enzymes such as the LDH are released. Consequently, the presence of LDH in the bronchioalveolar lavage fluid is indicative of a chronic lung inflammation and of the occurrence of a cellular damage. Since this damage tends to be repaired thereafter, it can be judged as not too adverse [Diezi, 1999]. We therefore classify this effect in category 3 and characterize it by a $DALY_p$ of 0.11 [yr/pers].

• **Methylmercury**

The abnormalities in neurological development induced by methylmercury in children are significant. Since neurotoxicity is part of category 2 in table 3.6, a $DALY_p$ of 1.1 [yr/pers] is selected. A higher value could be recommended, since some toxicologists would rank neurotoxicity in category 1 [Burke et al., 1996]. This indicates that the selected $DALY_p$ is to be understood as a subjective value that implies a value judgement. However, we prefer to explicitly calculate the $DALY_p$ rather than implicitly assuming it is equal than the $DALY_p$ of other adverse effects.

• **Beryllium**

No $DALY_p$ is provided by Murray and Lopez [1996(a)] for small intestinal lesions induced after an oral exposure to beryllium. These lesions occur predominantly in the small intestine and to a lesser extent in the stomach and large intestine. Since the gastrointestinal toxicity is not reported in table 3.6, we apply the default $DALY_p$ of 1.1 [yr/pers].

For the inhalation exposure, the induced chronic beryllium disease is an inflammatory respiratory disease. Based on the classification proposed in table 3.6, we classify beryllium disease in category 2 and a $DALY_p$ of 1.1 [yr/pers] is selected.

• **Lead**

No $DALY_p$ is provided by Murray and Lopez [1996(a)] for blood pressure increase resulting from the oral exposure to lead. Based on table 3.6, we classify blood pressure increase in category 2 (heart disease). A $DALY_p$ of 1.1 [yr/pers] is therefore selected.

• **Inorganic arsenic**

The skin toxicity associated with the oral exposure to inorganic arsenic is not reported in table 3.6. We therefore apply the default $DALY_p$ of 1.1 [yr/pers] for the oral exposure to inorganic arsenic.

3.8 EFFECT FACTORS

The ultimate objective of this chapter is to derive the effect factor for a large number of chemicals and for the metals selected in section 1.3.2. We presented in section 2.8.1 how the slope factor and the Disability Adjusted Life Years per affected Person can be combined together to derive the effect factor (see equation (2.19)). Effects factors are presented here for the compounds studied in this chapter and are summarized in appendix 1.1.

3.8.1 Effect factors for metals

The calculation of the effect factors for metals is summarized in table 3.7. Effect factors range from $9.2 \cdot 10^{-8}$ for chromium(VI) up to $1.3 \cdot 10^{-3}$ [yr lost/mg absorbed] for an inhalation exposure to beryllium, showing a factor 10^4 between the highest and the lowest value. Beryllium has the highest effect factor after inhalation, due to its very low NOAEL reported in the IRIS database for an occupational study. This effect factor, as well as the effect factors after an oral exposure to chromium(VI), chromium(III), lead and inorganic arsenic, are presented in italic in table 3.7 since they are derived from a slope factor based on a No Observable Adverse Effect Level. Their confidence is consequently lower than for the effect factors evaluated after fitting the dose-response curve at the level of the observed bioassay data. The effect factor of lead is particularly uncertain, since there is no consensus on a NOAEL for lead, as explained in section 3.6.7. Values indicated in brackets in table 3.7 are indicative values provided for an excessive exposure to chromium(III) and copper.
For cadmium, methylmercury, lead and inorganic arsenic, the effect factor has been determined only for the oral route of exposure. The absence of adequate data for one route of exposure has already been discussed in section 3.6.1., as well as the reasons for not extrapolating the inhalation risk from the oral risk for these metals. It should not be interpreted that the risk is zero for inhalation of cadmium, methylmercury, lead and inorganic arsenic; the abbreviation "n.e." in table 3.7 means that their effect factor can not be evaluated, and not that it is equal to zero.

Metal	CAS RN	Route of exposure	Data type	Critical endpoint	β_{ED10} [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
1 Cadmium	7440-43-9	Oral	Human	Kidney	4.10E+01	0.11	2.5E-06
		Inhalation		n.e.	n.e.		n.e.
2 Chromium(VI)	18540-29-9	Oral	Rat	Non appearance of effects	*1.5E-01*	1.1	*9.2E-08*
		Inhalation	Rat	LDH in bronchioalveolar lavage fluid	2.9E+01	0.11	1.8E-06
3 Chromium(III)	16065-83-1	Oral	Rat	(Non appearance of effects)	*0 (2.6E-4)*	1.1	*0 (1.6E-10)*
		Inhalation		n.e.	0 (n.e.)		0 (n.e.)
4 Copper	7440-50-8	Oral and inhalation		n.e.	0 (n.e.)		0 (n.e.)
5 Methylmercury	22967-92-6	Oral	Human	Abnormalities in neurological development of infants	3.0E+01	1.1	1.8E-05
		Inhalation		n.e.	n.e.		n.e.
6 Beryllium	7440-41-7	Oral	Dog	Intestinal lesions	1.2E-01	1.1	7.4E-08
		Inhalation	Human	Chronic beryllium disease (lung lesion)	*2.2E+03*	1.1	*1.3E-03*
7 Lead (1)	7439-92-1	Oral	Rat	High blood pressure	*2.7E+02*	1.1	*1.7E-04*
		Inhalation		n.e.	n.e.		n.e.
8 Inorganic arsenic	7440-38-2	Oral	Human	Hyperpigmentation and keratosis	*7.8E+01*	1.1	*4.8E-05*
		Inhalation		n.e.	n.e.		n.e.

Table 3.7 Evaluation of the effect factor EF from the slope factor β_{ED10} and the Disability Adjusted Life Years per affected Person $DALY_p$, for the studies metals (n.e. = not estimated).
LDH: lactate dehydrogenate

3.8.2 Effect factors for the other chemicals studied in this chapter

The effect factors for the other chemicals studied in sections 3.3 and 3.4 are calculated in appendices 3.2.2 and 3.3, and are summarized in appendix 1.1. They range from $4.2 \cdot 10^{-12}$ for 1-Chloro-1,1-difluoroethane to $1.3 \cdot 10^{-3}$ [yr lost / mg absorbed] for beryllium.

The effect factor for the respiratory effects of fine particles, sulfur dioxide, nitrogen oxide and carbon monoxide are presented in appendix 3.1, using values calculated by Hofstetter [1998]. Carbon monoxide presents the lowest effect factor ($1.3 \cdot 10^{-8}$ [yr lost / mg absorbed]) and $PM_{2.5}$ the highest effect factor ($7 \cdot 10^{-5}$ [yr lost / mg absorbed]).

3.9 COMPARISON WITH OTHER METHODS

We classified in section 3.1.2 the LCIA methods into different levels of sophistication. We compare in this section the evaluation of noncarcinogenic effects by the ED_{10}-procedure with the damage-oriented method Eco-Indicator 99 and with not damage-oriented methods based on acceptable levels like the reference dose.

3.9.1 Comparison with the Eco-Indicator 99

Both the ED_{10}-procedure and the Eco-Indicator 99 are damage-oriented approaches (level 2 in the classification proposed in section 3.1.2). The major respiratory effects of criteria air pollutants are comprehensively quantified in the Eco-Indicator 99, using results of the ExternE study. It is for that reason that we used in section 3.8.2 the data reported in the Eco-Indicator 99 to derive the effect factor of fine particles, sulfur dioxide, nitrogen oxide and carbon monoxide. Thus, for these substances, our effect factors are just the same as those of Eco-Indicator 99.

We can not compare the noncarcinogenic effect factors summarized in appendix 1.1 with the Eco-Indicator 99, since the Eco-Indicator 99 does not provide a risk quantification of noncancer health outcomes for other compounds than criteria air pollutants. As an example, noncarcinogenic effects of metals such as damages to the liver, kidney or nervous system are not modeled. This may cause a distortion of the LCA results, as acknowledged by Goedkoop and Spriensma [1999]. The ED_{10}-approach is applicable to more substances, since it is less sophisticated: it is based on the consideration of the critical adverse effect of a compound, while all the major endpoints associated with a substance are taken into account in the Eco-Indicator 99. Interestingly, effect factors derived from the ED_{10}-approach are expressed in units compatible with those reported in the Eco-Indicator 99. Factors provided in the Eco-Indicator 99 for damages on humans not studied in this dissertation (ionising radiation, summer smog, ozone layer depletion, climate change) can thus be used as a complement to our study. Reciprocally, effect factors for metals listed in table 3.7 and for compounds reported in appendix 1.1 could be used in addition to the factors reported in the Eco-Indicator 99, assuming that the critical endpoint is a good indicator of the total effect.

3.9.2 Comparison with methods using acceptable levels

The ED_{10}-approach can also be compared with LCIA methods developed by Huijbregts [1999] and Hertwich [1999], which are based on acceptable levels like the Reference Dose (RfD). These methods do not quantify the probability of occurrence of an adverse effect. On the contrary, the ED_{10}-approach enables quantifying the noncancer risk and comparing it with the cancer risk and other quantified damages on humans. Consequently,

only the relative weight attributed to chemicals by LCIA methods using the RfD and by the ED_{10}-approach can be compared.

When the ED_{10h} can be directly assessed from the dose-response curve plotted at the level of data observed in a bioassay, it corresponds to the same fixed response level for all chemicals. On the contrary, the NOAEL can correspond to different response levels. This introduces a bias in LCIA methods using the RfD for comparing chemicals. This is a fundamental difference between the ED_{10}-approach and methods based on acceptable levels like the RfD. As an order of magnitude, this difference can reach a factor 100 when two substances having a NOAEL associated with a response level of 0.1% and 10% respectively are compared.
The ED_{10h} has been evaluated for most chemicals from the $NOAEL_a$ (see section 3.4). Applying the RfD or the slope factor derived from the $NOAEL_a$ with equation (3.9) would not change the relative comparison of chemicals if we had adopted in our procedure the uncertainty factors developed in Risk Assessment. However, we used in section 3.4 conversion factors that are less conservative than the uncertainty factors of Risk Assessment, in order to get "best" estimates of the slope factor and thereby limit the bias in the comparison of chemicals. Consequently, the relative comparison of chemicals is different whether we use the RfD or the slope factor that we derive from the $NOAEL_a$. The more conservative the uncertainty factors used in Risk Assessment, the higher this difference. This difference can be up to 100 when our conversion factors are 100-folds lower than the uncertainty factors used in Risk Assessment. The relative weight of substances having large uncertainty factors is thus decreased in the ED_{10}-approach.

A third difference can finally be mentioned. The severity of the critical effect is incorporated in the ED_{10}-approach by using the $DALY_p$, while methods based on the reference dose do not consider the type of endpoint. However, since a default $DALY_p$ is used for most chemicals (see section 3.7.2), this difference does not presently change the comparison of most compounds. It may play a relevant role in the future if we succeed to assess the severity associated with each compound more precisely.

3.10 CONCLUSIONS

Effect factors have been calculated in this chapter for more than 300 substances, by combining their slope factors $\beta ED10$ with their Disability Adjusted Life Years per affected Person ($DALY_p$). Metals have been studied with specific attention. Like for carcinogenic effects, we found a factor larger than 100 million-folds between the lowest and the highest effect factor, and most of the variation among the effect factors is due to differences in the slope factors. We also found that the lethal dose LD_{50a} should not be used to extrapolate the effect factor for data-poor substances.

We already discussed in section 2.9 some advantages of the ED_{10}-procedure, such as its applicability to both cancer and noncancer endpoints. Specific interesting characteristics of the ED_{10}-approach for the evaluation of noncarcinogenic effects can be concluded from this chapter:

- The ED_{10}-approach is damage-oriented, that is makes it possible to quantify the risk of noncarcinogenic adverse effects of a relatively large number of chemicals. This is a new input for LCIA, where noncarcinogenic effects are usually not quantified or only for a limited number of substances like in the Eco-indicator 99 method of Goedkoop and Spriensma [1999].
- The application in LCIA of the ED_{10h} instead of an acceptable level like the reference dose RfD permits to reduce the bias in the comparison of chemicals. Indeed, while the RfD is associated with an unspecified response level, the ED_{10h} corresponds to a fixed 10% added risk over the background level. Every chemical can therefore be characterized on a similar basis, which reduces the bias in the comparison of compounds in LCIA. Furthermore, the conservative values of the uncertainty factors incorporated in the RfD are excluded from the ED_{10}-approach; the human-to-human uncertainty factor is not included since it is inappropriate for an application in LCIA, where we aim to assess the risk for the general population. This discussion indicates that we adapted in this chapter the values developed in Risk Assessment to the specific characteristic of LCIA. We showed that the use of non-conservative animal-to-human and subchronic-to-chronic conversion factors decreases the relative weight of substances having large uncertainty factors.
- A first screening of the severity of noncarcinogenic endpoints can be integrated, after a simplified adaptation of the Disability Adjusted Life Years per affected Person concept.

The limitations of the ED_{10}-procedure due to the hypotheses of linearity and non-threshold have already been discussed in section 2.9. Specific limitations for the characterization of noncarcinogenic effects are listed here:

- The extrapolation of the ED_{10h} from the $NOAEL_a$ should be used only to get a first order of magnitude of the slope factor, due to the drawbacks of the $NOAEL_a$. For a more reliable estimate of the slope factor, the ED_{10h} should be evaluated by plotting the dose-response curve at the level of the observed data.

- The ED_{10h} defined in this chapter is associated with the critical endpoint of each substance. The use of the endpoint exhibiting the lowest No Observable Adverse Effect Level of relevance for humans can be justified, since human exposures are likely to be at the low end of the dose-response curve. However, endpoints other than the critical one may occur at low human exposure levels. This is not accounted for in the slope factor, which consequently quantifies the risk of a potential health outcome rather than the risk of the health outcome occurring under any circumstances.
- The severity of the critical endpoint associated with each chemical has been evaluated subjectively by applying a default $DALY_p$ for all substances, with the exception of metals and substances with epidemiological data. A more precise evaluation could be undertaken in the future, by focusing on compounds playing a major role in LCA case studies.

4. FATE AND EXPOSURE OF AIR POLLUTANTS

ABSTRACT

This chapter aims to quantify the fate and exposure of atmospheric releases for carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_X), fine particles and the metals selected in section 1.3.2. Methods currently applied in Life Cycle Impact Assessment (LCIA) for the fate and exposure assessment, mainly based on multimedia models developed in Risk Assessment, are presented and their potentials and shortcomings are discussed. In order to offer an alternative to multimedia models, a semi-empirical approach is developed in this chapter. It uses the concept of exposure efficiency, which is defined as the ratio between the dose absorbed by the population and the emission inducing that absorption. In this chapter, concentrations of the studied atmospheric pollutants are empirically estimated, using measurements reported in the literature. Based on these concentrations and a ventilation rate of 20 [m^3/pers-day], the mass absorbed by the population and the exposure efficiency can be derived. Three types of exposure efficiency are defined for a world release into air of a compound. A specific exposure efficiency, directly based on rural and urban concentrations inhaled by humans, is defined. A continental exposure efficiency is also defined by considering an uniform world continental concentration over urban and rural inhabited regions (marine and desert regions are excluded). A global exposure efficiency is similarly based on the global world concentration of a substance, which is defined as an area-weighted average of the urban and the background concentrations.

We calculated the exposure efficiencies for fine particles, CO, NO_X and SO_2. The specific exposure efficiency ranges from $3.9 \cdot 10^{-6}$ to $2.4 \cdot 10^{-5}$ [mg absorbed / mg emitted], demonstrating that only a small fraction of an atmospheric release is inhaled by humans. Carbon monoxide presents the highest exposure efficiency, by a factor 6 compared to sulfur dioxide. The exposure efficiency by inhalation of indoor releases is also calculated for these substances and is higher than the exposure efficiency of outdoor releases by a factor 10^2 to 10^3. The exposure efficiency of metals released into air and absorbed by inhalation is assumed to be equal to the efficiency of fine particles, since airborne metals are mostly attached to particulate matter. If atmospheric deposition on an agricultural soil occurs, humans can be exposed after a transfer into food products. A first evaluation of this transfer indicates that it can increase the exposure efficiency of metals released into air by a factor 5 up to 70 compared to simple inhalation.
The specific exposure efficiency is selected in this chapter to describe the fate and exposure of atmospheric releases, since it gives a better picture of the actual exposure than the other exposure efficiencies. The specific exposure efficiency is higher by a factor 3 and by a factor 10 than the continental and global exposure efficiency respectively. This demonstrates that the global exposure efficiency, and to a less extent the continental

exposure efficiency, underestimate the exposure that can be expected in the real world. It can be concluded that the use of a one-box continental model without differentiation of urban and rural concentrations leads to an underestimation of the exposure efficiency. This is due to the fact that higher emissions occur in highly populated regions. As a first approximation, the factor 3 could be used as a corrective factor to derive the specific exposure efficiency from the efficiency predicted by a one-box continental model.

As explained in chapter 1 and summarized in figure 1.2, the damage induced by toxic releases on human health can be evaluated by combining their fate and exposure with their harmful potential. While chapters 2 and 3 focus on the effect assessment, this chapter deals with the evaluation of the fate and exposure in the air compartment. Only a brief description of the fate of metals in agricultural soils is provided for comparison in section 4.4.5.

4.1 INTRODUCTION

First, the concept of exposure efficiency is presented in this introduction. Then, Life Cycle Impact Assessment (LCIA) methods for fate and exposure modeling are reviewed together with their drawbacks and the objectives of the chapter are set.

4.1.1 Exposure efficiency

Evans et al. [1997] defined the exposure efficiency as the ratio between the dose absorbed by the population and the emission inducing that absorption. Jolliet and Crettaz [1998] proposed to use the exposure efficiency concept to carry out the fate and exposure assessment in LCIA.

Figure 4.1 presents how the exposure efficiency combines the fate assessment with the exposure assessment. In a first stage, the concentration increase induced by the emission of a substance i is calculated. The fate factor, linking the emission to the concentration increase, can be used for that purpose [Jolliet and Crettaz, 1998]. Then, the absorbed dose is deduced via an exposure factor. By combining these two steps, the dose absorbed by humans can be directly deduced from the emission, applying the exposure efficiency.

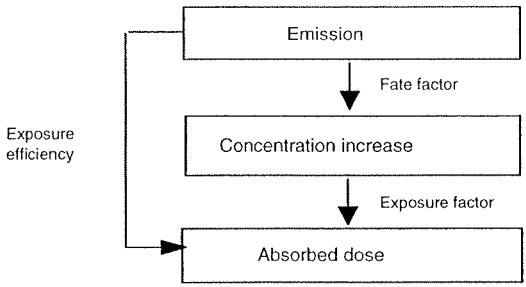

Figure 4.1 Fate and exposure assessment using the exposure efficiency, for a substance released into air and inhaled by humans.

4.1.2 Existing methods for Life Cycle Impact Assessment: potentials and drawbacks

The characterization of the fate and exposure of toxic releases by some of the most frequently used LCIA methods is presented here, by classifying methods among three classes.

a) No or partial fate assessment

Some methods applied in LCIA do not consider the fate and exposure of compounds, that is they assume that all substances have the same fate properties. The Critical Volume approach [BUS, 1984] is an example. This is clearly not a valid assumption, since the persistence of atmospheric pollutants can vary by a factor higher than 10000 [Dinkel et al., 1994]. Other methodologies, such as the Danish EDIP approach [Hauschild, 1994], are limited to a partial fate analysis.

b) Full fate analysis, based on multimedia models

Multimedia fate models predicting the concentrations in the environment are available. Mackay models (fugacity models) are the most widely used. The multimedia fate model Simplebox, implemented in the Uniform System for the Evaluation of Substances (USES), has been applied in LCIA by Guinée et al. [1996], Hofstetter [1998], Goedkoop and Spriensma [1999] and Huijbregts [1999]. This model was first developed by the Dutch National Institute of Public Health (RIVM) [Jager et al., 1994]. The fate and exposure model CalTOX was used by Hertwich [1999]. These Mackay level III models rely on fugacity coefficients to determine the partitioning of chemicals between the different environmental compartments.

Multimedia models have the advantage to take the intermedia transfer directly into account. On the other hand, there is no general agreement in the scientific community about the accuracy and reliability of these models. They poorly represent the atmosphere compartment with a box of a fixed height (e.g. 1000 [m] in USES) and require the knowledge of a large number of parameters. Default values are often used when available data are missing, making data quality a substantial problem. Furthermore, these models have been developed for Risk Assessment and therefore are conservative, while a best estimate of the fate and exposure is needed in LCIA. It would not be consistent to be conservative for human toxicity and not for other environmental classes such as global warming, ozone depletion, etc. Finally, and especially important in the context of the present chapter, the validity of multimedia models is limited to some types of chemicals. Multimedia models are not directly applicable to heavy metals [Guinée and Heijungs, 1993] as well as to CO, NO_X, SO_2 and fine particles [Hofstetter, 1998], since the modeling of these substances requires numerous assumptions.

c) Full fate analysis, alternative approaches

- Semi-empirical approach: Critical Surface-Time 94

In order to offer an alternative to modeling approach and to check fugacity models against empirical measurements, Jolliet [1994] suggested a semi-empirical approach. If measurements of the concentration and estimates of the emission flow are available for a given area, the fate coefficient can be directly determined as the ratio between the mean

measured concentration at the earth level and the corresponding total emission flow per unit area. Jolliet [1994] calculated the first empirical estimates of fate factors at a regional scale (Switzerland).
In these calculations, Jolliet used the global Swiss concentration, obtained by an area-weighted average of the urban and the non-urban concentrations. Since emissions listed in a Life Cycle Inventory can take place all over the world, it would be desirable not to model the Swiss environment, but some "average" world.
- **Approach based on chemical and physical properties of compounds**
Another alternative to fugacity models has been proposed by Hauschild and Jolliet [1998] who developed a model for determining the residence time of substances released into air. All the removal processes (wet and dry deposition; transformation by hydrolysis, photolysis and chemical oxidation) are evaluated in this model through physical and chemical properties of the chemicals. The fate factor is deduced as the ratio of the residence time to the volume of dilution, assuming a fixed volume of dilution of 1000 [m^3/m^2].

4.1.3 Objectives

Some of the main LCIA procedures available to characterize the fate and exposure of toxic releases and their drawbacks have been discussed. This chapter has the following objectives:

1) To determine the fate and exposure for atmospheric releases of NO_X, SO_2, CO, fine particles and of the metals selected in section 1.3.2, by assessing the exposure efficiency in a semi-empirical manner.
2) To compare the exposure efficiency based upon a global concentration with the exposure efficiency based on a continental and a specific concentration.
3) To compare indoor and outdoor exposure to atmospheric pollutants.
4) To test if the semi-empirical approach developed in this chapter can be used to validate multimedia models for well-known substances.

A global, continental and specific exposure efficiency are defined in section 4.2. Data required to evaluate these exposure efficiencies for carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_X), fine particles and metals are presented in section 4.3. The different types of exposure efficiencies are compared in section 4.4, as well as indoor and outdoor releases. The exposure efficiency of atmospheric releases of metals after deposition and transfer into food products is also discussed and compared to the direct exposure after inhalation. Conclusions are drawn in section 4.5.

4.2 EXPOSURE EFFICIENCY

The concept of exposure efficiency has been introduced in section 4.1.1. It is further defined here for characterizing atmospheric pollutants. The exposure efficiency at a global scale is then distinguished from a continental and a specific exposure efficiency.

4.2.1 Definition

The exposure efficiency has been defined in a general manner in section 4.1. More specifically, the exposure efficiency EE_i^{aa} for atmospheric substances is the fraction of a substance i emitted into air that is inhaled by humans (see equation (4.1)).
Pollutants released into air can de deposited to soil or water and then reach humans. The intermedia transfer coefficient f_i^{an}, representing the fraction of the atmospheric emission of a substance i reaching medium n, is introduced to account for the deposition from air to soil or water. Then, the exposure efficiency EE_i^{an} represents the fraction of substance i emitted into air which is ingested by humans through route n (n= food products or water). It is presented in equation (4.2).

$$EE_i^{aa} = \frac{M_{i\text{-abs}}^{a}}{M_i^{a}} \qquad \text{Equation (4.1)}$$

$$EE_i^{an} = f_i^{an} \cdot EE_i^{nn} \qquad \text{Equation (4.2)}$$

where:

EE_i^{aa}: Exposure efficiency of substance i (i) released into air (a), reaching humans by inhalation (a) [$mg_{absorbed}$ / $mg_{emitted}$]

EE_i^{an} : Exposure efficiency of substance i released into air (a), reaching humans by route n (n) [$mg_{absorbed}$ / $mg_{emitted}$]

EE_i^{nn}: Exposure efficiency of substance i released into medium n (n), reaching humans by route n (n) [$mg_{absorbed}$ / $mg_{emitted}$]

M_i^a: Emission flow of a substance i into air [kg/yr]

$M_{i\text{-abs}}^a$: Mass of substance i which is absorbed (i-abs) by humans by inhalation (a), after the emission flow M_i^a [kg/yr]

f_i^{an}: Intermedia transfer coefficient, from air (a) to medium n [-]

We can now define the exposure efficiency at a global and continental level, as well as a more specific exposure efficiency.

4.2.2 Global exposure efficiency

a) Definition

We have mentioned in the introduction some issues involved with the empirical approach developed by Jolliet [1994]. In order to model some "average" world and not to have to budget the import and export flows across regional borders, we propose here to consider the world scale (global scale) for assessing the exposure efficiency of air pollutants. Assuming a uniform concentration C_g at the earth surface for a given substance and a uniform world population density at the earth surface (ρ_g=12 [pers/km^2]), equation (4.3) can be derived. This equation is demonstrated in appendix 4.1, where the fate and exposure assessment are detailed. In equation (4.3), the fate coefficient is given as the ratio of the global concentration at the earth level to the corresponding total emission flow per unit area. The exposure factor accounts for the volume of air inhaled by humans and the density of population exposed to the concentration.

$$EE_{i\text{-}g}^{aa} = F_{i\text{-}g}^{aa} \cdot E_{i\text{-}g}^{aa} = \left[\frac{C_{i\text{-}g}}{M_i^a / A_g}\right] \cdot [V^{in} \cdot \rho_g \cdot N_{365}] = \frac{C_{i\text{-}g}}{M_i^a} \cdot V^{in} \cdot P_W \cdot N_{365} \qquad \text{Equation (4.3)}$$

where:

$EE_{i\text{-}g}^{aa}$: Global (g) exposure efficiency of substance i released into air (a), reaching humans by inhalation (a) [mg$_{absorbed}$ / mg$_{emitted}$]

$F_{i\text{-}g}^{aa}$ Global fate factor of substance i released into air, reaching humans by inhalation [yr-m^2/m^3]

$E_{i\text{-}g}^{aa}$ Global exposure factor of substance i released into air, reaching humans by inhalation [m^3/yr-m^2]

$C_{i\text{-}g}$ Global concentration of substance i at the earth level [mg/m^3]

M_i^a Total world emission flow of substance i in air [kg/yr]

A_g: Global (world) area over which the emission occurs [m^2] ($A_g = 5.1 \cdot 10^{14}$ m^2)

V^{in}: Volume of air inhaled (in) by humans [m^3/pers-day] (V^{in} = 20 m^3/pers-day)

ρ_g: Global world population density [pers/m^2] (ρ_g = 12 pers/km^2)

P_W: World (w) population [pers] ($P_W = 6 \cdot 10^9$ pers)

N_{365}: Number of days per year [days/year]

The fate factor can be expressed as the ratio of the residence time to the volume of dilution, as demonstrated in appendix 4.1. Equation (4.3) can then be rewritten as equation (4.4):

$$EE_{i\text{-}g}^{aa} = \frac{\tau_i^a}{V_i^a} \cdot V^{in} \cdot \rho_g \cdot N_{365} \qquad \text{Equation (4.4)}$$

where:

τ_i^a: Residence time of substance i in air [yr]

V_i^a: Volume of dilution of substance i in air, per unit surface (also called height of dilution) [m^3/m^2]

b) Global concentration

The assessment of the global exposure efficiency requires the evaluation of the global concentration of a given substance at the earth surface. While pollutants with a long residence time such as greenhouse gases are uniformly distributed at the earth surface, pollutants with a short residence time like NO_X, SO_2, particles and CO have a non-uniform distribution at the earth surface. We propose to calculate their mean global concentration as an area-weighted average of the urban and the background concentrations. Since background areas include oceans, desert areas and rural inhabited areas, the world global concentration can be expressed as:

$$C_g = f_m \cdot C_m + f_d \cdot C_d + f_r \cdot C_r + f_u \cdot C_u \qquad \text{Equation (4.5)}$$

where:

C_g : Global (g) concentration [mg/m^3]

C_m : Marine (m) concentration [mg/m^3]

C_d : Concentration in desert (d) regions [mg/m^3]

C_r : Concentration in rural (r) inhabited regions [mg/m^3]

C_u : Urban (u) concentration [mg/m^3]

f_m : Percentage of marine areas in the world [%]

f_d : Percentage of desert areas in the world [%]

f_r : Percentage of rural inhabited areas in the world [%]

f_u : Percentage of urban areas in the world [%]

The total background concentration C_b can be defined as:

$$C_b = f_m \cdot C_m + f_d \cdot C_d + f_r \cdot C_r \qquad \text{Equation (4.6)}$$

4.2.3 Continental exposure efficiency

Since no humans are living in marine and desert areas, the global world scale can be restricted to a world continental scale including only rural inhabited areas and urban areas. Assuming a uniform world continental concentration C_c and a uniform world continental

population density ρ_c, the continental exposure efficiency can be expressed as shown in equation (4.7). This corresponds to models with one continental box.

$$EE^{aa}_{i\text{-}c} = \left[\frac{C_{i\text{-}c}}{M^a_i / A_c}\right] \cdot [V^{in} \cdot \rho_c \cdot N_{365}] = \frac{C_{i\text{-}c}}{M^a_i} \cdot V^{in} \cdot P_W \cdot N_{365} \qquad \text{Equation (4.7)}$$

where:

$EE^{aa}_{i\text{-}c}$ Continental (c) exposure efficiency of substance i released into air (a), reaching humans by inhalation (a) [$mg_{absorbed}$ / $mg_{emitted}$]

$C_{i\text{-}c}$ Continental concentration of substance i at the earth level [mg/m^3]

A_c: Continental area over which the emission occurs [m^2]

ρ_c: Continental population density [pers/m^2] (ρ_c = 153 pers/km^2)

The world continental concentration is expressed as the area-weighted average of the urban and rural concentration:

$$C_c = f_{r\text{-}c} \cdot C_r + f_{u\text{-}c} \cdot C_u \qquad \text{Equation (4.8)}$$

where:

$f_{r\text{-}c}$: Percentage of rural inhabited areas of the world continental areas [%]

$f_{u\text{-}c}$: Percentage of urban areas of the world continental areas [%]

4.2.4 Specific exposure efficiency

Approaches adopted in sections 4.2.2 and 4.2.3 assume a uniform world population density either over the whole world or over the inhabited continental world surface. If the population were uniformly distributed, then the global concentration C_g and the continental concentration C_c would have a toxicological significance: they would represent the concentration that humans would inhale. However, the human population is not uniformly distributed and urban regions are characterized by higher population densities than inhabited rural regions. Consequently, the global concentration C_g and the continental concentration C_c have not a real meaning towards human toxicity (no human inhales these concentrations).

Therefore, we propose here to consider an approximation of the actual inhaled concentration, in order to give a better picture of the real world. Equation (4.3) can then be rewritten as equation (4.9). Equation (4.9) takes into account that people living in rural regions inhale the rural concentration C_r, whereas people in cities inhale the urban concentration C_u. The population density and the concentration are assumed to be uniform in both rural and urban regions. The resulting exposure efficiency is called the specific exposure efficiency, since it is based on concentrations inhaled in urban and rural inhabited regions, and is thus more specific than the global and the continental exposure efficiencies.

$$EE_{i\text{-}s}^{aa} = \frac{Cu \cdot \rho u \cdot Au + Cr \cdot \rho r \cdot Ar}{\frac{a}{Mi}} \cdot V^{in} \cdot N365$$

$$= \frac{Cu \cdot Pu + Cr \cdot Pr}{\frac{a}{Mi}} \cdot V^{in} \cdot N365$$

Equation (4.9)

where

$EE_{i\text{-}s}^{aa}$: Specific (s) exposure efficiency of substance i released into air (a), reaching humans by inhalation (a) [$mg_{absorbed}$ / $mg_{emitted}$]

ρ_u: Population density in urban regions [pers/m^2] (ρ_u = 760 [pers/km^2])

ρ_r: Population density in rural regions [pers/m^2] (ρ_r = 90 [pers/km^2])

A_u: Urban area [m^2]

A_r: Inhabited rural area [m^2]

P_u: World population living in urban regions [pers] ($P_u = 2.7 \cdot 10^9$ pers)

P_r: World population living in rural regions [pers] ($P_r = 3.3 \cdot 10^9$ pers)

4.3 DATA REQUIREment

We distinguished in section 4.2 different types of exposure efficiencies. Equations (4.3), (4.7) and (4.9) indicate that the urban, rural, global and continental concentrations are required for the evaluation of these exposure efficiencies, as well as the total world emissions into air. These data are presented in this section for carbon monoxide (CO), sulfur dioxide (SO_2), nitrogen oxides (NO_X) and fine particles.

4.3.1 Emission flows

Table 4.1 summarizes the world emission flows found in the literature for CO, SO_2, NO_X and fine particles. In this table, emission flows consist of anthropogenic and natural emissions. Residence times are also provided for information.

Substance	Annual emission 10^6 [tons/yr]	Reference	Residence time [day]	Reference
NO_x	131	[UNEP, 1989]	1	[Seinfeld and Pandis, 1998]
SO_2	300	[UNEP, 1989]	4	[Dinkel et al, 1994]
Fine particles	447	[IPCC, 1995]	7	[IPCC, 1995]
CO	2730	[UNEP, 1989]	60	[Seinfeld and Pandis, 1998]

Table 4.1 World total (natural and anthropogenic) emissions of CO, SO_2, NO_X and fine particles, with their approximated residence time.

4.3.2 Concentrations

Estimated values of the urban and rural concentrations, as well as of the global and continental concentrations, are presented in figure 4.2 for the selected pollutants. Appendix 4.2 reviews the literature used to derive these concentrations. For all pollutants, the continental concentration mainly depends on the rural concentration, while the global concentration is very close to the concentration in desert regions. The urban concentration is higher than the global concentration by a factor 10 to 100, and higher than the continental concentration by less than a factor 10. Figure 4.2 also shows that carbon monoxide presents the highest concentration, which is in accordance with its higher emission and residence time than the other pollutants.

For calculating the global concentration according to equation (4.5), the percentage of the different areas has been determined as: $f_m = 70\%$, $f_d = 23.4\%$, $f_r = 6\%$ and $f_u = 0.6\%$. For calculating the continental concentration according to equation (4.8), the percentage of

inhabited rural and urban regions are respectively determined as $f_{r\text{-}c} = 91\%$ and $f_{u\text{-}c} = 9\%$. These values are based on the world area occupied by oceans (70% of the earth surface) and on the assumption that 2.1% of the continental areas are worldwide urbanized. This urbanization value was extrapolated from European data reported by the Economic Commission for Europe [ECE, 1992]. The inhabited rural area is set up for a first screening as 10-folds higher than the urban area, assuming that the population density is 10 times lower in rural regions than in cities.

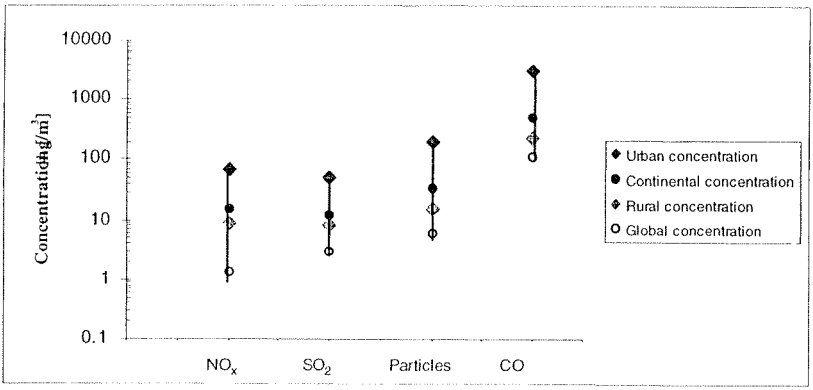

Figure 4.2 Concentrations for urban (C_u), rural (C_r), global (C_g, see equation (4.5)) and continental (C_c, see equation (4.8)) regions.

4.4 RESULTS

4.4.1 Calculations

The global, continental and specific exposure efficiencies have been calculated, using equations (4.3), (4.7) and (4.9) respectively and the data gathered in section 4.3 for CO, NO_X, SO_2 and fine particles. The exposure efficiency for indoor releases has also been calculated, by introducing the following indoor parameters into equation (4.4): population density = 10^{-2} [pers/m^2], volume of dilution = 3 [m] and residence time = 3 [hr] (approximate renewal rate of indoor air).

4.4.2 Comparison of the exposure efficiencies

The specific exposure efficiency is listed in table 4.2 and plotted in figure 4.3 for SO_2, NO_X, CO, fine particles and metals. It ranges from $3.9 \cdot 10^{-6}$ to $2.4 \cdot 10^{-5}$ [mg absorbed / mg emitted]. This range indicates that only a very small fraction of an atmospheric release (1 in 10^6 to 1 in 10^5 depending on the substance) is inhaled by humans. Carbon monoxide presents the highest exposure efficiency, by a factor 6 compared to sulfur dioxide. For metals, the exposure efficiency is approximated by the exposure efficiency of fine particles. The rationale is that airborne metals are attached to particulate matter and their main fate is to be dispersed with particles by the wind before coming down to earth by dry or wet deposition [ATSDR, 1999]. Large metal-particles remain airborne for shorter periods of time than small particles. Consequently, the exposure efficiency determined for fine particles should only be applied to fine metal-particles, since it would overestimate the fate behaviour of metals attached to large particles.

Figure 4.3 enables comparing the three types of exposure efficiency defined in this chapter. It indicates that for all compounds, the specific exposure efficiency is higher than the global exposure efficiency, by a factor 10 or even more. This was expected, since concentrations inhaled in urban regions are higher by at least a factor 10 than the global concentration C_g (see figure 4.2). Since NO_X is characterized by the largest difference between the urban and the global concentrations, it presents the highest difference between the global and the specific exposure efficiency. The continental exposure efficiency lays between the global and the specific efficiency. It is higher than the global efficiency, since desert and marine regions are excluded from the analysis. It is lower than the specific efficiency by a factor 3, since the uniform continental concentration is lower than the urban concentration considered in the specific exposure. As a first approximation, this factor 3 could eventually be used as a corrective factor to derive the specific exposure efficiency from the efficiency predicted by a one-box continental model.

That comparison shows that the global exposure efficiency, and to a less extent the continental exposure efficiency, underestimate the exposure efficiency that can be expected in the real world. Since there is no toxicological justification to assume a uniform global concentration C_g or a uniform continental concentration C_c, we selected in this dissertation the specific exposure efficiency to describe the fate and exposure behaviour of toxic releases within LCIA. This exposure efficiency is expected to give a better picture of the actual exposure resulting from an air release efficiency than the two other efficiencies.

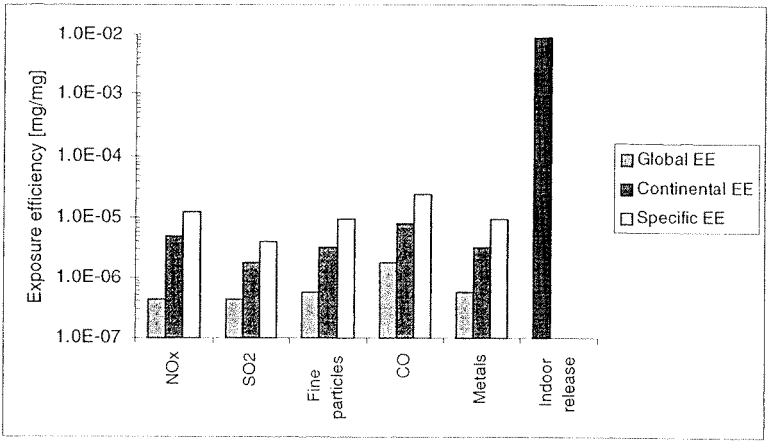

Figure 4.3 Global, continental and specific exposure efficiencies for NO_X, SO_2, fine particles, CO and metals. The exposure efficiency for an indoor release is provided for comparison.

Substance	Global EE_g [mg absorbed/mg emitted]	Continental EE_c [mg absorbed/mg emitted]	Specific EE_s [mg absorbed/mg emitted]
NO_X	4.4E-07	5.1E-06	1.2E-05
SO_2	4.4E-07	1.8E-06	3.9E-06
Fine particles	5.7E-07	3.3E-06	9.6E-06
CO	1.8E-06	8.1E-06	2.4E-05
Metals	5.7E-07	3.3E-06	9.6E-06

Table 4.2 Global, continental and specific exposure efficiencies for NO_X, SO_2, fine particles, CO and metals.

4.4.3 Indoor versus outdoor releases

Figure 4.3 indicates that the indoor release of a substance is much more efficient for reaching humans by inhalation than an outdoor release, by a factor 10^2 to 10^3 when compared to the specific exposure efficiency. The reason is that while the residence time is lower for an indoor exposition due to the constant renewal of indoor air, the indoor population density is higher and the indoor volume of dilution is lower than in outdoor conditions. This indicates that indoor pollution should not be approximated by outdoor pollution in LCIA.

We have to be careful when comparing the indoor and outdoor releases of metals, since the atmospheric deposition of outdoor releases of metals and their transfer into food products can be an important exposure pathway for humans. Consequently, the exposure efficiency of a metal i released into air and reaching humans by food products should be evaluated. A screening of this evaluation is discussed in the next section.

4.4.4 Exposure efficiency of metals in agricultural soils

a) Principle

The exposure efficiency of a metal i released into air and reaching humans by food products (including dairy products, fishes and drinking water) is evaluated here. This requires to assess the transfer coefficient from air to farming land and to evaluate the exposure efficiency of metals in agricultural soils (see equation (4.10)). Since agricultural soils represent 35% of the world continental area [Atlas, 1983] or 11.5% of the whole earth area, a transfer coefficient from air to agricultural soils f^{as} of 0.115 is used for all metals.

$$EEi^{af} = f^{as} \cdot EEi^{sf} \qquad \text{Equation (4.10)}$$

$$EEi^{sf} = fi \cdot EEi^{ff} \qquad \text{Equation (4.11)}$$

where

EEi^{af} : Exposure efficiency of a metal i released into air (a), reaching humans by food (f) products [$mg_{absorbed}$ / $mg_{emitted}$]

EEi^{sf} : Exposure efficiency of a metal i released into agricultural soils (s), reaching humans by food (f) products [$mg_{absorbed}$ / $mg_{emitted}$]

EEi^{ff} : Exposure efficiency of a metal i in food (f), reaching humans by oral exposure (f) [$mg_{absorbed}$ / $mg_{emitted}$]

f^{as} : Transfer factor from air to agricultural soils for metals [-]

fi^{sf} : Transfer factor for a metal i from an agricultural soil to food products [-]

The exposure efficiency for a metal i released into agricultural soils and reaching humans by food products is expressed in equation (4.11). We assume that the full content of each metal in food is taken in by humans ($EE_i^{ff} = 1$). The proper evaluation of the transfer factor from soil to food products could be studied in a chapter of its own. To describe the behavior of heavy metals in the soil compartment, Jolliet and Crettaz [1997] proposed a simple mass balance to account for losses by erosion and the export by plants. However, their first estimates provided unrealistically high estimate of the transfer into food (up to 77%). Taking into account the leaching, a transfer of about 4% has been evaluated for lead by Jolliet and Crettaz [1998]. Further developments of this approach would disserve attention in future research. In the meantime, we run the USES 2.0 model to estimate the fate and exposure in agricultural soils of metals selected in section 1.3.2. This model was developed by the Dutch National Institute of Public Health [RIVM, 1998] and adapted to LCA by Huijbregts [1999]. In this model, transfers into leafs, roots, meat, dairy products, fishes, drinking water and soil ingestion are accounted for. Results are summarized in table 4.3. They indicate that the exposure efficiency after atmospheric deposition and transfer into food products EE^{af} range from $4.7 \cdot 10^{-5}$ for beryllium up to $6.5 \cdot 10^{-4}$ [$mg_{absorbed}$ / $mg_{emitted}$] for copper (factor 14 between the lowest and the highest exposure efficiency).

Metal	EE^{sf} [mg absorbed / mg emitted]	Main route of exposure	EE^{af} [mg absorbed / mg emitted]
Cadmium	3.2E-03	Leaf and root	3.6E-04
Chromium (III) and chromium(VI)	4.3E-04	Drinking water and meat	5.0E-05
Copper	5.6E-03	Leaf and meat	6.5E-04
Methylmercury	8.1E-04	Drinking water and fish	9.4E-05
Beryllium	4.1E-04	Drinking water and leaf	4.7E-05
Lead	9.8E-04	Root and drinking water	1.1E-04
Inorganic arsenic	1.0E-03	Leaf and drinking water	1.1E-04

Table 4.3 Exposure efficiency EE^{sf} of the selected metals released into agricultural soils and reaching humans by food products; Exposure efficiency EE^{af} of the metals released into air and reaching humans by food products.

b) Relevance of the atmospheric deposition for metals

The exposure efficiencies for metals released into air and transferred into food products after atmospheric deposition are summarized in figure 4.4. While the exposure efficiency of fine particles is used to assess the fate and exposure after inhalation of all atmospheric emissions of metals, the fate and exposure in soil is specific to each metal. The atmospheric deposition on agricultural soils and its subsequent transfer into food products increases the exposure efficiency of outdoor releases by a factor 5 to 70. Atmospheric deposition consequently plays a central role for the human exposure to metals, indicating that it is crucial to include the intermedia transfer between air and soil. It should however not be concluded from figure

4.4 that only the indirect exposure after deposition and transfer into food products is relevant, since the effect factor can be higher by inhalation than after an oral exposure (see chapters 2 and 3).
Finally, it is important to underline that a validation of the soil to food transfer coefficient derived from the USES 2.0 model is essential before drawing final conclusions. The dependency of the adsorption coefficient Kd to soil characteristics, particularly to the soil pH, should be accounted for. Exposure efficiencies after transfer into food as presented in table 4.3 must thus be understood only as indicative values.

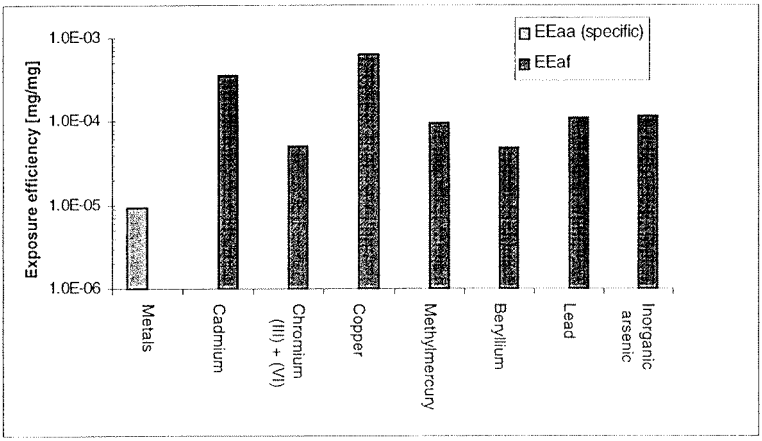

Figure 4.4 Exposure efficiencies of metals released into air, reaching humans by inhalation (EE^{aa}) or by food products after atmospheric deposition (EE^{af}).

4.4.5 Comparison with other approaches

LCIA methods currently used by LCA practitioners do not calculate the exposure efficiency. But the results of their fate analysis can be compared with our evaluation.

- **Modeling versus semi-empirical approach**

The global fate factors determined in this chapter for SO_2 and NO_X have been compared to the fate coefficients calculated by the modeling approach of Guinée et al. [1996]. The comparison was carried out in two steps. In the first comparison, we run the USES model to calculate explicitly the fate factor as the ratio of the Predicted Environmental Concentration (PEC) to the emission per unit area. A residence time of 180 and 226 [day] was gained for NO_X and SO_2 respectively, while typical values reported in the literature are only of a few days. A check of the model parameters used in the USES model indicated that some default values were unsuitable for these pollutants. Final results published by Guinée et al. [1996] gave fate factors of the same order of magnitude than our global empirical fate factors.

This comparison illustrates that the semi-empirical approach developed in this chapter can be used to validate multimedia models for well-known substances, to check the order of magnitude of their results and to find out inadequate default values used in multimedia models.

• **Comparison with Hofstetter [1998]**

Hofstetter [1998] also applied in his dissertation the USES model to predict the fate of substances. However, he acknowledged that particles and heavy metals do not fulfil the modeling requirements. He calculated the fate values with the USES model for arsenic, cadmium, chromium(VI) and nickel. He concluded that they are obviously too low, since they correspond to atmospheric residence times of only a few hours , while metals bound to particles present a significantly higher residence time. Consequently, Hofstetter [1998] recalculated the fate of these metals, by considered a wet deposition of 5 days for all metals (same value as for particles) and their dry deposition velocities. Resulting fate factors are listed in table 4.4. They are more than one order of magnitude larger than the fate factors obtained by the multimedia model and are in good accordance with the global fate factor that we calculated.

For particles, Hofstetter [1998] calculated the residence time for three particle classes. Fate factors are derived as the ratio of the residence time to the volume of dilution. They are also in good accordance with the global fate value that we estimated for fine particles. Fate factors reported in table 4.4 for the different metals and particles classes indicate that these substances have similar fate behaviour. Thus, our assumption that the fate of metals is equal to the fate of particles is acceptable as a first approximation.

Substance	Fate factor [m^2-yr/m^3] Hofstetter [1998] a)	Residence time [hr] ($V=1000\ m^3/m^2$) a)	Fate factor [m^2-yr/m^3] Hofstetter [1998] b)	Global fate factor [m^2-yr/m^3] This study
Particles				
TSP			8.9E-06	
PM_{10}			1.5E-05	
$PM_{2.5}$			1.7E-05	6.3E-06
Metals				
Arsenic	3.7E-07	3.2	8.0E-06	6.3E-06
Cadmium	5.3E-07	4.6	1.6E-05	6.3E-06
Chromium(VI)	5.0E-07	4.4	5.3E-06	6.3E-06
Nickel	2.9E-07	2.5	4.5E-06	6.3E-06

Table 4.4 Comparison of the global fate factors predicted in this chapter with those reported by Hofstetter [1998] using a) the USES model b) an alternative approach to the USES model.
TSP: Total Suspended Particles.
PM_{10}: Particles with a diameter lower than 10 [μm].
$PM_{2.5}$: Particles with a diameter lower than 2.5 [μm].

4.5 CONCLUSIONS

In this chapter, the concept of exposure efficiency has been made operational for LCIA. It has been applied to carry out the fate and exposure assessment of atmospheric releases of the selected metals, CO, NO_X, SO_2 and fine particles. We showed that the exposure efficiency is a powerful parameter to estimate the fraction of a release which is absorbed by humans. Since the exposure efficiency is defined upon measured concentrations and releases, our semi-empirical approach offers an interesting alternative to multimedia models; the comparison with the fate behaviour predicted for NO_X and SO_2 by the Uniform System for the Evaluation of Substances model (USES) has illustrated how the procedure developed in this chapter can be used to validate multimedia models and check their orders of magnitude. The comparison of specific and continental exposure efficiencies also showed that the consideration of a uniform continental concentration tends to underestimate the exposure efficiency that can actually be expected. The comparison of indoor versus outdoor releases indicated that indoor pollution should not be approximated by outdoor pollution in LCIA, since they are characterized by exposure efficiencies higher by a factor 10^2 to 10^3.

Limitations of the approach proposed in this chapter should be mentioned to conclude. It is applicable only to well-known substances for which atmospheric releases are estimated and a dense net of concentrations monitoring exists. Even for these substances, the evaluation of the emissions and associated concentrations can be uncertain. In addition, while the influence of different speciations was studied for the toxic effects of heavy metals (see chapters 2 and 3), it has not been addressed for the exposure efficiency. This is a shortcoming that should be explored in the future.
Finally, the specific exposure efficiency does not take into account that the actual exposure efficiency occurring after a release can strongly vary from one emission site to another, due to specific population densities and concentrations around the site of release. No attempt was made in this chapter to account for local conditions at the site of release, mainly because the many non-localized processes reported in a typical Life Cycle Inventory make it difficult.

5. HUMAN DAMAGE FACTORS

ABSTRACT

In this chapter, exposure efficiencies determined in chapter 4 and effect factors determined in chapters 2 and 3 are multiplied to derive the so-called Human Damage Factors (HDF). A framework is developed for that purpose. The damage factor is expressed in years of life lost per emitted mass. It therefore enables quantifying the damage induced on humans by a toxic release in terms of years of life lost, due either to premature death or to a decrease in the quality of life.

We calculated in this chapter the damage factors for NO_X, SO_2, CO and fine particles, as well as for the metals selected in section 1.3.2 and released into air or into agricultural soils. When transfer into food products is not accounted for, the damage factor of the studied metals range from $1.7 \cdot 10^{-11}$ for chromium(VI) up to $1.3 \cdot 10^{-8}$ [yr lost / mg emitted] for beryllium. Lead has the highest damage factor ($1.9 \cdot 10^{-8}$ [yr lost / mg emitted]), if transfer into food products is considered. Appendices 1.2.1 to 1.2.3 summarize the calculation of the damage factors for metals: they indicate that most of the variation among the damage factors for metals is due to differences among the effect factors, since the exposure efficiencies change by less than a factor 10 from one metal to another, for a given route of exposure. The inhalation and oral routes of exposure, as well as the carcinogenic and noncarcinogenic effects, are also compared. This indicates that atmospheric deposition on an agricultural soil, and its subsequent transfer into food, is the dominant route of exposure for cadmium, arsenic, lead and methylmercury, but not for chromium(VI) and beryllium. Indoor emissions of metals result in damage factors higher by a factor 10^3 than the inhalation of outdoor releases, since the exposure efficiency is 10^3 times higher for indoor releases. We have also shown that the noncarcinogenic effect of a given metal is characterized by a higher damage factor than its carcinogenic effect, except for an atmospheric release of chromium(VI) and for indoor releases.

Damage factors ranging from $2.7 \cdot 10^{-10}$ to $6.7 \cdot 10^{-10}$ [yr lost / mg emitted] are found for NO_X, SO_2 and fine particles, while carbon monoxide is characterized by a damage factor 10^3-folds lower. Per emitted mass, metals inhaled by humans induce damages of the same order of magnitude as NO_X, SO_2 and fine particles, except for beryllium whose damage factor is higher by a factor 20; when atmospheric deposition on agricultural soils and its subsequent transfer into food are accounted for, metals present higher damage factors.

A careful interpretation and use of the damage factors are required, since they are characterized by many uncertainties sources. A quantitative uncertainty analysis is out of the scope of this chapter. Some of the main uncertainties associated with the effect factor are qualitatively discussed and approaches that could be followed in the future to characterize uncertainties are mentioned. An indirect validation of the damage factors, which is required before they can be used as a reliable support for decision making in Life Cycle Assessment (LCA), is discussed and presented for SO_2, NO_X, CO, fine particles and five metals (Pb, Cd, Hg, Cr(VI), As) by applying their damage factors to their total emissions over Switzerland and Europe. The evaluated damages are plausible and in accordance with values reported in other studies.

As explained in chapter 1 and summarized in figure 1.2, the damage induced by toxic releases on human health can be assessed by combining the fate and exposure assessment with their harmful potential. Chapters 2 to 4 have presented the effect analysis as well as the fate and exposure analysis. In the present chapter, a framework linking these two steps is developed in section 5.1 and the human damage factor is defined so that the damage on human health can be directly assessed from an emission. Human damage factors are calculated and discussed in section 5.2 for NO_X, SO_2, CO and fine particles, as well as for releases into air and agricultural soils of the metals selected in section 1.3.2. An indirect validation of these damage factors and a discussion of their uncertainty is presented in sections 5.3 and 5.4. Conclusions are drawn in section 5.5.

5.1 COMBINING THE EXPOSURE EFFICIENCY WITH THE EFFECT FACTOR

The framework proposed to evaluate the damage on humans induced by substances has been put forwards in the introduction of this dissertation (section 1.3.3). Based on the developments presented in chapters 2 to 4, this framework is presented in further detail in this section for atmospheric releases and for emissions of metals into agricultural soils.

5.1.1 Key steps

Figure 5.1 summarizes the two stages required for assessing the damage on human health. In the fate and exposure analysis (first step), the fate factor links the emission of a substance i to the resulting concentration increase. Then, the exposure factor makes it possible to derive the dose absorbed by humans. The absorbed dose can be directly deduced from the emission, applying the exposure efficiency EE_i^{aa} (see chapter 4).
In the effect analysis (second stage), the damage induced by the absorbed dose is assessed. The slope factor β_{ED10} links the absorbed dose to the persons affected by the specific endpoint associated with a substance i. The severity of the endpoint is taken into account using the Disability Adjusted Life Years per affected Person concept. The damage on humans is derivable from the absorbed dose, applying the effect factor EF_i^a (see chapters 2 and 3).

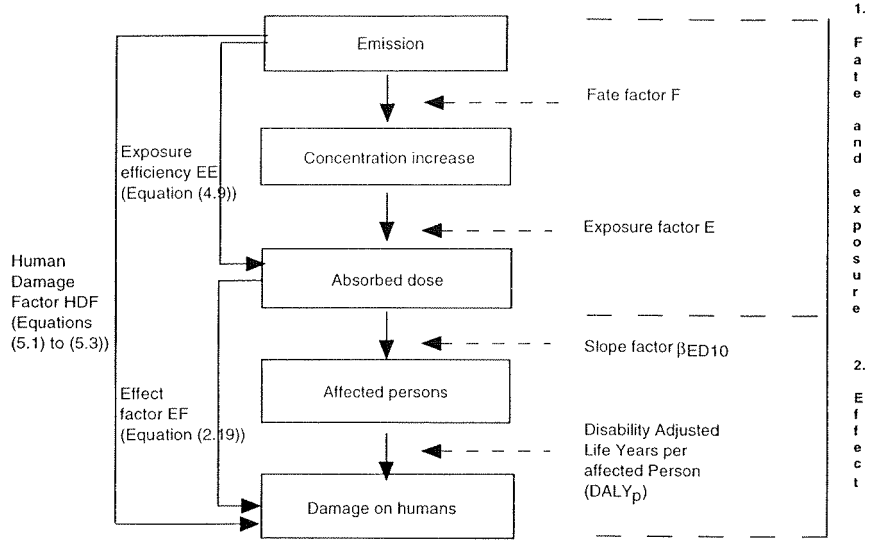

Figure 5.1 Overview of the framework proposed for assessing the damage induced on human health by a toxic released into air (only the direct exposure by inhalation is presented).

5.1.2 Human damage factors

a) Air release, direct exposure by inhalation

By combining the exposure efficiency and the effect factor, the factor converting the atmospheric emission of a substance i into the damage induced on humans can be derived. We denote this factor the Human Damage Factor (HDF), as indicated in figure 5.1. It is expressed in equation (5.1) for a substance released into air and reaching humans by inhalation. The unit of this factor is years of life lost per emitted mass. The damage factor therefore enables quantifying the damage induced by a release in terms of a number of years of life lost, due either to premature death or to a decrease of the quality of life.

$$HDF_i^{aa} = EE_i^{aa} \cdot EF_i^{a} \qquad \text{Equation (5.1)}$$

where

HDF_i^{aa} : Human damage factor of a substance i released in air (a), reaching humans by inhalation (a) [yr lost / mg$_{emitted}$]

EE_i^{aa} : Exposure efficiency of a substance i released in air (a), reaching humans by inhalation (a) [mg$_{absorbed}$ / mg$_{emitted}$]

EF_i^a : Effect factor of a substance i by inhalation (a) [yr lost / $mg_{absorbed}$]

b) Air release, with deposition on agricultural soils

We explained in section 4.4.4 that the transfer from air toward agricultural soils by atmospheric deposition and its subsequent transfer into food products can be a relevant exposure path for metals. To take this transfer into account, we introduced in chapter 4 the intermedia transfer coefficient f^{as} representing the fraction of a metal released into air which is deposited on agricultural soils. The overall damage factor, including both direct and indirect impact of a metal i on humans, is expressed in equation (5.2). It requires the evaluation of the damage factor of a metal i released into agricultural soils, which is presented in equation (5.3).

$$HDF_i^a = HDF_i^{aa} + f^{as} \cdot HDF_i^{sf} \qquad \text{Equation (5.2)}$$

$$HDF_i^{sf} = EE_i^{sf} \cdot EF_i^f \qquad \text{Equation (5.3)}$$

where:

HDF_i^a : Human damage factor for a metal i released in air (a), reaching humans by direct inhalation and after oral exposure following a transfer into food products [yr lost / $mg_{emitted}$]

HDF_i^{sf} : Human damage factor for a metal i, released into agricultural soils (s) and transferred into food (f) products [yr lost / $mg_{emitted}$]

EE_i^{sf} : Exposure efficiency for a metal i, released to agricultural soils (s) and transferred into food products (f) [$mg_{absorbed}$ / $mg_{emitted}$]

EF_i^f : Effect factor for a metal i via food (f) consumption [yr lost / $mg_{absorbed}$]

f^{as} : Transfer factor from air (a) to agricultural soils (s) for metals [-]

5.2 RESULTS

The human damage factors are calculated and discussed in this section for the metals studied in this dissertation as well as for NO_X, SO_2, CO and fine particles. The damage factors of these toxic releases are compared and the role of the route of exposure is discussed for metals. An example of application is also presented.

5.2.1 Human damage factors for metals

a) Calculation and results

Damage factors for indoor and outdoor air releases, as well as for emissions to agricultural soils, are calculated in appendices 1.2.1 to 1.2.3 for the metals studied throughout this thesis, using equations (5.1) to (5.3). As an example, the detailed calculations are presented in appendix 5 for cadmium.

Damage factors are summarized in figure 5.2. In this figure, the direct damage after inhalation is separated from the indirect damage occurring after atmospheric deposition and transfer into food products. Damage factors for carcinogenic and noncarcinogenis effects are purposefully kept apart, in order to facilitate the discussion.

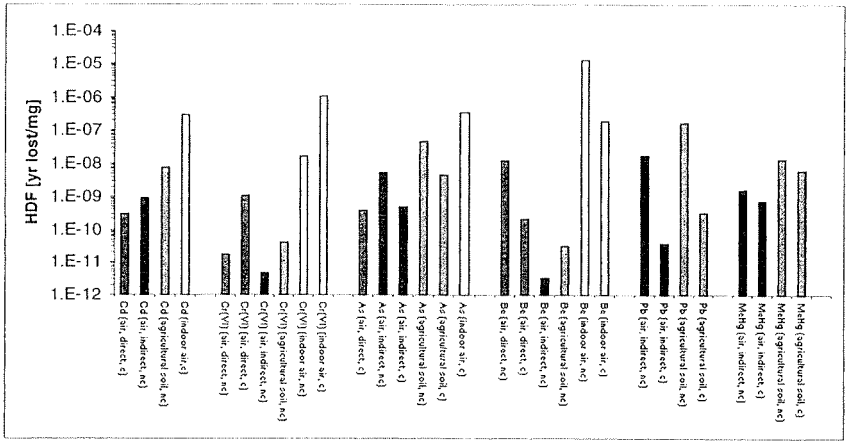

Figure 5.2 Human damage factors for atmospheric releases and emissions into agricultural soils.
Cd: cadmium; Cr(VI): chromium(VI); As: inorganic arsenic; Be: beryllium;
Pb: lead; MeHg: methylmercury; Air, direct: damage after inhalation (in blue).
Air, indirect: damage after deposition and transfer into food (in red).
Agricultural soil: damage after a release to agricultural soils (in green).
Indoor air: damage after an indoor release (in white).

b) Discussion

- Variation of the damage factors among metals

When transfer into food products is not accounted for, the damage factor for metals ranges from $1.7 \cdot 10^{-11}$ for chromium(VI) up to $1.3 \cdot 10^{-8}$ [yr lost / mg emitted] for beryllium. The high damage factor for beryllium by inhalation is due to its high effect factor by this route of exposure. Lead has the highest damage factor ($1.9 \cdot 10^{-8}$ [yr lost / mg emitted]) if transfer into food products after atmospheric deposition is considered. Its high noncarcinogenic damage factor is due to its low No Observable Adverse Effect Level on which no consensus exists (refer to section 3.6.7).

Appendices 1.2.1 to 1.2.3 indicate that most of the variation in the damage factors between metals is due to differences in the effect factor, since the exposure efficiency changes by less than a factor 10 from one metal to another.

- Exposure pathways

Firstly, the route of exposure by which a metal induces the highest damage can be identified. When a metal is known to be adverse by inhalation, indoor emissions result in a damage factor higher by a factor 10^3 than the inhalation of outdoor releases, since the exposure efficiency for indoor emissions is higher by a factor 10^3. Atmospheric deposition on agricultural soils, and subsequent transfer into food, is the dominant route of exposure for cadmium, arsenic, lead and methylmercury, but not for chromium(VI) or beryllium.

Secondly, the route of exposure plays a role in the type of damage. For instance, a cancer risk is linked to the inhalation of cadmium, whereas a kidney damage is evaluated in our procedure for an oral exposure. Like cadmium, chromium(VI) and beryllium are known to be carcinogenic by inhalation while no estimate is provided for the oral route. Conversely, methylmercury and lead are recognized in our procedure to induce a carcinogenic damage only after an oral exposure, while arsenic is known to be carcinogenic for both routes.

- Carcinogenic versus noncarcinogenic effects

Carcinogenic and noncarcinogenic effects can be compared. Except for an atmospheric release of chromium(VI) and indoor releases, noncarcinogenic outcomes dominate carcinogenic endpoints by a factor up to 500 for lead (see figure 5.2). For this comparison, it must be kept in mind that the Disability Adjusted Life Years per affected Person have been less precisely evaluated for noncarcinogenic endpoints than for carcinogenic effects. In addition, the noncarcinogenic damage was evaluated from the No Observable Adverse Effect Level for some metals. This evaluation may add extra uncertainty not encountered for carcinogenic endpoints. Nevertheless, the comparison indicates that effects other than the development of neoplasia may play a major role in LCIA.

5.2.2. Human damage factors for key air pollutants

a) Calculation

Hofstetter [1998] provided in his dissertation damage factors for criteria air pollutants. Since these factors have the same unit as the HDFs defined in section 5.1, we could directly use

them to compare the damages induced by metals and criteria air pollutants. However, the fate and exposure analysis conducted by Hofstetter [1998] gave different estimates than our analysis presented in chapter 4. In order to be consistent with the damage factors calculated above for metals, we calculated the damage factor for NO_X, SO_2, CO and fine particles by combining their specific exposure efficiencies presented in section 4.4.2 with their effect factors calculated by Hofstetter [1998] (see appendix 3.1). The calculations are summarized in table 5.1, while figure 5.3 plots the damage factors for the atmospheric pollutants and for metals released into air.

Pollutant	Exposure efficiency EE [mg absorbed /mg emitted] [This study]	Effect factor EF [yr lost / mg absorbed] [Hofstetter, 1998]	Human Damage Factor HDF [yr lost / mg emitted] [This study]
NO_x	1.2E-05	4.3E-05	5.3E-10
SO_2	3.9E-06	7.0E-05	2.7E-10
CO	2.4E-05	1.3E-08	3.1E-13
Fines particles	9.6E-06	7.0E-05	6.7E-10

Table 5.1 Determination of the human damage factors for NO_X, SO_2, CO and fine particles, using their specific exposure efficiencies and effect factors.

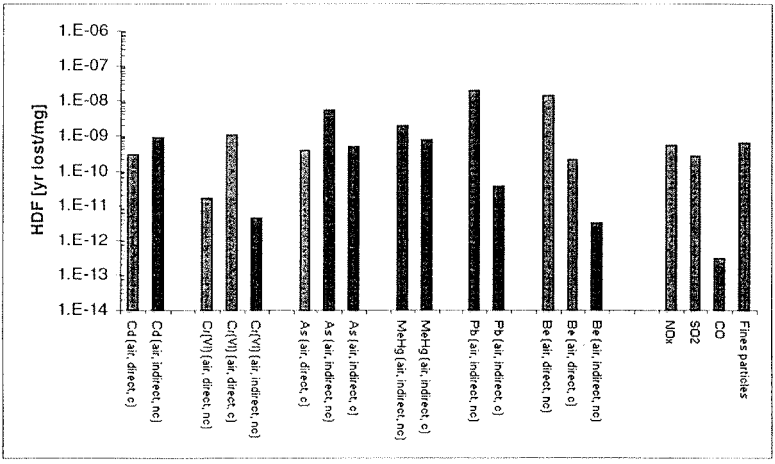

Figure 5.3 Human damage factors for NO_X, SO_2, CO, fine particles and metals released into air.
Air, direct: damage after inhalation (in blue).
Air, indirect: damage after deposition and transfer into food (in red).
c: carcinogenic effect; nc: non carcinogenic effect.

b) Discussion

NO_X, SO_2 and fine particles present similar damage factors, due to exposure efficiencies and effect factors of the same order of magnitude. The damage factor of carbon monoxide is lower by a factor 10^3. Indeed, while carbon monoxide has only a slightly higher exposure efficiency (up to a factor 6), its effect factor is lower by more than a factor 10^3. Therefore, carbon monoxide can have a significant influence on human health only if it is released in high amounts. The validation presented in section 5.3 indicates that this is not the case for the total releases occurring in Switzerland or in Europe.

Per emitted mass unit, inhalation of metals released into air induces damages of the same order of magnitude than NO_X, SO_2 and fine particles, except for beryllium which presents a damage factor higher by a factor 20. When the atmospheric deposition on agricultural soils and its subsequent transfer into food is accounted for, all metals present a higher damage factor.

A careful interpretation of these results is required. Firstly, damage factors are characterized by high uncertainties (see section 5.4) and a small difference between the damage factors of two compounds may therefore not be relevant. Furthermore, atmospheric releases of metals are lower than those of classical air pollutants by many order of magnitudes. Thus, conclusions drawn above are only valid per emitted mass. Other conclusions can be reached per functional unit (see for instance the case study in section 6.4.3) or when the actual releases over a region are considered (see section 5.3).

5.2.3 Example of application

The determination of the human damage factors requires a comprehensive study for each substance. However, their application is straightforward: the emission of a substance i simply has to be multiplied by its damage factors to derive its damage on human health. Table 5.2 presents a summarized example of application, using the inventory data of the reference scenario (scenario CONV) defined in chapter 6 for the Cycleaupe study.

Substance	Mi [mg/FU]	HDF [yr lost/mg]	Mi * HDF [yr lost/FU]
Air			
CO	107	3.1E-13	3.3E-11
NO_x	102	5.3E-10	5.4E-08
SO_2	278	2.7E-10	7.6E-08
particles	41	6.6E-10	2.7E-08
Pb	0.036	1.9E-08	6.8E-10
Agricultural soil			
As	3.5E-04	4.8E-08	1.7E-11
Cd	1.9E-03	8.0E-09	1.5E-11
Cr(VI)	4.4E-03	4.0E-11	1.8E-13
Pb	3.8E-02	1.7E-07	6.5E-09

Table 5.2 Application of the human damage factors to a summarized inventory data set.

5.3 VALIDATION

A framework for assessing the damage on humans induced by chemicals has been presented in section 5.1 and applied to selected metals and air pollutants in section 5.2. Some kind of validation is required before this procedure can become a reliable tool for decision support in LCA. A proper validation in a classical manner is not possible, since the damage induced by a release can not be measured in the real world. LCA does not include any temporal or spatial dimensions, which makes it impossible to measure changes caused by an LCA study. We can therefore not validate the framework proposed in this chapter by classical experiments and measurements. The comparison with other approaches is thus particularly important to check the orders of magnitude. It has been carried out at the effect level (sections 2.3.4 and 3.9) and at the fate and exposure level, where we provided an example of validation of multimedia models using our semi-empirical fate assessment (section 4.4.5). When differences were found, they were explained by looking at their causes. We also validated the ED10h-TD50a and the ED10a-NOAELa relationships, by comparing them with correlations reported in the literature or based on theoretical arguments. This section presents an indirect validation of some of the damage factors calculated in section 5.2.

5.3.1 Validation for atmospheric releases

The damage factors of SO_2, NO_X, CO and fine particles can be indirectly validated. The approach for that validation is to apply these damage factors to the total emission over a region of each pollutant and to check whether the evaluated damage is plausible and in accordance with results reported by other studies. Since considering a large scale like the world would add uncertainties in the releases estimate, the damage due to the Swiss releases is verified. These releases for 1995 are reported by the Swiss Agency for the Environment, Forests and Landscape [BUWAL, 2000]. Multiplying these emissions by the damage factors for SO_2, NO_X, CO and fine particles determined in section 5.2, the years of life lost due to each pollutant can be derived (see table 5.3). This table indicates that these four pollutants contribute to about 98000 years of life lost per year in Switzerland.

Substance	HDF [yr lost/mg]	SWITZERLAND Annual emission [tons/yr]	Damage on humans [yr lost / yr]	EUROPE Annual emission [tons/yr]	Damage on humans [yr lost / yr]
CO	3.1E-13	510000	159	4.7E+07	1.4E+04
SO_2	2.7E-10	38000	10374	1.2E+07	3.3E+06
NO_x	5.3E-10	136000	71944	1.3E+07	6.8E+06
Fine particles	6.6E-10	24200	15851	5.2E+06	3.4E+06
			98328		1.3E+07
Pb	1.9E-08	226	4294	1.3E+04	2.5E+05
Cd	1.2E-09	2.5	3	1.9E+02	2.3E+02
Hg	2.7E-09	3.3	9	1.3E+02	3.4E+02
As	6.1E-09			3.6E+02	2.2E+03
Cr	1.1E-09			4.2E+02	4.7E+02

Table 5.3 Years of life lost per year due to the Swiss (European) releases of SO_2, NO_X, CO, fine particles, lead, cadmium, mercury, arsenic and chromium. For mercury, the HDF of methylmercury is used as a first approximation.

Assuming a discount rate of zero and no age-weighting, Murray and Lopez [1996(a)] calculated that 161.5 million of years of life are lost per year in the Established Market Economies (EME include Europe, USA, Japan, etc., that is 798 million people). This gives 1.4 million of years lost per year in Switzerland. Comparing that total number of years lost with the one due to the SO_2, NO_X, CO and fine particles, these pollutants contribute to about 7% of the total years of life lost. This estimate can be compared with estimates reported in the literature. A Swiss study on externalities due to atmospheric pollution revealed that air pollution in Switzerland causes 3800 deaths per year [BUWAL, 1997], that is about 6% of the 63000 deaths reported in 1997 by the Swiss Federal Office for Statistics [OFS, 1999(b)]. The damage predicted by our procedure is thus in the same order of magnitude as this study.

NO_X is responsible of more years of life lost than fine particles when applying our damage factors, since both pollutants have more or less the same damage factor, but releases of particles are lower (see table 5.3). This is surprising at first glance, since the European Environmental Agency reported that the effects due to particles are the most important in Europe [EEA, 1999]. An explanation to that finding is that particle releases in Switzerland are low compared to the those occuring in other European countries. The consideration of the emissions in 17 European countries (380 million inhabitants) reported by Goedkoop and Spriensma [1999] confirms that particles play a more important role at the European level (see table 5.3). The estimated damage reported in table 5.3 for particles in Europe is in the same order of magnitude as the 40000 to 150000 extra deaths due to respiratory diseases per year reported by the European Environmental Agency [EEA, 1999].

The damages estimated for atmospheric releases of lead, cadmium, mercury, arsenic and chromium are also reported in table 5.3. Only lead appears to induce a significant damage.

Its damage occurs after atmospheric deposition on agricultural soils and transfer into food products. This damage must be interpreted with caution. The uncertainty of the damage factor for lead is indeed high, due to large uncertainties in both the fate assessment in agricultural soils and the noncarcinogenic effect based on a debatable No Observable Adverse Effect Level. The human damage factor for lead should therefore be interpreted and used only for a first screening. However, it indicates that the effect of lead can not be neglected and should not be set as zero.

5.3.2 Validation for carcinogenic chemicals

We checked the order of magnitude of the damage predicted by our methodology for SO_2, NO_X, CO, fine particles and some metals. The Environmental Protection Agency [EPA, 1990] similarly estimated the cancer risk for the exposure to 90 air pollutants, using their 1986 emissions in the USA, their unit risk estimates and their ambient concentrations. 2000 cases of cancer per year were estimated to be caused by the studied substances, which represents about 0.4% of the 500000 cancer deaths yearly reported in the USA. The comparison between the β_{ED10} and the q_1^* (see section 2.3.4) indicated that the slope factor β_{ED10} is lower by a factor 2 than the upper confidence limit q_1^*. Therefore, a lower cases of cancer (around 1000) would be found if we were applying the procedure developed in this thesis to the same releases, assuming a similar exposure. This estimate is in accordance with other values reported in the literature, for instance the 2% proportion of cancer deaths due to pollution reported by Doll and Peto [1981]. It can also be concluded from this discussion that the cancer risk from outdoor exposure to air toxicants is lower than the noncarcinogenic risk due to SO_2, NO_X and fine particles, on a lost life years-equivalent basis.

5.4 UNCERTAINTY SOURCES

The different components of the LCIA procedure proposed in this dissertation for assessing the damage on humans are summarized in figure 5.1. Each of them has some uncertainties. Not considering these uncertainties can lead to an inappropriate comparison of different toxic releases, since the degree of uncertainty can vary among chemicals. A quantitative uncertainty analysis would therefore increase the confidence in the human damage factors. An uncertainty analysis is out of the scope of the present dissertation, mainly because of the lack of reliable information on input data variability. However, we qualitatively discuss here some of the main uncertainties of the effect factor. The uncertainty of the exposure efficiency could similarly be discussed. Approaches that could be followed in the future to characterize uncertainties are also mentioned.

5.4.1 Sources of uncertainty in the effect factor

As indicated in equation (2.19), the effect factor depends on two main parameters: the ED_{10h} and the $DALY_p$. For carcinogens, table 2.3 indicates that the years of life lived with a disability per affected Person (YLD_p) make up only a small share of the total $DALY_p$. Consequently, the value choice concerning the disability weight incorporated in the YLD_p has little influence. Furthermore, table 2.3 also indicates that Disability Adjusted Life Years per affected Person ($DALY_p$) is about the same for all types of cancer. Therefore, the uncertainty concerning the specific affected cancer site is of limited concern. Finally, the $DALY_p$ for carcinogenic effects is calculated from hospital registers reported in the literature and therefore has a limited uncertainty. On the contrary, the $DALY_p$ for noncarcinogenic effects is based upon a subjective judgement for classifying these effects into a default effect category, due to the limited data availability. It is thus much more uncertain.

Concerning the ED_{10h}, the main uncertainties sources are summarized in table 5.4 and are discussed below.

a) Consideration of animal data

Using animal data poses 4 challenges, which are to determine whether the animal data is relevant to humans, to determine a human equivalent dose (concentration), to extrapolate from high to low doses and to know whether responses measured at high doses can be used to predict carcinogenicity [Rees and Hattis, 1994]. We already discussed the derivation of the human equivalent dose or concentration (section 2.1.4.e)) and the extrapolation from high to low doses (sections 2.3.6 and 3.3.3).

For the extrapolation from animals to humans (point 1 in table 5.4), it is assumed that chemicals toxic to animals also present a risk to humans, except if differences in

pharmacokinetics, physiological responses or susceptibility to the tested substance exist between species. We use this assumption in this thesis as a way to by determine if, under this hypothesis, risk is low enough that a substance can be eliminated from further considerations. A closer examination of a compound could be undertaken if it plays an important role in a particular LCA case study.
The Maximum Tolerable Dose (MTD) is the highest dose usually used in animal cancer bioassay [Pitot and Dragan, 1996]. Testing at the MTD is a source of uncertainty (point 4 in table 5.4), since saturation of the DNA repair system and saturation of detoxification pathways occurring at the MTD may produce effects at high doses that are not encountered at ambient concentration [EPA, 1996(a)]. It is assumed that effects seen at the highest dose are appropriate for the assessment, except if adequate data demonstrate that the effects are solely the result of a saturation process rather than carcinogenicity.

b) Route-to-route extrapolation
The route-to-route extrapolation should be a case-by-case analysis of available data. We therefore based our judgement on the recommendation of experts. For instance, we derived the effect factor by inhalation from the oral effect factor only for carcinogens for which this extrapolation is carried out in the IRIS database [EPA, 1998]. For these substances, the same effect factor is consequently judged to be valid for both the oral and the inhalation exposure routes (see appendix 2.1.2). A route-to-route extrapolation was not carried out for the other chemicals, particularly for metals. Metals are indeed expected to have different toxicity by the inhalation and the oral routes of exposure [EPA, 1994] and a route-to-route extrapolation would therefore be too uncertain.

c) Interaction of chemicals
Humans are exposed to a cocktail of chemicals that may interact with each other in additive, synergic or antagonistic manner. We assumed additivity for the effects of all compounds, since data are generally not available for accounting for synergic or antagonistic effects. This assumption may induce large uncertainties. For instance, the toxicity of carbaryl is enhanced 200-fold by the presence of synergists [Beck et al., 1994].

d) Causality
It is not always possible to know with certainty that the relationship between the dose and the response is a causal one, especially when epidemiological studies are used. These studies can be often characterized by the lack of good exposure information (for both chemicals species and actual concentrations) and by the existence of confounding factors (e.g. smoking) [Rees and Hattis, 1994]. To reduce uncertainties, we only used peer-reviewed data.

e) Other factors
Extrapolation from subchronic to chronic effects is often required, since we aim to evaluate the lifetime effect induced by substances. The default extrapolation factor of 3.3 determined by Lewis et al. [1990] (see section 3.1.4.a)) has been applied for that adjustment. It may be inaccurate for some substances.

Pharmacokinetic differences and sensitivity differences due to factors such as age, gender and genetic constitution exist among humans. Within LCIA, we aim to assess the risk for the general population. In that perspective, epidemiological studies on healthy adult male workers may induce uncertainty in the prediction of the health effects in the general population.
To limit the uncertainties associated with bioassays of poor reliability, we only used peer-reviewed data from recognized sources and also avoided an evaluation of the chronic risk from the lethal dose (see sections 2.5 and 3.5). We also referred to the judgement of experts for the choice of the critical endpoint, with the exception of lead for which no consensus exists in the literature (see section 3.6.7); for that substance, the uncertainty is therefore enhanced.

Uncertainty sources	Assumption-proposal
1 Animal to human extrapolation	Positive effect in animals => Effect in humans, except if differences exist
2 Animal to human dose (concentration)	Toxicokinetic adjustment or surface scaling (for doses)
3 High to low dose extrapolation	Linear extrapolation, without threshold (flagging when linearity)
4 Testing at the MTD (for carcinogens)	Use results at the MTD, except if saturation occurs
5 Route to route extrapolation	Case-by-case analysis by experts; not possible for metals
6 Synergic/antagonistic effects	Suppose additivity
7 Causality	Assume causality
8 Subchronic to lifetime exposure	Default extrapolation by a factor 3.3
9 Variation among humans	Estimate the risk for the general population
10 Bioassay quality	Use only peer-reviewed data
11 Choice of the critical effect	Follow the judgement of experts (EPA, ATSDR)

Table 5.4 Uncertainty sources in the evaluation of the ED_{10h}, and thereby of the effect factor and of the human damage factor.

5.4.2 Approaches for an uncertainty analysis

Some of the main sources of uncertainty for the effect factor have been discussed. The same review could be carried out for the exposure efficiency. A quantitative uncertainty analysis of the human damage factor is out of the scope of the present study. We only suggest here how it could be evaluated in a future study. In chapter 6, sensitivity analyses are carried out to characterize uncertainties in the Cycleaupe case study. Similarly, we could have tested

different values of the parameters affecting the damage factor. A sensitivity analysis has only been carried out by testing the influence of the curve-fitting model on the ED10h. This analysis showed that the ED10h is fairly independent from the model (see sections 2.3.3 and 3.3.2).

A Monte Carlo simulation could also be performed in the future, by providing a distribution of the parameters affecting the damage factor. A probability density function for the human damage factor could be derived. It would contain more information than the single-number human damage factor provided in section 5.2. The dominant sources of uncertainties and their order of magnitude could be identified and compared to uncertainties encountered in the Life Cycle Inventory. As an indication, Hofstetter [1998] calculated the lower and upper values of the 95% confidence interval for the damage factor. He obtained a range of 10^2 to 10^3 between the lowest and the highest estimate for criteria air pollutants (SO_2, NO_X, CO and particles) and a range from 10 up to 10^5 for the carcinogenic effects of different compounds.

5. 5 CONCLUSIONS

The human damage factor has been defined in this chapter by combining the effect factor with the exposure efficiency. This damage factor makes it possible to quantify the damage induced by a toxic release in terms of years of life lost, due either to premature death or to a decrease in the quality of life. The procedure developed in this chapter is therefore damage-oriented. As an example of application, damage factors for the selected metals, NO_X, SO_2, CO and fine particles have been calculated. Most of the variation in the damage factors among metals is due to differences in their effect factors, since the exposure efficiency changes by less than a factor 10 from one metal to another. We have also shown that when atmospheric deposition on agricultural soils and its subsequent transfer into food are accounted for, metals present higher damage factors than NO_X, SO_2 and fine particles. As demonstrated for metals, the carcinogenic and noncarcinogenic effect of toxic releases can be compared on a similar basis. It should also be possible in the long term to compare the years of life lost due to chemicals' exposure with the years of life lost due to other causes, for instance due to road or work accidents reported in a LCA case study. Based on the framework proposed in this chapter and the effect factors summarized in appendix 1.1 for more than 900 substances, a large set of damage factors could be calculated in the near future by combining the effect factors with new fate and exposure factors.

The uncertainty of the damage factors should finally be emphasized. Uncertainty sources affecting the effect factor have been discussed. Due to these uncertainties and those affecting the exposure efficiency, damage factors should be used with caution when assessing the relative impact of chemicals within LCIA. The background of these factors should be understood by practitioners. The application of the damage factors beyond the intended scope of LCIA, for instance for evaluating the absolute damage induced on humans by toxic releases, should presently be avoided.

6. CASE STUDY ON DOMESTIC RAINWATER USE

ABSTRACT

Systems using rainwater or reducing drinking water consumption have been developed for toilet flushing. This chapter presents the CYCLAUPE I project that was launched to quantify the environmental impacts of these systems, in comparison with a conventional water supply system. This project, sponsored by the Swiss Agency for the Environment, Forests and Landscape (BUWAL), aims to go beyond the dogmatic positions concerning rainwater recuperation by identifying key factors which make each system interesting. To achieve these goals, a Life Cycle Assessment (LCA) has been performed on the drinking water supply system, the rainwater recuperation system and the wastewater treatment system. This LCA is the first one carried out on the whole water cycle. Five scenarios have been defined for flushing the toilet. A complex treatment for the drinking water, as well as energy consumptions of 0.35 [kWh/m^3] for the conventional water supply and of 0.09 [kWh/m^3] for pumping the rainwater, are selected to define the scenarios.

Results show that economic toilets (3.5 [l/flushing]) lead to a significant reduction of the energy requirements in comparison to conventional toilets (9 [l/flushing]). A conventional water supply and the rainwater recuperation with an individual storage tank of 10 m^3 are characterized by a similar energy consumption. A rainwater storage tank of 20 m^3, designed to be independent of the conventional water supply system, is energetically disadvantageous. Calorific losses, linked to the temperature increase of flushing water in the house, has a significant contribution to the energy requirements.
In a first stage, a Life Cycle Impact Assessment (LCIA) was performed with the critical surface-time CST95 method of Jolliet and Crettaz [1997] and the CML96 method of Guinée et al. [1996]. Both methods indicate that the conventional scenario with economic toilets (CONVeco) is the most advantageous for all impact classes. With the CST95 approach, this scenario is even more favorable for human toxicity after consideration of the transfer of pollutants contained in flushing water, since drinking water is less polluted than rainwater. In a second stage, the human damage factors developed in this thesis (see chapter 5) have been applied. The conventional scenario (CONVeco) is then still characterized by lower impacts on humans than the recuperation scenario (REC10eco). However, the substances having the major effect on human health are different than with the CST95 method: while CST95 identifies metals as major contributors, NO_X, SO_2 and fine particles are responsible of the total damage when the damage factors are applied. These air pollutants have much higher releases and damage factors close or not very lower than metals, explaining why they have a much higher impact.

Sensitivity analysis have been carried out and show that the rainwater recuperation scenario (RECeco) has a lower energy consumption than the conventional scenario (CONVeco) only when the energy required for the water supply is higher than 0.8 [kWh/m^3], assuming a complex water treatment; this threshold is equal to 1.3 [kWh/m^3] for a simple treatment. However, the scenario CONVeco remains preferable for all other impact classes. A high energy consumption of the pump, in order to reach pressures suitable for garden watering, strongly penalizes the rainwater recuperation, as well as a storage tank in concrete.

6.1 INTRODUCTION

Regions where water shortages may occur are limited in countries like Switzerland. However, unpolluted water is becoming more and more of a scare resource and the cost of water supply and treatment is constantly increasing. A moderated use of water is therefore recommended by the Swiss regulation on water protection [VGL, 1996]. Different ways to diminish water consumption are proposed, among them the use of low-flow toilets (referred to as economic toilets in this chapter). Moreover, rainwater recuperation is proposed as an alternative to the use of drinking water for toilet flushing. Different systems using rainwater or reducing water consumption have been recently developed as an alternative to conventional toilets supply.
Rainwater recuperation is a much debated subject. For its supporters, it does not make any sense to transport water on long distances, to treat it, and then to use it for toilet flushing. Instead, rainwater could be used as part of a sustainable management of water resources [Schudel, 1996 ; Vahrenholt, 1992]. For the opponents of rainwater recuperation, its use is questionable in areas where there is no shortage of water. Their arguments are that energy savings are illusory and that some hygienic problems may occur [Kamm and Peter, 1995].

No study with an overall view of the issues involved on the whole cycle of water production and treatment has ever been presented, neither by supporters nor by opponents of the rainwater recuperation. To fill this gap and to go beyond the dogmatic position concerning this subject, the CYCLEAUPE I study was launched on the request of the Swiss Agency for the Environment, Forests and Landscape (BUWAL). We carried out a Life Cycle Assessment to quantify the environmental burdens on the whole chain of processes required for toilet flushing. The structure of this chapter is based on the four steps of a LCA. In section 6.2, the aim of the study, the scenarios, the functional unit and the system boundaries are defined. The emissions of substances and the consumption of resources are quantified in section 6.3. Their environmental impact on humans and ecosystems are evaluated in section 6.4 using different impact assessment methods presented in the previous chapters and the human damage factors developed in this dissertation. The interpretation analysis carries out some sensitivity analyses in section 6.5. Conclusions are presented in section 6.6.

6.2 GOAL DEFINITION

6.2.1 Aims

The Life Cycle Assessment presented in this chapter aims to quantify the environmental impacts of systems using rainwater or reducing water consumption for toilet flushing, in comparison to conventional toilet flushing. Advantages and disadvantages of these systems have to be identified. Conditions making each system interesting from an environmental point of view must be determined as well as processes responsible for the main environmental burdens. Human damage factors determined in chapter 5 for metals and air pollutants are tested on this case study. Results obtained after their application are compared to those obtained by other LCIA methods.

It should be pointed out that this study is restricted to rainwater use for toilet flushing. Garden watering is studied in the sensitivity analysis, while the use of rainwater to wash the laundry has been considered in the Cyclaupe II project [Bronchi et al., 1999].

6.2.2 Scenarios

The five scenarios studied in this case study are summarized in table 6.1 and described below. Variants of the drinking water treatment and supply, as well as variants of the storage tank and the pump, are discussed in sensitivity analyses (see section 6.5).

Scenario type	Toilets supply	Recovery fraction c	Type of toilet
1 CONV	Conventional supply	-	Normal: 54 [l/pers-day]
2 REC 10	Rain water recuperation in a storage tank of 10 m^3	57%	Normal
3 CONVeco	Conventional supply	-	Economic: 21 [l/pers-day]
4 REC 10eco	Rain water recuperation in a storage tank of 10 m^3	97%	Economic
5 REC100%	Rain water recuperation in a storage tank of 20 m^3	100%	Economic

Table 6.1 Scenarios studied in the Cyclaupe study.
CONV: Conventional water supply; REC : Recuperation: eco : Low-flow toilets.

a) Conventional scenario: CONV

This reference scenario is characterized by a conventional water supply for the toilets. Rainwater is infiltrated in the soil. As reference values for this study, we selected:

- A complex drinking water treatment (treatment with chlorine, activated carbon, ozone and flocculation). The drinking water treatment plant of Betteraz (Porrentruy, JU) is selected as representative of a complex treatment.
- An Swiss average energy requirement of 0.35 [kWh/m^3] for the water supply [Pelli et al., 1996].
- A typical wastewater treatment plant, as described by Zimmermann et al. [1996].
- A two level house (2 families of 4 persons per level, 100 m^2 of living area for each family).
- A Swiss electricity production for the water supply, the drinking water plant and the wastewater treatment plant. Major energy sources of the Swiss electricity are hydroelectric (58.7%) and nuclear energy (38.3%) [Frischknechet et al., 1996].
- Conventional toilets characterized by a water consumption of 9 [l/flushing], according to Orlando and Cuanillon [1997]. An average of 6 flushings per person and per day is assumed, leading to a water consumption of 54 [l/pers-day].

b) Recuperation scenario: REC10

In this scenario, rainwater is stored in a individual storage tank made of polyester and is pumped towards the toilets (see figure 6.1). Additional sanitary installations such as a filter, pipes, etc., are required. As calculated by Crettaz et al. [1998], a 10 m^3 storage tank leads to a recovery fraction of 57%. This fraction means that 57% of the water consumption for toilets flushing can be provided by the recuperation system, while 43% of the consumption must be provided by the conventional water supply system. The house is still connected to the conventional water distribution in order to flush the toilets when the rainwater storage tank is empty.

As reference value for this study, an energy requirement of 0.09 [kWh/m^3] for pumping the rainwater from the storage tank to the toilets has been selected [Orlando and Cuanillon, 1997].

c) Independent recuperation scenario, economic toilets: REC100%

A 20 m^3 storage tank leads to a recovery fraction of 100% if economic toilets (3.5 [l/flushing]) are used [Crettaz et al., 1998]. This means that 100% of the water consumption for toilets flushing is provided by the recuperation system. Independence from the conventional water supply is therefore provided, allowing to reduce the size of this latter as explained in section 6.3.1.

d) Conventional scenario with economic toilets: CONVeco

This scenario is based on the same water supply system than the scenario CONV. The only difference is that economic toilets, characterized by a reduced consumption of 3.5 [l/flushing], are selected.

e) Recuperation scenario with economic toilets: REC10eco

This scenario is similar to scenario REC10. The only difference is that economic toilets are selected here, leading to a recovery fraction of 97% [Crettaz et al., 1999].

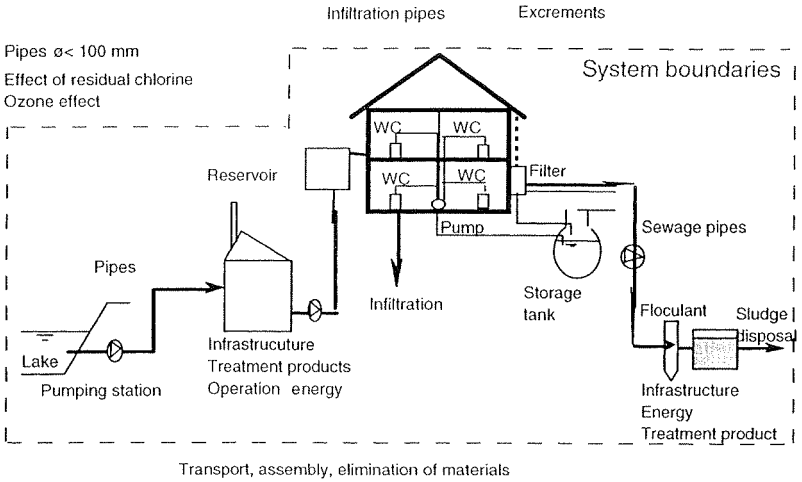

Figure 6.1 Elements included and excluded of the system boundaries.
Only main elements of the recuperation system are presented on this figure.

6.2.3 Functional unit and system boundaries

The goal of the system is to flush toilets with a satisfactory level of hygiene. The functional unit is therefore the Flushing of a toilet for one Person during one Day, in abbreviation FPD. All the inventory emissions must be reported to this unit.

System boundaries are set in order to include all processes required to accomplish the function of the system. Elements considered in the system boundaries are presented in figure 6.1. The drinking water distribution and treatment, the sanitary installations required for rainwater recuperation and the wastewater treatment are included in the system boundaries. Rainwater infiltration is also considered as well as the energy production and the calorific losses. This loss is due to the warming of flushing water in the house (see appendix 6.4). All together, more than 160 different processes have been considered, together with their related emissions and energy use.

Elements similar in the different scenarios can be excluded from the LCA. For instance, pipes with a diameter lower than 100 mm are kept out of the system boundaries, since their sizing depends on the fire flow. Excrements and infiltration pipes are excluded from the system boundaries, since they are similar in each scenario. The transport and elimination of the different inputs are also excluded because of the lack of information.

6.3 INVENTORY

6.3.1 Inputs and emission flows

Emissions of toxic releases into air, water and soil as well as the energy consumption can be deduced from input flows and emission factors. Input flows are the quantities of materials, energy, transport, etc., required for each process. The input flows for the wastewater treatment plant are available in the study conducted by Zimmermann et al. [1996]. This study determines the energy and products requirements as a function of the wastewater quality. For drinking water distribution and treatment, as well as for the sanitary installations required for the recuperation, little data are available in the literature and input flows have been determined in a technical report carried out for the Cyclaupe study by Orlando and Cuanillon [1997]. Table 6.2 summarizes the required quantities of some main input flows.
Emission factors quantify the emissions and energy consumption per unit of input. The emission factors proposed by Frischknecht et al. [1996] are retained. For products specific to the drinking water treatment such as activated carbon, hydrogen peroxide and WAC (chemical used for flocculation), specific research has been carried out by asking the producers for information. For instance, we contacted Bayer AG [Wildner, 1997] for information on activated carbon.

The input requirements have been reported per m^3 for each infrastructure. The specific emissions in m^3 can then been automatically calculated. The fraction F of these emissions to consider for each scenario, as well as details of the inventory calculations, are presented by Crettaz et al. [1998]. The principle for these calculations is that elements dimensioned in relation to the peak flow of the water requirement (general reservoir, infrastructure of the drinking water treatment plant) can be reduced only if the toilets supply is independent from the conventional water distribution system, even during dry periods. On the contrary, elements dimensioned in relation to the mean flow in the water distribution system (pumping station, energy and products requirement for the drinking water treatment plant, energy for the water supply) can be reduced even if the recuperation does not yield a recovery fraction of 100%.

Input	Drinking water [kg/m³]	WTP [kg/m³]	Storage tank [kg/pers-jour]
Steel	3.1E-03	3.4E-02	3.8E-04
Concrete	3.5E-01	7.8E-01	1.5E-03
Cast iron	7.5E-03	1.9E-03	3.5E-04
Polyester	0.0E+00	7.3E-03	1.4E-03

Table 6.2 Quantities of some main input flows for the drinking water plant, the wastewater treatment plant (WTP) and the rainwater storage tank.

6.3.2 Direct transfer of pollutants contained in flushing water

In addition to the emissions related to the various input flows, the direct transfer of pollutants contained in water has to be evaluated. Pollutant concentrations in rainwater and drinking water have been evaluated on the basis of values reported by Truffer [1997] and Mottier [1995]. It appears that heavy metal contents is much higher in rainwater than in drinking water for lead and cooper and only slightly higher for zinc and cadmium (see appendix 6.2).

The fate of pollutants contained in water changes from one scenario to another. In the conventional scenarios, rainwater is infiltrated and drinking water used for toilet flushing is transferred to the wastewater treatment plant, where pollutants are transferred to air, water and sludges. A transfer into food products occurs if sludges are used as a fertilizer in agriculture. In the recuperation scenarios, rainwater used to flush toilets is sent to the wastewater treatment plant as long as the storage tank is not empty. In that latter case, drinking water is used for the flushing. Infiltration of rainwater occurs only when the storage tank is full. More details on the transfer of substances contained in water are presented in appendix 6.3.

It should be emphasized that pollutants contained in rainwater are emitted by cars, industries, heating, etc and could therefore be allocated to these activities. However, rainwater recuperation modifies the fate of these pollutants. Therefore, the impact of these pollutants is presented in section 6.4 separately from the other processes.

6.3.3 Inventory results

a) Energy

Figure 6.2 presents the primary energy requirement of the main scenarios. Scenarios CONV and REC10 have similar energy requirements, since the energy reduction induced in the recuperation scenario by the decrease of the drinking water supply is compensated by the energy increase due the sanitary installations and the pump. Systems reducing water consumption lead to a strong decrease of the energy requirement. Economic toilets are therefore beneficial in regards to the energy consumption. The scenario REC100% shows that a total independence from the conventional water supply is unfavorable in comparison with the scenario CONVeco, as the energy required for the additional installations is not compensated by the reduction of the conventional water distribution system.

Figure 6.2 also indicates that the calorific loss represents a high energy consumption in all scenarios. It decreases with economic toilets, proportionally to the reduction of water consumption. This loss is induced by the temperature increase of flushing water in the house, within the pipes and in the flushing tank. Detailed calculations of the calorific loss are presented in appendix 6.4.

The calorific loss due to the flushing of the toilets and the energy requirement for heating a house can be compared. The calorific loss due to the flushing is evaluated to 2700 [MJfinal/house-year], for a house with 16 persons and a heating yield of 0.85 (see appendix 6.4). The energy requirement for heating a house of 400 m^2 is around 100000

[MJfinal/house-year] (250 MJfinal/m^2-yr · 400 m^2). The calorific loss represents therefore 2.7% of the total energy requirement and must not be neglected.

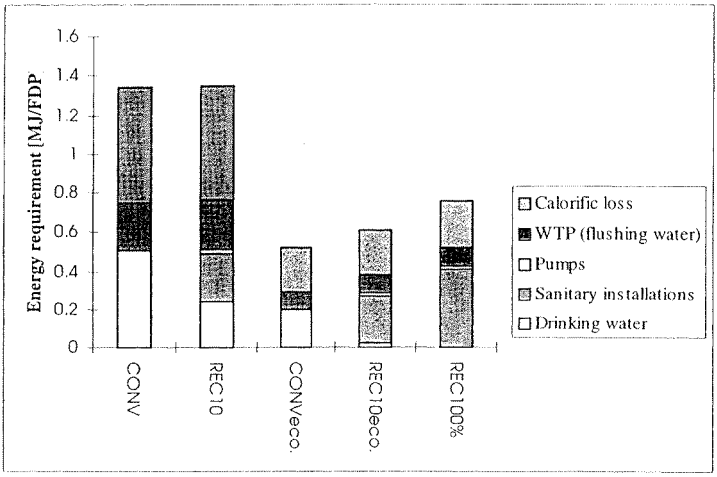

Figure 6.2 Energy requirement for the main scenarios per FPD (Flushing for one Person during one Day).
WTP stands for Wastewater Treatment Plant.
CONV: Conventional water supply, W.-C. conventional
REC10: Rainwater recuperation, V=10 m^3, W.-C. conventional
CONVeco :Conventional water supply, W.-C. economic
REC10eco: Rainwater recuperation, V=10 m^3, W.-C. economic
REC100%: Rainwater recuperation, V=20 m^3, W.-C. economic

Main contributions to the energy consumption are summarized in table 6.3. For the drinking water supply, the energy required for the drinking water treatment plant (44%) and for the water supply (38%) take the main share in the energy consumption. Treatment products such as activated carbon and ozone also play a significant role (10%). Sewers (50%) and infrastructure (40%) represent the highest energy requirement for the wastewater treatment plant, while polyester (68%) and steel (16%) are the main contributions for the sanitary installations of the rainwater recuperation.

Process	Elements	unit	Contribution MJ/unit	%
Drinking water supply & treatment	Energy for the water treatment plant	m^3	4.14	44
	Energy for the water supply	m^3	3.53	38
	Products (O3, Cactif)	m^3	0.95	10
	Drinking water plant (steel, concrete)	m^3	0.49	5
	Others	m^3	0.28	3
	Total		9.40	100
Wastewater treatment plant	Sewers (steel, concrete)	m^3	2.26	50
	Infrastructure (steel, concrete)	m^3	1.8	40
	Operating energy	m^3	0.47	10
	Total		4.53	100
Sanitary installations	Polyester	pers-day	0.17	68
	Steel	pers-day	0.04	16
	Cast iron	pers-day	0.02	8
	Others	pers-day	0.02	8
	Total		0.25	100

Table 6.3 Main contributions to the energy requirement for the water supply, the wastewater treatment and the sanitary installations

b) Emissions

We calculated the emissions for more than sixty substances. Table 6.4 summarizes some of the main emissions for the different scenarios and is discussed here. The full inventory table is presented in appendix 6.5.

- Air and water pollutants

Emissions of air and water pollutants are linked to the energy consumption. They are lower for a conventional water supply. Recuperation scenarios are highly unfavorable for N and C substances (NH_3, COD), due to their higher concentration in rainwater and their transfer at the wastewater treatment plant.

Table 6.4 indicates that toilets with low water consumption tend to have lower emissions. The scenario CONVeco is the most favorable, while scenario REC100% frequently presents higher emissions than scenario REC10eco because of the larger size of its storage tank.

- Heavy metals

Heavy metals emissions must be discussed specifically, since they mainly result from their transfer from flushing water. Emissions into water are higher in the recuperation scenarios, due to the higher heavy metal content of rainwater than of drinking water and because of the transfer of metals at the wastewater treatment plant.

Soil emissions cannot be directly compared, since they occur in different types of soil. Transfer at the wastewater treatment plant of metals contained in flushing water induces

emissions into agricultural soils, following the application of sludges as a fertilizer. Emissions in the infiltration soil occur when rainwater is infiltrated. For these emissions, it is essential to consider the fate of metals and their impacts on humans and ecosystems. This is carried out in the impact assessment presented in section 6.4.

Pollutants	Unit	CONV [unit/FPD]	REC10 [unit/FPD]	CONVeco [unit/FPD]	REC10eco [unit/FPD]	REC100% [unit/FPD]
AIR						
Cd	µg	2.4	**3.7**	0.9	2.3	**2.8**
CO	mg	107.0	**157.0**	41.1	91.1	**116.8**
CO2	g	61.0	**69.0**	23.4	31.9	**35.3**
Cr	µg	5.1	**6.4**	2.0	3.3	**3.6**
Cu	µg	43.3	**68.9**	16.1	**41.9**	39.3
Hg	µg	1.1	**1.3**	0.4	0.7	**0.8**
CH4	mg	104.1	**130.2**	39.8	67.7	**81.1**
NMHC	mg	124.1	**205.6**	48.3	130.1	**197.8**
NOx	mg	102.5	**125.0**	39.1	62.9	**72.1**
particles	mg	41.5	**53.3**	15.8	27.9	**28.5**
Pb	µg	36.1	**44.6**	14.0	22.8	**22.9**
SOx	mg	278.5	**440.7**	108.0	273.3	**274.2**
WATER						
chloride	mg	455.8	**568.8**	177.3	293.2	**370.9**
COD	mg	2.8	**19.5**	1.1	12.7	**14.2**
Cu	mg	0.1	**1.4**	0.0	0.9	**1.0**
NH3	mg	1.1	**18.9**	0.4	12.3	**12.9**
oil	mg	13.2	**16.8**	5.1	8.8	**11.7**
Pb	µg	131.0	**227.5**	49.0	121.9	**123.1**
phenol	µg	97.5	**513.5**	37.9	454.2	**835.3**
Zn	µg	4839.1	**600.9**	186.3	279.7	**284.6**
INFILTRATION SOIL						
Cd	µg	**10.8**	0.4	**4.2**	2.5	2.4
Cr	µg	**40.5**	1.7	**15.7**	9.5	8.9
Cu	mg	**6.8**	0.3	**2.6**	1.6	1.5
Pb	mg	**1.1**	0.045	**0.4**	0.26	0.24
Zn	mg	**1.1**	0.047	**0.5**	0.27	0.25
AGRICULTURAL SOIL						
Cd	µg	1.9	**2.3**	0.7	1.0	**1.0**
Cr	µg	4.4	**10.8**	1.7	6.3	**7.3**
Cu	mg	0.012	**1.3**	0.0048	0.88	**0.91**
Pb	µg	38.3	**279.5**	14.9	173.8	**178.5**
Zn	µg	275.0	**340.1**	106.9	151.1	**154.9**

Table 6.4 Emissions into air, water and soil, for the main pollutants per FPD (Flushing for one Person during one Day). Substances contained in flushing water are taken into account.

6.4 IMPACT ASSESSMENT

The inventory for each scenario has been presented in section 6.3. In this section, the environmental impacts on humans and ecosystems are evaluated using two impact assessment methods presented in chapter 1 (CST95 and CML96) and the human damage factors developed in this dissertation.

6.4.1 Results with CST95

a) Comparison of the scenarios

Results of the characterization carried out with the CST95 method of Jolliet and Crettaz [1997] are presented in figure 6.3, without considering the effect of pollutants contained in flushing water. The score of the conventional scenario CONV is fixed at 100%, since it is the reference scenario. Scores of the scenario REC10 are higher then those of the scenario CONV. The recuperation scenario is especially unfavorable for the aquatic ecosystem, because of high phenol releases linked to the material of the rainwater storage tank (PET). Economic toilets are clearly advantageous for all environmental classes. This is in accordance with the energy requirement and the emissions discussed in section 6.3.3. The scenario CONVeco is the most favorable from an environmental point of view. It presents scores 39% lower than scores of the scenario CONV, this decrease corresponding to the water saving after the introduction of economic toilets (21l/54l = 0.39). For the recuperation scenarios, this decrease is not proportional to the water reduction and is less important.

The scenario CONVeco is even more favorable if the impact of pollutants contained in flushing water is included (see figure 6.4). These pollutants are transferred at the wastewater treatment plant. Since this transfer is proportional to the water contamination and since rainwater is more polluted than drinking water, rainwater recuperation induces an extra load on human toxicity. This extra load results from the transfer of metals into sludges of the wastewater treatment plant; the use of these sludges in agriculture induces a bioaccumulation of metals in the food chain (see section 6.3.2). The hypothesis to allocate heavy metals to the rainwater recuperation or to industrial activities is therefore crucial for the human toxicity.

In the impact assessment, we assumed that the infiltration of rainwater near the house has no effect on humans. This assumes no contamination of the ground water and no transfer into surface water. These hypotheses are reasonable if the infiltration occurs at a sufficient distance of the water table (if required through an absorbing layer) and if the infiltration is deep enough. A sensibility analysis is carried out in section 6.5 in order to evaluate the effect on humans if the ground water is contaminated.

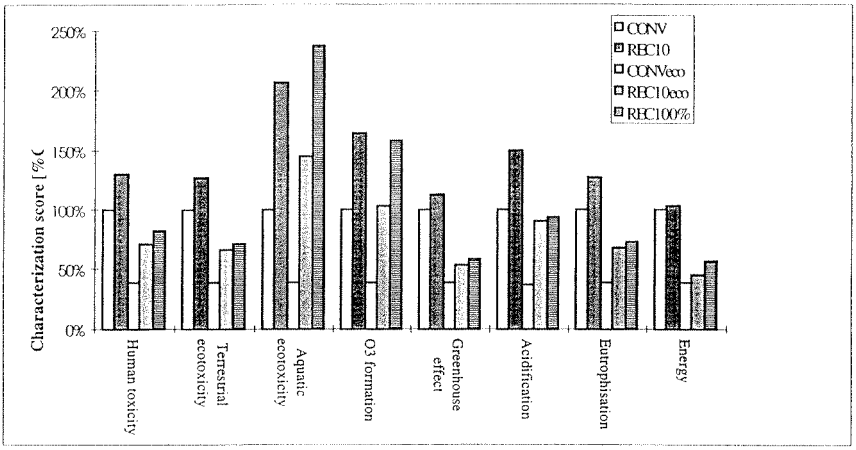

Figure 6.3 Characterization scores with the CST95 method [Jolliet and Crettaz, 1997], without considering the transfer of pollutants contained in flushing water.

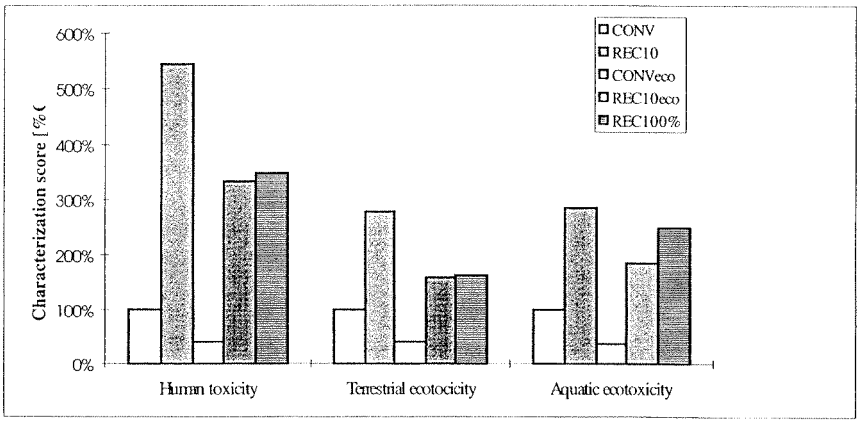

Figure 6.4 Characterization scores with the CST95 method [Jolliet and Crettaz, 1997], when only the transfer of pollutants contained in flushing water is considered.

b) Substances contributing to human toxicity

Figure 6.5 compares the scenarios CONV and REC10, without considering the transfer of pollutants contained in flushing water. Among the 40 substances affecting human health, lead, nickel, mercury and cadmium released into air have the highest impact. Their effect does not occur after inhalation, but after deposition on agricultural soils and transfer into food products. On the contrary, deposition on surface water is without significant effect.

Direct releases of chromium and arsenic into soil also play a significant role. These emissions are related to the inputs and it is unclear on what kind of soil they occur, since no indication has been found in [Frischknecht et al., 1996]. An agricultural soil has been chosen in order to estimate their maximal impact.

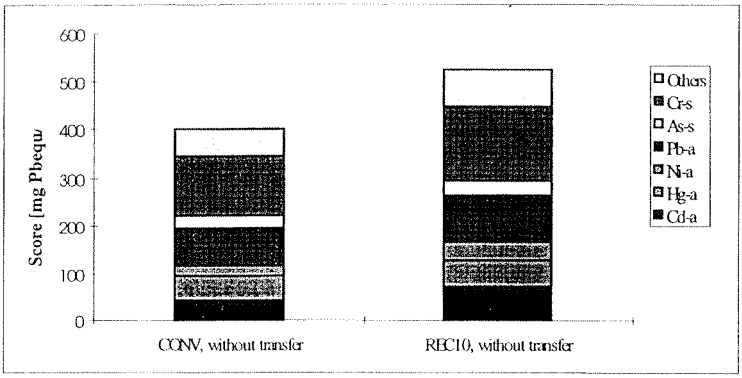

Figure 6.5 Characterization for human toxicity with the CST95 method [Jolliet and Crettaz, 1997], without considering the transfer of pollutants contained in flushing water.
a: emission into air.
s: emission into agricultural soils.

Figure 6.6 considers the impact of pollutants contained in flushing water. It shows that the transfer at the wastewater treatment plant is responsible of the main burden on human health, whereas atmospheric deposition of metals plays only a secondary role. Lead, copper, cadmium and chromium have the highest contribution. The conventional scenario is by far more favorable than the recuperation scenario, since the contamination of rainwater in metals is higher than the one of drinking water.
We should mention that the average Swiss disposal of sludge (49% agriculture, 32% incineration and 19% landfill) has been chosen in the calculations. The effect on humans would be lower if a 100% incineration scenario was selected. Chemical fertilizers or manure would then be required instead of sludges.

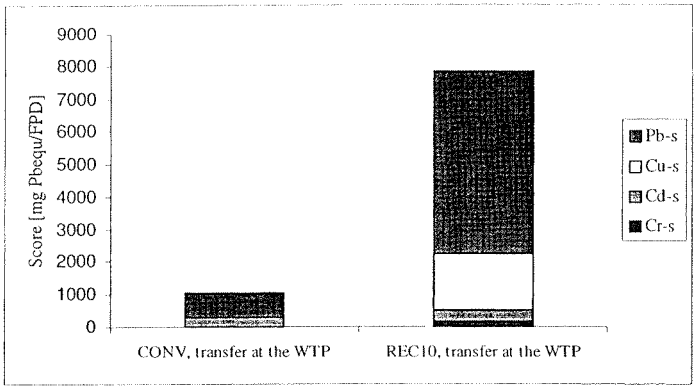

Figure 6.6 Characterization for human toxicity with the CST95 method [Jolliet and Crettaz, 1997], when only the transfer of pollutants contained in flushing water is considered.

c) Contribution of the different elements of the production chain

The different contributions to the energy requirement have been presented in table 6.3. Elements having the highest contribution on human health for the wastewater treatment and the sanitary installations are the same as those having the highest energy contributions. The treatment plant, the treatment products and the reservoir have the highest contribution on human health for the drinking water supply (see table 6.5).

Process	Elements	unit	Contribution kgPb/unit	%
Drinking water supply & treatment	Energy for the water treatment plant	m^3	1.1E-04	12%
	Energy for the water supply	m^3	9.6E-05	10%
	Products (O_3, activated carbon)	m^3	1.1E-04	12%
	Water treatment plant (steel, concrete)	m^3	4.1E-04	43%
	Reservoir (concrete, steel)	m^3	1.5E-04	16%
	Pumping station (steel)	m^3	6.4E-05	7%
	Total		9.4E-04	100%
Wastewater treatment	Sewers (steel, concrete)	m^3	1.7E-03	52%
	Infrastructure (steel, concrete)	m^3	1.6E-03	47%
	Operating energy	m^3	4.6E-05	1%
	Total		3.3E-03	100%
Sanitary installations	Polyester	pers-day	6.7E-05	46%
	Steel	pers-day	3.2E-05	22%
	Cast iron	pers-day	2.4E-05	17%
	Others	pers-day	2.2E-05	15%
	Total	pers-day	1.5E-04	100%

Table 6.5 Contribution to human toxicity of the elements involved in the water supply, wastewater treatment and sanitary installations.

6.4.2 Results with CML96

Characterization scores according to the CML96 methodology of Guinée et al. [1996] are presented in figure 6.7, without considering pollutants contained in flushing water. The scenario CONVeco is the most favorable for all impact classes, confirming results found with the CST95 approach. Eutrophisation scores are lower with CST95, since this approach considers the regional sensibility to nutrients by excluding N emissions. The order of magnitude is the same for the toxicity classes with both methods. Characterization scores for acidification, global warming and ozone formation are not represented in figure 6.7, since CML96 and CST95 apply the same characterization coefficients for these classes.

The impact of pollutants contained in flushing water has also been calculated. It is not significant and does not change the results presented in figure 6.7, since the CML96 method attributes higher characterization factor to atmospheric emissions of metals than to metals released into soil.

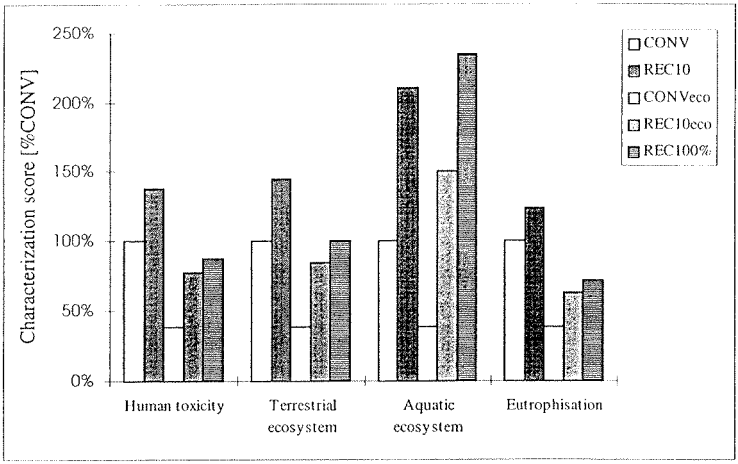

Figure 6.7 Characterization scores with the CML96 method Guinée et al. [1996], without considering pollutants contained in flushing water.

6.4.3 Results with the Human Damage Factors

a) Substances contributing to human toxicity

Figure 6.8 compares the scenarios CONV and REC10, after application of the human damage factors developed in chapter 5 of this dissertation. The transfer of pollutants contained in the flushing water is not considered. The damage on humans is higher by a factor 1.4 for the scenario REC10. While a similar conclusion is obtained with CST95 (see figure 6.5), substances having the highest impact on humans are different. CST95 identifies metals released into air as major contributors (see section 6.4.1.b)), whereas NOx, SO_2 and fine particles are responsible of more than 99% of the total damage when using the damage factors (see figure 6.8).

The contribution of metals is 10^2 to 10^5 times lower than the contribution of SO_2, NO_x and fine particles, as indicated in table 6.6. Metals therefore play an insignificant role compared to NO_x, SO_2 and fine particles, mainly because these criteria air pollutants have much higher releases and their damage factors are close or not very lower than those of metals. Due to the uncertainty of the human damage factors, the robustness of the conclusions should be discussed. The comparison of the two studied scenarios is robust, since the recuperation scenario is characterized by higher emissions for all substances.

Reasons for the different contribution after the application of CST95 and the damage factors can be given. The exposure efficiency of metals released into agricultural soils is overestimated in the CST95 method, since their leaching is not accounted for. On the contrary, the exposure efficiency of atmospheric pollutants is underestimated, since it is

based on the global concentration defined in section 4.2.2. Furthermore, epidemiological data provided by Hofstetter [1998] are incorporated in the damage factors, instead of acceptable daily intakes; this increases the effect factor of NO_X, SO_2 and fine particles in comparison to metals.

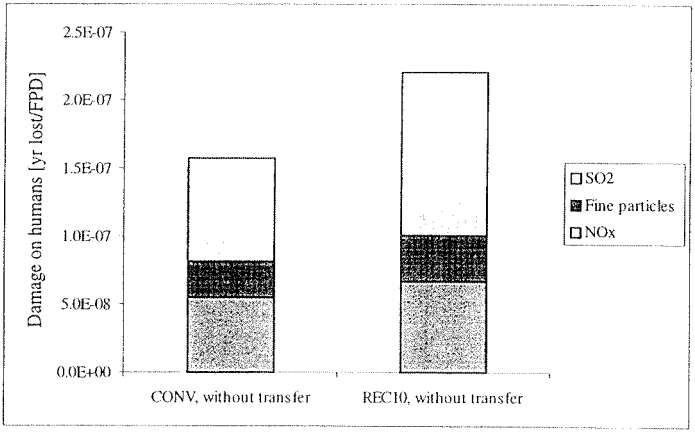

Figure 6.8 Contribution of the toxic releases to human toxicity, after application of the human damage factors developed in chapter 5.
The transfer of polluants contained in flushing water is not considered.

	CONV, without transfer Damage on humans [yr lost / FPD]	REC10, without transfer Damage on humans [yr lost / FPD]
Air		
Cd	2.9E-12	4.5E-12
CO	3.3E-11	4.9E-11
Cr	5.2E-12	6.5E-12
NO_x	5.4E-08	6.6E-08
Fine particles	2.7E-08	3.5E-08
Pb	7.0E-10	8.5E-10
SO_2	7.6E-08	1.2E-07
Agricultural soil		
As	1.8E-11	2.3E-11
Cd	1.4E-13	1.7E-12
Cr	1.8E-13	2.2E-13
Pb	8.6E-11	1.1E-10

Table 6.6 Contribution of the toxic releases to human toxicity, after application of the human damage factors developed in chapter 5.
The transfer of pollutants contained in flushing water is not considered.

Figure 6.9 presents the same comparison, when the impact of pollutants contained in flushing water is considered in addition to the other releases. While lead, copper, cadmium and chromium released into soil have the highest contribution according to the CST95 method (see figure 6.6), lead released into an agricultural soil is the only metal that plays a role when applying the damage factors. It contributes to about 4% of the total score for the scenario CONV and to 15% for the scenario REC10. It is the high noncarcinogenic effect factor of lead, based on a low No Observable Adverse Effect Level, which explains that lead emerges from the analysis. As already emphasized, no consensus regarding a No Observable Adverse Effect Level for lead exists in the literature (see section 3.6.7) and its transfer coefficient from agricultural soil into food products (see section 4.4.4) must be validated before drawing final conclusions. Therefore, only the potential damage of lead is estimated here.

Due to the uncertainty of the damage factor, in particular for lead, the robustness of the conclusion needs to be discussed. Again, results of the comparison of the conventional and recuperation scenarios are robust, since the recuperation scenario is characterized by higher emissions for all substances. If the soil-to-food transfer coefficient calculated by Jolliet and Crettaz [1998] had been used for the evaluation of the damage factor, then a coefficient higher by a factor 40 had been found. Lead would then have had the highest impact on humans. This indicates that an interval of confidence of the damage factor would help to discuss the results. As an indication, Hofstetter [1998] calculated the lower and upper values of the 95% confidence interval for a parameter similar than the damage factor. He obtained a range of 10^2 to 10^3 between the lowest and the highest estimate for SO_2, NO_X, CO and particles. This range should be compared in further studies with the 95% confidence interval for metals, in particular for lead.

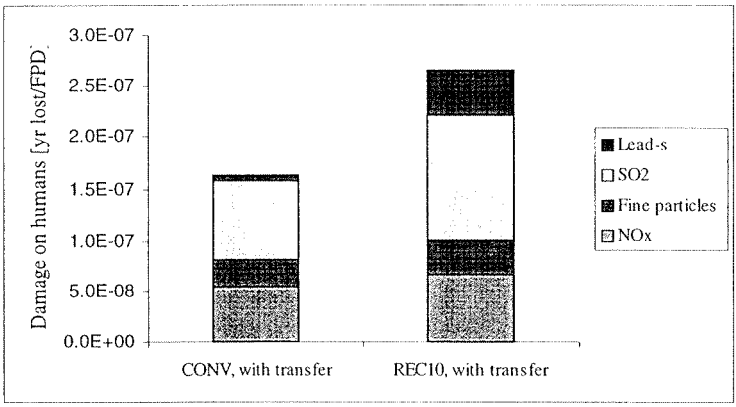

Figure 6.9 Contribution of the toxic releases to human toxicity, after application of the human damage factors developed in chapter 5.
The impact of pollutants contained in flushing water is considered in addition to the other releases.
s: emission into agricultural soils.

b) Comparison of the scenarios

The damage on human health for the five scenarios are compared in figure 6.10, after application of the human damage factors and without considering the impact of pollutants contained in the flushing water. The score of the scenario CONV is fixed at 100%, since it is the reference scenario. Damages for the scenario REC10 are higher than those of the scenario CONV and economic toilets are clearly advantageous, in a similar proportion as when the CST95 method is applied. The conventional scenarios are even more favorable if the impact of pollutants contained in flushing water is included.

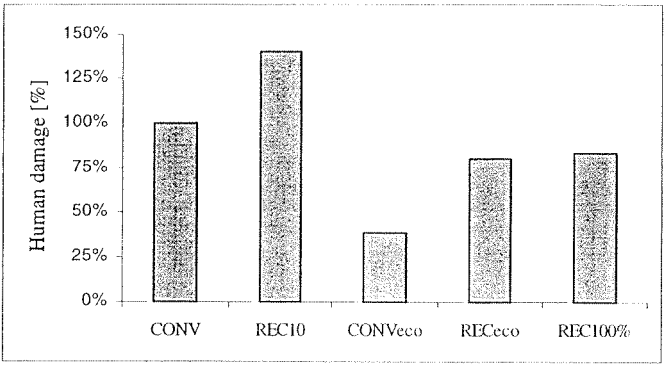

Figure 6.10 Damages on human health, after application of the human damage factors developed in chapter 5.
The transfer of pollutants contained in flushing water is not considered.

6.5 INTERPRETATION AND SENSITIVITY ANALYSES

The inventory and the LCIA have been presented for the five main scenarios. We carry out in this section some sensitivity analyses to find out how changes in key parameters influence the results. Only economic toilets are investigated here, since we have shown that they are clearly favorable.

Figure 6.11 indicates that the scenario REC10eco remains energetically unfavorable when an extreme drinking water treatment is selected. Its energy requirement is similar to the one of the scenario CONVeco if an European electricity supply is selected instead of a Swiss production. The scenario REC10eco becomes advantageous only if the energy required for the water supply is extreme (1.5 [kWh/m^3] according to Pelli et al. [1996]). A threshold value of 0.8 [kWh/m^3] for a complex drinking water treatment and of 1.3 [kWh/m^3] for a simple treatment is deduced. Above these thresholds, the scenario REC10eco has a lower energy requirement, but still remains unfavorable for the other impact classes.
The reference value used in this chapter for the energy requirement of the pump (0.09 [kWh/m^3]) is based on a total pressure of 1.5 bar. This pressure is adapted for toilet flushing. However, it is not appropriate for other uses such as to water the garden using sprinklers. If a pressure of 4 bar is required for sprinklers, a high energy requirement (1 [kWh/m^3]) is required for the pumping [Orlando and Cuanillon, 1997]. This utilization of rainwater is to be avoided, since it induces an increase in the energy consumption of about 30% for the scenario REC10eco (see figure 6.11).

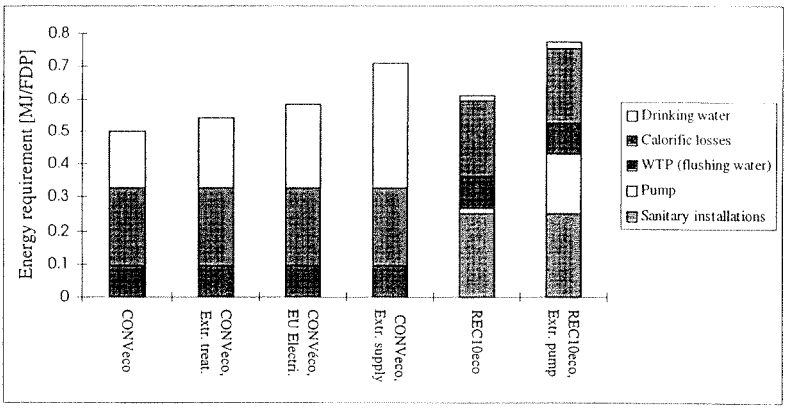

Figure 6.11 Energy requirement for variants of the scenarios CONVeco and REC10eco.
CONVeco, Extr.treat: 0.1 [kWh/m^3] for ozone and 25 [mg/m^3] for AC.
CONVeco, EU Electri.: European electricity is provided.
CONVeco, Extr.supply: 1.5 [kWh/m^3] for the water supply.
REC10eco, Extr.pump: 1 [kWh/m^3] for pumping the water from the tank.

Other sensitivity analyses than those presented in figure 6.11 have been performed. They indicate that a storage tank in concrete penalize the recuperation. Furthermore, it has been assumed in section 6.4.1 that rainwater infiltration has no effect on humans and on the aquatic ecosystem. A sensitivity analysis assuming that pollutants contained in infiltration water reach the ground water has been carried out, using the CST95 method.
The effect of infiltration is then significant on the aquatic ecosystem, which characterization score becomes similar for the scenarios CONVeco and REC10eco [Crettaz et al., 1999]. On the contrary, infiltration has not a significant effect on humans in comparison with the transfer into food products. It must be stressed that this conclusion has been reached by using the CST95 method, which only provides a screening evaluation of the fate and exposure after infiltration. This method takes into account that only a small fraction of the infiltrated water is reaching humans; however, in specific cases, the infiltration could play a significant role. A validation of the impact on humans after infiltration of rainwater is therefore required before drawing final conclusions.

6.6 CONCLUSIONS

A Life Cycle Assessment has been carried out in this chapter to compare systems using rainwater or reducing drinking water consumption with a conventional toilet flushing. A quantitative database for decision making concerning domestic use of rainwater and reduction of water consumption has been provided. Results have indicated that economic toilets are favorable for all impact classes, in comparison to conventional toilets. They are also economically attractive (see appendix 6.6). Rainwater recuperation appears unfavorable from an environmental point of view, when an average energy requirement for the water supply and a complex drinking water treatment are selected. It becomes energetically advantageous only when the energy required for the water distribution is extremely high. The Cyclaupe II project [Bronchi et al., 1999] indicated that the use of rainwater to wash clothes permits to reduce the quantity of applied powder in regions where water is hard. Thus, rainwater recuperation can be economically viable and environmentally interesting in these hard water areas.

The impact assessment step has illustrated that substances contributing to human health can significantly change depending on the selected LCIA methodology. Applying the human damage factors developed in this thesis, we found that the substances inducing the major hazard on humans are NO_X, SO_2, fine particles, as well as lead released on agricultural soils when the impact of metals contained in the flushing water is considered. These contributions significantly differ from those obtained when applying the CST95 method of Jolliet and Crettaz [1997]; reasons for that change have been discussed.

Different recommendations can finally be deduced from this study:
- A reduction of the water consumption for toilet flushing has to be promoted. This is a clear priority.
- An insulation of the flushing tank could significantly diminish the calorific losses occurring within the house.
- If rainwater recuperation is undertaken, a pump adapted to the use is required. For toilet flushing, a pressure of 1.5 bar is sufficient and a pump characterized by a high energy consumption should be avoided. Rainwater recuperation for garden watering under pressure has to be avoided.

7. CONCLUSIONS

A procedure for Life Cycle Impact Assessment (LCIA) has been developed in this thesis. Human damage factors, which combine the effect factor and the exposure efficiency of a toxic release, have been calculated for a set of selected metals and criteria air pollutants. The damages induced by these toxic releases have been quantified in years of life lost per emitted mass and compared. The quantification of the damage linked to noncarcinogenic effects is a new input for LCIA, since noncarcinogenic effects are often not quantified in LCIA or only for a limited number of substances like in the Eco-indicator 99 method of Goedkoop and Spriensma [1999]. In the long term, years of life lost due to chemicals' exposure could be compared with the years of life lost due to other causes, for instance due to road or work accidents.

Concerning the effect assessment, the ED_{10}-procedure has been explored for the first time in LCIA and applied to more than 900 chemicals. A factor larger than 100 million-folds has been found between the lowest and the highest effect factor for both carcinogenic and noncarcinogenic endpoints; it reflects that the adverse effects can widely vary between toxic releases. Most of the variation of the effect factor among chemicals is due to differences in the slope factor. It has been shown how concepts developed in Risk Assessment can be adapted to the specific requirements of LCIA. For instance, the maximum likelihood estimate ED_{10h} has been used as a point of departure instead of the lower confidence limit BMD_{10h}; conservative uncertainty factors incorporated in the Reference Dose have been replaced in the ED_{10}-approach by non-conservative values, and the human-to-human uncertainty factor has not been applied. The ED_{10}-approach is therefore, as far as possible, a "best estimates" approach. We have used the ED_{10}-approach for both carcinogenic and noncarinogenic health outcomes; the benefit is to be able to compare these effects on a common framework, to take into account their different severity and eventually to aggregate these effects into a single score for human health. It has also been found that the lethal dose LD_{50a} can not be used to extrapolate in a reliable way the effect factor for data-poor substances.

Concerning the fate and exposure assessment, the concept of exposure efficiency has been made operational in LCIA. It has been applied to the atmospheric releases of the selected metals, CO, NO_x, SO_2 and fine particles. The exposure efficiency provides a powerful parameter to estimate the fraction of a release which is absorbed by humans. We have illustrated how the developed approach can be used for well-known substances to validate multimedia models. The comparison of specific and continental exposure efficiencies has demonstrated that the consideration of a uniform continental concentration underestimates the exposure efficiency that can actually be expected by a factor close to 3. The comparison of indoor versus outdoor releases indicated that indoor emissions should not be approximated by outdoor releases in LCIA, since they are characterized by exposure efficiencies higher by a factor 10^2 to 10^3.

The application to the Cycleaupe case study of the impact assessment methodology developed in this dissertation has revealed that the impacts of metals was overestimated in the CST95 method of Jolliet and Crettaz [1997]. Concerning the specific goals of the Cycleaupe study, it has been found that a reduction of the water consumption for toilet flushing has to be promoted and that rainwater recuperation for toilet flushing becomes energetically favorable only in extreme situations. An insulation of the flushing tank may also be recommended to diminish the calorific losses occurring within the house.

After this overview of the main conclusions of this research, **limitations** of the LCIA procedure developed in this thesis have to be discussed. Effect factors are characterized by different uncertainty sources that have been reviewed. In the ED_{10}-approach, the same linear and non-threshold mechanism of action has been assumed for all chemicals. This is a simplified representation of the mechanism of action. It is likely to overestimate the risk in case of a nonlinear dose-response and does not enable taking into account that two compounds having the same ED_{10h} can have different slopes at low exposure levels. In addition, the extrapolation of the ED_{10h} from the No Observable Adverse Effect Level should only be used to get a first order of magnitude of the slope factor, due to the limitations of the $NOAEL_a$. This extrapolation is less reliable than the extrapolation of the slope factor from the tumor dose TD_{50a}, since the TD_{50a} is associated with a fixed response level while the response at the $NOAEL_a$ can vary among chemicals. Furthermore, the severity of the critical endpoint associated with noncarcinogenic effects has been subjectively evaluated and the effect factor does not take into account that endpoints other than the critical one may occur at low human exposure range.

Concerning the semi-empirical procedure proposed for the fate and exposure assessment, it is applicable only to well-known substances for which concentrations and emissions are available. It must therefore be considered as an interesting possibility to test the fate modeling approaches which will be applied for other pollutants. In addition, the specific exposure efficiency does not take into account the local variation in actual exposure efficiency which can vary from one emission site to another, due to specific population densities and concentrations around the site of release.

Due to these limitations, the human damage factors and the effect factors summarized in appendix 1 should be used with caution. Damage factors should only be used in LCIA for assessing the relative damage of toxic releases on human health. Their application beyond the intended scope of LCIA, for instance for evaluating the absolute damage induced by toxic releases, should presently be avoided. While some practitioners are advocating to abandon the LCIA because of its uncertainties and because it is not achievable in its most sophisticated form, we rather support that LCIA is bringing useful information if we make transparent the limitations and uncertainties. A transparent impact assessment, regularly updated to the newest available state of the art, is required for a sound decision-making process.

Finally, **proposals and recommendations** for future research can be presented:

- The ED_{10}-approach has been used in this research as a default screening procedure. Departure from this procedure could be made if new information improves the understanding of the mechanisms of action to the point that the low dose-response curve can be assessed from this understanding. For instance, the development of biologically based dose-response models could help in the future to reflect the biological characteristics of carcinogenesis as accurately as possible. Critical events along the causal pathway between exposure and effect could be described for well-known chemicals, by including information on pharmacokinetic and pharmacodynamic. The identification of changes in the kinetics over a dose range, over different routes of exposure and over species could be used for a more reliable projection of risk beyond the range of possible observations in terms of dose, route of exposure and species.

- Instead of deriving the ED_{10h} from the $NOAEL_a$, its evaluation by plotting the dose-response curve at the level of the data observed in a bioassay should be encouraged. The application of this ED_{10h} instead of acceptable levels like the reference dose would permit to reduce the bias in the comparison of chemicals.

- A first screening for integrating the severity of noncarcinogenic endpoints has been proposed. A closer examination of the critical endpoint for a compound, and its classification into another category than the default one, could be undertaken if that chemical plays an important role in a LCA case study. For this examination, a close collaboration with toxicologists has to be continued.

- The incorporation of all the relevant health outcomes associated with a compound would enhance the damage evaluation. It could be tested on some releases of particular importance.

- The soil to food transfer coefficient for heavy metals, derived from the Uniform System for the Evaluation of Substances (USES 2.0 model), should be validated before drawing final conclusions about their fate in agricultural soils. The dependency of the adsorption coefficient Kd to soil characteristics, particularly to the soil pH, should be accounted for.

- A quantitative uncertainty analysis would increase the confidence in the human damage factors. The dominant sources of uncertainty and their order of magnitude could be identified and compared to those encountered in the Life Cycle Inventory.

- Based on the framework developed in this thesis and the effect factors summarized in appendix 1.1, a large set of damage factors could be derived in the near future by combining them with new fate and exposure factors. This would enhance the pertinence and applicability of the procedure developed in this thesis, and would permit to extend the comparison of damage factors to other substances than the metals and air pollutants studied in this thesis.

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Visiting fellow at the Harvard School of Public Health (March to July 1998)

Swiss Federal Institute of Technology, Lausanne, Switzerland
Master in Rural and Surveying Engineering, Environmental Specialization (1990-1995)

McGill University, Montreal, Canada
Exchange student in Civil Engineering (1992-93)

Employment:

Swiss Federal Office of Public Health, Department of Chemical Products, Bern, Switzerland; May 2000 up to now.
Responsible for the classification of pesticides into one of the five classes of toxicants reported in the Swiss Ordinance for Toxic Substances. Participation to the elaboration of ordinances for the new Regulation on Chemicals. Research on Risk Assessment of pesticides.

Laboratory of Ecosystem Management, Swiss Federal Institute of Technology, Lausanne, Switzerland; August 1998 – August 2000.
Conception of a procedure for quantifying the potential carcinogenic and noncarinogenic effects of more than 900 chemicals.
Contribution to the SETAC international working group on "Human Toxicity". Collaboration with the Harvard School of Public Health.

Department of Environmental Health, Harvard School of Public Health, Harvard University, Boston, USA; March 1998 - July 1998
Quantification of the risk induced by toxic releases on human health.
Creation of a professional connections network with specialists of Risk Assessment. Adaptation to the American way of life and work.

Land and Water Management Institute, Swiss Federal Institute of Technology, Lausanne, Switzerland; November 1996 - February 1998
In charge of the realization of the project CYCLAUPE "Case study on drinking water management and domestic use of rainwater", in collaboration with the consulting office RWB SA (sponsored by the Swiss EPA). Budget: frs. 100'000.
Organization of meetings with different specialists of water management.

Swiss Federal Research Station for Agricultural Economics and Engineering (FAT), Tänikon; August - October 1996.
Research program aiming to quantify the toxic releases associated with energy agents as well as the emissions of agricultural inputs.

Land and Water Management Institute, Swiss Federal Institute of Technology, Lausanne, Switzerland; June 1995 - July 1996.
Evaluation of the environmental impact of agricultural systems, within the framework of a European project (Swiss budget: frs. 60'000).
Collaboration within a team of 10 European scientists.
Co-organization of a working meeting. Evaluation of the exposure efficiency for some main atmospheric pollutants. Comparison of the impact for indoor and outdoor air pollution.

Catholic mission, Pointe-Noire, Congo; April - May 1995
Humanitarian aid (teaching, construction).

Chemical laboratory of the Tunis University, Tunisia; October 1994-February 1995.
Study of Tunisian harbors contamination in organotin compounds, sponsored by the association "Ingénieurs du Monde".
Collection of water samples, contacts and negotiations with local authorities. Laboratory analyses using gas chromatography.

Teaching

In charge of the following lectures:
"Life Cycle Assessment as a support tool for the ISO 14001 standard", IFCAM, Lausanne , October 1999.
"Perspective en écobilan", Institut National d'Agriculture, Tunis, 1999.
"Environmental Life Cycle Assessment: methodology and challenges", Harvard School of Public Health, Boston, USA, 1998.
"Pollution Prevention", Harvard University, Boston, USA, 1998.
"Architecture et développement durable", master at the EPFL, 1996-98.
"Life Cycle Assessment and ISO 14000 standards: perspectives", master at the EPFL, 1997.
Know how gained from teaching: capacity to structure and present a thematic in public, to supervise students' works and to keep the attention of an audience.

Computer skills :

Use of PC/Macintosh, of standard softwares (PowerPoint, Excel, ...) and of specific softwares: SimaPro (environmental impact of products), MSTAGE

and BMDS (toxicity evaluation), JMP (statistic analysis), etc.
Development of a web site.

Languages : French: mother tongue.
English: fluent (one year at McGill University and 5 months at Harvard University; articles, dissertation and conferences in English).
German: good scientific knowledge (4 months training at the Forchungsanstal Tänikon, German articles/conferences)

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APPENDICES

APPENDICES 1. SUMMARY OF THE RESULTS

Appendix 1.1 Effect factors

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
1	A-alpha-C	26148-68-5	eat	5.0E-02	1.1E+01	3.1E-07				
2	Acenaphthene	83-32-9					oral	1.5E-02	1.1E+00	9.4E-09
3	**Acephate**	**30560-19-1**	**oral**	**1.0E-02**	**1.1E+01**	**6.2E-08**				
4	Acetaldehyde s	75-07-0	inh	1.6E-02	1.1E+01	1.0E-07	inh	3.8E-02	1.1E+00	2.3E-08
5	Acetaldehyde methylformylhydrazone	16568-02-8	gav	1.0E+00	1.1E+01	6.2E-06				
6	Acetamide	60-35-5	eat	1.4E-02	1.1E+01	8.6E-08				
7	Acetaminophen	103-90-2	eat	5.1E-03	1.1E+01	3.1E-08				
8	Acetochlor	34256-82-1					oral	5.0E-02	1.1E+00	3.1E-08
9	Acetone	67-64-1					oral	1.2E-02	1.1E+00	7.6E-09
10	Acetone[4-(5-nitro-2-furyl)-2-thiazolyl]	18523-69-8	eat	4.1E-01	1.1E+01	2.6E-06				
11	Acetonitrile	75-05-8					oral	4.2E-02	1.1E+00	2.6E-08
12	Acetophenone	98-86-2					oral	2.9E-03	1.1E+00	1.8E-09
13	Acetoxime	127-06-0	wat	2.1E-01	1.1E+01	1.3E-06				
14	1'-Acetoxysafrole	34627-78-6	eat	1.0E-01	1.1E+01	6.2E-07				
15	4-Acetylaminobiphenyl	4075-79-0	eat	2.1E+00	1.1E+01	1.3E-05				
16	2-Acetylaminofluorene s	53-96-3	eat	2.0E+00	1.1E+01	1.3E-05				
17	N'-Acetyl-4-(hydroxymethyl)	65734-38-5	wat	1.0E-02	1.1E+01	6.4E-08				
18	1-Acetyl-2-isonicotinoylhydrazine	1078-38-2	wat	7.6E-03	1.1E+01	4.7E-08				
19	1-Acetyl-2-phenylhydrazine	114-83-0	wat	4.9E-02	1.1E+01	3.0E-07				
20	Acifluorfen	50594-66-6	eat	1.8E-02	1.1E+01	1.1E-07				
21	Acifluorfen sodium	62476-59-9					oral	3.0E-01	1.1E+00	1.8E-07
22	Acronycine	7008-42-6	ipj	5.0E+00	1.1E+01	3.1E-05				
23	**Acrylamide**	**79-06-1**	**oral + inh.**	**1.3E+00**	**1.1E+01**	**7.8E-06**	**oral**	**6.2E+00**	**1.1E+00**	**3.8E-06**
24	Acrylic acid	79-10-7					oral	7.1E-03	1.1E+00	4.4E-09
25	Acrylonitrile	107-13-1	inh	1.5E-01	1.1E+01	9.2E-07				
	Acrylonitrile	**107-13-1**	**oral**	**3.2E-01**	**1.1E+01**	**2.0E-06**				
26	Actinomycin D	50-76-0	ipj	2.3E+03	1.1E+01	1.4E-02				
27	Aflatoxicol	29611-03-8	eat	1.0E+03	1.1E+01	6.3E-03				
28	Aflatoxin B1 s	1162-65-8	eat	7.8E+02	1.1E+01	4.8E-03				
29	Aflatoxin, crude	---	eat	8.4E+02	1.1E+01	5.2E-03				
30	AF-2 s	3688-53-7	eat	8.5E-02	1.1E+01	5.3E-07				
31	Alachlor	15972-60-8					oral	1.0E-01	1.1E+00	6.2E-08
32	Alar	1596-84-5					oral	2.5E-02	1.1E+00	1.5E-08
33	Aldicarb	116-06-3					oral	6.3E+00	1.1E+00	3.8E-06
34	Aldicarb sulfone	1646-88-4					oral	9.1E-01	1.1E+00	5.6E-07
35	**Aldrin**	**309-00-2**	**oral + inh.**	**8.5E+00**	**1.1E+01**	**5.3E-05**				
36	Ally	74223-64-6					oral	1.5E-02	1.1E+00	9.2E-09
37	Ally alcohol	107-18-6					oral	2.6E-01	1.1E+00	1.6E-07

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
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38	Allyl chloride	107-05-1					inh.	9.1E-02	1.1E+00	5.6E-08
39	Allyl glycidyl ether	106-92-3	inh	1.4E-02	1.1E+01	8.5E-08				
40	Allyl isothiocyanate	57-06-7	gav	2.6E-02	1.1E+01	1.6E-07				
41	Allyl isovalerate	2835-39-4	gav	2.0E-02	1.1E+01	1.3E-07				
42	Allylhydrazine.HCl	52207-83-7	wat	7.3E-02	1.1E+01	4.5E-07				
43	1-Allyl-1-nitrosourea	760-56-5	gav	7.3E+00	1.1E+01	4.6E-05				
44	Aluminium phosphide	20859-73-8					oral	8.7E+00	1.1E+00	5.4E-06
45	Amdro	67485-29-4					oral	1.0E+00	1.1E+00	6.2E-07
46	Ametryn	834-12-8					oral	1.4E-01	1.1E+00	8.9E-08
47	2-Aminoanthraquinone	117-79-3	eat	2.5E-02	1.1E+01	1.5E-07				
48	o-Aminoazotoluene	97-56-3	eat	6.2E-01	1.1E+01	3.8E-06				
49	4-Aminodiphenyl	92-67-1	gav	1.2E+00	1.1E+01	7.4E-06				
50	4-Aminodiphenyl.HCl	2113-61-3	gav	2.6E+00	1.1E+01	1.6E-05				
51	2-Aminodiphenylene oxide	3693-22-9	eat	5.9E-01	1.1E+01	3.7E-06				
52	3-Amino-4-ethoxyacetanilide	17026-81-2	eat	1.2E-03	1.1E+01	7.5E-09				
53	3-Amino-9-ethylcarbazole mixture	mixture	eat	9.5E-02	1.1E+01	5.9E-07				
54	3-Amino-9-ethylcarbazole.HCl	6109-97-3	eat	4.4E-02	1.1E+01	2.7E-07				
55	1-Amino-2-methylanthraquinone	82-28-0	eat	4.2E-02	1.1E+01	2.6E-07				
56	2-Amino-5-(5-nitro-2-furyl)-1,3,4-oxadiazole	3775-55-1	eat	6.8E-01	1.1E+01	4.2E-06				
57	2-Amino-5-(5-nitro-2-furyl)-1,3,4- thiadiazole	712-68-5	eat	3.8E+00	1.1E+01	2.3E-05				
58	2-Amino-4-(5-nitro-2-furyl)thiazole	38514-71-5	eat	4.3E-01	1.1E+01	2.7E-06				
59	trans-5-Amino-3[2-(5-nitro-2-furyl)vinyl]-1.2,4-oxadiazole	28754-68-9	eat	2.2E-02	1.1E+01	1.4E-07				
60	2-Amino-4-nitrophenol	99-57-0	gav	3.0E-03	1.1E+01	1.8E-08				
61	2-Amino-5-nitrophenol	121-88-0	gav	2.3E-02	1.1E+01	1.4E-07				
62	4-Amino-2-nitrophenol	119-34-6	eat	8.1E-03	1.1E+01	5.0E-08				
63	2-Amino-4-(p-nitrophenyl)thiazole	08.09.04	eat	2.5E-01	1.1E+01	1.6E-06				
64	2-Amino-5-nitrothiazole	121-66-4	eat	5.6E-02	1.1E+01	3.5E-07				
65	3-Aminotriazole s	61-82-5	eat	2.5E-01	1.1E+01	1.6E-06				
66	11-Aminoundecanoic acid	2432-99-7	eat	2.3E-03	1.1E+01	1.4E-08				
67	Amitraz	33089-61-1					oral	4.0E-01	1.1E+00	2.5E-07
68	Ammonia	7664-41-7					inh.	9.5E-02	1.1E+00	5.8E-08
69	Ammonium sulfamate	7773-06-0					oral	5.8E-03	1.1E+00	3.6E-09
70	1-Amyl-1-nitrosourea	10589-74-9	gav	4.5E+00	1.1E+01	2.8E-05				
71	Amylopectin sulfate	9047-13-6	eat	8.8E-03	1.1E+01	5.5E-08				
72	**Aniline**	**62-53-3**	**oral**	**1.3E-02**	**1.1E+01**	**8.0E-08**	**inh.**	**9.7E-02**	**1.1E+00**	**5.9E-08**
73	Aniline.HCl	142-04-1	eat	9.3E-03	1.1E+01	5.8E-08				
74	o-Anisidine.HCl	134-29-2	eat	8.4E-02	1.1E+01	5.2E-07				
75	Anthracene	120-12-7					oral	2.7E-03	1.1E+00	1.6E-09
76	*Antimony trioxide*	*1309-64-4*					*inh.*	*5.3E+00*	*1.1E+00*	*3.2E-06*
77	Apollo	74115-24-5					oral	8.0E-02	1.1E+00	4.9E-08
78	**Aramite**	**140-57-8**	**oral + inh.**	**4.2E-02**	**1.1E+01**	**2.6E-07**				
79	Arecoline.HCl	61-94-9	gav	6.3E-02	1.1E+01	3.9E-07				
80	Aroclor 1016	12674-11-2					oral	5.3E+01	1.1E+00	3.3E-05
81	Aroclor 1254	27323-18-8	eat	2.6E-01	1.1E+01	1.6E-06				
82	Aroclor 1260	11096-82-5	eat	1.4E+00	1.1E+01	8.9E-06				
83	*Arsenic inorganic*	7440-38-2	oral	7.5E-01	1.1E+01	4.7E-06	oral	7.8E+01	1.1E+00	4.8E-05
	Arsenic inorganic	7440-38-2	inh	7.5E+00	9.0E+00	3.8E-05				
84	Arsine	7784-42-1					inh.	7.1E+00	1.1E+00	4.4E-06
85	Asbestos	1332-21-4	inh	1.3E+01	1.1E+01	8.3E-05				

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			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
86	Assure	76578-14-8					oral	3.4E-01	1.1E+00	2.1E-07
87	Atrazine	1912-24-9	eat	7.9E-02	1.1E+01	4.9E-07	oral	1.1E-01	1.1E+00	6.6E-08
88	Auramine-O	2465-27-2	eat	2.3E-01	1.1E+01	1.4E-06				
89	5-Azacytidine	320-67-2	ipj	1.5E+01	1.1E+01	9.1E-05				
90	Azaserine	115-02-6	ipj	3.2E+00	1.1E+01	2.0E-05				
91	Azathioprine	446-86-6	eat	2.8E-01	1.1E+01	1.7E-06				
92	**Azobenzene**	**103-33-3**	**oral + inh.**	**7.1E-02**	**1.1E+01**	**4.4E-07**				
93	Azoxymethane	25843-45-2	wat	5.4E+01	1.1E+01	3.3E-04				
94	1-Azoxypropane	---	gav	1.0E+04	1.1E+01	6.4E-02				
95	2-Azoxypropane	---	gav	9.3E+02	1.1E+01	5.8E-03				
96	Barbital, sodium	144-02-5	eat	2.4E-02	1.1E+01	1.5E-07				
97	Barium and compounds	7440-39-3					oral	3.0E-01	1.1E+00	1.8E-07
98	Bayleton	43121-43-3					oral	1.5E-01	1.1E+00	9.2E-08
99	Baythroid	68359-37-5					oral	1.5E-01	1.1E+00	9.2E-08
100	Bemitradine	88133-11-3	eat	4.6E-03	1.1E+01	2.8E-08				
101	Benefin	1861-40-1					oral	4.0E-03	1.1E+00	2.5E-09
102	Bentazon	25057-89-0					oral	3.1E-02	1.1E+00	1.9E-08
103	Benzaldehyde	100-52-7	gav	1.7E-03	1.1E+01	1.0E-08	oral	8.7E-03	1.1E+00	5.3E-09
104	Benzene	71-43-2	gav	1.5E-02	1.1E+01	9.2E-08				
105	Benzidine	92-87-5	inh	1.4E+00	1.1E+01	9.0E-06				
	Benzidine	92-87-5	oral	1.2E+02	1.1E+01	7.1E-04				
106	Benzidine.2HCl	531-85-1	wat	1.3E-01	1.1E+01	7.9E-07				
107	Benzo(a)pyrene	50-32-8	wat	2.6E+00	1.1E+01	1.6E-05				
108	Benzofuran	271-89-6	gav	5.9E-03	1.1E+01	3.7E-08				
109	Benzoic acid	65-85-0					oral	1.8E-03	1.1E-01	1.1E-10
110	1,4-Benzoquinone	106-51-4	gav	4.9E-01	1.1E+01	3.1E-06				
111	**Benzotrichloride**	**98-07-7**	**oral**	**8.3E+00**	**1.1E+01**	**5.2E-05**				
112	Benzoyl hydrazine	613-94-5	wat	2.6E-01	1.1E+01	1.6E-06				
113	Benzyl acetate	140-11-4	gav	1.7E-03	1.1E+01	1.1E-08				
114	**Benzyl chloride**	**100-44-7**	**oral**	**8.0E-02**	**1.1E+01**	**5.0E-07**				
115	o-Benzyl-p-chlorophenol	120-32-1	gav	1.9E-03	1.1E+01	1.1E-08				
116	Benzylhydrazine.2HCl	20570-96-1	wat	2.9E-02	1.1E+01	1.8E-07				
117	*Beryllium*	7440-41-7	inh.	4.2E+00	9.0E+00	2.1E-05	inh.	2.2E+03	1.1E+00	1.3E-03
	Beryllium	*7440-41-7*					*oral*	*1.2E-01*	*1.1E+00*	*7.2E-08*
118	Bidrin	141-66-2					oral	1.2E+01	1.1E+00	7.6E-06
119	Biphenthrin	82657-04-3					oral	6.7E-02	1.1E+00	4.1E-08
120	1,1-Biphenyl	92-52-4					oral	7.5E-03	1.1E+00	4.6E-09
121	2-Biphenylamine.HCl	2185-92-4	eat	2.2E-03	1.1E+01	1.4E-08				
122	Bis-2-chloroethylether	111-44-4	orl	2.1E-01	1.1E+01	1.3E-06				
	Bis-2-chloroethylether	111-44-4	inh	5.8E-01	1.1E+01	3.6E-06				
123	Bis(2-chloroisopropyl) ether	39638-32-9					oral	2.3E-02	1.1E+00	1.4E-08
124	Bis-1,4-(chloromethoxy)-p-xylene	56894-91-8	ipj	8.0E-01	1.1E+01	5.0E-06				
125	Bis-1,2-(chloromethoxy)ethane	13483-18-6	ipj	5.4E-01	1.1E+01	3.4E-06				
126	Bis-(chloromethyl)ether	542-88-1	ihn	7.0E+02	1.1E+01	4.3E-03				
	Bis-(chloromethyl)ether	542-88-1	oral	1.1E+02	1.1E+01	6.8E-04				
127	Bis(2-chloro-1-methylethyl)ether	108-60-1	gav	1.3E-02	1.1E+01	8.1E-08				
128	Bis(2,3-dibromopropyl)phosphate,	36711-31-6	eat	7.8E-02	1.1E+01	4.8E-07				
129	4-Bis(2-hydroxyethyl)amino-2-(5-nitro-2thienyl)quinazoline	33372-39-3	eat	8.0E-01	1.1E+01	4.9E-06				
130	Bis-2-hydroxyethyldithiocarbamic acid	23746-34-1	orl	6.6E-02	1.1E+01	4.1E-07				

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131	C.I. direct black 38	1937-37-7	eat	1.8E+00	1.1E+01	1.1E-05				
132	HC blue no. 1	2784-94-3	eat	3.6E-03	1.1E+01	2.2E-08				
133	HC blue no. 1 (purified)	2784-94-3	eat	3.2E-02	1.1E+01	2.0E-07				
134	C.I. direct blue 6	2602-46-2	eat	1.4E+00	1.1E+01	9.0E-06				
135	C.I. direct blue 15	2429-74-5	wat	9.1E-02	1.1E+01	5.6E-07				
136	C.I. direct blue 218	28407-37-6	eat	1.6E-03	1.1E+01	9.9E-09				
137	C.I. disperse blue 1	2475-45-8	eat	1.6E-02	1.1E+01	9.9E-08				
138	Boron (Boron and Borates only)	7440-42-8					oral	1.1E-02	1.1E+00	7.0E-09
139	Bromate, potassium	02.01.58	wat	2.5E-01	1.1E+01	1.6E-06				
140	**Bromodichloromethane**	**75-27-4**	**oral**	**4.2E-02**	**1.1E+01**	**2.6E-07**				
141	Bromoethane	74-96-4	inh	1.7E-02	1.1E+01	1.0E-07				
142	Bromoethanol	540-51-2	wat	3.3E-02	1.1E+01	2.0E-07				
143	**Bromoform**	**75-25-2**	**oral + inh.**	**5.8E-03**	**1.1E+01**	**3.6E-08**	**oral**	**6.9E-02**	**1.1E+00**	**4.3E-08**
144	Bromomethane	74-83-9					oral	8.8E-01	1.1E+00	5.4E-07
145	Bromoxynil	1689-84-5					oral	7.5E-02	1.1E+00	4.6E-08
146	Bromoxynil octanoate	1689-99-2					oral	5.1E-02	1.1E+00	3.2E-08
147	C.I. direct brown 95	16071-86-6	eat	1.2E+00	1.1E+01	7.5E-06				
148	Budesonide	51333-22-3	wat	8.6E+00	1.1E+01	5.3E-05				
149	1,3-Butadiene	106-99-0	inh	9.6E-03	1.1E+01	5.9E-08				
150	n-Butanol	71-36-3					oral	9.9E-03	1.1E+00	6.1E-09
151	Butyl benzyl phthalate	85-68-7					oral	7.8E-03	1.1E+00	4.8E-09
152	Butylate	2008-41-5					oral	2.0E-02	1.1E+00	1.2E-08
153	Butylated hydroxyanisole s	25013-16-5	eat	3.4E-03	1.1E+01	2.1E-08				
154	Butylated hydroxytoluene	128-37-0	eat	3.8E-03	1.1E+01	2.4E-08				
155	N-n-Butyl-N-formylhydrazine	16120-70-0	wat	1.3E-01	1.1E+01	8.0E-07				
156	1,1-di-n-Butylhydrazine	7422-80-2	wat	5.5E-02	1.1E+01	3.4E-07				
157	1,2-di-n-Butylhydrazine.2HCl	78776-28-0	wat	5.4E-02	1.1E+01	3.4E-07				
158	n-Butylhydrazine.HCl	56795-65-4	wat	2.1E-01	1.1E+01	1.3E-06				
159	N-Butyl-N-(4-hydroxybutyl)	06.11.17	wat	5.5E+00	1.1E+01	3.4E-05				
160	N-n-Butyl-N-nitrosourea	869-01-2	wat	4.8E+00	1.1E+01	3.0E-05				
161	Butylphthalyl butylglycolate	85-70-1					oral	3.8E-04	1.1E+00	2.3E-10
162	beta-Butyrolactone	3068-88-0	gav	1.8E-01	1.1E+01	1.1E-06				
163	*Cadmium*	7440-43-9	inh	6.1E+00	9.0E+00	3.1E-05	oral	4.1E+01	1.1E-01	2.5E-06
164	Cadmium chloride s	10108-64-2	inh	2.2E+02	1.1E+01	1.4E-03				
165	Cadmium sulphate (1:1) s	10124-36-4	inh	1.2E+02	1.1E+01	7.2E-04				
166	Caffeic acid	331-39-5	eat	8.4E-03	1.1E+01	5.2E-08				
167	Calciferol	50-14-6	eat	6.3E-02	1.1E+01	3.9E-07				
168	Calcium cyanide	592-01-8					oral	2.0E-02	1.1E+00	1.2E-08
169	Caprolactam	105-60-2					oral	7.5E-03	1.1E+00	4.6E-09
170	Capsaicin	404-86-4	eat	1.5E-02	1.1E+01	9.3E-08				
171	Captafol	01.06.25	eat	4.2E-02	1.1E+01	2.6E-07				
172	Captan	133-06-2					oral	3.0E-02	1.1E+00	1.8E-08
173	Carbamyl hydrazine.HCl	563-41-7	wat	1.1E-02	1.1E+01	7.0E-08				
174	1-Carbamyl-2-phenylhydrazine	103-03-7	wat	1.5E-02	1.1E+01	9.4E-08				
175	Carbaryl	63-25-2	gav	1.8E-01	1.1E+01	1.1E-06	oral	3.9E-02	1.1E+00	2.4E-08
176	Carbazole	86-74-8	eat	1.5E-02	1.1E+01	9.5E-08				
177	Carbofuran	1563-66-2					oral	2.0E-01	1.1E+00	1.2E-07
178	Carbon disulfide	75-15-0					oral	3.4E-02	1.1E+00	2.1E-08
	Carbon disulfide	*75-15-0*					*inh.*	*3.3E-02*	*1.1E+00*	*2.0E-08*

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
179	**Carbon tetrachloride**	**56-23-5**	**oral + inh.**	**8.4E-02**	**1.1E+01**	**5.2E-07**	**oral**	**1.8E+00**	**1.1E+00**	**1.1E-06**
180	Carbosulfan	55285-14-8					oral	3.8E-01	1.1E+00	2.3E-07
181	Carboxin	5234-68-4					oral	1.2E-01	1.1E+00	7.6E-08
182	Carboxymethylnitrosourea	60391-92-6	wat	5.8E-01	1.1E+01	3.6E-06				
183	Carrageenan, acid-degraded	---	eat	1.1E-03	1.1E+01	6.7E-09				
184	Catechol	120-80-9	eat	2.1E-02	1.1E+01	1.3E-07				
185	Chloral hydrate	302-17-0	wat	2.4E-02	1.1E+01	1.5E-07				
186	Chloramben	133-90-4	eat	4.8E-04	1.1E+01	3.0E-09				
187	Chlorambucil	305-03-3	ipj	2.8E+00	1.1E+01	1.7E-05				
188	Chlordane	12789-03-6	oral + inh.	1.8E-01	1.1E+01	1.1E-06	oral	5.4E+00	1.1E+00	3.3E-06
189	Chlordane, technical grade	57-74-9	eat	8.4E-01	1.1E+01	5.2E-06				
190	Chlorendic acid	115-28-6	eat	6.1E-02	1.1E+01	3.8E-07				
191	Chlorimuron-ethyl	90982-32-4					oral	1.6E-02	1.1E+00	9.8E-09
192	Chlorinated paraffins (C12, 60% chlorine)	63449-39-8	gav	1.1E-02	1.1E+01	7.0E-08				
193	Chlorine	7782-50-5					oral	2.6E-02	1.1E+00	1.6E-08
194	Chlorine cyanide	506-77-4					oral	1.5E-02	1.1E+00	9.1E-09
195	Chloroacetaldehyde	107-20-0	wat	6.9E-02	1.1E+01	4.3E-07				
196	4-Chloro-4'-aminodiphenylether	101-79-1	eat	6.6E-02	1.1E+01	4.1E-07				
197	p-Chloroaniline.HCl	20265-96-7	gav	3.3E-01	1.1E+01	2.0E-06				
198	Chlorobenzene	108-90-7	gav	1.0E-02	1.1E+01	6.3E-08	oral	1.7E-02	1.1E+00	1.1E-08
199	Chlorobenzilate	510-15-6	eat	2.7E-02	1.1E+01	1.7E-07	oral	7.5E-02	1.1E+00	4.6E-08
200	1-Chloro-1,1-difluoroethane	75-68-3					inh.	6.8E-06	1.1E+00	4.2E-12
201	Chlorodifluoromethane	75-45-6					inh.	6.2E-05	1.1E+00	3.8E-11
202	2-Chloro-5-(3,5-dimethylpiperidino-sulphonyl)benzoic acid	37087-94-8	eat	5.2E-01	1.1E+01	3.2E-06				
203	Chloroethane	75-00-3	inh	1.4E-03	1.1E+01	8.6E-09				
204	1-Chloroethylnitroso-3-(2-hydroxypropyl)	---	wat	2.0E+01	1.1E+01	1.3E-04				
205	Chlorofluoromethane	593-70-4	gav	9.1E-02	1.1E+01	5.6E-07				
206	**Chloroform**	**67-66-3**	**oral**	**4.2E-03**	**1.1E+01**	**2.6E-08**				
	Chloroform	67-66-3	inh	4.0E-02	1.1E+01	2.5E-07				
207	Chloromethyl methyl ether s	107-30-2	inh	4.5E-01	1.1E+01	2.8E-06				
208	3-Chloro-2-methylpropene	563-47-3	gav	2.2E-02	1.1E+01	1.4E-07				
209	3-(Chloromethyl)pyridine.HCl	6959-48-4	gav	5.8E-03	1.1E+01	3.6E-08				
210	beta-Chloronaphthalene	91-58-7					oral	1.1E-02	1.1E+00	6.6E-09
211	1-Chloro-2-nitrobenzene	88-73-3	eat	1.6E-02	1.1E+01	9.9E-08				
212	1-Chloro-4-nitrobenzene	100-00-5	eat	5.3E-03	1.1E+01	3.3E-08				
213	2-Chlorophenol	95-57-8					oral	2.5E-01	1.1E+00	1.5E-07
214	3-(p-Chlorophenyl)-1,1-dimethylurea	150-68-5	eat	1.9E-02	1.1E+01	1.2E-07				
215	4-Chloro-m-phenylenediamine	5131-60-2	eat	7.9E-03	1.1E+01	4.9E-08				
216	4-Chloro-o-phenylenediamine	95-83-0	eat	1.2E-02	1.1E+01	7.3E-08				
217	1-(4-Chlorophenyl)-1-phenyl-2-propynyl	10473-70-8	eat	2.8E-01	1.1E+01	1.8E-06				
218	2-Chloropropanal	683-50-1	gav	1.9E-01	1.1E+01	1.2E-06				
219	1-Chloropropene	590-21-6	gav	5.0E-01	1.1E+01	3.1E-06				
220	Chlorothalonil	1897-45-6	eat	1.1E-03	1.1E+01	6.8E-09	oral	6.7E-02	1.1E+00	4.1E-08
221	o-Chlorotoluene	95-49-8					oral	6.2E-02	1.1E+00	3.8E-08
222	5-Chloro-o-toluidine	95-79-4	eat	1.3E-02	1.1E+01	8.0E-08				
223	4-Chloro-o-toluidine.HCl	3165-93-3	eat	9.7E-02	1.1E+01	6.0E-07				
224	2-Chloro-1,1,1-trifluoroethane	75-88-7	gav	2.9E-02	1.1E+01	1.8E-07				
225	[4-Chloro-6-(2,3-xylidino)-2-pyrimidinylthio]acetic acid	50892-23-4	eat	2.6E-01	1.1E+01	1.6E-06				
226	4-Chloro-6-(2,3-xylidino)-2-pyrimidinylthio(N-beta-hydroxyethyl)	65089-17-0	eat	3.9E-01	1.1E+01	2.4E-06				

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227	Chlorozotocin	54749-90-5	ipj	6.7E+01	1.1E+01	4.1E-04				
228	Chlorpropham	101-21-3					oral	7.5E-03	1.1E+00	4.6E-09
229	Chlorpyrifos	2921-88-2					oral	2.1E+00	1.1E-01	1.3E-07
230	Chlorsulfuron	64902-72-3					oral	7.5E-02	1.1E+00	4.6E-08
231	*Chromium(III), insoluble salts*	16065-83-1					oral	2.6E-04	1.1E+00	1.6E-10
232	*Chromium(VI)*	18540-29-9					oral	1.5E-01	1.1E+00	9.2E-08
	Chromium(VI)	*18540-29-9*	*inh*	*2.1E+01*	*9.0E+00*	*1.1E-04*	*inh.*	*2.9E+01*	*1.1E-01*	*1.8E-06*
233	Chrysazin	117-10-2	eat	1.0E-02	1.1E+01	6.3E-08				
234	Cinnamyl anthranilate	87-29-6	eat	2.1E-04	1.1E+01	1.3E-09				
235	Ciprofibrate	52214-84-3	eat	1.2E+00	1.1E+01	7.2E-06				
236	Citrinin	518-75-2	eat	3.3E-01	1.1E+01	2.1E-06				
237	Clivorine	33979-15-6	wat	5.0E+00	1.1E+01	3.1E-05				
238	Clofibrate	637-07-0	eat	1.5E-02	1.1E+01	9.2E-08				
239	Clophen A 30	55600-34-5	eat	1.6E-02	1.1E+01	9.9E-08				
240	Coke oven emissions	8007-45-2	inh	1.1E+00	1.1E+01	6.7E-06				
241	Compound LY171883	88107-10-2	eat	2.2E-02	1.1E+01	1.4E-07				
242	*Copper cyanide*	544-92-3					oral	2.5E-01	1.1E+00	1.5E-07
243	Coumarin s	91-64-5	gav	1.8E-01	1.1E+01	1.1E-06				
244	m-Cresidine	#REF!	gav	5.3E-03	1.1E+01	3.3E-08				
245	p-Cresidine	120-71-8	eat	2.6E-02	1.1E+01	1.6E-07				
246	Crotonaldehyde	123-73-9	wat	6.0E-01	1.1E+01	3.7E-06				
247	Cumene	98-82-8					oral	1.1E-02	1.1E+00	6.9E-09
248	Cupferron	135-20-6	eat	3.0E-01	1.1E+01	1.9E-06				
249	Cyanide, free	57-12-5					oral	3.5E-02	1.1E+00	2.1E-08
250	Cyanogen	460-19-5					oral	1.7E-02	1.1E+00	1.1E-08
251	Cyanogen bromide	506-68-3					oral	8.5E-03	1.1E+00	5.2E-09
252	Cyclamate, sodium	139-05-9	wat	3.7E-03	1.1E+01	2.3E-08				
253	Cyclochlorotine	12663-46-6	eat	1.1E-01	1.1E+01	6.6E-07				
254	Cyclohexanone	108-94-1					oral	8.1E-04	1.1E+00	5.0E-10
255	Cyclohexylamine	108-91-8					oral	2.1E-02	1.1E+00	1.3E-08
256	Cyclophosphamide	50-18-0	ipj	1.1E+00	1.1E+01	7.0E-06				
257	Cyhalothrin/Karate	68085-85-8					oral	7.5E-01	1.1E+00	4.6E-07
258	Cypermethrin	52315-07-8					oral	1.0E-01	1.1E+00	6.2E-08
259	Cyromazine	66215-27-8					oral	1.3E-01	1.1E+00	8.2E-08
260	Cytembena	16170-75-5	ipj	9.0E-01	1.1E+01	5.6E-06				
261	Dacarbazine	04.03.42	ipj	3.5E+00	1.1E+01	2.2E-05				
262	Dacthal	1861-32-1					oral	3.8E-01	1.1E+00	2.3E-07
263	Dalapon, sodium salt	75-99-0					oral	4.4E-02	1.1E+00	2.7E-08
264	Daminozide	1596-84-5	wat	1.0E-03	1.1E+01	6.2E-09				
265	Danitol	39515-41-8					oral	4.0E-02	1.1E+00	2.5E-08
266	Dapsone	80-08-0	eat	1.1E-01	1.1E+01	6.9E-07				
267	p,p'-DDD	72-54-8	eat	8.1E-02	1.1E+01	5.1E-07				
268	**p,p'-Dichlorodiphenyldichloroethylene**	**72-55-9**	**oral**	**1.5E-01**	**1.1E+01**	**9.4E-07**				
269	DDT s	50-29-3	eat	3.0E-02	1.1E+01	1.8E-07	oral	7.5E+00	1.1E+00	4.6E-06
	DDT s	50-29-3	inh	1.7E-01	1.1E+01	1.1E-06				
270	Decabromodiphenyl ether (DBDPE)	1163-19-5	eat	7.5E-04	1.1E+01	4.6E-09	oral	3.8E-01	1.1E+00	2.3E-07
271	Dehydroepiandrosterone acetate	853-23-6	eat	8.0E-02	1.1E+01	4.9E-07				
272	Dextran sulfate sodium (DS-M-1)	9011-18-1	eat	1.3E-02	1.1E+01	7.9E-08				
273	N-1-Diacetamidofluorene	63019-65-8	eat	1.3E-01	1.1E+01	8.2E-07				

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274	Diallate	2303-16-4	orl	9.4E-02	1.1E+01	5.8E-07				
275	1,1-Diallylhydrazine	04.11.64	wat	8.4E-02	1.1E+01	5.2E-07				
276	1,2-Diallylhydrazine.2HCl	26072-78-6	wat	7.4E-02	1.1E+01	4.6E-07				
277	Diallylnitrosamine s	16338-97-9	wat	7.4E-02	1.1E+01	4.6E-07				
278	2,4-Diaminoanisole sulfate	39156-41-7	eat	1.4E-02	1.1E+01	8.5E-08				
279	4,6-Diamino-2-(5-nitro-2-furyl)-S-triazine	720-69-4	eat	1.5E+00	1.1E+01	9.1E-06				
280	2,4-Diaminophenol.2HCl	137-09-7	gav	1.7E-02	1.1E+01	1.1E-07				
281	2,4-Diaminotoluene	95-80-7	eat	1.0E+00	1.1E+01	6.3E-06				
282	2,4-Diaminotoluene.2HCl	636-23-7	eat	5.7E-01	1.1E+01	3.5E-06				
283	3-Diazotyramine.HCl	---	wat	6.6E-02	1.1E+01	4.1E-07				
284	Dibenz(a,h)anthracene	53-70-3	wat	4.3E-01	1.1E+01	2.6E-06				
285	3-Dibenzofuranamine	4106-66-5	eat	1.0E+00	1.1E+01	6.3E-06				
286	1,4-Dibromobenzene	106-37-6					oral	1.2E-01	1.1E+00	7.6E-08
287	**Dibromochloromethane**	**124-48-1**	**oral**	**3.1E-02**	**1.1E+01**	**1.9E-07**	**oral**	**5.8E-02**	**1.1E+00**	**3.6E-08**
288	1,2-Dibromo-3-chloropropane	96-12-8	gav	9.7E+00	1.1E+01	6.0E-05	inh.	1.9E+00	1.1E+00	1.2E-06
289	Dibromodulcitol	10318-26-0	ipj	3.0E-01	1.1E+01	1.9E-06				
290	1,2-Dibromoethane	106-93-4	wat	1.6E+00	1.1E+01	1.0E-05				
	1,2-Dibromoethane	106-93-4	oral	4.3E+01	1.1E+01	2.6E-04				
	1,2-Dibromoethane	106-93-4	inh	3.9E-01	1.1E+01	2.4E-06				
291	Dibromomannitol	488-41-5	ipj	9.1E-02	1.1E+01	5.6E-07				
292	Dibutyl phthalate	84-74-2					oral	9.9E-03	1.1E+00	6.1E-09
293	1,3-Dibutyl-1-nitrosourea	56654-52-5	wat	5.8E-01	1.1E+01	3.6E-06				
294	Dicamba	1918-00-9					oral	1.3E-01	1.1E+00	7.7E-08
295	Dichloroacetic acid	79-43-6	wat	5.1E-02	1.1E+01	3.1E-07				
296	Dichloroacetylene	7572-29-4	inh	7.0E-01	1.1E+01	4.3E-06				
297	1,4-Dichlorobenzene	106-46-7	gav	3.9E-03	1.1E+01	2.4E-08	inh.	1.3E-03	1.1E+00	8.2E-10
298	1,2-Dichlorobenzene	95-50-1					oral	1.4E-02	1.1E+00	8.9E-09
299	3,3'-Dichlorobenzidine s	91-94-1	eat	8.9E-02	1.1E+01	5.5E-07				
300	trans-1,4-Dichlorobutene-2	110-57-6	ipj	1.6E+00	1.1E+01	1.0E-05				
301	Dichlorodifluoromethane	75-71-8					oral	2.5E-02	1.1E+00	1.5E-08
302	3,5-Dichloro(N-1,1-dimethyl-2-propynyl)benzamide	23950-58-5	eat	2.1E-02	1.1E+01	1.3E-07				
	Pronamide	23950-58-5					oral	1.3E-02	1.1E+00	8.2E-09
303	1,2-Dichloroethane	107-06-2	gav	3.1E-01	1.1E+01	1.9E-06				
	1,2-Dichloroethane	107-06-2	inh	4.6E-02	1.1E+01	2.8E-07				
304	**1,1-Dichloroethylene**	**75-35-4**	**oral**	**2.2E-01**	**1.1E+01**	**1.3E-06**				
	Vinylidene chloride	**75-35-4**	**inh**	**7.2E-02**	**1.1E+01**	**4.5E-07**				
305	trans-1,2-Dichloroethylene	156-60-5					oral	1.6E-01	1.1E+00	9.7E-08
306	**Dichloromethane**	**75-09-2**	**oral**	**2.4E-03**	**1.1E+01**	**1.5E-08**	**oral**	**6.4E-02**	**1.1E+00**	**3.9E-08**
	Methylene chloride	**75-09-2**	**inh**	**3.5E-03**	**1.1E+01**	**2.1E-08**				
307	2,4-Dichlorophenol	120-83-2					oral	1.3E+00	1.1E+00	7.7E-07
308	2,4-Dichlorophenoxyacetic acid (2,4-D)	94-75-7					oral	3.8E-01	1.1E+00	2.3E-07
309	4-(2,4-Dichlorophenoxy)butyric acid	94-82-6					oral	4.1E-02	1.1E+00	2.5E-08
310	2,6-Dichloro-p-phenylenediamine	609-20-1	eat	3.1E-03	1.1E+01	1.9E-08				
311	1,2-Dichloropropane	78-87-5	gav	9.1E-03	1.1E+01	5.6E-08				
312	2,3-Dichloropropanol	616-23-9					oral	1.2E-01	1.1E+00	7.6E-08
313	1,3-Dichloropropene	542-75-6					oral	4.1E-01	1.1E+00	2.5E-07
	Telone II	542-75-6	gav	2.7E-02	1.1E+01	1.7E-07				
314	Dichlorvos	62-73-7	gav	6.0E-01	1.1E+01	3.7E-06	oral	2.0E+00	1.1E+00	1.2E-06
315	Dicofol	115-32-2	eat	7.6E-02	1.1E+01	4.7E-07				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
316	Dieldrin s	60-57-1	eat	2.7E+00	1.1E+01	1.7E-05	oral	7.5E+01	1.1E+00	4.6E-05
	Dieldrin s	60-57-1	inh	8.1E+00	1.1E+01	5.0E-05				
317	Diesel engine emissions	---					inh.	6.4E-01	1.1E+00	3.9E-07
318	Diethyl phthalate	84-66-2					oral	1.7E-03	1.1E+00	1.0E-09
319	Diethylacetamide	685-91-6	gav	2.8E-01	1.1E+01	1.8E-06				
320	Diethylene glycol	111-46-6	eat	1.5E-03	1.1E+01	9.3E-09				
321	**Di(2-ethylhexyl)adipate**	**103-23-1**	**oral**	**7.2E-04**	**1.1E+01**	**4.5E-09**	**oral**	**2.2E-03**	**1.1E+00**	**1.4E-09**
322	**Di(2-ethylhexyl)phthalate**	**117-81-7**	**oral**	**6.0E-03**	**1.1E+01**	**3.7E-08**				
323	N,N-Diethyl-4-(4'-(pyridyl-1'-oxide)azo)	7347-49-1	eat	1.5E+00	1.1E+01	9.5E-06				
324	Diethylstilbestrol	56-53-1	eat	2.2E+01	1.1E+01	1.4E-04				
325	N,N'-Diethylthiourea	105-55-5	eat	1.0E-01	1.1E+01	6.5E-07				
326	Difenzoquat	43222-48-6					oral	1.5E-02	1.1E+00	9.2E-09
327	Diflubenzuron	35367-38-5					oral	5.0E-02	1.1E+00	3.1E-08
328	1,1-Difluoroethane	75-37-6					inh.	8.3E-06	1.1E+00	5.1E-12
329	1,2-Diformylhydrazine	628-36-4	wat	3.7E-03	1.1E+01	2.3E-08				
330	Diftalone	21626-89-1	eat	2.9E-03	1.1E+01	1.8E-08				
331	Diglycidyl resorcinol ether	101-90-6	gav	6.6E-01	1.1E+01	4.1E-06				
332	3,4-Dihydrocoumarin	119-84-6	gav	8.4E-04	1.1E+01	5.2E-09				
333	3,6-Dihydro-2-nitroso-2H-1,2-oxazine	3276-41-3	wat	2.8E-02	1.1E+01	1.7E-07				
334	1,2-Dihydro-2-(5-nitro-2-thienyl)	33389-33-2	eat	1.6E+00	1.1E+01	1.0E-05				
335	Dihydrosafrole	94-58-6	orl	1.7E-02	1.1E+01	1.1E-07				
336	Diisopropyl methylphosphonate (DIMP)	1445-75-6					oral	4.4E-03	1.1E+00	2.7E-09
337	Dimethipin	55290-64-7					oral	1.9E-01	1.1E+00	1.2E-07
338	Dimethoate	60-51-5					oral	7.5E+00	1.1E+00	4.6E-06
339	Dimethoxane	828-00-2	wat	3.5E-03	1.1E+01	2.2E-08				
340	2,5-Dimethoxy-4'-aminostilbene	5803-51-0	eat	3.5E+00	1.1E+01	2.2E-05				
341	3,3'-Dimethoxybenzidine-4,4'-	91-93-0	orl	1.5E-03	1.1E+01	9.5E-09				
342	3,3'-Dimethoxybenzidine.2HCl	20325-40-0	wat	2.4E+00	1.1E+01	1.5E-05				
343	5,6-Dimethoxysterigmatocystin	65176-75-2	eat	6.9E+00	1.1E+01	4.3E-05				
344	Dimethyl hydrogen phosphite	868-85-9	gav	1.8E-02	1.1E+01	1.1E-07				
345	Dimethyl methylphosphonate	756-79-6	gav	3.6E-03	1.1E+01	2.2E-08				
346	Dimethyl morpholinophosphoramidate	597-25-1	gav	4.1E-03	1.1E+01	2.5E-08				
347	N,N-Dimethyl-4-aminoazobenzene s	60-11-7	eat	7.6E-01	1.1E+01	4.7E-06				
348	6-Dimethylamino-4,4-diphenyl-3-heptanol	43033-72-3	eat	3.7E-02	1.1E+01	2.3E-07				
349	Dimethylaminoethylnitrosoethylurea, nitrite salt	---	gav	3.6E+00	1.1E+01	2.2E-05				
350	trans-2-[(Dimethylamino)methylimino]	55738-54-0	eat	1.1E-01	1.1E+01	6.9E-07				
351	N,N-Dimethylaniline	121-69-7	gav	2.0E-02	1.1E+01	1.2E-07				
352	7,12-Dimethylbenz(a)anthracene	57-97-6	eat	3.0E+01	1.1E+01	1.8E-04				
353	3,3'-Dimethylbenzidine.2HCl	612-82-8	wat	4.0E+00	1.1E+01	2.5E-05				
354	Dimethylcarbamyl chloride s	79-44-7	inh	4.7E-01	1.1E+01	2.9E-06				
355	1,1-Dimethylhydrazine s	57-14-7	wat	6.3E-01	1.1E+01	3.9E-06				
356	1,2-Dimethylhydrazine.2HCl s	306-37-6	wat	2.2E+01	1.1E+01	1.4E-04				
357	2-(2,2-Dimethylhydrazino)	26049-69-4	eat	6.1E+00	1.1E+01	3.8E-05				
358	Dimethylnitramine	4164-28-7	wat	4.6E+00	1.1E+01	2.8E-05				
359	4,6-Dimethyl-2-(5-nitro-2-furyl)	59-35-8	eat	1.8E+00	1.1E+01	1.1E-05				
360	1,2-Dimethyl-5-nitroimidazole	551-92-8	eat	1.5E-01	1.1E+01	9.1E-07				
361	2,4-Dimethylphenol	105-67-9					oral	5.4E-02	1.1E+00	3.3E-08
362	2,6-Dimethylphenol	576-26-1					oral	2.1E+00	1.1E+00	1.3E-06
363	3,4-Dimethylphenol	95-65-8					oral	8.8E-01	1.1E+00	5.4E-07

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
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364	Dimethylvinyl chloride	513-37-1	gav	7.9E-02	1.1E+01	4.9E-07				
365	m-Dinitrobenzene	99-65-0					oral	3.1E+00	1.1E+00	1.9E-06
366	Dinitrosohomopiperazine	55557-00-1	wat	4.1E+01	1.1E+01	2.5E-04				
367	Dinitrosopiperazine	140-79-4	gav	6.9E-01	1.1E+01	4.3E-06				
368	2,4-Dinitrotoluene	121-14-2					oral	5.0E-01	1.1E+00	3.1E-07
369	2,6-Dinitrotoluene	606-20-2	eat	4.4E+00	1.1E+01	2.7E-05				
370	**2,4-/2,6-Dinitrotoluene**	**25321-14-6**	**oral**	**2.3E-01**	**1.1E+01**	**1.4E-06**				
371	**1,4-Dioxane**	**123-91-1**	**oral**	**7.8E-03**	**1.1E+01**	**4.8E-08**				
372	Dipentylnitrosamine	13256-06-9	eat	6.2E-01	1.1E+01	3.9E-06				
373	Diphenamid	957-51-7					oral	3.3E-02	1.1E+00	2.1E-08
374	Diphenylamine	122-39-4					oral	4.0E-02	1.1E+00	2.5E-08
375	5,5-Diphenylhydantoin	57-41-0	eat	4.2E-02	1.1E+01	2.6E-07				
376	Dipyrone	68-89-3	wat	4.0E-03	1.1E+01	2.5E-08				
377	Diquat	85-00-7					oral	1.7E+00	1.1E+00	1.0E-06
378	Diuron	330-54-1					oral	1.6E-01	1.1E+00	9.8E-08
379	Dodine	195681					oral	8.0E-02	1.1E+00	4.9E-08
380	Endosulfan	115-29-7					oral	6.3E-01	1.1E+00	3.8E-07
381	Endothall	145-73-3					oral	5.0E-02	1.1E+00	3.1E-08
382	Endrin	72-20-8					oral	4.0E+00	1.1E+00	2.5E-06
383	Enovid	8015-30-3	eat	9.0E+00	1.1E+01	5.6E-05				
384	Epichlorohydrin	106-89-8	gav	8.4E-01	1.1E+01	5.2E-06	inh.	9.1E-01	1.1E+00	5.6E-07
	Epichlorohydrin	106-89-8	inh	2.1E-03	1.1E+01	1.3E-08				
385	1,2-Epoxybutane	106-88-7	inh	1.1E-02	1.1E+01	7.1E-08				
386	Estradiol	50-28-2	eat	8.9E+00	1.1E+01	5.5E-05				
387	Estradiol mustard	22966-79-6	gav	1.7E+00	1.1E+01	1.1E-05				
388	Estragole	140-67-0	eat	4.8E-02	1.1E+01	3.0E-07				
389	Ethion	563-12-2					oral	1.3E+00	1.1E-01	7.7E-08
390	Ethionamide	536-33-4	gav	3.6E-02	1.1E+01	2.2E-07				
391	Ethionine	13073-35-3	eat	5.0E-01	1.1E+01	3.1E-06				
392	dl-Ethionine	67-21-0	eat	2.7E-01	1.1E+01	1.7E-06				
393	o-Ethoxybenzamide	938-73-8	eat	4.9E-03	1.1E+01	3.0E-08				
394	2-Ethoxyethanol	110-80-5					inh.	4.8E-03	1.1E+00	3.0E-09
395	Ethyl acetate	141-78-6					oral	1.4E-03	1.1E+00	8.5E-10
396	Ethyl acrylate	140-88-5	gav	2.1E-02	1.1E+01	1.3E-07				
397	Ethyl alcohol	64-17-5	wat	2.7E-04	1.1E+01	1.7E-09				
398	Ethyl benzene	100-41-4	gav	2.1E-03	1.1E+01	1.3E-08	oral	1.3E-02	1.1E+00	7.8E-09
399	Ethyl chloride	75-00-3					inh.	2.5E-05	1.1E+00	1.5E-11
400	S-Ethyl dipropylthiocarbamate (EPTC)	759-94-4					oral	1.5E-01	1.1E+00	9.2E-08
401	Ethyl ether	60-29-7					oral	2.5E-03	1.1E+00	1.5E-09
402	Ethyl p-nitrophenyl phenylphosphorothioate	2104-64-5					oral	1.2E+02	1.1E+00	7.6E-05
403	Z-Ethyl-O,N,N-azoxyethane	16301-26-1	wat	1.1E+02	1.1E+01	7.1E-04				
404	Z-Ethyl-O,N,N-azoxymethane	57497-29-7	wat	1.3E+02	1.1E+01	8.2E-04				
405	Ethylene glycol	107-21-1					oral	1.9E-03	1.1E+00	1.2E-09
406	Ethylene imine	151-56-4	orl	6.6E+00	1.1E+01	4.1E-05				
407	Ethylene oxide	75-21-8	inh	1.2E-01	1.1E+01	7.3E-07				
408	Ethylene thiourea	96-45-7	eat	3.2E-01	1.1E+01	2.0E-06				
409	N-Ethyl-N-formylhydrazine	74920-78-8	wat	8.9E-01	1.1E+01	5.5E-06				
410	Ethylhydrazine.HCl	18413-14-4	wat	3.8E-01	1.1E+01	2.4E-06				
411	N-Ethyl-N'-nitro-N-nitrosoguanidine	63885-23-4	wat	8.8E-01	1.1E+01	5.5E-06				

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412	Ethylnitrosocyanamide	38434-77-4	wat	6.8E-01	1.1E+01	4.2E-06				
413	1-Ethylnitroso-3-(2-hydroxyethyl)-urea	---	wat	4.8E+00	1.1E+01	3.0E-05				
414	1-Ethylnitroso-3-(2-oxopropyl)-urea	---	gav	1.4E+01	1.1E+01	8.6E-05				
415	1-Ethyl-1-nitrosourea	759-73-9	wat	2.6E+00	1.1E+01	1.6E-05				
416	Ethylphthalyl ethylglycolate (EPEG)	84-72-0					oral	1.5E-03	1.1E+00	9.2E-10
417	4-Ethylsulphonylnaphthalene-1-sulfonamide	842-00-2	eat	1.2E-01	1.1E+01	7.4E-07				
418	Express	101200-48-0					oral	1.3E-01	1.1E+00	7.8E-08
419	Fenamiphos	22224-92-6					oral	4.0E+00	1.1E+00	2.5E-06
420	Fluometuron	2164-17-2					oral	9.9E-02	1.1E+00	6.1E-08
421	Fluoranthene	206-44-0					oral	2.1E-02	1.1E+00	1.3E-08
422	Fluorene	86-73-7					oral	2.1E-02	1.1E+00	1.3E-08
423	N-(2-Fluorenyl)-2,2,2-trifluoroacetamide	363-17-7	eat	1.5E+00	1.1E+01	9.6E-06				
424	Fluorine (soluble fluoride)	7782-41-4					oral	1.0E+00	1.1E-01	6.4E-08
425	4'-Fluoro-4-aminodiphenyl	324-93-6	gav	2.2E+00	1.1E+01	1.4E-05				
426	N-4-(4'-Fluorobiphenyl)acetamide	398-32-3	eat	2.5E+00	1.1E+01	1.5E-05				
427	2-Fluoroethyl-nitrosourea	69112-98-7	gav	2.0E+01	1.1E+01	1.2E-04				
428	5-Fluorouracil	51-21-8	ipj	8.4E-01	1.1E+01	5.2E-06				
429	Fluridone	59756-60-4					oral	4.7E-02	1.1E+00	2.9E-08
430	Flurprimidol	56425-91-3					oral	2.1E-01	1.1E+00	1.3E-07
431	Fluvalinate	69409-94-5					oral	3.8E-01	1.1E+00	2.3E-07
432	**Folpet**	**133-07-3**	**oral**	**2.4E-03**	**1.1E+01**	**1.5E-08**	**oral**	**1.0E-02**	**1.1E+00**	**6.2E-09**
433	Fonofos	944-22-9					oral	5.0E-01	1.1E+00	3.1E-07
434	Formaldehyde s	50-00-0	inh	1.1E+00	1.1E+01	7.1E-06	oral	2.5E-02	1.1E+00	1.5E-08
435	**Formesafen**	**72178-02-0**	**oral**	**8.8E-02**	**1.1E+01**	**5.4E-07**				
436	Formic acid 2-(4-methyl-2-thiazolyl)	32852-21-4	eat	1.7E-01	1.1E+01	1.1E-06				
437	Formic acid 2-[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazide s	3570-75-0	eat	4.9E-01	1.1E+01	3.1E-06				
438	Formylhydrazine	624-84-0	wat	6.9E-02	1.1E+01	4.3E-07				
439	Fosetyl Al	39148-24-8	eat	6.8E-04	1.1E+01	4.2E-09	oral	4.0E-04	1.1E+00	2.5E-10
440	Fumonisin B1	116355-83-0	eat	2.2E+00	1.1E+01	1.3E-05				
441	Furan	110-00-9	gav	6.3E+00	1.1E+01	3.9E-05	oral	1.9E+00	1.1E+00	1.2E-06
442	Furfural s	98-01-1	gav	3.7E-03	1.1E+01	2.3E-08				
443	**Furmecyclox**	**60568-05-0**	**oral**	**1.9E-02**	**1.1E+01**	**1.1E-07**				
444	Furosemide	54-31-9	eat	3.4E-03	1.1E+01	2.1E-08				
445	Gentian violet	548-62-9	eat	2.8E-02	1.1E+01	1.7E-07				
446	Glufosinate-ammonium	77182-82-2					oral	3.1E+00	1.1E+00	1.9E-06
447	Glu-P-1	67730-11-4	eat	5.3E-01	1.1E+01	3.3E-06				
448	Glu-P-2	67730-10-3	eat	5.9E-02	1.1E+01	3.7E-07				
449	N2-gamma-Glutamyl-p-hydrazinobenzoic acid	---	gav	9.0E-03	1.1E+01	5.6E-08				
450	Glycidaldehyde	765-34-4					oral	1.1E+00	1.1E+00	7.0E-07
451	Glycidol s	556-52-5	gav	5.8E-01	1.1E+01	3.6E-06				
452	Glyphosate	1071-83-6					oral	3.8E-02	1.1E+00	2.3E-08
453	FD & C green no. 1	4680-78-8	eat	4.1E-04	1.1E+01	2.6E-09				
454	FD & C green no. 2	5141-20-8	eat	4.4E-04	1.1E+01	2.8E-09				
455	Griseofulvin s	126-07-8	eat	1.5E-03	1.1E+01	9.3E-09				
456	Haloxyfop-methyl	69806-40-2					oral	7.5E+01	1.1E+00	4.6E-05
457	Harmony	79277-27-3					oral	3.0E-01	1.1E+00	1.8E-07
458	HCDD mixture	mixture	gav	4.2E+03	1.1E+01	2.6E-02				
	HCDD mixture	19408-74-3	inh	2.3E+03	1.1E+01	1.4E-02				
459	Hematoxylin	517-28-2	eat	2.5E-03	1.1E+01	1.6E-08				

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460	Heptachlor	76-44-8	eat	2.1E+00	1.1E+01	1.3E-05	oral	2.5E+00	1.1E+00	1.5E-06
	Heptachlor	76-44-8	inh	2.3E+00	1.1E+01	1.4E-05				
461	Heptachlor epoxide	1024-57-3	oral + inh.	4.6E+00	1.1E+01	2.8E-05				
462	Hexabromobenzene	87-82-1					oral	6.2E-01	1.1E+00	3.8E-07
463	**Hexachlorobenzene**	**118-74-1**	**oral + inh.**	**1.3E+00**	**1.1E+01**	**8.3E-06**	**oral**	**4.7E+00**	**1.1E+00**	**2.9E-06**
464	**Hexachlorobutadiene**	**87-68-3**	**oral + inh.**	**3.4E-02**	**1.1E+01**	**2.1E-07**				
465	**alpha-lindane**	**319-84-6**	**oral + inh.**	**6.9E+00**	**1.1E+01**	**4.3E-05**				
466	**technical lindane**	**608-73-1**	**oral + inh.**	**7.7E-01**	**1.1E+01**	**4.8E-06**				
467	beta-1,2,3,4,5,6-Hexachlorocyclohexane	319-85-7	eat	9.0E-02	1.1E+01	5.6E-07				
	beta-1,2,3,4,5,6-Hexachlorocyclohexane	319-85-7	inh	9.3E-01	1.1E+01	5.8E-06				
468	gamma-1,2,3,4,5,6-Hexachlorocyclohexane	58-89-9	eat	8.1E-02	1.1E+01	5.1E-07	oral	3.8E+00	1.1E+00	2.3E-06
469	Hexachlorocyclopentadiene (HCCPD)	77-47-4					oral	1.8E-01	1.1E+00	1.1E-07
470	**Hexachloroethane**	**67-72-1**	**oral + inh.**	**4.7E-03**	**1.1E+01**	**2.9E-08**	**oral**	**1.2E+00**	**1.1E+00**	**7.6E-07**
471	**Hexahydro-1,3,5-trinitro-1,3,5-triazine**	**121-82-4**	**oral**	**5.7E-02**	**1.1E+01**	**3.5E-07**	**oral**	**1.3E+00**	**1.1E+00**	**7.7E-07**
472	1,6-Hexamethylene diisocyanate	822-06-0					inhalation	9.9E+01	1.1E+00	6.1E-05
473	Hexamethylmelamine	531-18-0	eat	2.5E-01	1.1E+01	1.5E-06				
474	Hexanal methylformylhydrazone	---	gav	1.1E+00	1.1E+01	6.7E-06				
475	Hexanamide	628-02-4	eat	1.3E-03	1.1E+01	8.0E-09				
476	n-Hexane	110-54-3					inhalation	8.6E-03	1.1E+00	5.3E-09
477	Hexazinone	51235-04-2					oral	3.8E-02	1.1E+00	2.3E-08
478	N-Hexylnitrosourea	18774-85-1	gav	4.9E+00	1.1E+01	3.0E-05				
479	**Hydrazine**	**302-01-2**	**oral + inh.**	**1.6E+00**	**1.1E+01**	**1.0E-05**				
480	**Hydrazine sulfate s**	**10034-93-2**	**gav**	**6.1E-02**	**1.1E+01**	**3.8E-07**				
481	2-Hydrazino-4-(p-aminophenyl)thiazole	26049-71-8	eat	2.4E+00	1.1E+01	1.5E-05				
482	p-Hydrazinobenzoic acid.HCl	24589-77-3	wat	4.5E-03	1.1E+01	2.8E-08				
483	2-Hydrazino-4-(5-nitro-2-furyl)thiazole	26049-68-3	eat	7.8E-01	1.1E+01	4.9E-06				
484	2-Hydrazino-4-(p-nitrophenyl)	26049-70-7	eat	7.8E-01	1.1E+01	4.8E-06				
485	1,2-Diphenylhydrazine	122-66-7	oral + inh.	5.0E-02	1.1E+01	3.1E-07				
486	Hydrogen cyanide	74-90-8					oral	3.3E-02	1.1E+00	2.1E-08
487	Hydrogen peroxide	7722-84-1	wat	3.3E-04	1.1E+01	2.1E-09				
488	Hydrogen sulfide	"7783-06-4"					oral	2.7E-01	1.1E+00	1.6E-07
489	Hydroquinone	123-31-9	eat	3.0E-02	1.1E+01	1.9E-07				
490	N-Hydroxy-2-acetylaminofluorene s	53-95-2	eat	2.5E+03	1.1E+01	1.6E-02				
491	1-Hydroxyanthraquinone	129-43-1	eat	4.2E-02	1.1E+01	2.6E-07				
492	3-Hydroxy-p-butyrophenetidide	1083-57-4	eat	4.5E-04	1.1E+01	2.8E-09				
493	1'-Hydroxyestragole	51410-44-7	eat	4.3E-02	1.1E+01	2.7E-07				
494	1-(2-Hydroxyethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinc	03.03.36	eat	1.5E-01	1.1E+01	9.3E-07				
495	4-(2-Hydroxyethylamino)-2-(5-nitro-2-thienyl)quinazoline	33389-36-5	eat	1.3E+00	1.1E+01	8.3E-06				
496	2-Hydroxyethylhydrazine s	109-84-2	orl	6.3E+00	1.1E+01	3.9E-05				
497	1-(2-Hydroxyethyl)-nitroso	---	wat	3.2E+00	1.1E+01	2.0E-05				
498	1-(2-Hydroxyethyl)-nitroso-3-ethylurea	---	wat	4.4E+00	1.1E+01	2.8E-05				
499	1-(2-Hydroxyethyl)-1-nitrosourea	13743-07-2	wat	1.9E+01	1.1E+01	1.2E-04				
500	1-(3-Hydroxypropyl)-1-nitrosourea	71752-70-0	gav	2.6E+00	1.1E+01	1.6E-05				
501	1'-Hydroxysafrole	5208-87-7	eat	1.4E-01	1.1E+01	8.4E-07				
502	ICRF-159	21416-87-5	ipj	2.3E-01	1.1E+01	1.5E-06				
503	Imazalil	35554-44-0					oral	8.0E-02	1.1E+00	4.9E-08
504	Imazaquin	81335-37-7					oral	4.0E-03	1.1E+00	2.5E-09
505	Indolidan	100643-96-7	eat	1.2E+00	1.1E+01	7.7E-06				
506	Iodinated glycerol	5634-39-9	gav	2.5E-02	1.1E+01	1.5E-07				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
507	Iprodione	36734-19-7					oral	2.4E-02	1.1E+00	1.5E-08
508	IQ s	76180-96-6	eat	1.5E+00	1.1E+01	9.5E-06				
509	IQ.HCl	---	gav	7.6E-01	1.1E+01	4.7E-06				
510	Isobutyl alcohol	78-83-1					oral	3.9E-03	1.1E+00	2.4E-09
511	Isomazole	86315-52-8	eat	3.5E-02	1.1E+01	2.2E-07				
512	Isoniazid s	54-85-3	gav	1.7E-02	1.1E+01	1.0E-07				
513	Isonicotinic acid vanillylidenehydrazide	149-17-7	gav	9.1E-02	1.1E+01	5.7E-07				
514	Isophorone	78-59-1	gav	2.1E-03	1.1E+01	1.3E-08	oral	2.2E-03	1.1E+00	1.4E-09
515	Isophosphamide	3778-73-2	ipj	3.4E+00	1.1E+01	2.1E-05				
516	Isopropalin	33820-53-0					oral	8.3E-02	1.1E+00	5.1E-08
517	Isopropyl methyl phosphonic acid (IMPA)	1832-54-8					oral	4.4E-03	1.1E+00	2.7E-09
518	Isoxaben	82558-50-7					oral	7.5E-02	1.1E+00	4.6E-08
519	Kepone	143-50-0	eat	8.4E-01	1.1E+01	5.2E-06				
520	Lasiocarpine	303-34-4	eat	5.3E+00	1.1E+01	3.3E-05				
521	*Lead acetate (C4H6O4Pb)*	301-04-2	wat	5.4E-02	1.1E+01	3.3E-07				
522	*Lead subacetate (C4H8O6Pb2)*	1335-32-6	eat	1.4E-02	1.1E+01	8.6E-08				
523	Leupeptin	24365-47-7	eat	4.5E-02	1.1E+01	2.8E-07				
524	d-Limonene	5989-27-5	gav	1.2E-02	1.1E+01	7.6E-08				
525	Londax	83055-99-6					oral	5.0E-03	1.1E+00	3.1E-09
526	Luteoskyrin	21884-44-6	eat	1.3E-01	1.1E+01	8.3E-07				
527	Malathion	121-75-5					oral	2.7E-01	1.1E-01	1.7E-08
528	Maleic anhydride	108-31-6					oral	3.8E-02	1.1E+00	2.3E-08
529	Malonaldehyde, sodium salt	24382-04-5	gav	2.0E-02	1.1E+01	1.3E-07				
530	Maneb	12427-38-2					oral	7.4E-02	1.1E+00	4.6E-08
531	Manganese	7439-96-5					oral	4.5E-01	1.1E+00	2.7E-07
532	Manganese ethylenebisthiocarbamate	12427-38-2	gav	1.6E-02	1.1E+01	9.9E-08				
533	*MDI*	*101-68-8*					*inh.*	*3.7E+00*	*1.1E+00*	*2.3E-06*
534	MeA-alpha-C	68006-83-7	eat	1.1E-01	1.1E+01	7.0E-07				
535	MeIQ	77094-11-2	eat	2.0E-01	1.1E+01	1.3E-06				
536	MeIQx	77500-04-0	eat	1.3E+00	1.1E+01	7.8E-06				
537	Melamine	108-78-1	eat	3.4E-03	1.1E+01	2.1E-08				
538	Melphalan	148-82-3	ipj	2.7E+01	1.1E+01	1.7E-04				
539	Mepiquat chloride	24307-26-4					oral	1.3E-02	1.1E+00	8.1E-09
540	2-Mercaptobenzothiazole	149-30-4	gav	7.3E-03	1.1E+01	4.5E-08				
541	*Mercuric chloride*	7487-94-7	gav	8.0E-01	1.1E+01	5.0E-06				
542	*Mercurymethylchloride*	115-09-3	eat	1.3E+00	1.1E+01	8.1E-06				
543	Merphos	150-50-5					oral	1.2E+01	1.1E+00	7.6E-06
544	Merphos oxide	78-48-8					oral	1.2E+01	1.1E+00	7.6E-06
545	Metalaxyl	57837-19-1					oral	1.6E-02	1.1E+00	9.8E-09
546	Metepa	57-39-6	gav	5.6E-01	1.1E+01	3.5E-06				
547	Methacrylonitrile	126-98-7					oral	9.7E-01	1.1E+00	6.0E-07
548	Methanol	67-56-1					oral	2.5E-03	1.1E+00	1.5E-09
549	Methapyrilene.HCl s	135-23-9	eat	2.7E-01	1.1E+01	1.7E-06				
550	Methidathion	950-37-8	eat	4.1E-01	1.1E+01	2.6E-06	oral	1.0E+00	1.1E+00	6.2E-07
551	Methimazole	60-56-0	eat	2.2E+00	1.1E+01	1.4E-05				
552	Methomyl	16752-77-5					oral	4.0E-02	1.1E+00	2.5E-08
553	3-Methoxy-4-aminoazobenzene	3544-23-8	eat	4.2E-02	1.1E+01	2.6E-07				
554	2-Methoxy-3-aminodibenzofuran	5834-17-3	eat	8.6E-02	1.1E+01	5.4E-07				
555	Methoxychlor	72-43-5					oral	7.5E-02	1.1E+00	4.6E-08

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
556	2-Methoxyethanol	109-86-4					inh.	1.9E-02	1.1E+00	1.2E-08
557	8-Methoxypsoralen	298-81-7	gav	7.7E-02	1.1E+01	4.8E-07				
558	Methyl tert-butyl ether (MTBE)	1634-04-4					inh.	3.8E-04	1.1E+00	2.4E-10
559	Methyl carbamate	598-55-0	gav	3.0E-03	1.1E+01	1.8E-08				
560	Methyl clofenapate	21340-68-1	eat	2.7E-01	1.1E+01	1.7E-06				
561	Methyl ethyl ketone (MEK)	78-93-3					oral	7.0E-04	1.1E+00	4.3E-10
562	Methyl methacrylate	80-62-6					oral	9.1E-03	1.1E+00	5.6E-09
	Methyl methacrylate	*80-62-6*					*inh.*	*3.9E-02*	*1.1E+00*	*2.4E-08*
563	Methyl methanesulfonate	66-27-3	wat	7.9E-02	1.1E+01	4.9E-07				
564	Methyl parathion	298-00-0					oral	1.5E+01	1.1E+00	9.2E-06
565	Z-Methyl-O,N,N-azoxyethane	57497-34-4	wat	2.2E-01	1.1E+01	1.3E-06				
566	alpha-Methylbenzyl alcohol	98-85-1	gav	5.5E-03	1.1E+01	3.4E-08				
567	3-Methylbutanal methylformylhydrazone	---	gav	1.1E+00	1.1E+01	7.0E-06				
568	4-(2-Methyl-4-chlorophenoxy) butyric acid	94-81-5					oral	2.8E-02	1.1E+00	1.7E-08
569	2-Methyl-4-chlorophenoxyacetic acid	94-74-6					oral	6.7E-01	1.1E+00	4.1E-07
570	2-(2-Methyl-4-chlorophenoxy)propionic acid	93-65-2					oral	4.1E-01	1.1E+00	2.5E-07
571	3-Methylcholanthrene s	56-49-5	gav	5.1E+00	1.1E+01	3.2E-05				
572	1-Methyl-1,4-dihydro-7-[2-(5-nitrofuryl)	---	eat	3.1E-01	1.1E+01	1.9E-06				
573	3'-Methyl-4-dimethylaminoazobenzene s	55-80-1	eat	7.6E-01	1.1E+01	4.7E-06				
574	N-Methyl-N,4-dinitrosoaniline	99-80-9	ipj	1.9E+00	1.1E+01	1.2E-05				
575	**4,4'-Methylene bis(N,N'-dimethyl)aniline**	**101-61-1**	**oral**	**1.0E-01**	**1.1E+01**	**6.3E-07**				
576	4,4'-Methylene-bis(2-	64049-29-2	eat	3.8E-02	1.1E+01	2.3E-07				
577	4,4'-Methylene-bis(2-methylaniline)	838-88-0	eat	3.4E-01	1.1E+01	2.1E-06				
578	4,4'-Methylene-bis(2-chloroaniline) s	101-14-4	eat	1.3E-01	1.1E+01	8.0E-07				
579	4,4'-Methylenedianiline.2HCl	13552-44-8	wat	1.3E-01	1.1E+01	7.8E-07				
580	N-Methyl-N-formylhydrazine s	758-17-8	wat	1.8E+00	1.1E+01	1.1E-05				
581	Methylhydrazine s	60-34-4	wat	3.3E-01	1.1E+01	2.1E-06				
582	Methylhydrazine sulfate	302-15-8	wat	9.2E-01	1.1E+01	5.7E-06				
583	*Methylmercury*	22967-92-6	oral	1.3E+00	1.1E+01	8.1E-06	*oral*	*3.0E+01*	*1.1E+00*	*1.9E-05*
584	Methylnitramine	598-57-2	gav	1.4E-01	1.1E+01	8.9E-07				
585	N-Methyl-N'-nitro-N-nitrosoguanidine s	70-25-7	wat	2.9E+00	1.1E+01	1.8E-05				
586	2-Methyl-1-nitroanthraquinone	129-15-7	eat	2.9E-02	1.1E+01	1.8E-07				
587	4-Methyl-1-[(5-nitrofurfurylidene)	21638-36-8	eat	4.7E-01	1.1E+01	2.9E-06				
588	4-(Methylnitrosamino)-1-(3-pyrridyl)-1-butanol	---	wat	2.4E+01	1.1E+01	1.5E-04				
589	4-(Methylnitrosamino)-1-(3-pyrridyl)-1-(butanone)	64091-91-4	wat	1.4E+01	1.1E+01	8.5E-05				
590	4-(4-N-Methyl-N-nitrosaminostyryl)	16699-10-8	eat	3.6E+00	1.1E+01	2.2E-05				
591	(N-6)-(Methylnitroso)adenine	---	wat	1.4E-01	1.1E+01	8.6E-07				
592	(N-6)-(Methylnitroso)adenosine	21928-82-5	wat	1.4E-01	1.1E+01	8.5E-07				
593	N-Methyl-N-nitrosobenzamide	63412-06-6	wat	7.7E-01	1.1E+01	4.8E-06				
594	N-(N-Methyl-N-nitrosocarbamoyl)-l-ornithine	63642-17-1	ipj	3.2E+00	1.1E+01	2.0E-05				
595	Methylnitrosocyanamide	33868-17-6	wat	5.2E+00	1.1E+01	3.2E-05				
596	R(-)-2-Methyl-N-nitrosopiperidine	14026-03-0	wat	1.2E-01	1.1E+01	7.6E-07				
597	S(+)-2-Methyl-N-nitrosopiperidine	36702-44-0	wat	1.9E-01	1.1E+01	1.2E-06				
598	N-Methylolacrylamide	924-42-5	gav	9.4E-02	1.1E+01	5.8E-07				
599	2-Methylphenol	95-48-7					oral	2.5E-02	1.1E+00	1.5E-08
600	3-Methylphenol	108-39-4					oral	2.5E-02	1.1E+00	1.5E-08
601	Metolachlor	51218-45-2					oral	2.5E-02	1.1E+00	1.5E-08
602	Metribuzin	21087-64-9					oral	4.0E-02	1.1E+00	2.5E-08
603	Metronidazole	443-48-1	eat	4.6E-03	1.1E+01	2.9E-08				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
604	Michler's ketone	90-94-8	eat	4.4E-01	1.1E+01	2.8E-06				
605	Mirex	2385-85-5	eat	1.4E+00	1.1E+01	8.8E-06	oral	5.4E+00	1.1E+00	3.3E-06
606	Mirex, photo	39801-14-4	eat	1.7E+00	1.1E+01	1.1E-05				
607	Mitomycin-C	50-07-7	ipj	2.5E+03	1.1E+01	1.5E-02				
608	Molinate	2212-67-1					oral	1.9E+00	1.1E+00	1.2E-06
609	Monoacetyl hydrazine	1068-57-1	gav	2.5E-01	1.1E+01	1.6E-06				
610	Monochloramine	10599-90-3					oral	3.9E-02	1.1E+00	2.4E-08
611	Monocrotaline	315-22-0	gav	2.7E+00	1.1E+01	1.7E-05				
612	1-5-Morpholinomethyl-3-[(5-nitrofurfurylidene)amino]-2-nitrofurfur	3031-51-4	eat	3.9E-01	1.1E+01	2.5E-06				
613	4-Morpholino-2-(5-nitro-2-thienyl)	58139-48-3	eat	5.0E-01	1.1E+01	3.1E-06				
614	Nafenopin	3771-19-5	eat	1.1E-01	1.1E+01	7.0E-07				
615	Naled	300-76-5					oral	1.9E+00	1.1E+00	1.2E-06
616	Nalidixic acid	389-08-2	eat	1.2E-02	1.1E+01	7.7E-08				
617	*Naphthalene*	*91-20-3*	*inh*	*1.5E-02*	*1.1E+01*	*9.5E-08*	*oral*	*1.7E-02*	*1.1E+00*	*1.1E-08*
618	1,5-Naphthalenediamine	2243-62-1	eat	3.6E-02	1.1E+01	2.2E-07				
619	2-Naphthylamine s	91-59-8	gav	4.1E-02	1.1E+01	2.5E-07				
620	Napropamide	15299-99-7					oral	1.3E-02	1.1E+00	7.7E-09
621	Nickel, soluble salts	Various					oral	7.5E-02	1.1E+00	4.6E-08
622	Nickel refinery dust		inh	4.2E-01	1.1E+01	2.6E-06				
623	Nickel subsulfide	12035-72-2	inh	8.4E-01	1.1E+01	5.2E-06				
624	Nicotinic acid hydrazide	553-53-7	wat	1.1E-02	1.1E+01	6.8E-08				
625	Nithiazide	139-94-6	eat	1.9E-02	1.1E+01	1.2E-07				
626	Nitrate	14797-55-8					oral	3.9E-02	1.1E+00	2.4E-08
627	Nitrilotriacetic acid	139-13-9	eat	1.4E-03	1.1E+01	8.8E-09				
628	Nitrilotriacetic acid, trisodium salt, monohydrate	18662-53-8	eat	6.8E-03	1.1E+01	4.2E-08				
629	Nitrite	147975-0					oral	6.3E-02	1.1E+00	3.9E-08
630	Nitrite, sodium s	7632-00-0	eat	1.5E-02	1.1E+01	9.3E-08				
631	5-Nitroacenaphthene s	602-87-9	eat	2.9E-01	1.1E+01	1.8E-06				
632	3-Nitro-p-acetophenetide	1777-84-0	eat	1.1E-03	1.1E+01	6.8E-09				
633	5-Nitro-o-anisidine	99-59-2	eat	4.6E-02	1.1E+01	2.9E-07				
634	o-Nitroanisole	91-23-6	eat	1.6E-01	1.1E+01	9.9E-07				
635	6-Nitrobenzimidazole	94-52-0	eat	6.7E-03	1.1E+01	4.2E-08				
636	p-Nitrobenzoic acid	62-23-7	eat	8.7E-03	1.1E+01	5.4E-08				
637	Nitrofen	1836-75-5	eat	6.0E-03	1.1E+01	3.7E-08				
638	5-Nitro-2-furaldehyde semicarbazone	59-87-0	eat	3.6E-01	1.1E+01	2.2E-06				
639	1-[(5-Nitrofurfurylidene)amino]-2-imidazolidinone	555-84-0	eat	4.8E-01	1.1E+01	2.9E-06				
640	1-[(5-Nitrofurfurylidene)amino]hydantoin	67-20-9	eat	1.5E-02	1.1E+01	9.5E-08				
641	N-{[3-(5-Nitro-2-furyl)-1,2,4-oxadiazole-5-yl]-methyl}acetamide	36133-88-7	eat	4.2E-02	1.1E+01	2.6E-07				
642	N-[5-(5-Nitro-2-furyl)-1,3,4-thiadiazol-2-yl]acetamide	2578-75-8	eat	2.8E-01	1.1E+01	1.8E-06				
643	3-(5-Nitro-2-furyl)-imidazo(1,2-alpha)pyridine	75198-31-1	eat	1.8E-01	1.1E+01	1.1E-06				
644	5-(5-Nitro-2-furyl)-1,3,4-oxadiazole-2-ol	2122-86-3	eat	2.9E-01	1.1E+01	1.8E-06				
645	N,N'-[6-(5-Nitro-2-furyl)-S-triazine-2,4-diyl]bisacetamide	51325-35-0	eat	1.8E-01	1.1E+01	1.1E-06				
646	4-(5-Nitro-2-furyl)thiazole	53757-28-1	eat	3.3E-01	1.1E+01	2.0E-06				
647	N-[4-(5-Nitro-2-furyl)-2-thiazolyl]	531-82-8	eat	1.4E-01	1.1E+01	8.7E-07				
648	N-[4-(5-Nitro-2-furyl)-2-thiazolyl]	24554-26-5	eat	5.9E-01	1.1E+01	3.7E-06				
649	Nitrogen mustard	51-75-2	ivj	2.2E+02	1.1E+01	1.4E-03				
650	Nitrogen mustard N-oxide	126-85-2	ivj	3.3E+00	1.1E+01	2.0E-05				
651	Nitroguanidine	556-88-7					oral	3.9E-03	1.1E+00	2.4E-09
652	3-Nitro-3-hexene	4812-22-0	inh	2.9E-01	1.1E+01	1.8E-06				

Nr	Chemical	CAS NR	Main route of exposure	Carcinogenic effects $\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	Noncarcinogenic effects $\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
653	2-Nitro-p-phenylenediamine	5307-14-2	eat	4.1E-03	1.1E+01	2.5E-08				
654	8-Nitroquinoline	607-35-2	eat	2.5E-01	1.1E+01	1.6E-06				
655	N-Nitrosoallyl-2,3-dihydroxypropylamine	88208-16-6	wat	3.0E+00	1.1E+01	1.9E-05				
656	N-Nitrosoallylethanolamine	91308-69-9	wat	5.1E+00	1.1E+01	3.2E-05				
657	N-Nitrosoallyl-2-hydroxypropylamine	91308-70-2	wat	2.9E+00	1.1E+01	1.8E-05				
658	N-Nitrosoallyl-2-oxopropylamine s	91308-71-3	gav	7.5E+00	1.1E+01	4.6E-05				
659	Nitrosoamylurethan	64005-62-5	wat	2.5E+00	1.1E+01	1.5E-05				
660	Nitrosoanabasine	1133-64-8	wat	2.1E-01	1.1E+01	1.3E-06				
661	Nitroso-Baygon	38777-13-8	gav	6.9E+00	1.1E+01	4.3E-05				
662	N-Nitrosobenzthiazuron	51542-33-7	gav	2.2E+00	1.1E+01	1.4E-05				
663	N-Nitrosobis(2-hydroxypropyl)amine	53609-64-6	wat	3.0E+00	1.1E+01	1.8E-05				
664	N-Nitrosobis(2-oxopropyl)amine	60599-38-4	gav	5.1E+00	1.1E+01	3.2E-05				
665	N-Nitroso-bis-(4,4,4-trifluoro-N-butyl)	83335-32-4	gav	3.3E+00	1.1E+01	2.1E-05				
666	Nitrosodibutylamine	924-16-3	gav	3.6E+00	1.1E+01	2.2E-05				
	Nitrosodibutylamine	924-16-3	inh	2.8E+00	1.1E+01	1.7E-05				
667	**N-Nitrosodiethanolamine**	**1116-54-7**	**oral**	**1.0E+00**	**1.1E+01**	**6.3E-06**				
668	N-Nitrosodiethylamine s	55-18-5	wat	1.1E+02	1.1E+01	6.5E-04				
	N-Nitrosodiethylamine s	55-18-5	oral + inh.	7.5E+01	1.1E+01	4.7E-04				
669	1-Nitroso-5,6-dihydrouracil	16813-36-8	wat	2.5E+01	1.1E+01	1.6E-04				
670	N-Nitroso-2,3-dihydroxypropyl-2-hydroxypropylamine s	89911-79-5	gav	4.7E+01	1.1E+01	2.9E-04				
671	Nitroso-2,3-dihydroxypropyl-2-oxopropylamine s	92177-50-9	gav	7.1E+01	1.1E+01	4.4E-04				
672	N-Nitroso-2,3-dihydroxypropylethanolamine s	89911-78-4	wat	4.2E-01	1.1E+01	2.6E-06				
673	1-Nitroso-3,5-dimethyl-4-benzoylpiperazine	61034-40-0	wat	2.6E-01	1.1E+01	1.6E-06				
674	N-Nitrosodimethylamine s	62-75-9	gav	2.0E+01	1.1E+01	1.3E-04				
	N-Nitrosodimethylamine s	62-75-9	inh	2.5E+01	1.1E+01	1.5E-04				
675	N-Nitrosodiphenylamine	86-30-6	eat	1.5E-02	1.1E+01	9.3E-08				
676	p-Nitrosodiphenylamine	156-10-5	eat	1.2E-02	1.1E+01	7.7E-08				
677	N-Nitrosodipropylamine s	621-64-7	ipj	1.3E+01	1.1E+01	8.3E-05				
	N-Nitrosodipropylamine s	621-64-7	oral	3.5E+00	1.1E+01	2.2E-05				
678	Nitrosododecamethyleneimine	40580-89-0	gav	2.3E-01	1.1E+01	1.4E-06				
679	N-Nitrosoephedrine	17608-59-2	gav	2.6E-02	1.1E+01	1.6E-07				
680	Nitrosoethylmethylamine	10595-95-6	gav	5.0E+01	1.1E+01	3.1E-04				
681	Nitrosoethylurethan	614-95-9	wat	2.8E+01	1.1E+01	1.7E-04				
682	Nitrosoheptamethyleneimine	20917-49-1	wat	6.6E+01	1.1E+01	4.1E-04				
683	N-Nitrosohexamethyleneimine	932-83-2	wat	7.0E+00	1.1E+01	4.3E-05				
684	1-Nitrosohydantoin	42579-28-2	wat	5.7E-02	1.1E+01	3.5E-07				
685	1-Nitroso-1-hydroxyethyl-3-chloroethylurea	96806-34-7	gav	1.1E+01	1.1E+01	6.8E-05				
686	1-Nitroso-1-(2-hydroxypropyl)-3- chloroethylurea	96806-35-8	gav	2.9E+00	1.1E+01	1.8E-05				
687	N-Nitroso-3-hydroxypyrrolidine	56222-35-6	wat	3.3E-01	1.1E+01	2.0E-06				
688	N-Nitroso-N-isobutylurea	760-60-1	wat	5.3E-01	1.1E+01	3.3E-06				
689	N-Nitrosomethyl-2,3-dihydroxypropylamine s	86451-37-8	gav	3.9E+00	1.1E+01	2.4E-05				
690	2-Nitrosomethylaminopyridine	16219-98-0	gav	1.2E+01	1.1E+01	7.3E-05				
691	Nitrosomethylaniline	614-00-6	wat	1.8E+01	1.1E+01	1.1E-04				
692	N-Nitroso-N-methyldecylamine	75881-22-0	gav	2.0E+00	1.1E+01	1.2E-05				
693	N-Nitroso-N-methyl-N-dodecylamine	55090-44-3	gav	4.7E+00	1.1E+01	2.9E-05				
694	N-Nitroso-N-methyl-4-fluoroaniline	937-25-7	wat	9.8E+00	1.1E+01	6.1E-05				
695	N-Nitrosomethyl-(2-hydroxyethyl)amine	26921-68-6	gav	1.9E+00	1.1E+01	1.2E-05				
696	N-Nitrosomethyl-(3-hydroxypropyl)	70415-59-7	gav	1.5E+00	1.1E+01	9.3E-06				
697	N-Nitrosomethyl-2-hydroxypropylamine	75411-83-5	wat	5.4E+01	1.1E+01	3.4E-04				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
698	N-Nitrosomethyl(2-oxopropyl)amine	55984-51-5	gav	1.5E+02	1.1E+01	9.0E-04				
699	Nitroso-N-methyl-N-(2-phenyl)	13256-11-6	wat	2.5E+02	1.1E+01	1.6E-03				
700	N-Nitroso-N-methyl-N-tetradecylamine	75881-20-8	gav	1.5E+00	1.1E+01	9.4E-06				
701	N-Nitrosomethyl-(2-tosyloxyethyl)	---	gav	5.2E-01	1.1E+01	3.2E-06				
702	Nitrosomethylundecylamine	68107-26-6	gav	1.1E+00	1.1E+01	6.5E-06				
703	N-Nitroso-N-methylurea s	684-93-5	eat	2.7E+01	1.1E+01	1.7E-04				
704	N-Nitrosomorpholine s	59-89-2	wat	2.3E+01	1.1E+01	1.4E-04				
705	N'-Nitrosonornicotine-1-N-oxide s	78246-24-9	wat	2.9E+00	1.1E+01	1.8E-05				
706	3-Nitroso-2-oxazolidinone	38347-74-9	wat	6.5E+00	1.1E+01	4.0E-05				
707	Nitroso-2-oxopropylethanolamine s	92177-49-6	gav	1.4E+00	1.1E+01	8.6E-06				
708	di(N-Nitroso)-perhydropyrimidine	15973-99-6	ipj	1.5E+01	1.1E+01	9.3E-05				
709	N-Nitrosopiperazine	5632-47-3	wat	2.8E-01	1.1E+01	1.8E-06				
710	N-Nitrosopiperidine s	100-75-4	wat	1.7E+00	1.1E+01	1.1E-05				
711	**N-Nitrosopyrrolidine**	**930-55-2**	**oral + inh.**	**1.3E+00**	**1.1E+01**	**8.1E-06**				
712	Nitroso-1,2,3,6-tetrahydropyridine	55556-92-8	wat	4.2E+01	1.1E+01	2.6E-04				
713	N-Nitrosothialdine	81795-07-5	gav	5.2E+00	1.1E+01	3.2E-05				
714	N-Nitrosothiomorpholine	26541-51-5	wat	4.6E-01	1.1E+01	2.9E-06				
715	o-Nitrosotoluene	611-23-4	eat	4.9E-02	1.1E+01	3.1E-07				
716	N-Nitroso(2,2,2-trifluoroethyl)	82018-90-4	gav	9.9E-01	1.1E+01	6.2E-06				
717	N-Nitroso-2,2,4-trimethyl-1,2-dihydroquinoline polymer	29929-77-9	ipj	7.6E-01	1.1E+01	4.7E-06				
718	1-Nitroso-3,4,5-trimethylpiperazine s	75881-18-4	gav	1.7E+01	1.1E+01	1.0E-04				
719	5-Nitro-o-toluidine	99-55-8	eat	9.0E-03	1.1E+01	5.6E-08				
720	Norflurazon	27314-13-2					oral	2.7E-02	1.1E+00	1.6E-08
721	Norlestrin s	01.12.15	gav	1.3E+00	1.1E+01	8.0E-06				
722	NuStar	85509-19-9					oral	5.0E-01	1.1E+00	3.1E-07
723	Ochratoxin A	303-47-9	eat	2.4E+01	1.1E+01	1.5E-04				
724	Octabromodiphenyl ether	32536-52-0					oral	4.9E-01	1.1E+00	3.0E-07
725	Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	2691-41-0					oral	2.5E-02	1.1E+00	1.5E-08
726	C.I. acid orange 3	6373-74-6	gav	1.5E-03	1.1E+01	9.1E-09				
727	Oryzalin	19044-88-3					oral	2.0E-02	1.1E+00	1.2E-08
728	Oxadiazon	19666-30-9					oral	7.5E-01	1.1E+00	4.6E-07
729	Oxamyl	23135-22-0					oral	1.5E-01	1.1E+00	9.2E-08
730	Oxazepam	604-75-1	eat	7.0E-02	1.1E+01	4.3E-07				
731	N-(9-Oxo-2-fluorenyl)acetamide	3096-50-2	eat	4.1E-01	1.1E+01	2.5E-06				
732	4,4'-Oxydianiline	101-80-4	eat	2.6E-01	1.1E+01	1.6E-06				
733	N-Oxydiethylene thiocarbamyl-N-oxydiethylene sulfenamide	13752-51-7	eat	2.8E-02	1.1E+01	1.7E-07				
734	Oxyfluorfen	42874-03-3					oral	2.7E+00	1.1E+00	1.7E-06
735	Ozone	10028-15-6	inh	1.3E+00	1.1E+01	8.3E-06				
736	Paclobutrazol	76738-62-0					oral	9.9E-02	1.1E+00	6.1E-08
737	Paraquat	1910-42-5					oral	2.2E-01	1.1E+00	1.4E-07
738	Pendimethalin	40487-42-1					oral	8.0E-03	1.1E+00	4.9E-09
739	Pentabromodiphenyl ether	32534-81-9					oral	7.0E-01	1.1E+00	4.3E-07
740	Pentachloroanisole	1825-21-4	gav	1.0E-01	1.1E+01	6.3E-07				
741	Pentachloroethane	76-01-7	gav	4.4E-02	1.1E+01	2.7E-07				
742	Pentachloronitrobenzene	82-68-8	orl	3.5E-02	1.1E+01	2.2E-07	oral	1.3E-01	1.1E+00	8.2E-08
743	**Pentachlorophenol**	**87-86-5**	**oral**	**6.1E-02**	**1.1E+01**	**3.8E-07**	**oral**	**1.3E-01**	**1.1E+00**	**7.7E-08**
744	2,3,4,5,6-Pentachlorophenol	87-86-5	eat	1.0E-01	1.1E+01	6.5E-07				
745	Pentanal methylformylhydrazone	57590-20-2	gav	7.3E-01	1.1E+01	4.5E-06				
746	n-Pentylhydrazine.HCl	1119-68-2	wat	4.3E-01	1.1E+01	2.6E-06				

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			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
747	Permethrin	52645-53-1					oral	7.5E-02	1.1E+00	4.6E-08
748	Petasitenine	60102-37-6	wat	2.7E+00	1.1E+01	1.7E-05				
749	Phenacetin	62-44-2	eat	2.0E-03	1.1E+01	1.2E-08				
750	Phenazone	60-80-0	eat	2.0E-03	1.1E+01	1.3E-08				
751	Phenazopyridine.HCl	136-40-3	eat	8.3E-03	1.1E+01	5.1E-08				
752	Phenesterin	09.10.46	gav	4.8E+00	1.1E+01	3.0E-05				
753	Phenmedipham	13684-63-4					oral	1.5E-02	1.1E+00	9.2E-09
754	Phenobarbital s	50-06-6	eat	4.1E-01	1.1E+01	2.5E-06				
755	Phenobarbital, sodium	57-30-7	wat	2.9E-02	1.1E+01	1.8E-07				
756	Phenol	108-95-2					oral	6.3E-03	1.1E+00	3.8E-09
757	Phenoxybenzamine.HCl	63-92-3	ipj	2.3E+00	1.1E+01	1.4E-05				
758	1-Phenylazo-2-naphthol	842-07-9	eat	8.5E-02	1.1E+01	5.3E-07				
759	Phenylbutazone	50-33-9	gav	2.2E-03	1.1E+01	1.3E-08				
760	1-Phenyl-3,3-dimethyltriazene	7227-91-0	gav	1.1E+00	1.1E+01	6.7E-06				
761	m-Phenylenediamine	108-45-2					oral	2.1E-01	1.1E+00	1.3E-07
762	o-Phenylenediamine.2HCl	615-28-1	eat	1.0E-02	1.1E+01	6.3E-08				
763	Phenylethylhydrazine sulfate	156-51-4	wat	1.7E-01	1.1E+01	1.1E-06				
764	Phenylglycidyl ether	122-60-1	inh	5.7E-02	1.1E+01	3.5E-07				
765	Phenylhydrazine.HCl	59-88-1	gav	3.5E-02	1.1E+01	2.2E-07				
766	Phenylmercuric acetate	62-38-4					oral	4.5E+01	1.1E+00	2.7E-05
767	o-Phenylphenate, sodium	132-27-4	eat	4.6E-03	1.1E+01	2.8E-08				
768	o-Phenylphenol	90-43-7	eat	1.1E-02	1.1E+01	6.7E-08				
769	PhIP.HCl	---	eat	5.0E-01	1.1E+01	3.1E-06				
770	Phorbol	17673-25-5	ipj	1.1E+00	1.1E+01	7.0E-06				
771	Phosmet	732-11-6					oral	1.9E-01	1.1E+00	1.2E-07
772	Phosphine	7803-51-2					oral	1.4E+01	1.1E+00	8.9E-06
773	*Phosphoric acid*	*7664-38-2*					*inh.*	*2.3E-01*	*1.1E+00*	*1.4E-07*
774	Picloram	5145					oral	1.4E-02	1.1E+00	8.8E-09
775	Piperonyl sulfoxide	120-62-7	eat	4.0E-02	1.1E+01	2.5E-07				
776	Pirimiphos-methyl	29232-93-7					oral	2.5E-01	1.1E-01	1.5E-08
777	Pivalolactone	1955-45-9	gav	1.2E-02	1.1E+01	7.4E-08				
778	Polybrominated biphenyl mixture	67774-32-7	eat	7.8E+00	1.1E+01	4.8E-05				
779	Potassium cyanide	151-50-8					oral	1.4E-02	1.1E+00	8.5E-09
780	Potassium silver cyanide	506-61-6					oral	4.5E-03	1.1E+00	2.8E-09
781	Prednimustine	29069-24-7	gav	1.3E-01	1.1E+01	8.1E-07				
782	Prednisolone	50-24-8	wat	1.6E+00	1.1E+01	1.0E-05				
783	Probenecid	57-66-9	gav	4.6E-03	1.1E+01	2.9E-08				
784	Procarbazine	671-16-9	ivj	6.2E-01	1.1E+01	3.9E-06				
785	Procarbazine.HCl s	366-70-1	ipj	7.1E+00	1.1E+01	4.4E-05				
786	Prochloraz	67747-09-5	oral	7.5E-02	1.1E+01	4.7E-07	oral	1.1E-01	1.1E+00	6.8E-08
787	Prometon	1610-18-0					oral	8.3E-02	1.1E+00	5.1E-08
788	Prometryn	7287-19-6					oral	2.7E-02	1.1E+00	1.6E-08
789	Propachlor	1918-16-7					oral	2.5E-02	1.1E+00	1.5E-08
790	Propane sultone	1120-71-4	gav	6.5E-01	1.1E+01	4.0E-06				
791	Propanil	709-98-8					oral	7.5E-02	1.1E+00	4.6E-08
792	Propargite	2312-35-8					oral	4.4E-03	1.1E+00	2.7E-09
793	Propargyl alcohol	107-19-7					oral	2.5E-01	1.1E+00	1.5E-07
794	Propazine	139-40-2					oral	7.5E-02	1.1E+00	4.6E-08
795	Propham	122-42-9					oral	2.5E-02	1.1E+00	1.5E-08

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
796	Propiconazole	60207-90-1					oral	8.0E-02	1.1E+00	4.9E-08
797	beta-Propiolactone	57-57-8	gav	1.7E+00	1.1E+01	1.1E-05				
798	Propylene glycol monomethyl ether	107-98-2					inh.	5.0E-04	1.1E+00	3.1E-10
799	**1,2-Propylene oxide**	**75-56-9**	**inh**	**3.4E-02**	**1.1E+01**	**2.1E-07**				
	Propylene oxide	**75-56-9**	**oral**	**1.3E-01**	**1.1E+01**	**8.1E-07**				
800	N-N'-Propyl-N-formylhydrazine	77337-54-3	wat	2.8E-01	1.1E+01	1.8E-06				
801	Propylhydrazine.HCl	56795-66-5	wat	5.5E-02	1.1E+01	3.4E-07				
802	N-Propyl-N'-nitro-N-nitrosoguanidine	13010-07-6	wat	1.9E+00	1.1E+01	1.2E-05				
803	N-Propyl-N-nitrosourea	816-57-9	wat	6.6E-01	1.1E+01	4.1E-06				
804	Propylthiouracil	51-52-5	eat	1.8E-01	1.1E+01	1.1E-06				
805	Pursuit	81335-77-5					oral	4.0E-03	1.1E+00	2.5E-09
806	Pydrin	51630-58-1					oral	1.5E-01	1.1E+00	9.2E-08
807	Pyrene	129-00-0					oral	3.6E-02	1.1E+00	2.2E-08
808	Pyridine	110-86-1					oral	1.2E+00	1.1E+00	7.6E-07
809	Pyrilamine maleate	59-33-6	eat	8.9E-03	1.1E+01	5.5E-08				
810	Quercetin	117-39-5	eat	2.5E-01	1.1E+01	1.5E-06				
811	Quinalphos	13593-03-8					oral	2.0E+00	1.1E+00	1.2E-06
812	p-Quinone dioxime	105-11-3	eat	2.4E-02	1.1E+01	1.5E-07				
813	C.I. acid red 114	6459-94-5	wat	6.4E-01	1.1E+01	4.0E-06				
814	C.I. pigment red 3	2425-85-6	eat	2.1E-03	1.1E+01	1.3E-08				
815	D & C red no. 5	3761-53-3	eat	6.0E-03	1.1E+01	3.7E-08				
816	D & C red no. 9	01.02.60	eat	1.7E-02	1.1E+01	1.1E-07				
817	FD & C red no. 1	08.09.64	eat	4.8E-03	1.1E+01	3.0E-08				
818	FD & C red no. 2	915-67-3	eat	1.7E-03	1.1E+01	1.1E-08				
819	FD & C red no. 4 s	4548-53-2	eat	3.1E-04	1.1E+01	1.9E-09				
820	Reserpine	50-55-5	eat	8.2E+00	1.1E+01	5.1E-05				
821	Rifampicin	13292-46-1	wat	7.4E-02	1.1E+01	4.6E-07				
822	Ripazepam	26308-28-1	eat	2.2E-02	1.1E+01	1.4E-07				
823	p-Rosaniline.HCl s	569-61-9	eat	6.3E-02	1.1E+01	3.9E-07				
824	Rotenone	83-79-4					oral	9.9E-01	1.1E+00	6.1E-07
825	Saccharin, sodium	128-44-9	eat	1.2E-03	1.1E+01	7.3E-09				
826	Safrole	94-59-7	eat	5.7E-03	1.1E+01	3.5E-08				
827	Salbutamol	18559-94-9	eat	6.3E-02	1.1E+01	3.9E-07				
828	Savey	78587-05-0					oral	4.0E-02	1.1E+00	2.5E-08
829	Selenious acid	7783-00-8					oral	4.2E+00	1.1E-01	2.6E-07
830	Selenium and Compounds	7782-49-2					oral	4.2E+00	1.1E-01	2.6E-07
831	Selenium diethyldithiocarbamate	5456-28-0	orl	1.7E+00	1.1E+01	1.0E-05				
832	Selenium sulfide	7446-34-6	gav	3.1E-01	1.1E+01	1.9E-06				
833	Senkirkine	2318-18-5	ipj	1.5E+00	1.1E+01	9.1E-06				
834	Sesamol	533-31-3	eat	1.9E-03	1.1E+01	1.1E-08				
835	Sethoxydim	74051-80-2					oral	1.1E-02	1.1E+00	6.9E-09
836	Silver cyanide	506-64-9					oral	6.7E-03	1.1E+00	4.1E-09
837	Simazine	122-34-9					oral	7.2E-01	1.1E+00	4.4E-07
838	Sodium azide	26628-22-8					oral	3.5E-01	1.1E+00	2.1E-07
839	Sodium cyanide	143-33-9					oral	1.8E-02	1.1E+00	1.1E-08
840	Sodium diethyldithiocarbamate	148-18-5					oral	4.1E-02	1.1E+00	2.5E-08
841	Sodium fluoroacetate	62-74-8					oral	2.5E+01	1.1E+00	1.5E-05
842	Sterigmatocystin s	10048-13-2	eat	1.6E+01	1.1E+01	1.0E-04				
843	Streptozotocin	18883-66-4	ipj	2.6E+00	1.1E+01	1.6E-05				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
844	Strobane	8001-50-1	orl	2.8E+00	1.1E+01	1.8E-05				
845	Strontium	7440-24-6					oral	2.0E-03	1.1E+00	1.2E-09
846	Styrene	100-42-5	inh	1.1E-01	1.1E+01	6.7E-07	oral	1.7E-03	1.1E+00	1.0E-09
847	Styrene oxide	96-09-3	gav	4.5E-02	1.1E+01	2.8E-07				
848	Sulfallate	95-06-7	eat	9.6E-02	1.1E+01	5.9E-07				
849	Sulfamethazine	57-68-1	eat	1.7E-03	1.1E+01	1.0E-08				
850	4,4'-Sulfonylbisacetanilide	77-46-3	eat	4.5E-02	1.1E+01	2.8E-07				
851	Symphytine	22571-95-5	ipj	1.3E+00	1.1E+01	8.1E-06				
852	Systhane	88671-89-0					oral	1.5E-01	1.1E+00	9.3E-08
853	Tebuthiuron	34014-18-1					oral	5.4E-02	1.1E+00	3.3E-08
854	Terbacil	5902-51-2					oral	8.0E-02	1.1E+00	4.9E-08
855	Terbutaline	23031-25-6	eat	6.1E-03	1.1E+01	3.8E-08				
856	Terbutryn	886-50-0					oral	3.8E+00	1.1E+00	2.3E-06
857	3,3',4,4'-Tetraaminobiphenyl.4HCl	7411-49-6	eat	6.3E-03	1.1E+01	3.9E-08				
858	1,2,4,5-Tetrachlorobenzene	95-94-3					oral	3.6E+00	1.1E+00	2.2E-06
859	2,3,7,8-Tetrachlorodibenzo-p-dioxin	1746-01-6	gav	5.5E+04	1.1E+01	3.4E-01				
860	1,1,2,2-tetrachloroethane	79-34-5	oral + inh.	1.1E-01	1.1E+01	6.8E-07				
861	**1,1,1,2-tetrachloroethane**	**630-20-6**	**oral + inh.**	**9.7E-03**	**1.1E+01**	**6.0E-08**				
862	**1,1,2,2-Tetrachloroethane**	**79-34-5**	**gav**	**6.5E-02**	**1.1E+01**	**4.1E-07**				
863	Tetrachloroethylene	127-18-4	gav	2.5E-02	1.1E+01	1.5E-07	oral	1.9E-01	1.1E+00	1.2E-07
864	2,3,4,6-Tetrachlorophenol	58-90-2					oral	5.0E-02	1.1E+00	3.0E-08
865	Tetrachlorvinphos	961-11-5	eat	1.1E-02	1.1E+01	6.8E-08	oral	3.2E-02	1.1E+00	2.0E-08
866	Tetraethyldithiopyrophosphate	3689-24-5					oral	2.5E+00	1.1E+00	1.5E-06
867	*1,1,1,2 Tetrafluoroethane*	*811-97-2*					*inh.*	*2.4E-05*	*1.1E+00*	*1.5E-11*
868	Tetrafluoro-m-phenylenediamine.2HCl	63886-77-1	eat	2.9E-02	1.1E+01	1.8E-07				
869	Tetrahydro-2-nitroso-2H-1,2-oxazine	40548-68-3	wat	1.0E-01	1.1E+01	6.4E-07				
870	Tetranitromethane	509-14-8	inh	5.6E+00	1.1E+01	3.5E-05				
871	Thallium acetate	563-68-8					oral	4.8E+00	1.1E+00	2.9E-06
872	Thallium carbonate	6533-73-9					oral	5.4E+00	1.1E+00	3.3E-06
873	Thallium chloride	7791-12-0					oral	5.4E+00	1.1E+00	3.3E-06
874	Thallium nitrate	10102-45-1					oral	4.8E+00	1.1E+00	2.9E-06
875	Thallium(I) sulfate	7446-18-6					oral	5.0E+00	1.1E+00	3.0E-06
876	Thioacetamide	62-55-5	eat	2.2E-01	1.1E+01	1.3E-06				
877	Thiobencarb	28249-77-6					oral	3.8E-01	1.1E+00	2.3E-07
878	4,4'-Thiodianiline	139-65-1	eat	6.7E-01	1.1E+01	4.2E-06				
879	beta-Thioguanine deoxyriboside	64039-27-6	ipj	1.2E+00	1.1E+01	7.4E-06				
880	Thiophanate-methyl	23564-05-8					oral	4.7E-02	1.1E+00	2.9E-08
881	Thio-TEPA	52-24-4	ipj	1.5E+01	1.1E+01	9.5E-05				
882	Thiouracil	141-90-2	eat	2.1E-01	1.1E+01	1.3E-06				
883	Thiourea	62-56-6	wat	2.5E-02	1.1E+01	1.6E-07				
884	Thiram	137-26-8					oral	7.5E-02	1.1E+00	4.6E-08
885	Toluene	108-88-3	gav	3.5E-03	1.1E+01	2.2E-08	oral	1.7E-03	1.1E+00	1.0E-09
886	2,4-/2,6-Toluene diisocyanate mixture	26471-62-5					inh.	1.1E+02	1.1E+00	6.7E-05
	Toluene diisocyanate, commercial grade	26471-62-5	gav	7.4E-02	1.1E+01	4.6E-07				
887	o-Toluenesulfonamide	88-19-7	gav	6.3E-04	1.1E+01	3.9E-09				
888	m-Toluidine.HCl	638-03-9	eat	1.7E-03	1.1E+01	1.1E-08				
889	o-Toluidine.HCl	636-21-5	eat	5.7E-02	1.1E+01	3.6E-07				
890	p-Toluidine.HCl	540-23-8	eat	3.0E-02	1.1E+01	1.9E-07				
891	p-Tolylurea	622-51-5	eat	1.2E-02	1.1E+01	7.5E-08				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Extr.}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
892	**Toxaphene**	**8001-35-2**	**oral + inh.**	**3.6E-01**	**1.1E+01**	**2.2E-06**				
893	Tralomethrin	66841-25-6					oral	5.0E-01	1.1E+00	3.1E-07
894	Trenimon	68-76-8	ivj	5.0E+02	1.1E+01	3.1E-03				
895	Triallate	2303-17-5					oral	7.8E-02	1.1E+00	4.8E-08
896	Triamcinolone acetonide	76-25-5	wat	4.7E+01	1.1E+01	2.9E-04				
897	Triamterene	396-01-0	eat	4.2E-02	1.1E+01	2.6E-07				
898	Triasulfuron	82097-50-5					oral	6.8E-01	1.1E+00	4.2E-07
899	1,2,4-Tribromobenzene	615-54-3					oral	2.5E-01	1.1E+00	1.5E-07
900	*Tributyltin oxide*	*56-35-9*					*oral*	*1.1E+01*	*1.1E+00*	*6.8E-06*
901	2,4,6-Trichloroaniline	634-93-5	eat	9.7E-03	1.1E+01	6.0E-08				
902	1,2,4-Trichlorobenzene	120-82-1					oral	8.4E-02	1.1E+00	5.1E-08
903	**1,1,2-Trichloroethane**	**79-00-5**	**oral + inh.**	**2.0E-02**	**1.1E+01**	**1.2E-07**	**oral**	**6.9E-01**	**1.1E+00**	**4.2E-07**
904	Trichloroethylene s	79-01-6	inh	3.7E-03	1.1E+01	2.3E-08				
	Trichloroethylene	79-01-6	gav	7.3E-03	1.1E+01	4.5E-08				
905	**2,4,6-Trichlorophenol**	**88-06-2**	**oral + inh.**	**6.3E-03**	**1.1E+01**	**3.9E-08**				
906	2,4,5-Trichlorophenol	95-95-4					oral	1.2E-02	1.1E+00	7.6E-09
907	2 (2,4,5-Trichlorophenoxy) propionic acid	93-72-1					oral	1.3E-01	1.1E+00	8.2E-08
908	2,4,5-Trichlorophenoxyacetic acid (2,4,5-T)	93-76-5					oral	1.3E-01	1.1E+00	7.7E-08
909	1,1,2-Trichloropropane	598-77-6					oral	8.3E-02	1.1E+00	5.1E-08
910	1,2,3-Trichloropropane	96-18-4	gav	1.9E+00	1.1E+01	1.1E-05	oral	2.2E-01	1.1E+00	1.3E-07
911	1,1,2-Trichloro-1,2,2-trifluoroethane (CFC-113)	76-13-1					oral	2.3E-04	1.1E-01	1.4E-11
912	Tridiphane	58138-08-2					oral	1.1E+00	1.1E+00	7.0E-07
913	Triethanolamine	102-71-6	eat	2.5E-02	1.1E+01	1.6E-07				
914	Triethylamine	121-44-8					inh.	1.7E-02	1.1E+00	1.0E-08
915	2,2,2-Trifluoro-N-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide	42011-48-3	eat	3.7E-01	1.1E+01	2.3E-06				
916	**Trifluralin**	**1582-09-8**	**oral**	**3.4E-03**	**1.1E+01**	**2.1E-08**	**oral**	**1.3E-01**	**1.1E+00**	**8.2E-08**
917	2,4,5-Trimethylaniline	137-17-7	eat	7.4E-02	1.1E+01	4.6E-07				
918	2,4,5-Trimethylaniline.HCl	21436-97-5	eat	2.5E-02	1.1E+01	1.6E-07				
919	2,4,6-Trimethylaniline.HCl	08.11.34	eat	4.8E-01	1.1E+01	3.0E-06				
920	Trimethylphosphate	512-56-1	gav	7.5E-03	1.1E+01	4.6E-08				
921	Trimethylthiourea	2489-77-2	eat	9.7E-02	1.1E+01	6.0E-07				
922	1,3,5-Trinitrobenzene	99-35-4					oral	1.4E-01	1.1E+00	8.6E-08
923	2,4,6-Trinitro-1,3-dimethyl-5-tert-butylbenzene	81-15-2	eat	2.0E-02	1.1E+01	1.2E-07				
924	Trinitroglycerin	55-63-0	eat	9.5E-03	1.1E+01	5.9E-08				
925	**2,4,6-trinitrotoluene (TNT)**	**118-96-7**	**oral**	**2.3E-02**	**1.1E+01**	**1.4E-07**				
926	Tris(2-chloroethyl)phosphate	115-96-8	gav	2.9E-02	1.1E+01	1.8E-07				
927	Tris-1,2,3-(chloromethoxy)propane	38571-73-2	ipj	7.3E-01	1.1E+01	4.5E-06				
928	Tris(2,3-dibromopropyl)phosphate	126-72-7	eat	6.5E-01	1.1E+01	4.1E-06				
929	Tris(2-ethylhexyl)phosphate	78-42-2	gav	9.8E-04	1.1E+01	6.1E-09				
930	Trp-P-1 acetate	75104-43-7	eat	4.3E+00	1.1E+01	2.7E-05				
931	Trp-P-2 acetate	72254-58-1	eat	3.8E-01	1.1E+01	2.3E-06				
932	Uracil	66-22-8	eat	3.7E-03	1.1E+01	2.3E-08				
933	Urethane s	51-79-6	wat	6.1E-02	1.1E+01	3.8E-07				
934	Vanadium pentoxide	1314-62-1					oral	4.2E-01	1.1E+00	2.6E-07
935	Vernam	1929-77-7					oral	1.2E+00	1.1E+00	7.6E-07
936	Vinclozolin	50471-44-8					oral	4.0E-02	1.1E+00	2.5E-08
937	Vinyl acetate	108-05-4	wat	1.2E-02	1.1E+01	7.7E-08	inh.	2.0E-02	1.1E+00	1.2E-08
938	Vinyl bromide	593-60-2	inh	1.4E-01	1.1E+01	8.4E-07				
939	Vinyl carbamate	15805-73-9	ipj	2.0E+01	1.1E+01	1.3E-04				

Nr	Chemical	CAS NR	Carcinogenic effects				Noncarcinogenic effects			
			Main route of exposure	$\beta_{ED10\text{-}Ext}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Route of exposure	$\beta_{ED10\text{-}Ext}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
940	Vinyl chloride s	75-01-4	inh	1.3E-01	1.1E+01	8.1E-07				
941	4-Vinylcyclohexene	100-40-3	gav	2.4E-02	1.1E+01	1.5E-07				
942	FD & C violet no. 1	1694-09-3	eat	4.1E-03	1.1E+01	2.5E-08				
943	White phosphorus	7723-14-0					oral	8.3E+01	1.1E+00	5.1E-05
944	Xylene mixture (m-xylene, o-xylene,	mixture	gav	4.8E-03	1.1E+01	3.0E-08				
945	Xylenes	1330-20-7					oral	2.1E-03	1.1E+00	1.3E-09
946	2,4-Xylidine.HCl	21436-96-4	eat	2.0E-01	1.1E+01	1.3E-06				
947	2,5-Xylidine.HCl	51786-53-9	eat	1.6E-02	1.1E+01	1.0E-07				
948	C.I. disperse yellow 3	2832-40-8	eat	6.6E-03	1.1E+01	4.1E-08				
949	C.I. vat yellow 4	128-66-5	eat	2.3E-04	1.1E+01	1.4E-09				
950	Zearalenone	17924-92-4	eat	6.4E-02	1.1E+01	4.0E-07				
951	Zinc cyanide	557-21-1					oral	1.5E-02	1.1E+00	9.5E-09
952	Zinc dimethyldithiocarbamate	137-30-4	eat	6.1E-02	1.1E+01	3.8E-07				
953	Zinc ethylenebisthiocarbamate	12122-67-7	gav	9.8E-03	1.1E+01	6.1E-08				

Appendix 1.1 Effect factors EF derived from the slope factor β_{ED10} and the Disability Adjusted Life Years per affected Person $DALY_p$ using equation (2.19), for carcinogenic and noncarcinogenic effects of more than 900 chemicals.
Detailed calculations are provided in appendices 2.1.2, 2.2, 3.2.2 and 3.3.
In bold: Substances from carcinogenic bioessays reported in IRIS, studied into details in appendix 2.1.
In italic: Substances from carcinogenic bioessays reported in IRIS, studied into details in appendix 3.2.

Route of exposure: wat=water; eat=diet; gav=gavage; inh=inhalation;
orl=gavage preweanling, followed by diet; ipj=intraperitoneal injection; ivj=intravenous injection.

Appendix 1.2 Human damage factors

Metal and path of exposure	EE [mg absorbed / mg emitted]	NONCANCER EFFECTS EFnc [yr lost /mg absorbed]	NONCANCER EFFECTS HDFnc [yr lost /mg emitted]	CANCER EFFECTS EFc [yr lost /mg absorbed]	CANCER EFFECTS HDFc [yr lost /mg emitted]
CADMIUM					
Inhalation	9.6E-06	n.e.	n.e.	3.1E-05	3.0E-10
Deposition and food transfer	3.6E-04	2.5E-06	9.0E-10	n.e.	n.e.
Total exposure			9.0E-10		3.0E-10
CHROMIUM(VI)					
Inhalation	9.6E-06	1.8E-06	1.7E-11	1.1E-04	1.1E-09
Deposition and food transfer	5.0E-05	*9.2E-08*	*4.6E-12*	n.e.	n.e.
Total exposure			2.2E-11		1.1E-09
CHROMIUM(III)					
Inhalation	9.6E-06	0 (n.e.)	0 (n.e.)	n.e.	n.e.
Deposition and food transfer	5.0E-05	*0 (1.6E-10)*	*0 (8.0E-15)*	n.e.	n.e.
Total exposure			*0 (8.0E-15)*		n.e.
COOPER					
Inhalation	9.6E-06	0 (n.e.)	0 (n.e.)	n.e.	n.e.
Deposition and food transfer	6.5E-04	0 (n.e.)	0 (n.e.)	n.e.	n.e.
Total exposure			0 (n.e.)		n.e.
BERYLLIUM					
Inhalation	9.6E-06	*1.40E-03*	*1.3E-08*	2.1E-05	2.0E-10
Deposition and food transfer	4.7E-05	7.4E-08	3.5E-12	n.e.	n.e.
Total exposure			*1.3E-08*		2.0E-10
METHYLMERCURY					
Inhalation	9.6E-06	n.e.	n.e.	n.e.	n.e.
Deposition and food transfer	9.4E-05	1.8E-05	1.7E-09	*8.10E-06*	*7.6E-10*
Total exposure			1.7E-09		*7.6E-10*
LEAD					
Inhalation	9.6E-06	n.e.	n.e.	n.e.	n.e.
Deposition and food transfer	1.1E-04	*1.7E-04*	*1.9E-08*	*3.40E-07*	*3.7E-11*
Total exposure			*1.9E-08*		*3.7E-11*
INORGANIC ARSENIC					
Inhalation	9.6E-06	n.e.	n.e.	3.8E-05	3.6E-10
Deposition and food transfer	1.1E-04	*4.8E-05*	*5.3E-09*	4.5E-06	5.0E-10
Total exposure			*5.3E-09*		8.6E-10

Appendix 1.2.1 Determination of the human damage factors HDF for an outdoor air release of the selected metals, by combining their exposure efficiencies EE and effect factors EF (see equation 5.1).
In italic: values derived using the NOAEL (for noncarcinogens) and the TD_{50a} (for carcinogens); n.e.: not estimated.

Metal	EE [mg absorbed / mg emitted]	NONCANCER EFFECTS EFnc [yr lost /mg absorbed]	NONCANCER EFFECTS HDFnc [yr lost /mg emitted]	CANCER EFFECTS EFc [yr lost /mg absorbed]	CANCER EFFECTS HDFc [yr lost /mg emitted]
Cadmium	3.2E-03	2.5E-06	8.0E-09	n.e.	n.e.
Chromium(VI)	4.3E-04	*9.2E-08*	*4.0E-11*	n.e.	n.e.
Chromium(III)	4.3E-04	*0 (1.6E-10)*	*0 (6.8E-14)*	n.e.	n.e.
Copper	5.6E-03	0 (n.e.)	0 (n.e.)	n.e.	n.e.
Beryllium	4.1E-04	7.4E-08	3.0E-11	n.e.	n.e.
Methylmercury	8.1E-04	1.8E-05	1.5E-08	*8.1E-06*	*6.6E-09*
Lead	9.8E-04	*1.7E-04*	*1.7E-07*	*3.4E-07*	*3.3E-10*
Inorganic arsenic	1.0E-03	*4.8E-05*	*4.8E-08*	4.5E-06	4.5E-09

Appendix 1.2.2 Determination of the human damage factors HDF for a release into an agricultural so of the selected metals, by combining their exposure efficiencies EE and effect factoı EF (see equation 5.3).
In italic: values derived using the NOAEL (for noncarcinogens) and the TD50a (for carcinogens); n.e.: not estimated.

Metal	EE [mg absorbed / mg emitted]	NONCANCER EFFECTS EFnc [yr lost /mg absorbed]	NONCANCER EFFECTS HDFnc [yr lost /mg emitted]	CANCER EFFECTS EFc [yr lost /mg absorbed]	CANCER EFFECTS HDFc [yr lost /mg emitted]
Cadmium	9.1E-03	n.e.	n.e.	3.1E-05	2.8E-07
Chromium(VI)	9.1E-03	1.8E-06	1.6E-08	1.1E-04	1.0E-06
Chromium(III)	9.1E-03	0 (n.e.)	0 (n.e.)	n.e.	n.e.
Copper	9.1E-03	0 (n.e.)	0 (n.e.)	n.e.	n.e.
Beryllium	9.1E-03	*1.4E-03*	*1.3E-05*	2.1E-05	1.9E-07
Methylmercury	9.1E-03	n.e.	n.e.	n.e.	n.e.
Lead	9.1E-03	n.e.	n.e.	n.e.	n.e.
Inorganic arsenic	9.1E-03	n.e.	n.e.	3.8E-05	3.5E-07

Appendix 1.2.3 Determination of the human damage factors HDF for an indoor air release of the selected metals, by combining their exposure efficiencies EE and effec factors EF.
In italic: values derived using the NOAEL; n.e.: not estimated.

Pollutant	Exposure efficiency EE [mg absorbed /mg emitted] [This study]	Effect factor EF [yr lost / mg absorbed] [Hofstetter, 1998]	Human Damage Factor HDF [yr lost / mg emitted] [This study]
NO_x	1.2E-05	4.3E-05	5.3E-10
SO_2	3.9E-06	7.0E-05	2.7E-10
CO	2.4E-05	1.3E-08	3.1E-13
Fines particles	9.6E-06	7.0E-05	6.7E-10

Appendix 1.2.4 Determination of the human damage factors HDF for NO_X, SO_2, CO and fine particles, by combining their specific exposure efficiencies EE and effect factors EF (see equation 5.1).

APPENDICES CHAPTER 2

Appendix 2.1 Detailed analysis for 44 compounds

	Chemical	CAS RN	Tested anima	Tumor site	Groupe 1 Dose [mg/kg-day]	Response	Groupe 2 Dose [mg/kg-day]	Response	Groupe 3 Dose [mg/kg-day]	Response	Groupe 4 Dose [mg/kg-day]	Response	Groupe 5 Dose [mg/kg-day]	Response	Groupe 6 Dose [mg/kg-day]	Response
1	Acephate	30560-19-1	Mice	l.a.	0	1/62	0.63	3/61	3.33	0/62	13	15/62				
2	Acrylamide	79-06-1	Rats	g, u, o.c.	0	13/60	0.0010	18/60	0.02	14/60	0.076	21/60	0.305	46/60		
3	Acrylonitrile	107-13-1	Rats	b.a.	0	6/100	0.02	6/98	1.36	36/98						
			Rats	b.a.	0	5/200	0.02	4/100	0.04	5/100	0.14	7/100	0.43	20/100	1.39	34/100
			Rats	b.a.	0	4/80	0.58	18/47	1.46	36/48	3.620	45/48				
4	Aldrin	309-00-2	Mice	liv	0	2/53	0.104	72/85								
			Mice	liv	0	22/73	0.104	75/91								
			Mice	liv	0	3/20	0.04	16/49	0.08	25/45						
5	Aniline	62-53-3	Rats	s, f, ss, cs	0	0/64	1.23	0/90	3.69	1/90	12.29	31/90				
6	Aramite	140-57-8	Rats	l.n., c	0	2/193	0.78	2/93	1.57	3/100	3.14	20/90				
7	Azobenzene	103-33-3	Rats	a.c.s.	0	0/20	1.53	5/50	3.06	21/50						
8	Benzotrichloride	98-07-7	Mice	l, a	0	0/35	0.00	1/37	0.017	9/38	0.068	16/40				
9	Benzyl chloride	100-44-7	Rats	t, c	0	4/52	1.06	8/51	2.12	14/52						
10	Bromodichloromethane	75-27-4	Mice	k	0	1/46	1.5	2/49	3	9/50						
11	Bromoform	75-25-2	Rats	i	0	0/50	10.6	1/50	20.5	8/50						
12	Carbon tetrachloride	56-23-5	Hamsters	h.c.	0	0/80	1.02	10/19								
			Mice	h.c.	0	2/152	2.30	34/73								
			Mice	h.c.	0	6/157	55.4	89/89	110.8	90/93						
			Rats	h.c.	0	0/37	4.5	2/45	7.4	4/46	8.7	2/47	14.9	1/30		
13	Chloroform	67-66-3	Rats	k	0	1/50	3.4	6/313	6.9	7/148	14.8	3/48	28.9	7/50		
14	Di(2-ethylhexyl)adipate	103-23-1	Mice	a, c	0	3/50	255	19/50	625	18/49						
15	Di(2-ethylhexyl)phthalate	117-81-7	Mice	a, c	0	14/50	32	25/48	65	29/50						
16	Dibromochloromethane	124-48-1	Mice	a, c	0	6/50	2.83	10/49	5.66	19/50						
17	p,p'-Dichlorodiphenyldichloroethylene	72-55-9	Mice-female	h.c.	0	0/19	0.9	19/47	1.58	34/48						
			Mice-male	h.c.	0	0/19	0.9	7/41	1.58	17/47						
			Mice-female	h.c.	0	1/99	2.45	54/55								
			Mice-male	h.c.	0	33/98	2.45	39/53								
			Hamsters	h.c.	0	0/31	4.79	7/30	9.57	8/39						
			Hamsters	h.c.	0	0/42	4.79	4/39	9.57	6/39						
18	1,1-Dichloroethylene	75-35-4	Rats	a,p.	0	6/50	0.12	5/48	0.6	13/47						
19	Dichloromethane	75-09-2	Mice	h.c.	0	3/50	122	16/48	244	40/8						
			Mice	h.c.	0	24/125	4.5	51/200	9.4	30/100	14	31/99	18.9	35/125		
20	2,4-/2,6-Dinitrotoluene	25321-14-6	Rats	l, g	0	11/23	0.13	12/35	0.93	17/27	7.557	34/35				
21	1,4-Dioxane	123-91-1	Rats	n.t.	0	0/33	48	12/25	106	16/33						
22	1,2-Diphenylhydrazine	122-66-7	Rats	l.n.	0	6/95	4	13/49	15	37/49						
23	Folpet	133-07-3	Mice	d.t	0	1/104	7.4	2/80	40.2	8/80	102.6	41/80				
			Mice	d.t	0	0/104	7.6	1/80	41.2	8/80	102.7	41/80				
24	Fomesafen	72178-02-0	Mice	liv	0	30/127	0.01	26/63	0.06	17/64	1.3	27/64	5.600	42/64		
25	Furmecyclox	60568-05-0	Rats	l.n.	0	4/65	5	10/65	20	25/65	100	62/65				
26	Hexachlorobenzene	118-74-1	Rats	c	0	0/52	0.73	36/56	1.46	48/55						
27	Hexachlorobutadiene	87-68-3	Rats	r.t.a.	0	1/90	0.04	0/40	0.40	0/40	4	9/39				
28	alpha-lindane	319-84-6	Mice	h.c.	0	0/20	0.012	0/20	0.035	30/38	0.1	20/20				
29	technical lindane	608-73-1	Mice	l.n., h.c.	0	2/22	0.30	8/20	0.6	12/12						
30	Hexachloroethane	67-72-1	Mice	h.c.	0	3/20	27.8	15/50	55.5	31/49						
31	Hexahydro-1,3,5-trinitro-1,3,5-triazine	121-82-4	Mice	liv, h.c.	0	1/65	0.13	5/62	0.58	9/64	2.9	12/64				
32	Hydrazine-hydrazine sulfate	302-01-2	Mice	h	0	3/30	0.04	1/26	0.1	7/25	0.222	12/25	0.403	15/25		
33	4,4'-Methylene bis(N,N'-dimethyl)aniline	101-61-1	Rats	t, c	0	0/20	1.63	4/46	3.25	36/45						
34	N-Nitrosodiethanolamine	1116-54-7	Rats	h.c., c.c.	0	1/20	0.15	10/39	0.34	14/20						
35	N-Nitrosopyrrolidine	930-55-2	Rats	h.c.	0	0/61	0.05	5/60	0.17	17/62	0.51	31/38	1.700	14/24		
36	Pentachlorophenol	87-86-5	Mice	h.c.	0	5/31	1.4	12/48	2.7	15/46						
			Mice	h.c.	0	1/34	1.3	6/49	2.7	9/46	8.7	42/49				
37	Propylene oxide	75-56-9	Rats	fs	0	0/100	0.44	2/50	1.76	19/50						
38	1,1,1,2-tetrachloroethane	630-20-6	Mice	h.c.	0	5/49	14.8	13/46	27.6	30/48						
39	1,1,2,2-tetrachloroethane	79-34-5	Mice	h.c.	0	0/20	6.56	30/48	13.12	43/47						
40	Toxaphene	8001-35-2	Mice	h.c.	0	10/53	0.05	10/54	0.14	12/53	0.361	18/51				
41	1,1,2-Trichloroethane	79-00-5	Mice	h.c.	0	2/20	9.3	18/49	18.6	37/49						
42	2,4,6-Trichlorophenol	88-06-2	Rats	leuk	0	3/20	44.6	22/50	94.4	29/50						
43	Trifluralin	1582-09-8	Rats	r.c.	0	5/60	5.1	5/60	21.9	9/60	46.5	17/60				
44	2,4,6-trinitrotoluene (TNT)	118-96-7	Rats	u.b.	0	0/54	0.065	0/54	0.325	0/55	1.623	1/55	8.117	17/55		

Appendix 2.1.1 Carcinogenic bioassay data reported in the IRIS database [EPA, 1998] for 44 compounds, for an oral route of exposure.

a.c.s.	abnominal cavity sarcomas	d.t	digestive tract tumor	i	intestin	n.t.	nasal turbinates	u	uterus
a	adenoma	f	fibrosarcoma	k	kidney	o.c.	oral cavity	u.b.	urinary bladder
a.p.	adrenal pheochromocytomas	fs	forestomach	l.a.	liver adenomas	r.c.	renal carcinomas		
b.a.	brain and spinal cord astrocytomas	g	gland	l.n.	liver nodules	r.t.a.	renal tubular adenomas		
c	carcinoma	h	hepatoma	l	lung	s	spleen		

	Chemical	CAS RN	Formula [Chemfinder, 1999]	Production [OECD, 1997]	q1* [Risk / mg/kg-day]	q1 [Risk / mg/kg-day]	q1*/q1 -	Route of exposure	ED_{10h} [mg/kg-day]	β_{ED10} [Risk / mg/kg-day]	$DALY_p$ [yr lost /pers]	EF [yr lost / mg absorbed]	ED_{10a} [mg/kg-day]	BMD_{10h} [mg/kg-day]	TD_{50a} [mg/kg/day]	LD_{50a} [mg/kg]
					Calculated in this study, using Crouch [1985]				Calculated in this study, using Crouch [1985]				Calculated with [BMDS, 19		[Gold and Zeiger, 1997]	[NIOSH, 1998]
1	Acephate	30560-19-1	C4H10NO3PS		9.1E-03	<=0	infinite	oral	10	1.0E-02	11.1	6.2E-08	10	7.6	n.a.	700
2	Acrylamide	79-06-1	C3H5NO	HVP	4.2E+00	1.1E+00	3.9	oral + inh.	0.08	1.3E+00	11.1	7.8E-06	0.08	0.04	6.15	124
3	Acrylonitrile	107-13-1	C3H3N	HVP	5.4E-01	2.5E-01	2.1	oral	0.317	3.2E-01	11.1	2.0E-06	n.c.	n.c.	16.9	78
4	Aldrin	309-00-2	C12H8Cl6		1.6E+01	9.4E+00	1.7	oral + inh.	0.012	8.5E+00	11.1	5.3E-05	n.c.	n.c.	1.27	39
5	Aniline	62-53-3	C6H7N	HVP	5.7E-03	<=0	infinite	oral	7.75	1.3E-02	11.1	8.0E-08	7.75	6.73	n.a.	250
6	Aramite	140-57-8	C15H23ClO4S		2.8E-02	1.9E-04	149.7	oral + inh.	2.4	4.2E-02	11.1	2.6E-07	2.4	2.01	96.7	3900
7	Azobenzene	103-33-3	C12H10N2		1.1E-01	<=0	infinite	oral + inh.	1.4	7.1E-02	11.1	4.4E-07	1.4	0.86	24.1	1000
8	Benzotrichloride	98-07-7	C7H5Cl3	HVP	1.2E+01	9.2E+00	1.3	oral	0.012	8.3E+00	11.1	5.2E-05	0.012	0.012	n.a.	6000
9	Benzyl chloride	100-44-7	C7H7Cl	HVP	1.7E-01	6.0E-02	2.8	oral	1.25	8.0E-02	11.1	5.0E-07	1.25	0.68	61.5	1231
10	Bromodichloromethane	75-27-4	CHBrCl2		6.6E-02	<=0	infinite	oral	2.4	4.2E-02	11.1	2.6E-07	2.4	1.61	72.5	430
11	Bromoform	75-25-2	CHBr3		7.8E-03	<=0	infinite	oral + inh.	17.1	5.8E-03	11.1	3.6E-08	17.1	12.8	648	933
12	Carbon tetrachloride	56-23-5	CCl4	HVP	1.3E-01	8.9E-02	1.5	oral + inh.	1.19	8.4E-02	11.1	5.2E-07	n.c.	n.c.	2.29	2350
13	Chloroform	67-66-3	CHCl3	HVP	6.7E-03	3.3E-03	2.0	oral	23.7	4.2E-03	11.1	2.6E-08	23.7	15.7	262	908
14	Di(2-ethylhexyl)adipate	103-23-1	C22H42O4	HVP	1.2E-03	8.3E-04	1.4	oral	138	7.2E-04	11.1	4.5E-09	138	101	3880	9100
15	Di(2-ethylhexyl)phthalate	117-81-7	C24H38O4	HVP	1.4E-02	9.9E-03	1.4	oral	16.8	6.0E-03	11.1	3.7E-08	16.8	14.3	647	30000
16	Dibromochloromethane	124-48-1	CHBr2Cl		8.4E-02	9.0E-03	9.3	oral	3.2	3.1E-02	11.1	1.9E-07	3.2	1.5	139	370
17	p,p'-Dichlorodiphenyldichloroethylene	72-55-9	C14H8Cl4		4.2E-01	1.5E-01	2.8	oral	0.66	1.5E-01	11.1	9.4E-07	n.c.	n.c.	12.5	880
18	1,1-Dichloroethylene	75-35-4	C2H2Cl2	HVP	5.8E-01	<=0	infinite	oral	0.46	2.2E-01	11.1	1.3E-06	0.46	0.20	34.6	200
19	Dichloromethane	75-09-2	CH2Cl2	HVP	8.8E-03	4.5E-03	2.0	oral	42	2.4E-03	11.1	1.5E-08	n.c.	n.c.	724	1600
20	2,4-/2,6-Dinitrotoluene	25321-14-6	C7H6N2O4		6.8E-01	4.2E-01	1.6	oral	0.43	2.3E-01	11.1	1.4E-06	o.n.f.	o.n.f.	8.02	750
21	1,4-Dioxane	123-91-1	C4H8O2	HVP	1.1E-02	8.2E-03	1.3	oral	12.9	7.8E-03	11.1	4.8E-08	12.9	9.5	334	7120
22	1,2-Diphenylhydrazine	122-66-7	C12H12N2		9.9E-02	5.0E-02	2.0	oral + inh.	2	5.0E-02	11.1	3.1E-07	2	1.1	5.59	n.a.
23	Folpet	133-07-3	C9H4Cl3NO2S		3.6E-03	1.6E-03	2.2	oral	41.70	2.4E-03	11.1	1.5E-08	n.c.	n.c.	1170	7540
24	Formesafen	72178-02-0	C15H10ClF3N2O6S		1.9E-01	1.3E-01	1.5	oral	1.14	8.8E-02	11.1	5.4E-07	o.n.f.	o.n.f.	n.a.	1250
25	Furmecyclox	60568-05-0	C14H21NO3		3.0E-02	2.1E-02	1.4	oral	5.4	1.9E-02	11.1	1.1E-07	5.4	3.7	n.a.	3780
26	Hexachlorobenzene	118-74-1	C6Cl6	HVP	1.7E+00	1.4E+00	1.2	oral + inh.	0.075	1.3E+00	11.1	8.3E-06	0.075	0.06	3.51	10000
27	Hexachlorobutadiene	87-68-3	C4Cl6	HVP	7.3E-02	<=0	infinite	oral + inh.	2.98	3.4E-02	11.1	2.1E-07	o.n.f.	o.n.f.	65.8	82
28	alpha-lindane	319-84-6	C6H6Cl6		6.3E+00	<=0	infinite	oral + inh.	0.0145	6.9E+00	11.1	4.3E-05	n.r.	n.r.	11.2	177
29	technical lindane	608-73-1	C6H6Cl6		1.8E+00	<=0	infinite	oral + inh.	0.13	7.7E-01	11.1	4.8E-06	n.r.	n.r.	14.8	100
30	Hexachloroethane	67-72-1	C2Cl6	HVP	1.4E-02	<=0	infinite	oral + inh.	21.5	4.7E-03	11.1	2.9E-08	21.5	9.0	55.4	4460
31	Hexahydro-1,3,5-trinitro-1,3,5-triazine	121-82-4	C3H6N6O6	HVP	1.1E-01	6.4E-02	1.7	oral	1.75	5.7E-02	11.1	3.5E-07	1.75	1.03	n.a.	n.a.
32	Hydrazine	302-01-2	H4N2	HVP	3.0E+00	1.8E+00	1.7	oral + inh.	0.062	1.6E+00	11.1	1.0E-05	0.062	0.04	0.309	60
33	4,4'-Methylene bis(N,N'-dimethyl)anili	101-61-1	C17H22N2		5.4E-02	<=0	infinite	oral	0.98	1.0E-01	11.1	6.3E-07	0.98	0.8	16.4	3160
34	N-Nitrosodiethanolamine	1116-54-7	C4H10N2O3		2.8E+00	2.5E-01	11.4	oral	0.098	1.0E+00	11.1	6.3E-06	0.098	0.04	3.17	7500
35	N-Nitrosopyrrolidine	930-55-2	C4H8N2O		1.7E+00	1.4E+00	1.2	oral + inh.	0.077	1.3E+00	11.1	8.1E-06	0.077	0.06	0.799	900
36	Pentachlorophenol	87-86-5	C6HCl5O	HVP	1.3E-01	6.8E-02	1.9	oral	1.63	6.1E-02	11.1	3.8E-07	n.c.	n.c.	24	27
37	Propylene oxide	75-56-9	C3H6O	HVP	2.4E-01	3.3E-02	7.2	oral	0.765	1.3E-01	11.1	8.1E-07	0.765	0.43	74.4	380
38	1,1,1,2-tetrachloroethane	630-20-6	C2H2Cl4	HVP	2.6E-02	<=0	infinite	oral + inh.	10.3	9.7E-03	11.1	6.0E-08	10.3	4.7	182	670
39	1,1,2,2-tetrachloroethane	79-34-5	C2H2Cl4	HVP	2.0E-01	1.1E-01	1.8	oral + inh.	0.91	1.1E-01	11.1	6.8E-07	0.91	0.52	38.3	250
40	Toxaphene	8001-35-2	a)		1.1E+00	1.1E-01	9.9	oral + inh.	0.28	3.6E-01	11.1	2.2E-06	0.28	0.12	5.57	50
41	1,1,2-Trichloroethane	79-00-5	C2H3Cl3	HVP	5.7E-02	5.8E-03	9.8	oral + inh.	5.1	2.0E-02	11.1	1.2E-07	5.1	2.12	55	836
42	2,4,6-Trichlorophenol	88-06-2	C6H3Cl3O	HVP	1.1E-02	7.9E-03	1.4	oral + inh.	16	6.3E-03	11.1	3.9E-08	16	12	405	820
43	Trifluralin	1582-09-8	C13H16F3N3O4		7.7E-03	1.6E-03	4.8	oral	29	3.4E-03	11.1	2.1E-08	29	15.4	330	1930
44	2,4,6-trinitrotoluene (TNT)	118-96-7	C7H5N3O6	HVP	3.1E-02	<=0	infinite	oral	4.35	2.3E-02	11.1	1.4E-07	4.35	2.99	n.a.	n.a.

Appendix 2.1.2 Main parameters of the studied chemicals: q1 and q1*, effect factors EF derived from the Disability Adjusted Life Years per affected Person ($DALY_p$) and the slope factor β_{ED10} (see equation (2.19)), benchmark dose BMD_{10h} and effect dose ED_{10h} for humans, tumor dose TD_{50a} and lethal dose LD_{50a} for animals.

n.c.: not calculated; n.r.: no results; o.n.f.: optimal not found; n.a.: not available.

HVP (High Volume Production) chemicals are compounds whose production or importated quantity exceeds 1000 tonnes in at least one OECD country [OECD, 1997].

a) Toxaphene is a mixture of many individual substances and can therefore not be adequately represented by a single molecular structure.

	Chemical	CASRN	MULTISTAGE MODEL		QUANTAL LINEAR MODEL		QUANTAL QUADRATIC MODEL		WEIBULL MODEL		LOGISTIC MODEL		Max value/Min value of the ED_{10h}
			ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/kg-day]	
1	Acephate	30560-19-1	10	1.1E-02	6.932	1.4E-02	8.96	1.1E-02	11.38	8.8E-03	9.6	1.0E-02	1.6
2	Acrylamide	79-06-1	0.08	1.3E+00	0.038	2.6E+00	0.1	1.0E+00	0.078	1.3E+00	0.065	1.5E+00	2.6
3	Aniline	62-53-3	7.75	1.6E-02	4.44	2.3E-02	6.41	1.6E-02	7.82	1.3E-02	9.165	1.1E-02	2.1
4	Aramite	140-57-8	2.4	4.4E-02	2.15	4.7E-02	2.23	4.5E-02	2.5	4.0E-02	c.f.	-	1.2
5	Azobenzene	103-33-3	1.4	7.2E-02	0.78	1.3E-01	1.4	7.1E-02	1.53	6.5E-02	1.8	5.6E-02	2.3
6	Benzotrichloride	98-07-7	0.012	8.7E+00	0.012	8.3E+00	0.032	3.1E+00	0.012	8.3E+00	0.03	3.3E+00	2.7
7	Benzyl chloride	100-44-7	1.25	7.9E-02	1.1	9.1E-02	1.5	6.7E-02	1.26	7.9E-02	c.f.	-	1.4
8	Bromodichloromethane	75-27-4	2.4	4.1E-02	2.35	4.3E-02	2.5	4.0E-02	2.57	3.9E-02	c.f.	-	1.1
9	Bromoform	75-25-2	17.1	5.9E-03	17.2	5.8E-03	17.2	5.8E-03	17.6	5.7E-03	c.f.	-	1.0
10	Chloroform	67-66-3	23.7	4.2E-03	24.5	4.1E-03	25	4.0E-03	23.5	4.3E-03	25.5	3.9E-03	1.1
11	Di(2-ethylhexyl)adipate	103-23-1	138	7.2E-04	137	7.3E-04	367	2.7E-04	138	7.2E-04	270	3.7E-04	2.7
12	Di(2-ethylhexyl)phthalate	117-81-7	16.8	5.9E-03	17	5.9E-03	35	2.9E-03	17	5.9E-03	23	4.3E-03	2.1
13	Dibromochloromethane	124-48-1	3.2	3.1E-02	2.2	4.5E-02	3.5	2.9E-02	3.15	3.2E-02	c.f.	-	1.6
14	1,1-Dichloroethylene	75-35-4	0.46	2.3E-01	0.36	2.8E-01	0.45	2.2E-01	0.57	1.8E-01	c.f.	-	1.6
15	2,4-/2,6-Dinitrotoluene	25321-14-6	n.f.	-	0.5	2.0E-01	2	5.0E-02	0.43	2.3E-01	0.8	1.3E-01	4.7
16	1,4-Dioxane	123-91-1	12.9	7.8E-03	12.9	7.8E-03	34.2	2.9E-03	12.9	7.8E-03	35.5	2.8E-03	2.8
17	1,2-Diphenylhydrazine	122-66-7	2	4.9E-02	1.3	7.7E-02	4.25	2.4E-02	2.2	4.5E-02	3.7	2.7E-02	3.3
18	Fomesafen	72178-02-0	n.f.	-	1.1	9.1E-02	2.5	4.0E-02	1.1	9.1E-02	1.6	6.3E-02	2.3
19	Furmecyclox	60568-05-0	5.4	1.8E-02	4.3	2.3E-02	18	5.6E-03	6.4	1.6E-02	13	7.7E-03	4.2
20	Hexachlorobenzene	118-74-1	0.075	1.3E+00	0.075	1.3E+00	0.29	3.4E-01	0.075	1.3E+00	0.27	3.7E-01	3.9
21	Hexachlorobutadiene	87-68-3	n.f.	-	1.9	5.3E-02	2.6	3.8E-02	3.39	2.9E-02	3.3	3.0E-02	1.8
22	alpha-lindane	319-84-6	n.r.	-	0.0028	3.6E+01	0.0097	1.0E+01	0.025	4.0E+00	0.031	3.2E+00	11.1
23	technical lindane	608-73-1	n.r.	-	0.046	2.2E+00	0.13	7.7E-01	0.235	4.3E-01	0.13	7.7E-01	5.1
24	Hexachloroethane	67-72-1	21.5	4.7E-03	8.2	1.2E-02	21	4.8E-03	23	4.3E-03	17	5.9E-03	2.8
25	Hexahydro-1,3,5-trinitro-1,3,5-triazine	121-82-4	1.75	5.9E-02	1.75	5.7E-02	2.6	3.8E-02	1.75	5.7E-02	c.f.	-	1.5
26	Hydrazine-hydrazine sulfate	302-01-2	0.06	1.6E+00	0.052	1.9E+00	0.14	7.1E-01	0.075	1.3E+00	0.11	9.1E-01	2.7
27	4,4'-Methylene bis(N,N'-dimethyl)aniline	101-61-1	0.98	1.0E-01	0.4	2.5E-01	0.99	1.0E-01	1.7	5.9E-02	1.72	5.8E-02	4.3
28	N-Nitrosodiethanolamine	1116-54-7	0.098	1.0E+00	0.045	2.2E+00	0.11	9.1E-01	0.099	1.0E+00	0.1	1.0E+00	2.4
29	N-Nitrosopyrrolidine	930-55-2	0.077	1.3E+00	0.078	1.3E+00	0.49	2.0E-01	0.078	1.3E+00	0.32	3.1E-01	6.4
30	Propylene oxide	75-56-9	0.765	1.3E-01	0.47	2.1E-01	0.82	1.2E-01	0.76	1.3E-01	1.1	9.1E-02	2.3
31	1,1,2,2-tetrachloroethane	79-34-5	10.3	9.6E-03	0.64	1.6E-01	2.5	4.0E-02	1.23	8.1E-02	2.13	4.7E-02	16.1
32	1,1,1,2-tetrachloroethane	630-20-6	0.9	1.1E-01	4.6	2.2E-02	10.2	9.8E-03	11	9.1E-03	8.5	1.2E-02	12.2
33	Toxaphene	8001-35-2	0.28	3.7E-01	0.22	4.5E-01	0.27	3.7E-01	0.26	3.8E-01	c.f.	-	1.3
34	1,1,2-Trichloroethane	79-00-5	5.1	2.0E-02	1.9	5.3E-02	5.5	1.8E-02	5.2	1.9E-02	4.6	2.2E-02	2.9
35	2,4,6-Trichlorophenol	88-06-2	16	6.1E-03	16	6.3E-03	45	2.2E-03	16.4	6.1E-03	28	3.6E-03	2.8
36	Trifluralin	1582-09-8	29	3.5E-03	23	4.3E-03	31	3.2E-03	28.5	3.5E-03	c.f.	-	1.3
37	2,4,6-trinitrotoluene (TNT)	118-96-7	4.35	2.3E-02	2.9	3.4E-02	4.4	2.3E-02	4.3	2.3E-02	5.9	1.7E-02	2.0

Appendix 2.1.3.a) Effect dose ED_{10h} and slope factor β_{ED10}, derived by using five different curve-fitting models provided in the benchmark dose software [EPA, 1999]. n.f.: not found; n.r.: no results; c.f.: calculations failed.

	Chemical	CASRN	MULTISTAGE MODEL		QUANTAL LINEAR MODEL		QUANTAL QUADRATIC MODEL		WEIBULL MODEL		LOGISTIC MODEL		Max value/Min.value of the $ED_{0.001h}$
			$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	
1	Acephate	30560-19-1	8.7E-02	1.1E-04	6.6E-04	1.5E-02	8.8E-02	1.1E-04	2.1E+00	4.8E-06	3.5E-03	2.9E-03	3200
2	Acrylamide	79-06-1	8.0E-06	1.3E+00	4.0E-06	2.5E+00	9.0E-04	1.1E-02	2.0E-04	5.0E-02	6.5E-06	1.5E+00	225
3	Aniline	62-53-3	6.3E-02	1.6E-04	4.2E-04	2.4E-02	6.3E-02	1.6E-04	3.8E-01	2.6E-05	1.7E-02	5.9E-04	905
4	Aramite	140-57-8	2.0E-02	5.0E-04	2.0E-04	5.0E-02	2.0E-02	5.0E-04	2.0E-01	5.0E-05	c.f.	-	1000
5	Azobenzene	103-33-3	1.4E-02	7.1E-04	8.0E-05	1.3E-01	1.4E-02	7.1E-04	3.2E-02	3.1E-04	6.0E-04	1.7E-02	400
6	Benzotrichloride	98-07-7	1.2E-06	8.7E+00	1.2E-06	8.3E+00	3.0E-04	3.3E-02	1.2E-06	8.3E+00	3.0E-06	3.3E+00	261
7	Benzyl chloride	100-44-7	1.3E-04	7.7E-02	1.0E-04	1.0E-01	1.0E-02	1.0E-03	2.0E-03	5.0E-03	c.f.	-	100
8	Bromodichloromethane	75-27-4	2.0E-02	5.0E-04	2.3E-04	4.3E-02	2.0E-02	5.0E-04	1.2E-01	8.3E-05	c.f.	-	522
9	Bromoform	75-25-2	1.7E-01	6.0E-05	1.7E-03	5.9E-03	1.8E-01	5.6E-05	1.1E+00	9.5E-06	c.f.	-	618
10	Chloroform	67-66-3	3.0E-03	3.3E-03	2.5E-03	4.1E-03	2.5E-01	4.0E-05	2.0E-02	5.0E-04	6.0E-03	1.7E-03	102
11	Di(2-ethylhexyl)adipate	103-23-1	1.0E-02	1.0E-03	1.4E-02	7.3E-04	3.5E+00	2.9E-06	1.4E-02	7.1E-04	2.7E-02	3.7E-04	350
12	Di(2-ethylhexyl)phthalate	117-81-7	1.7E-03	5.9E-03	1.7E-03	5.9E-03	3.0E-01	3.3E-05	2.0E-03	5.0E-03	2.3E-03	4.3E-03	176
13	Dibromochloromethane	124-48-1	1.5E-03	6.7E-03	2.2E-04	4.5E-02	3.0E-02	3.3E-04	2.0E-02	5.0E-04	c.f.	-	136
14	1,1-Dichloroethylene	75-35-4	4.0E-03	2.5E-03	3.6E-05	2.8E-01	4.0E-03	2.5E-03	1.8E-01	5.6E-05	c.f.	-	5000
15	2,4-/2,6-Dinitrotoluene	25321-14-6	n.f.	-	5.0E-05	2.0E-01	2.0E-02	5.0E-04	4.0E-05	2.5E-01	8.0E-05	1.3E-01	500
16	1,4-Dioxane	123-91-1	1.2E-03	8.3E-03	1.3E-03	7.7E-03	3.5E-01	2.9E-05	1.3E-03	7.7E-03	5.0E-03	2.0E-03	292
17	1,2-Diphenylhydrazine	122-66-7	2.0E-04	5.0E-02	1.3E-04	7.7E-02	4.0E-02	2.5E-04	5.0E-04	2.0E-02	4.0E-04	2.5E-02	308
18	Fomesafen	72178-02-0	1.3E-04	7.7E-02	1.1E-04	9.1E-02	2.5E-02	4.0E-04	1.2E-04	8.3E-02	2.0E-04	5.0E-02	227
19	Furmecyclox	60568-05-0	7.0E-04	1.4E-02	4.3E-04	2.3E-02	1.8E-01	5.6E-05	3.0E-03	3.3E-03	1.3E-03	7.7E-03	419
20	Hexachlorobenzene	118-74-1	7.2E-06	1.4E+00	7.5E-06	1.3E+00	2.8E-03	3.6E-03	8.0E-06	1.3E+00	4.0E-05	2.5E-01	389
21	Hexachlorobutadiene	87-68-3	n.f.	-	1.9E-04	5.3E-02	2.5E-02	4.0E-04	6.2E-01	1.6E-05	6.0E-03	1.7E-03	3263
22	alpha-lindane	319-84-6	n.r.	-	2.8E-07	3.6E+01	9.5E-05	1.1E-01	7.5E-03	1.3E-03	2.0E-02	5.0E-04	71429
23	technical lindane	608-73-1	n.r.	-	4.6E-06	2.2E+00	1.5E-03	6.7E-03	4.0E-02	2.5E-04	3.0E-05	3.3E-01	8696
24	Hexachloroethane	67-72-1	2.0E-01	5.0E-05	8.2E-04	1.2E-02	1.5E-01	6.7E-05	3.0E-01	3.3E-05	2.0E-03	5.0E-03	366
25	Hexahydro-1,3,5-trinitro-1,3,5-triazine	121-82-4	2.0E-04	5.0E-02	1.8E-04	5.7E-02	3.0E-02	3.3E-04	1.8E-04	5.6E-02	c.f.	-	171
26	Hydrazine-hydrazine sulfate	302-01-2	5.0E-06	2.0E+00	5.2E-06	1.9E+00	1.5E-03	6.7E-03	3.0E-05	3.3E-01	1.2E-05	8.3E-01	300
27	4,4'-Methylene bis(N,N'-dimethyl)aniline	101-61-1	9.6E-03	1.0E-03	4.0E-05	2.5E-01	1.0E-02	1.0E-03	1.9E-01	5.3E-05	6.0E-04	1.7E-02	4750
28	N-Nitrosodiethanolamine	1116-54-7	5.0E-05	2.0E-01	4.5E-06	2.2E+00	1.2E-03	8.3E-03	8.0E-04	1.3E-02	2.0E-05	5.0E-01	267
29	N-Nitrosopyrrolidine	930-55-2	7.3E-06	1.4E+00	7.8E-06	1.3E+00	5.0E-03	2.0E-03	8.0E-06	1.3E+00	3.0E-05	3.3E-01	685
30	Propylene oxide	75-56-9	3.0E-04	3.3E-02	4.7E-05	2.1E-01	8.0E-03	1.3E-03	4.0E-03	2.5E-03	5.0E-04	2.0E-02	170
31	1,1,2,2-tetrachloroethane	79-34-5	1.0E-01	1.0E-04	6.4E-05	1.6E-01	2.5E-02	4.0E-04	1.2E-03	8.3E-03	2.0E-04	5.0E-02	1563
32	1,1,1,2-tetrachloroethane	630-20-6	9.0E-05	1.1E-01	5.0E-04	2.0E-02	9.0E-02	1.1E-04	1.5E-01	6.7E-05	9.0E-04	1.1E-02	1667
33	Toxaphene	8001-35-2	1.0E-04	1.0E-01	2.2E-05	4.5E-01	3.0E-03	3.3E-03	1.0E-03	1.0E-02	c.f.	-	136
34	1,1,2-Trichloroethane	79-00-5	2.0E-03	5.0E-03	1.9E-04	5.3E-02	5.0E-02	2.0E-04	4.0E-02	2.5E-04	6.0E-04	1.7E-02	263
35	2,4,6-Trichlorophenol	88-06-2	1.7E-03	6.1E-03	1.6E-03	6.3E-03	4.0E-01	2.5E-05	2.0E-03	5.0E-03	2.8E-03	3.6E-03	250
36	Trifluralin	1582-09-8	5.0E-03	2.0E-03	2.3E-03	4.3E-03	3.0E-01	3.3E-05	9.0E-02	1.1E-04	c.f.	-	130
37	2,4,6-trinitrotoluene (TNT)	118-96-7	4.2E-02	2.4E-04	2.9E-04	3.4E-02	4.5E-02	2.2E-04	3.5E-02	2.9E-04	5.0E-03	2.0E-03	155

Appendix 2.1.3.b) Effect dose $ED_{0.001h}$ and slope factor $\beta_{ED0.001}$, derived by using five different curve-fitting models provided in the benchmark dose software [EPA, 1999]. n.f.: not found; n.r.: no results; c.f.: calculations failed.

Appendix 2.1.4 q_1^* versus q_1

Only the upper confidence limit q_1^* is reported in the IRIS database [EPA, 1998] and the HEAST tables [EPA, 1992]. We calculated the maximum likelihood estimate q_1 (see appendix 2.1.2) to compare the q_1 and q_1^* parameters.

Figure A.1 presents the results of the comparison. It shows that the difference between q_1^* and q_1 is low (factor 1-4) for more than half (60%) of the substances. However, the ratio q_1^*/q_1 ranges from 4 to 150 for 15% of the substances. It is even infinite for 25% of the chemicals. These compounds have a maximum likelihood estimate q1 equal or lower than zero, resulting in an infinite q_1^*/q_1 ratio. They are plotted on the horizontal axis in figure A.1. The q_1^*/q_1 ratio mainly depends on the general shape of the dose-response function predicted by the multistage model: the more nonlinear the dose-response curve, the higher the ratio q_1^*/q_1 [Gray et al., 1991].

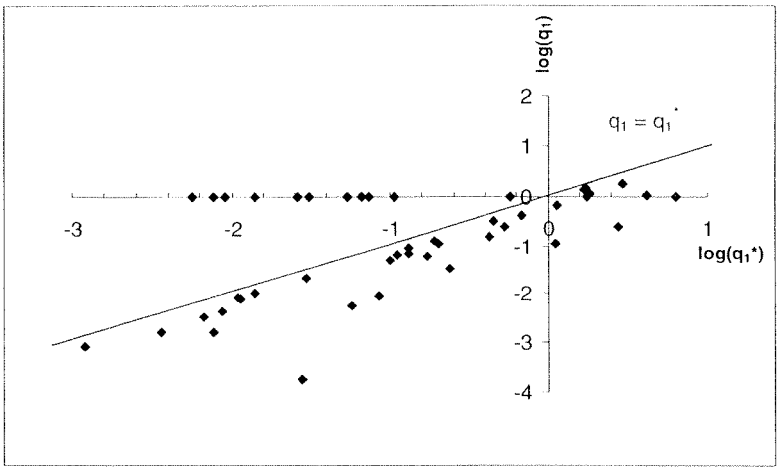

Figure A.1 Comparison of the Maximum Likelihood Estimate q_1 and the 95% Upper Confidence Limit q_1^*, for the 44 chemicals listed in appendix 2.1.2.
Chemicals for which q_1 is equal or lower than zero are plotted on the horizontal axis.

Appendix 2.2 Slope factors and effect factors derived from the TD_{50a}

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10b} [mg/kg-day]	$\beta_{ED10\text{-Extr.}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
1	A-alpha-C	26148-68-5		eat			49.8	2.0E+00	5.0E-02	11.1	3.1E-07	.	.	liv vsc	liv vsc
2	Acetaldehyde s	75-07-0	HVP	inh	-	153		6.1E+00	1.6E-02	11.1	1.0E-07	nas	nas	.	.
3	Acetaldehyde methylformylhydrazone	16568-02-8		gav			2.51	1.0E-01	1.0E+00	11.1	6.2E-06	.	.	lun pre	cli lun sto
4	Acetamide	60-35-5		eat	-	180	3010	7.2E+00	1.4E-02	11.1	8.6E-08	liv	liv	hmo	.
5	Acetaminophen	103-90-2	HVP	eat		495	1620	2.0E+01	5.1E-03	11.1	3.1E-08	liv ubl	liv ubl	liv	liv
6	Acetone[4-(5-nitro-2-furyl)-2-thiazolyl]	18523-69-8		eat		6.05		2.4E-01	4.1E-01	11.1	2.6E-06	.	sto	.	.
7	Acetoxime	127-06-0		wat		12.1		4.8E-01	2.1E-01	11.1	1.3E-06	liv	-	.	.
8	1'-Acetoxysafrole	34627-78-6		eat		25		1.0E+00	1.0E-01	11.1	6.2E-07	sto	.	-	.
9	N'-Acetyl-4-(hydroxymethyl)	65734-38-5		wat			241	9.6E+00	1.0E-02	11.1	6.4E-08	.	.	lun vsc	lun vsc
10	1-Acetyl-2-isonicotinoylhydrazine	1078-38-2		wat			330	1.3E+01	7.6E-03	11.1	4.7E-08	.	.	lun	lun
11	1-Acetyl-2-phenylhydrazine	114-83-0		wat	+		51.2	2.0E+00	4.9E-02	11.1	3.0E-07	.	.	vsc	vsc
12	4-Acetylaminobiphenyl	4075-79-0		eat		1.18		4.7E-02	2.1E+00	11.1	1.3E-05	.	mgl	.	.
13	2-Acetylaminofluorene s	53-96-3		eat		1.22	7.59	4.9E-02	2.0E+00	11.1	1.3E-05	liv mgl ski	liv mgl ski	liv ubl	liv ubl
14	Acifluorfen	50594-66-6		eat			141	5.6E+00	1.8E-02	11.1	1.1E-07	.	.	liv sto	liv sto
15	Acronycine	7008-42-6		ipj		0.505		2.0E-02	5.0E+00	11.1	3.1E-05	bon per	mgl per	l	l
16	**Acrylamide**	79-06-1	HVP	wat	?	6.15		2.5E-01	4.1E-01	11.1	2.5E-06	adr nrv per	mgl orc pit	.	.
17	**Acrylonitrile**	107-13-1	HVP	inh	+	16.9		6.8E-01	1.5E-01	11.1	9.2E-07	ezy nrv orc sm	iy mgl nas n	.	.
18	Actinomycin D	50-76-0		ipj		0.00111		4.4E-05	2.3E+03	11.1	1.4E-02	per	per	.	.
19	AF-2 s	3688-53-7		eat	+	29.4	131	1.2E+00	8.5E-02	11.1	5.3E-07	mgl	mgl	sto	sto
20	Aflatoxicol	29611-03-8		eat		0.00247		9.9E-05	1.0E+03	11.1	6.3E-03	liv	.	.	.
21	Aflatoxin B1 s	1162-65-8		eat		0.0032		1.3E-04	7.8E+02	11.1	4.8E-03	kid lgi liv	lgi liv	-	-
22	Aflatoxin, crude	---		eat		0.00299	0.343	1.2E-04	8.4E+02	11.1	5.2E-03	liv	.	hmo	.
23	**Aldrin**	309-00-2		eat	-		1.27	5.1E-02	2.0E+00	11.1	1.2E-05	-	-	liv	liv(B)
24	Allyl glycidyl ether	106-92-3	HVP	inh	+		182	7.3E+00	1.4E-02	11.1	8.5E-08	-	-	nas	-
25	Allyl isothiocyanate	57-06-7		gav	?	96		3.8E+00	2.6E-02	11.1	1.6E-07	ubl	-	-	-
26	Allyl isovalerate	2835-39-4		gav	-	123	62.8	4.9E+00	2.0E-02	11.1	1.3E-07	hmo	-	-	hmo
27	1-Allyl-1-nitrosourea	760-56-5		gav		0.341		1.4E-02	7.3E+00	11.1	4.6E-05	lgi lun sto	mgl sto ute	.	.
28	Allylhydrazine.HCl	52207-83-7		wat			34.2	1.4E+00	7.3E-02	11.1	4.5E-07	.	.	lun	lun vsc
29	3-Amino-4-ethoxyacetanilide	17026-81-2		eat	+		2070	8.3E+01	1.2E-03	11.1	7.5E-09	-	-	thy	-
30	3-Amino-9-ethylcarbazole.HCl	6109-97-3		eat	+	57.2	38.6	2.3E+00	4.4E-02	11.1	2.7E-07	ezy liv ski	ezy liv ute	liv	liv
31	3-Amino-9-ethylcarbazole mixture	mixture		eat		26.4	38	1.1E+00	9.5E-02	11.1	5.9E-07	ezy liv ski	ezy	liv	liv
32	1-Amino-2-methylanthraquinone	82-28-0		eat	+	59.2	174	2.4E+00	4.2E-02	11.1	2.6E-07	kid liv	liv	-	liv
33	2-Amino-5-(5-nitro-2-furyl)-1,3,4-oxadiazole	3775-55-1		eat		3.67		1.5E-01	6.8E-01	11.1	4.2E-06	.	id lun mgl s	.	.
34	2-Amino-5-(5-nitro-2-furyl)-1,3,4- thiadiazole	712-68-5		eat		0.662		2.6E-02	3.8E+00	11.1	2.3E-05	.	id lun mgl s	.	.
35	2-Amino-4-(5-nitro-2-furyl)thiazole	38514-71-5		eat		5.85	7.87	2.3E-01	4.3E-01	11.1	2.7E-06	.	sto ubl	.	sto
36	trans-5-Amino-3[2-(5-nitro-2-furyl)vinyl]-1,2,4-oxadiazole	28754-68-9		eat			112	4.5E+00	2.2E-02	11.1	1.4E-07	.	.	hmo sto	hmo sto
37	2-Amino-4-nitrophenol	99-57-0		gav	+	839		3.4E+01	3.0E-03	11.1	1.8E-08	kid	.	-	-
38	2-Amino-5-nitrophenol	121-88-0		gav	+	111		4.4E+00	2.3E-02	11.1	1.4E-07	pan	-	-	-

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-Exu.}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
39	4-Amino-2-nitrophenol	119-34-6		eat	+	309		1.2E+01	8.1E-03	11.1	5.0E-08	ubl	-	-	-
40	2-Amino-4-(p-nitrophenyl)thiazole	08.09.04		eat			9.95	4.0E-01	2.5E-01	11.1	1.6E-06	.	.	.	hmo
41	2-Amino-5-nitrothiazole	121-66-4	HVP	eat	+	44.6		1.8E+00	5.6E-02	11.1	3.5E-07	-	kid lun mgl	-	-
42	2-Aminoanthraquinone	117-79-3	HVP	eat		101	1190	4.0E+00	2.5E-02	11.1	1.5E-07	liv	-	liv	hmo liv
43	o-Aminoazotoluene	97-56-3		eat		4.04		1.6E-01	6.2E-01	11.1	3.8E-06	liv	liv	-	.
44	4-Aminodiphenyl	92-67-1		gav			2.1	8.4E-02	1.2E+00	11.1	7.4E-06	.	.	liv ubl	liv ubl
45	4-Aminodiphenyl.HCl	2113-61-3		gav		0.98		3.9E-02	2.6E+00	11.1	1.6E-05	.	mgl	.	.
46	2-Aminodiphenylene oxide	3693-22-9		eat			4.24	1.7E-01	5.9E-01	11.1	3.7E-06	.	.	liv ubl	liv
47	3-Aminotriazole s	61-82-5	HVP	eat	-	9.94	25.3	4.0E-01	2.5E-01	11.1	1.6E-06	thy	pit thy	liv	liv
48	11-Aminoundecanoic acid	2432-99-7	HVP	eat	-	1100		4.4E+01	2.3E-03	11.1	1.4E-08	liv ubl	-	-	-
49	1-Amyl-1-nitrosourea	10589-74-9		gav		0.555		2.2E-02	4.5E+00	11.1	2.8E-05	hmo lun sto	no lun mgl s	.	.
50	Amylopectin sulfate	9047-13-6		eat		283		1.1E+01	8.8E-03	11.1	5.5E-08	lgi	.	.	.
51	Aniline.HCl	142-04-1		eat	-	269		1.1E+01	9.3E-03	11.1	5.8E-08	per spl vsc	per	-	-
52	o-Anisidine.HCl	134-29-2		eat	+	29.7	966	1.2E+00	8.4E-02	11.1	5.2E-07	kid thy ubl	ubl	ubl	ubl
53	**Aramite**	**140-57-8**		eat		96.7	158	3.9E+00	2.6E-02	11.1	1.6E-07	liv(B)	liv(B)	liv	-
54	Arecoline.HCl	61-94-9		gav			39.5	1.6E+00	6.3E-02	11.1	3.9E-07	.	.	lun sto vsc	lun vsc
55	Aroclor 1254	27323-18-8		eat	-		9.58	3.8E-01	2.6E-01	11.1	1.6E-06	-	-	liv	.
56	Aroclor 1260	11096-82-5		eat		1.74		7.0E-02	1.4E+00	11.1	8.9E-06	liv	liv	.	.
57	Atrazine	1912-24-9	HVP	eat	-	31.7		1.3E+00	7.9E-02	11.1	4.9E-07	mgl	hmo ute	.	-
58	Auramine-O	2465-27-2		eat	+	11	62.7	4.4E-01	2.3E-01	11.1	1.4E-06	liv	.	liv	liv
59	5-Azacytidine	320-67-2		ipj	+	0.17	0.0774	6.8E-03	1.5E+01	11.1	9.1E-05	tes	I	hmo lun ski	hmo mgl ski
60	Azaserine	115-02-6		ipj		0.793		3.2E-02	3.2E+00	11.1	2.0E-05	pan(B)	pan(B)	.	.
61	Azathioprine	446-86-6		eat	+		8.92	3.6E-01	2.8E-01	11.1	1.7E-06	.	-	-	hmo vsc
62	**Azobenzene**	103-33-3		eat	+	24.1		9.6E-01	1.0E-01	11.1	6.4E-07	spl vsc	spl	-	-
63	Azoxymethane	25843-45-2		wat	+w	0.0466		1.9E-03	5.4E+01	11.1	3.3E-04	ezy kid lgi liv	.	.	.
64	1-Azoxypropane	---		gav		0.000241		9.6E-06	1.0E+04	11.1	6.4E-02	nas ski	.	.	.
65	2-Azoxypropane	---		gav		0.00268		1.1E-04	9.3E+02	11.1	5.8E-03	ski	.	.	.
66	Barbital, sodium	144-02-5		eat		105		4.2E+00	2.4E-02	11.1	1.5E-07	kid	.	.	.
67	Bemitradine	88133-11-3		eat		548		2.2E+01	4.6E-03	11.1	2.8E-08	liv thy	liv mgl thy	.	.
68	Benzaldehyde	100-52-7	HVP	gav	-		1490	6.0E+01	1.7E-03	11.1	1.0E-08	.	-	sto	sto
69	Benzene	71-43-2	HVP	gav	-	169	77.5	6.8E+00	1.5E-02	11.1	9.2E-08	ezy nas orc skizy	nas orc suzy	hag hmo luizy	hmo lun m
70	Benzidine	92-87-5		inh	+	1.73		6.9E-02	1.4E+00	11.1	9.0E-06	hmo(B) liv(B)	mo(B) liv(E	.	.
71	Benzidine.2HCl	531-85-1		wat	+		19.7	7.9E-01	1.3E-01	11.1	7.9E-07	.	.	hag liv	hag liv vsc
72	Benzo(a)pyrene	50-32-8		wat	+	0.956	11	3.8E-02	2.6E+00	11.1	1.6E-05	sto(B)	sto(B)	eso	.
73	Benzofuran	271-89-6		gav		424	25.1	1.7E+01	5.9E-03	11.1	3.7E-08	-	kid	liv lun sto	liv lun sto
74	1,4-Benzoquinone	106-51-4		gav			5.07	2.0E-01	4.9E-01	11.1	3.1E-06	.	.	hmo	hmo
75	Benzoyl hydrazine	613-94-5		wat			9.59	3.8E-01	2.6E-01	11.1	1.6E-06	.	.	hmo lun	hmo lun
76	Benzyl acetate	140-11-4	HVP	gav	-		1440	5.8E+01	1.7E-03	11.1	1.1E-08	-	-	liv sto	liv sto
77	**Benzyl chloride**	100-44-7	HVP	gav	+w		61.5	2.5E+00	4.1E-02	11.1	2.5E-07	-	-	sto	sto
78	o-Benzyl-p-chlorophenol	120-32-1		gav	-		1350	5.4E+01	1.9E-03	11.1	1.1E-08	-	-	kid	-
79	Benzylhydrazine.2HCl	20570-96-1		wat			85.3	3.4E+00	2.9E-02	11.1	1.8E-07	.	.	-	lun
80	2-Biphenylamine.HCl	2185-92-4		eat			1120	4.5E+01	2.2E-03	11.1	1.4E-08	-	-	-	vsc
81	Bis(2-chloro-1-methylethyl)ether	108-60-1		gav	+		191	7.6E+00	1.3E-02	11.1	8.1E-08	-	-	liv lun	lun
82	Bis-2-chloroethylether	111-44-4	HVP	orl	+w		11.7	4.7E-01	2.1E-01	11.1	1.3E-06	.	.	liv	-

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-Extr.}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
83	Bis-1,2-(chloromethoxy)ethane	13483-18-6		ipj			4.62	1.8E-01	5.4E-01	11.1	3.4E-06	.	.	.	per
84	Bis-1,4-(chloromethoxy)-p-xylene	56894-91-8		ipj			3.11	1.2E-01	8.0E-01	11.1	5.0E-06	.	.	.	per
85	Bis-(chloromethyl)ether	542-88-1		ihn		0.00357	0.182	1.4E-04	7.0E+02	11.1	4.3E-03	lun nas	.	lun	per
86	Bis(2,3-dibromopropyl)phosphate,	36711-31-6		eat		32		1.3E+00	7.8E-02	11.1	4.8E-07	eso smu sto	so liv smi st	.	.
87	4-Bis(2-hydroxyethyl)amino-2-(5-nitro-2thienyl)quinazoline	33372-39-3		eat		3.14		1.3E-01	8.0E-01	11.1	4.9E-06	mgl smu	.	.	.
88	Bis-2-hydroxyethyldithiocarbamic acid	23746-34-1		orl			37.7	1.5E+00	6.6E-02	11.1	4.1E-07	.	.	liv	.
89	C.I. direct black 38	1937-37-7		eat		1.39	71.6	5.6E-02	1.8E+00	11.1	1.1E-05	liv	liv	liv(B)	liv(B) mgl
90	C.I. direct blue 6	2602-46-2		eat		1.73		6.9E-02	1.4E+00	11.1	9.0E-06	liv	liv	.	.
91	C.I. direct blue 15	2429-74-5		wat		27.5		1.1E+00	9.1E-02	11.1	5.6E-07	ezy lgi liv orc ti	ezy hmo l	.	.
92	C.I. direct blue 218	28407-37-6		eat		1570	857	6.3E+01	1.6E-03	11.1	9.9E-09	orc	.	liv	liv
93	C.I. disperse blue 1	2475-45-8		eat		156		6.2E+00	1.6E-02	11.1	9.9E-08	ubl	ubl	.	.
94	HC blue no. 1	2784-94-3		eat		702	86.3	2.8E+01	3.6E-03	11.1	2.2E-08	.	lun	liv thy	liv
95	HC blue no. 1 (purified)	2784-94-3		eat			78.7	3.1E+00	3.2E-02	11.1	2.0E-07	.	.	.	liv
96	Bromate, potassium	02.01.58		wat		9.81		3.9E-01	2.5E-01	11.1	1.6E-06	kid per	kid	.	.
97	**Bromodichloromethane**	75-27-4		gav	-	72.5	47.7	2.9E+00	3.4E-02	11.1	2.1E-07	kid lgi	kid lgi liv	kid	liv
98	Bromoethane	74-96-4	HVP	inh		149	535	6.0E+00	1.7E-02	11.1	1.0E-07	adr lun nrv	.	.	ute
99	Bromoethanol	540-51-2		wat	+		76.1	3.0E+00	3.3E-02	11.1	2.0E-07	.	.	sto	sto
100	C.I. direct brown 95	16071-86-6		eat		2.07		8.3E-02	1.2E+00	11.1	7.5E-06	.	liv	.	.
101	Budesonide	51333-22-3		wat		0.291		1.2E-02	8.6E+00	11.1	5.3E-05	liv	.	.	.
102	1,3-Butadiene	106-99-0	HVP	inh	+	261	13.9	1.0E+01	9.6E-03	11.1	5.9E-08	tes	mgl	hag hmo kid liv	wag hmo liv lu
103	N-n-Butyl-N-formylhydrazine	16120-70-0		wat			19.3	7.7E-01	1.3E-01	11.1	8.0E-07	.	.	lun pre	eli lun
104	N-Butyl-N-(4-hydroxybutyl)	06.11.17		wat		0.457		1.8E-02	5.5E+00	11.1	3.4E-05	tes ubl	ubl	.	.
105	N-n-Butyl-N-nitrosourea	869-01-2		wat		0.517		2.1E-02	4.8E+00	11.1	3.0E-05	ezy eso hmo lgr	ezy eso hmo l	.	.
106	Butylated hydroxyanisole s	25013-16-5		eat	-	745	5530	3.0E+01	3.4E-03	11.1	2.1E-08	sto	sto	sto	B-
107	Butylated hydroxytoluene	128-37-0	HVP	eat	-		653	2.6E+01	3.8E-03	11.1	2.4E-08	-	-	liv lun	-
108	1,1-di-n-Butylhydrazine	7422-80-2		wat			45.2	1.8E+00	5.5E-02	11.1	3.4E-07	.	.	liv lun sto	lun sto
109	n-Butylhydrazine.HCl	56795-65-4		wat			12.1	4.8E-01	2.1E-01	11.1	1.3E-06	.	.	lun	lun
110	1,2-di-n-Butylhydrazine.2HCl	78776-28-0		wat			46.2	1.8E+00	5.4E-02	11.1	3.4E-07	.	.	hmo kid lun	hmo lun
111	beta-Butyrolactone	3068-88-0		gav	+	13.8		5.5E-01	1.8E-01	11.1	1.1E-06	.	sto	.	.
112	*Cadmium chloride s*	10108-64-2		inh	-	0.0114		4.6E-04	2.2E+02	11.1	1.4E-03	hmo lun pro tes	lun	.	.
113	*Cadmium sulphate (1:1) s*	10124-36-4	HVP	inh		0.0217		8.7E-04	1.2E+02	11.1	7.2E-04	lun	lun	.	.
114	Caffeic acid	331-39-5		eat		297	4900	1.2E+01	8.4E-03	11.1	5.2E-08	kid sto	sto	lun sto	kid sto
115	Calciferol	50-14-6		eat			39.6	1.6E+00	6.3E-02	11.1	3.9E-07	.	.	.	mgl
116	Capsaicin	404-86-4		eat			167	6.7E+00	1.5E-02	11.1	9.3E-08	.	.	lgi	lgi
117	Captafol	01.06.25		eat		59.4	108	2.4E+00	4.2E-02	11.1	2.6E-07	kid liv	kid liv	liv smi sto vsc	liv smi ste vsc
118	Carbamyl hydrazine.HCl	563-41-7		wat			223	8.9E+00	1.1E-02	11.1	7.0E-08	.	.	lun	lun vsc
119	1-Carbamyl-2-phenylhydrazine	103-03-7		wat			165	6.6E+00	1.5E-02	11.1	9.4E-08	.	.	lun	lun
120	Carbaryl	63-25-2		gav		14.1		5.6E-01	1.8E-01	11.1	1.1E-06	tba(B)	tba(B)	.	.
121	Carbazole	86-74-8	HVP	eat			164	6.6E+00	1.5E-02	11.1	9.5E-08	.	.	liv sto	liv sto
122	**Carbon tetrachloride**	56-23-5	HVP	gav	-	2.29	150	9.2E-02	1.1E+00	11.1	6.8E-06	liv	liv mgl	adr liv	adr liv
123	Carboxymethylnitrosourea	60391-92-6		wat		4.31		1.7E-01	5.8E-01	11.1	3.6E-06	ski	mgl smi	.	.
124	Carrageenan, acid-degraded	---		eat		2310		9.2E+01	1.1E-03	11.1	6.7E-09	lgi	lgi(B)	.	.
125	Catechol	120-80-9		eat	-	118	244	4.7E+00	2.1E-02	11.1	1.3E-07	sto	sto	sto	sto
126	Chloral hydrate	302-17-0		wat	+		106	4.2E+00	2.4E-02	11.1	1.5E-07	.	.	liv	.

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10th} [mg/kg-day]	$\beta_{ED10\text{-Exp.}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
127	Chloramben	133-90-4		eat			5230	2.1E+02	4.8E-04	11.1	3.0E-09	-	-	-	liv
128	Chlorambucil	305-03-3		ipj	+	0.896	0.133	3.6E-02	2.8E+00	11.1	1.7E-05	hmo	ezy mgl nrv	hmo lun	lun
129	Chlordane, technical grade	57-74-9		eat	+		2.99	1.2E-01	8.4E-01	11.1	5.2E-06	-	-	liv	liv
130	Chlorendic acid	115-28-6		eat	-	40.8	141	1.6E+00	6.1E-02	11.1	3.8E-07	liv pan	liv	liv	-
131	Chlorinated paraffins (C12, 60% chlorine)	63449-39-8	HVP	gav		222	113	8.9E+00	1.1E-02	11.1	7.0E-08	kid liv	liv thy	liv	liv thy
132	Chlorinated paraffins (C23, 43% chlorine)	63449-39-8	HVP	gav			6540	2.6E+02	3.8E-04	11.1	2.4E-09	-	-	hmo	-
133	4-Chloro-4'-aminodiphenylether	101-79-1		eat		37.6	346	1.5E+00	6.6E-02	11.1	4.1E-07	liv	.	-	ubl vsc
134	2-Chloro-5-(3,5-dimethylpiperidino-sulphonyl)benzoic acid	37087-94-8		eat		4.85		1.9E-01	5.2E-01	11.1	3.2E-06	liv	.		
135	3-Chloro-2-methylpropene	563-47-3	HVP	gav	-	113	77.7	4.5E+00	2.2E-02	11.1	1.4E-07	sto	sto	sto	sto
136	1-Chloro-2-nitrobenzene	88-73-3	HVP	eat	+		157	6.3E+00	1.6E-02	11.1	9.9E-08	-	.	liv	liv
137	1-Chloro-4-nitrobenzene	100-00-5	HVP	eat	+		473	1.9E+01	5.3E-03	11.1	3.3E-08	-	.	liv vsc	vsc
138	4-Chloro-m-phenylenediamine	5131-60-2		eat		315	1230	1.3E+01	7.9E-03	11.1	4.9E-08	adr	-	.	liv
139	4-Chloro-o-phenylenediamine	95-83-0		eat	+	214	1340	8.6E+00	1.2E-02	11.1	7.3E-08	sto ubl	sto ubl	liv	liv
140	5-Chloro-o-toluidine	95-79-4		eat	-		195	7.8E+00	1.3E-02	11.1	8.0E-08	-	-	liv vsc	liv vsc
141	4-Chloro-o-toluidine.HCl	3165-93-3		eat	-		25.8	1.0E+00	9.7E-02	11.1	6.0E-07	-	-	vsc	vsc
142	2-Chloro-1,1,1-trifluoroethane	75-88-7		gav		87.3		3.5E+00	2.9E-02	11.1	1.8E-07	tes	ute		
143	[4-Chloro-6-(2,3-xylidino)-2-pyrimidinylthio]acetic acid	50892-23-4		eat		9.69	10.8	3.9E-01	2.6E-01	11.1	1.6E-06	liv	.	liv	
144	4-Chloro-6-(2,3-xylidino)-2-pyrimidinylthio(N-beta-hydroxyethyl)	65089-17-0		eat		6.49	44.6	2.6E-01	3.9E-01	11.1	2.4E-06	liv	.	.	liv
145	Chloroacetaldehyde	107-20-0		wat			36.1	1.4E+00	6.9E-02	11.1	4.3E-07	.	.	liv	.
146	p-Chloroaniline.HCl	20265-96-7		gav		7.62	89.5	3.0E-01	3.3E-01	11.1	2.0E-06	spl	.	liv vsc	.
147	Chlorobenzene	108-90-7	HVP	gav	-	247		9.9E+00	1.0E-02	11.1	6.3E-08	liv	.	-	-
148	Chlorobenzilate	510-15-6		eat	-		93.9	3.8E+00	2.7E-02	11.1	1.7E-07	-	-	liv	liv
149	**Chlorodibromomethane**	124-48-1		gav	-		139	5.6E+00	1.8E-02	11.1	1.1E-07	-	-	-	liv
150	Chloroethane	75-00-3	HVP	inh			1810	7.2E+01	1.4E-03	11.1	8.6E-09	-	-	[	ute
151	1-Chloroethylnitroso-3-(2-hydroxypropyl)	---		wat		0.124		5.0E-03	2.0E+01	11.1	1.3E-04	lun	.	.	
152	Chlorofluoromethane	593-70-4		gav		27.5		1.1E+00	9.1E-02	11.1	5.6E-07	sto	sto	.	
153	**Chloroform s**	67-66-3	HVP	gav		262	90.3	1.0E+01	9.5E-03	11.1	5.9E-08	kid	liv	kid liv	liv
154	Chloromethyl methyl ether s	107-30-2	HVP	inh		5.5		2.2E-01	4.5E-01	11.1	2.8E-06	mix	.	.	
155	3-(Chloromethyl)pyridine.HCl	6959-48-4		gav	+	433	229	1.7E+01	5.8E-03	11.1	3.6E-08	sto	-	sto	sto
156	3-(p-Chlorophenyl)-1,1-dimethylurea	150-68-5		eat		131		5.2E+00	1.9E-02	11.1	1.2E-07	kid liv	-	-	-
157	1-(4-Chlorophenyl)-1-phenyl-2-propynyl	10473-70-8		eat		8.78		3.5E-01	2.8E-01	11.1	1.8E-06	nrv sma	.	.	
158	2-Chloropropanal	683-50-1		gav			12.9	5.2E-01	1.9E-01	11.1	1.2E-06	.	.	-	sto
159	1-Chloropropene	590-21-6		gav			5.05	2.0E-01	5.0E-01	11.1	3.1E-06	.	.	-	sto
160	Chlorothalonil	1897-45-6		eat	-	2270		9.1E+01	1.1E-03	11.1	6.8E-09	kid	kid	-	-
161	Chlorozotocin	54749-90-5		ipj		0.0375		1.5E-03	6.7E+01	11.1	4.1E-04	per	per		
162	Chrysazin	117-10-2		eat		245	201	9.8E+00	1.0E-02	11.1	6.3E-08	lgi		liv	
163	Cinnamyl anthranilate	87-29-6		eat	-	12100	2580	4.8E+02	2.1E-04	11.1	1.3E-09	kid pan	-	liv	liv
164	Ciprofibrate	52214-84-3		eat		2.16	6.2	8.6E-02	1.2E+00	11.1	7.2E-06	liv sto	sto	liv	
165	Citrinin	518-75-2		eat		7.48		3.0E-01	3.3E-01	11.1	2.1E-06	kid	.	.	
166	Clivorine	33979-15-6		wat		0.5		2.0E-02	5.0E+00	11.1	3.1E-05	liv(B) vsc(B)	iv(B) vsc(B	.	
167	Clofibrate	637-07-0		eat		169		6.8E+00	1.5E-02	11.1	9.2E-08	liv pan	.	.	.
168	Clophen A 30	55600-34-5		eat		157		6.3E+00	1.6E-02	11.1	9.9E-08	liv	.	.	
169	Compound LY171883	88107-10-2		eat			112	4.5E+00	2.2E-02	11.1	1.4E-07	.	.	-	liv
170	Coumarin s	91-64-5		gav	+	13.9	103	5.6E-01	1.8E-01	11.1	1.1E-06	kid	-	lun	liv lun

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-}Extr}$ (Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
171	m-Cresidine			gav	+	470		1.9E+01	5.3E-03	11.1	3.3E-08	ubl	ubl	I	-
172	p-Cresidine	120-71-8		eat	+	98	54.3	3.9E+00	2.6E-02	11.1	1.6E-07	liv nas ubl	nas ubl	ubl	liv ubl
173	Crotonaldehyde	123-73-9	HVP	wat	+	4.2		1.7E-01	6.0E-01	11.1	3.7E-06	liv	.	.	.
174	Cupferron	135-20-6		eat	+	8.35	585	3.3E-01	3.0E-01	11.1	1.9E-06	liv sto vsc	zy liv sto vs	vsc	zy hag liv vsc
175	Cyclamate, sodium	139-05-9		wat			667	2.7E+01	3.7E-03	11.1	2.3E-08	B-	B-	liv	tba
176	Cyclochlorotine	12663-46-6		eat			23.6	9.4E-01	1.1E-01	11.1	6.6E-07	.	.	liv	.
177	Cyclophosphamide	50-18-0		ipj		2.21	5.96	8.8E-02	1.1E+00	11.1	7.0E-06	hmo(B) nrv(B)	mo(B) nrv(I	lun	hmo lun
178	Cytembena	16170-75-5		ipj	+	2.77		1.1E-01	9.0E-01	11.1	5.6E-06	per	mgl	-	-
179	Dacarbazine	04.03.42		ipj	+	0.71	0.966	2.8E-02	3.5E+00	11.1	2.2E-05	.	hmo mgl ute	hmo lun vsc	mo lun ute vs
180	Daminozide	1596-84-5		wat		2500	1030	1.0E+02	1.0E-03	11.1	6.2E-09	-	ute	kid lun vsc	lun vsc
181	Dapsone	80-08-0		eat	-	22.4		9.0E-01	1.1E-01	11.1	6.9E-07	per spl	-	-	-
182	p,p'-DDD	72-54-8		eat			30.7	1.2E+00	8.1E-02	11.1	5.1E-07	-	-	liv lun	lun
183	p,p'-DDE s	72-55-9		eat	-		12.5	5.0E-01	2.0E-01	11.1	1.2E-06	-	-	liv	liv
184	DDT s	50-29-3	HVP	eat	-	84.7	12.3	3.4E+00	3.0E-02	11.1	1.8E-07	liv	liv	liv	hmo liv
185	Decabromodiphenyl oxide	1163-19-5	HVP	eat	-	3340		1.3E+02	7.5E-04	11.1	4.6E-09	liv	liv	-	-
186	Dehydroepiandrosterone acetate	853-23-6		eat		31.4		1.3E+00	8.0E-02	11.1	4.9E-07	liv	.	.	.
187	Dextran sulfate sodium (DS-M-1)	9011-18-1		eat		196		7.8E+00	1.3E-02	11.1	7.9E-08	.	.	.	.
188	N-1-Diacetamidofluorene	63019-65-8		eat		19		7.6E-01	1.3E-01	11.1	8.2E-07	.	.	.	.
189	Diallate	2303-16-4		orl			26.7	1.1E+00	9.4E-02	11.1	5.8E-07	.	.	liv	-
190	1,1-Diallylhydrazine	04.11.64		wat			29.6	1.2E+00	8.4E-02	11.1	5.2E-07	.	.	lun sto	lun sto
191	1,2-Diallylhydrazine.2HCl	26072-78-6		wat			33.8	1.4E+00	7.4E-02	11.1	4.6E-07	.	.	lun	lun
192	Diallylnitrosamine s	16338-97-9		wat		33.9		1.4E+00	7.4E-02	11.1	4.6E-07	nas	nas	.	.
193	4,6-Diamino-2-(5-nitro-2-furyl)-S-triazine	720-69-4		eat		1.71		6.8E-02	1.5E+00	11.1	9.1E-06	.	mgl	.	.
194	2,4-Diaminoanisole sulfate	39156-41-7		eat	+	183	906	7.3E+00	1.4E-02	11.1	8.5E-08	ezy pre ski thy	ii ezy mgl th	thy	thy
195	2,4-Diaminophenol.2HCl	137-09-7		gav	+		143	5.7E+00	1.7E-02	11.1	1.1E-07	-	-	kid	-
196	2,4-Diaminotoluene	95-80-7	HVP	eat	+	2.47	26.7	9.9E-02	1.0E+00	11.1	6.3E-06	liv	liv mgl	-	liv
197	2,4-Diaminotoluene.2HCl	636-23-7		eat		4.42	203	1.8E-01	5.7E-01	11.1	3.5E-06	liv sub	.	liv vsc	liv
198	3-Diazotyramine.HCl	---		wat		37.6		1.5E+00	6.6E-02	11.1	4.1E-07	orc	.	.	.
199	Dibenz(a,h)anthracene	53-70-3		wat	+		5.88	2.4E-01	4.3E-01	11.1	2.6E-06	.	.	lun	.
200	3-Dibenzofuranamine	4106-66-5		eat		2.48		9.9E-02	1.0E+00	11.1	6.3E-06	tba	.	.	.
201	1,2-Dibromo-3-chloropropane	96-12-8		gav	+	0.259	2.72	1.0E-02	9.7E+00	11.1	6.0E-05	nas orc sto	lr mgl nas o	lun nas sto	lun nas sto
202	Dibromodulcitol	10318-26-0		ipj	+	8.37	11	3.3E-01	3.0E-01	11.1	1.9E-06	ski	.	hmo lun	hmo lun
203	1,2-Dibromoethane	106-93-4	HVP	wat	+	1.52	7.45	6.1E-02	1.6E+00	11.1	1.0E-05	nas per pit sto	v lun mgl n	lun sto vsc	so lun mgl na
204	Dibromomannitol	488-41-5		ipj	+	27.6	14.9	1.1E+00	9.1E-02	11.1	5.6E-07	per ski	mgl per	lun	hmo lun
205	1,3-Dibutyl-1-nitrosourea	56654-52-5		wat		4.28		1.7E-01	5.8E-01	11.1	3.6E-06	.	hmo mgl	.	.
206	3,5-Dichloro(N-1,1-dimethyl-2-propynyl)benzamide	23950-58-5		eat			119	4.8E+00	2.1E-02	11.1	1.3E-07	.	.	liv	.
207	2,6-Dichloro-p-phenylenediamine	609-20-1		eat			803	3.2E+01	3.1E-03	11.1	1.9E-08	-	-	liv	liv
208	Dichloroacetic acid	79-43-6		wat			49.3	2.0E+00	5.1E-02	11.1	3.1E-07	.	.	liv	.
209	Dichloroacetylene	7572-29-4		inh		3.58	0.574	1.4E-01	7.0E-01	11.1	4.3E-06	kid liv	hmo kid liv	hag kid	hag kid
210	1,4-Dichlorobenzene	106-46-7	HVP	gav	-	644	398	2.6E+01	3.9E-03	11.1	2.4E-08	kid	-	liv	liv
211	3,3'-Dichlorobenzidine s	91-94-1	HVP	eat		28.1		1.1E+00	8.9E-02	11.1	5.5E-07	ezy hmo mgl	mgl	.	.
212	trans-1,4-Dichlorobutene-2	110-57-6	HVP	ipj			1.52	6.1E-02	1.6E+00	11.1	1.0E-05	.	.	.	per
213	1,2-Dichloroethane	107-06-2	HVP	gav	+	8.04	101	3.2E-01	3.1E-01	11.1	1.9E-06	sto sub vsc	mgl	lun	lun mgl ute
214	1,2-Dichloropropane	78-87-5		gav	+		276	1.1E+01	9.1E-03	11.1	5.6E-08	-	-	liv	liv

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
215	Dichlorvos	62-73-7	HVP	gav	+	4.16	70.4	1.7E-01	6.0E-01	11.1	3.7E-06	hmo pan	-	sto	sto
216	Dicofol	115-32-2	HVP	eat	-		32.9	1.3E+00	7.6E-02	11.1	4.7E-07	-	-	liv	-
217	Dieldrin s	60-57-1		eat	-		0.912	3.6E-02	2.7E+00	11.1	1.7E-05	-	-	liv	liv
218	N,N-Diethyl-4-(4'-[pyridyl-1'-oxide]azo)	7347-49-1		eat		1.63		6.5E-02	1.5E+00	11.1	9.5E-06	liv	.	.	.
219	Diethylacetamide	685-91-6		gav		8.85		3.5E-01	2.8E-01	11.1	1.8E-06	kid	.	.	.
220	Diethylene glycol	111-46-6	HVP	eat	-	1660		6.6E+01	1.5E-03	11.1	9.3E-09	ubl	.	.	.
221	Diethylstilbestrol	56-53-1		eat	-	0.114	0.0372	4.6E-03	2.2E+01	11.1	1.4E-04	adr pit	-	mgl pit tes thy	ngl ova pit thy
222	N,N'-Diethylthiourea	105-55-5		eat	-	24		9.6E-01	1.0E-01	11.1	6.5E-07	thy	thy	-	-
223	1,2-Diformylhydrazine	628-36-4		wat			668	2.7E+01	3.7E-03	11.1	2.3E-08	.	.	lun	lun
224	Diftalone	21626-89-1		eat			865	3.5E+01	2.9E-03	11.1	1.8E-08	.	.	vsc	liv vsc
225	Diglycidyl resorcinol ether	101-90-6		gav		3.78	24.3	1.5E-01	6.6E-01	11.1	4.1E-06	sto	sto	sto	sto
226	1,2-Dihydro-2-(5-nitro-2-thienyl)	33389-33-2		eat		1.53		6.1E-02	1.6E+00	11.1	1.0E-05	.	tba	.	.
227	3,6-Dihydro-2-nitroso-2H-1,2-oxazine	3276-41-3		wat		90.6		3.6E+00	2.8E-02	11.1	1.7E-07	tba(B)	tba(B)	.	.
228	3,4-Dihydrocoumarin	119-84-6		gav	-	2970	723	1.2E+02	8.4E-04	11.1	5.2E-09	kid	-	-	liv
229	Dihydrosafrole	94-58-6		orl		143	125	5.7E+00	1.7E-02	11.1	1.1E-07	eso(B)	eso(B)	liv	lun
230	Dimethoxane	828-00-2		wat	+	716		2.9E+01	3.5E-03	11.1	2.2E-08	hmo kid liv ski	.	.	.
231	2,5-Dimethoxy-4'-aminostilbene	5803-51-0		eat		0.721	95.9	2.9E-02	3.5E+00	11.1	2.2E-05	ezy ski smi sto	.	liv lun	-
232	3,3'-Dimethoxybenzidine-4,4'-	91-93-0		orl	+	1630		6.5E+01	1.5E-03	11.1	9.5E-09	hmo ski	hmo ute	-	-
233	3,3'-Dimethoxybenzidine.2HCl	20325-40-0		wat		1.04		4.2E-02	2.4E+00	11.1	1.5E-05	ezy hmo lgi liv	li ezy lgi liv	-	-
234	5,6-Dimethoxysterigmatocystin	65176-75-2		eat		0.364		1.5E-02	6.9E+00	11.1	4.3E-05	liv	.	.	.
235	N,N-Dimethyl-4-aminoazobenzene s	60-11-7		eat		3.31		1.3E-01	7.6E-01	11.1	4.7E-06	.	liv	.	.
236	Dimethyl hydrogen phosphite	868-85-9	HVP	gav	+w	139		5.6E+00	1.8E-02	11.1	1.1E-07	lun sto	-	-	-
237	Dimethyl methylphosphonate	756-79-6	HVP	gav	-	700		2.8E+01	3.6E-03	11.1	2.2E-08	kid	-	l	-
238	Dimethyl morpholinophosphoramidate	597-25-1		gav	-	614		2.5E+01	4.1E-03	11.1	2.5E-08	hmo	hmo	-	-
239	4,6-Dimethyl-2-(5-nitro-2-furyl)	59-35-8		eat		1.39		5.6E-02	1.8E+00	11.1	1.1E-05	.	d mgl smi s		
240	1,2-Dimethyl-5-nitroimidazole	551-92-8		eat		17		6.8E-01	1.5E-01	11.1	9.1E-07	.	mgl		.
241	6-Dimethylamino-4,4-diphenyl-3-heptanol	43033-72-3		eat		68		2.7E+00	3.7E-02	11.1	2.3E-07	liv	liv	-	-
242	trans-2-[(Dimethylamuno)methylimuno]	55738-54-0		eat		22.4		9.0E-01	1.1E-01	11.1	6.9E-07	.	n mgl smi s		
243	Dimethylaminoethylnitrosoethylurea, nitrite salt	---		gav		0.704		2.8E-02	3.6E+00	11.1	2.2E-05	-	mgl ute	.	.
244	N,N-Dimethylaniline	121-69-7	HVP	gav	-	125		5.0E+00	2.0E-02	11.1	1.2E-07	bon	-	-	-
245	7,12-Dimethylbenz(a)anthracene	57-97-6		eat	+		0.084	3.4E-03	3.0E+01	11.1	1.8E-04	.	.	.	vsc
246	3,3'-Dimethylbenzidine.2HCl	612-82-8		wat	+	0.629	28.6	2.5E-02	4.0E+00	11.1	2.5E-05	ezy lgi liv lun	li ezy lgi liv	lun	-
247	Dimethylcarbamyl chloride s	79-44-7		inh	+		5.37	2.1E-01	4.7E-01	11.1	2.9E-06	.	.	.	pet
248	1,1-Dimethylhydrazine s	57-14-7		wat			3.96	1.6E-01	6.3E-01	11.1	3.9E-06	-	-	liv lun vsc	lun vsc
249	1,2-Dimethylhydrazine.2HCl s	306-37-6		wat			0.114	4.6E-03	2.2E+01	11.1	1.4E-04	.	.	lun vsc	lun vsc
250	2-(2,2-Dimethylhydrazino)	26049-69-4		eat		0.41		1.6E-02	6.1E+00	11.1	3.8E-05	.	hmo mgl	.	.
251	Dimethylnitramine	4164-28-7		wat		0.547		2.2E-02	4.6E+00	11.1	2.8E-05	liv nas	liv nas	.	.
252	Dimethylvinyl chloride	513-37-1		gav	+	31.8	14.9	1.3E+00	7.9E-02	11.1	4.9E-07	eso nas ore ski	so nas ore st	pre sto	sto
253	Dinitrosohomopiperazine	55557-00-1		wat		0.0615		2.5E-03	4.1E+01	11.1	2.5E-04	.	so liv nas or	.	.
254	Dinitrosopiperazine	140-79-4		gav			3.6	1.4E-01	6.9E-01	11.1	4.3E-06	.	.	sto	sto
255	2,6-Dinitrotoluene	606-20-2	HVP	eat		0.574		2.3E-02	4.4E+00	11.1	2.7E-05	liv			
256	**Dinitrotoluene, technical grade**	25321-14-6	HVP	eat		8.02		3.2E-01	3.1E-01	11.1	1.9E-06	liv			
257	**1,4-Dioxane**	123-91-1	HVP	wat	-	334	838	1.3E+01	7.5E-03	11.1	4.6E-08	liv(B) nas	liv nas	liv	liv
258	Dipentylnitrosamine	13256-06-9		eat		4.03		1.6E-01	6.2E-01	11.1	3.9E-06	liv	liv	.	.

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
259	5,5-Diphenylhydantoin	57-41-0		eat	-		59.1	2.4E+00	4.2E-02	11.1	2.6E-07	-	-	-	liv
260	Dipyrone	68-89-3	HVP	wat			630	2.5E+01	4.0E-03	11.1	2.5E-08	-	-	liv	liv
261	Enovid	8015-30-3		eat			0.279	1.1E-02	9.0E+00	11.1	5.6E-05	.	.	-	pit
262	Epichlorohydrin	106-89-8	HVP	gav	+	2.96		1.2E-01	8.4E-01	11.1	5.2E-06	sto	sto		-
263	1,2-Epoxybutane	106-88-7	HVP	inh	+	220		8.8E+00	1.1E-02	11.1	7.1E-08	lun nas	-	-	-
264	Estradiol	50-28-2		eat			0.282	1.1E-02	8.9E+00	11.1	5.5E-05		.	.	mgl
265	Estradiol mustard	22966-79-6		gav			1.45	5.8E-02	1.7E+00	11.1	1.1E-05	-	-	hmo lun myc	stmo lun myc s
266	Estragole	140-67-0	HVP	eat	-		51.8	2.1E+00	4.8E-02	11.1	3.0E-07		.	.	liv
267	Ethionamide	536-33-4		gav	-		69.3	2.8E+00	3.6E-02	11.1	2.2E-07	-	-	-	thy
268	Ethionine	13073-35-3		eat		4.97		2.0E-01	5.0E-01	11.1	3.1E-06	liv		.	.
269	dl-Ethionine	67-21-0		eat	-	9.11	71.4	3.6E-01	2.7E-01	11.1	1.7E-06	liv	.	liv	liv
270	o-Ethoxybenzamide	938-73-8		eat			513	2.1E+01	4.9E-03	11.1	3.0E-08		.	liv	-
271	Ethyl acrylate	140-88-5	HVP	gav	-	120	324	4.8E+00	2.1E-02	11.1	1.3E-07	sto	sto	sto	sto
272	Ethyl alcohol	64-17-5	HVP	wat	-	9110		3.6E+02	2.7E-04	11.1	1.7E-09	adr liv pan pit	-	-	-
273	Z-Ethyl-O,N,N-azoxyethane	16301-26-1		wat		0.022		8.8E-04	1.1E+02	11.1	7.1E-04	eso liv nas vsc	.	.	.
274	Z-Ethyl-O,N,N-azoxymethane	57497-29-7		wat		0.0189		7.6E-04	1.3E+02	11.1	8.2E-04	lgi liv smi vsc	.	.	.
275	Ethyl benzene	100-41-4	HVP	gav	-	1210		4.8E+01	2.1E-03	11.1	1.3E-08	tba	tba	.	.
276	N-Ethyl-N-formylhydrazine	74920-78-8		wat			2.8	1.1E-01	8.9E-01	11.1	5.5E-06		.	gal liv lun pre	lun vsc
277	N-Ethyl-N'-nitro-N-nitrosoguanidine	63885-23-4		wat			2.84	1.1E-01	8.8E-01	11.1	5.5E-06		.	eso(B) smi(B)	eso(B) smi(B
278	1-Ethyl-1-nitrosourea	759-73-9		wat	+	0.948		3.8E-02	2.6E+00	11.1	1.6E-05	nrv smi thy	nrv smi	.	.
279	Ethylene imine	151-56-4	HVP	orl			0.377	1.5E-02	6.6E+00	11.1	4.1E-05	.	.	liv lun	lun
280	Ethylene oxide	75-21-8	HVP	inh		21.3	63.7	8.5E-01	1.2E-01	11.1	7.3E-07	hmo nrv per	nrv sto	bag lun	ag hmo lun m
281	Ethylene thiourea	96-45-7		eat	?	7.9	23.5	3.2E-01	3.2E-01	11.1	2.0E-06	liv(B) thy	liv(B) thy	liv pit thy	liv pit thy
282	**di(2-Ethylhexyl)adipate**	103-23-1	HVP	eat			3880	1.6E+02	6.4E-04	11.1	4.0E-09	-	-	liv	liv
283	**di(2-Ethylhexyl)phthalate**	117-81-7	HVP	eat		647	894	2.6E+01	3.9E-03	11.1	2.4E-08	liv	liv	liv	liv
284	Ethylhydrazine.HCl	18413-14-4		wat			6.56	2.6E-01	3.8E-01	11.1	2.4E-06	.	.	lun vsc	lun vsc
285	1-Ethylnitroso-3-(2-hydroxyethyl)-urea	---		wat		0.522		2.1E-02	4.8E+00	11.1	3.0E-05	ski	mgl ski ute	.	.
286	1-Ethylnitroso-3-(2-oxopropyl)-urea	---		gav		0.181		7.2E-03	1.4E+01	11.1	8.6E-05	lgi lun nrv per	a lun mgl ni	.	.
287	Ethylnitrosocyanamide	38434-77-4		wat		3.68		1.5E-01	6.8E-01	11.1	4.2E-06	nas	nas	.	.
288	4-Ethylsulphonylnaphthalene-1-sulfonamide	842-00-2		eat			21.1	8.4E-01	1.2E-01	11.1	7.4E-07	.	.	.	ubl
289	N-(2-Fluorenyl)-2,2,2-trifluoroacetamide	363-17-7		eat		1.62		6.5E-02	1.5E+00	11.1	9.6E-06	.	ezy liv mgl	.	.
290	4'-Fluoro-4-aminodiphenyl	324-93-6		gav			1.14	4.6E-02	2.2E+00	11.1	1.4E-05	.	.	liv	liv
291	N-4-(4'-Fluorobiphenyl)acetamide	398-32-3		eat		1.01		4.0E-02	2.5E+00	11.1	1.5E-05	kid	.	.	.
292	2-Fluoroethyl-nitrosourea	69112-98-7		gav		0.125		5.0E-03	2.0E+01	11.1	1.2E-04	sto	.	.	.
293	5-Fluorouracil	51-21-8		ipj	-		2.96	1.2E-01	8.4E-01	11.1	5.2E-06	-	.	lun	hmo lun
294	Formaldehyde s	50-00-0	HVP	inh	+	2.19	43.9	8.8E-02	1.1E+00	11.1	7.1E-06	hmo nas	hmo nas	nas	-
295	Formic acid 2-(4-methyl-2-thiazolyl)	32852-21-4		eat		14.4		5.8E-01	1.7E-01	11.1	1.1E-06	.	mgl	.	.
296	Formic acid 2-[4-(5-nitro-2-furyl)-2-thiazolyl]hydrazide s	3570-75-0		eat		5.06	10.8	2.0E-01	4.9E-01	11.1	3.1E-06	kid liv mgl	ezy hmo kid l	.	hmo sto
297	Formylhydrazine	624-84-0		wat			36.4	1.5E+00	6.9E-02	11.1	4.3E-07	.	.	lun	lun
298	Fosetyl Al	39148-24-8	HVP	eat		3660		1.5E+02	6.8E-04	11.1	4.2E-09	ubl	-	.	.
299	Fumonisin B1	116355-83-0		eat		1.16		4.6E-02	2.2E+00	11.1	1.3E-05	liv	.	.	.
300	Furan	110-00-9		gav	-	0.396	2.72	1.6E-02	6.3E+00	11.1	3.9E-05	hmo liv	hmo liv	adr liv	adr liv
301	Furfural s	98-01-1	HVP	gav	?	683	197	2.7E+01	3.7E-03	11.1	2.3E-08	liv	-	liv	liv
302	Furosemide	54-31-9		eat	-		732	2.9E+01	3.4E-03	11.1	2.1E-08	-	-	-	mgl

	Chemical	CAS RN	Production (OECD, 1997)	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
303	Gentian violet	548-62-9		eat			90.5	3.6E+00	2.8E-02	11.1	1.7E-07			hag liv	hag hmo liv
304	Glu-P-1	67730-11-4		eat		4.69	5.4	1.9E-01	5.3E-01	11.1	3.3E-06	ezy lgi liv sma	li ezy lgi liv	liv vsc	liv vsc
305	Glu-P-2	67730-10-3		eat		42.3	16	1.7E+00	5.9E-02	11.1	3.7E-07	ezy lgi liv nrv	li ezy lgi liv	liv vsc	liv vsc
306	N2-gamma-Glutamyl-p-hydrazinobenzoic acid	---		gav			277	1.1E+01	9.0E-03	11.1	5.6E-08			sub	
307	Glycidol s	556-52-5		gav	+	4.28	34.7	1.7E-01	5.8E-01	11.1	3.6E-06	ezy lgi mgl nrv	hmo mgl n	hag liv lun ski	hag mgl ski sut
308	FD & C green no. 1	4680-78-8		eat		6060		2.4E+02	4.1E-04	11.1	2.6E-09	hmo(B) liv	hmo(B) liv	-	
309	FD & C green no. 2	5141-20-8		eat		5640		2.3E+02	4.4E-04	11.1	2.8E-09	hmo(B)	hmo(B)	-	
310	Griseofulvin s	126-07-8		eat	-		1660	6.6E+01	1.5E-03	11.1	9.3E-09			liv	
311	HCDD mixture	mixture		gav		0.000596	0.00143	2.4E-05	4.2E+03	11.1	2.6E-02	-	liv	liv	liv
312	Hematoxylin	517-28-2		eat	-	1000		4.0E+01	2.5E-03	11.1	1.6E-08	hmo(B)	hmo(B)		
313	Heptachlor	76-44-8		eat			1.21	4.8E-02	2.1E+00	11.1	1.3E-05	-	-	liv	liv
314	**Hexachlorobenzene s**	118-74-1	HVP	eat	-	3.51	65.1	1.4E 01	7.1E-01	11.1	4.4E-06	liv	liv	liv	liv
315	**Hexachlorobutadiene**	87-68-3	HVP	eat	-	65.8		2.6E+00	3.8E-02	11.1	2.4E-07	kid	kid		
316	**Hexachlorocyclohexane, technical grade**	608-73-1		eat			14.8	5.9E-01	1.7E-01	11.1	1.0E-06			liv	liv
317	**alpha-1,2,3,4,5,6-Hexachlorocyclohexane**	319-84-6		eat		11.2	6.62	4.5E-01	2.2E-01	11.1	1.4E-06	liv		liv	
318	beta-1,2,3,4,5,6-Hexachlorocyclohexane	319-85-7		eat			27.8	1.1E+00	9.0E-02	11.1	5.6E-07			liv	liv
319	gamma-1,2,3,4,5,6-Hexachlorocyclohexane	58-89-9	HVP	eat			30.7	1.2E+00	8.1E-02	11.1	5.1E-07	-	-	liv	liv lun
320	**Hexachloroethane**	67-72-1	HVP	gav	-	55.4	338	2.2E+00	4.5E-02	11.1	2.8E-07	kid	-	liv	liv
321	Hexamethylmelamine	531-18-0		eat	-	10.2		4.1E-01	2.5E-01	11.1	1.5E-06		kid mgl		
322	Hexanal methylformylhydrazone	---		gav			2.33	9.3E-02	1.1E+00	11.1	6.7E-06			liv lun pre	liv lun
323	Hexanamide	628-02-4		eat	-		1950	7.8E+01	1.3E-03	11.1	8.0E-09	-	-	hmo	-
324	N-Hexylnitrosourea	18774-85-1		gav		0.513		2.1E-02	4.9E+00	11.1	3.0E-05	lgi lun sto	in mgl sto u		
325	**Hydrazine s**	302-01-2	HVP	inh		0.309	2.93	1.2E-02	8.1E+00	11.1	5.0E-05	lun nas	lun nas	lun	lun
326	Hydrazine sulfate s	10034-93-2		gav	+	40.8	7.59	1.6E+00	6.1E-02	11.1	3.8E-07	liv lun	lun	liv lun	liv lun
327	2-Hydrazino-4-(p-aminophenyl)thiazole	26049-71-8		eat		1.03	11.3	4.1E-02	2.4E+00	11.1	1.5E-05		hmo mgl		hmo
328	2-Hydrazino-4-(5-nitro-2-furyl)thiazole	26049-68-3		eat		3.19	16.4	1.3E-01	7.8E-01	11.1	4.9E-06		kid mgl		sto
329	2-Hydrazino-4-(p-nitrophenyl)	26049-70-7		eat		3.21	10.6	1.3E-01	7.8E-01	11.1	4.8E-06		mgl		hmo
330	p-Hydrazinobenzoic acid.HCl	24589-77-3		wat			561	2.2E+01	4.5E-03	11.1	2.8E-08			vsc	vsc
331	**Hydrazobenzene**	122-66-7		eat		5.59	26	2.2E-01	4.5E-01	11.1	2.8E-06	ezy liv	liv mgl	-	liv
332	Hydrogen peroxide	7722-84-1	HVP	wat			7540	3.0E+02	3.3E-04	11.1	2.1E-09			-	sma
333	Hydroquinone	123-31-9	HVP	eat	-	82.8	225	3.3E+00	3.0E-02	11.1	1.9E-07	kid	hmo	kid liv	liv
334	N-Hydroxy-2-acetylaminofluorene s	53-95-2		eat	+	0.000988	6.23	4.0E-05	2.5E+03	11.1	1.6E-02	liv	liv		eso kid liv sto
335	3-Hydroxy-p-butyrophenetidide	1083-57-4		eat			5530	2.2E+02	4.5E-04	11.1	2.8E-09			kid	-
336	1-Hydroxyanthraquinone	129-43-1		eat		59.2		2.4E+00	4.2E-02	11.1	2.6E-07	lgi liv sto			
337	1'-Hydroxyestragole	51410-44-7		eat			57.8	2.3E+00	4.3E-02	11.1	2.7E-07				liv
338	1-(2-Hydroxyethyl)-3-[(5-nitrofurfurylidene)amino]-2-imidazolidinone	03.03.36		eat		16.7		6.7E-01	1.5E-01	11.1	9.3E-07		mgl		
339	1-(2-Hydroxyethyl)-nitroso	---		wat		0.789		3.2E-02	3.2E+00	11.1	2.0E-05	liv	liv		
340	1-(2-Hydroxyethyl)-nitroso-3-ethylurea	---		wat		0.562		2.2E-02	4.4E+00	11.1	2.8E-05	ski	mgl		
341	1-(2-Hydroxyethyl)-1-nitrosourea	13743-07-2		wat		0.131	0.818	5.2E-03	1.9E+01	11.1	1.2E-04	bon hmo kid lgi	hmo mgl	hmo	hmo
342	4-(2-Hydroxyethylamino)-2-(5-nitro-2-thienyl)quinazoline	33389-36-5		eat		1.87		7.5E-02	1.3E+00	11.1	8.3E-06		tba		
343	2-Hydroxyethylhydrazine s	109-84-2		orl			0.397	1.6E-02	6.3E+00	11.1	3.9E-05			liv	-
344	1-(3-Hydroxypropyl)-1-nitrosourea	71752-70-0		gav		0.978		3.9E-02	2.6E+00	11.1	1.6E-05	sto	sto		
345	1'-Hydroxysafrole	5208-87-7		eat		18.4	71.2	7.4E-01	1.4E-01	11.1	8.4E-07	liv sto		vsc	liv
346	ICRF-159	21416-87-5		ipj		10.7	23.7	4.3E-01	2.3E-01	11.1	1.5E-06	-	ute	-	hmo

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rat}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-Exit}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
347	Indolidan	100643-96-7		eat		2.01		8.0E-02	1.2E+00	11.1	7.7E-06	adr	adr	.	.
348	Iodinated glycerol	5634-39-9		gav	+	101	138	4.0E+00	2.5E-02	11.1	1.5E-07	hmo thy	.	.	hag pit
349	IQ s	76180-96-6		eat		1.63	19.6	6.5E-02	1.5E+00	11.1	9.5E-06	ezy lgi liv orc	cli ezy lgi liv	liv lun sto	liv lun sto
350	IQ.HCl	---		gav		3.29		1.3E-01	7.6E-01	11.1	4.7E-06	.	zy liv mgl p		
351	Isomazole	86315-52-8		eat		70.5		2.8E+00	3.5E-02	11.1	2.2E-07	adr	adr		
352	Isoniazid s	54-85-3		gav		150	27.1	6.0E+00	1.7E-02	11.1	1.0E-07	liv lun	mgl	liv lun mgl(B)	liv lun mgl(B
353	Isonicotinic acid vanillylidenehydrazide	149-17-7		gav			27.4	1.1E+00	9.1E-02	11.1	5.7E-07	.	.	lun(B) mgl(B)	lun(B) mgl(B
354	Isophorone	78-59-1	HVP	gav	-	1210		4.8E+01	2.1E-03	11.1	1.3E-08	kid pre	.	.	.
355	Isophosphamide	3778-73-2		ipj		0.739	5.06	3.0E-02	3.4E+00	11.1	2.1E-05	.	ute	.	hmo
356	Kepone	143-50-0		eat		2.96	0.982	1.2E-01	8.4E-01	11.1	5.2E-06	.	liv	liv	liv
357	Lasiocarpine	303-34-4		eat	+	0.476		1.9E-02	5.3E+00	11.1	3.3E-05	liv ski smu vsc	hmo liv vsc		
358	*Lead acetate (C4H6O4Pb)*	301-04-2	HVP	wat	-	46.6		1.9E+00	5.4E-02	11.1	3.3E-07	kid	.	.	.
359	*Lead subacetate (C4H8O6Pb2)*	1335-32-6		eat		181	472	7.2E+00	1.4E-02	11.1	8.6E-08	kid	kid	kid	kid
360	Leupeptin	24365-47-7		eat			55.8	2.2E+00	4.5E-02	11.1	2.8E-07	.	.	liv	.
361	d-Limonene	5989-27-5	HVP	gav	-	204		8.2E+00	1.2E-02	11.1	7.6E-08	kid	.	.	.
362	Luteoskyrin	21884-44-6		eat			18.6	7.4E-01	1.3E-01	11.1	8.3E-07	.	.	liv	liv
363	Malonaldehyde, sodium salt	24382-04-5		gav		122	14.1	4.9E+00	2.0E-02	11.1	1.3E-07	pan thy	thy	.	liv
364	Manganese ethylenebisthiocarbamate	12427-38-2	HVP	gav		157		6.3E+00	1.6E-02	11.1	9.9E-08	tba(B)	tba(B)	.	.
365	MeA-alpha-C	68006-83-7		eat			22.2	8.9E-01	1.1E-01	11.1	7.0E-07	.	.	liv vsc	liv vsc
366	MeIQ	77094-11-2		eat			12.3	4.9E-01	2.0E-01	11.1	1.3E-06	.	.	sto	liv sto
367	MeIQx	77500-04-0		eat		1.99	24.3	8.0E-02	1.3E+00	11.1	7.8E-06	ezy liv ski	cli ezy liv	hmo liv	liv lun
368	Melamine	108-78-1	HVP	eat	-	735		2.9E+01	3.4E-03	11.1	2.1E-08	ubl	.	.	.
369	Melphalan	148-82-3		ipj	+	0.0938	0.15	3.8E-03	2.7E+01	11.1	1.7E-04	per	per	hmo lun	lun
370	2-Mercaptobenzothiazole	149-30-4	HVP	gav	-	344		1.4E+01	7.3E-03	11.1	4.5E-08	adr hmo pan pri	adr pit	.	.
371	*Mercuric chloride*	7487-94-7		gav	-	3.12		1.2E-01	8.0E-01	11.1	5.0E-06	sto	.	.	.
372	*Mercurymethylchloride*	115-09-3		eat			1.91	7.6E-02	1.3E+00	11.1	8.1E-06	.	.	kid	.
373	Metepa	57-39-6		gav		4.46		1.8E-01	5.6E-01	11.1	3.5E-06	hmo	.		.
374	Methapyrilene.HCl s	135-23-9		eat	-	9.13		3.7E-01	2.7E-01	11.1	1.7E-06	liv	liv		.
375	Methidathion	950-37-8	HVP	eat			6.04	2.4E-01	4.1E-01	11.1	2.6E-06	.	.	liv	.
376	Methimazole	60-56-0		eat		1.14		4.6E-02	2.2E+00	11.1	1.4E-05	thy	thy		.
377	3-Methoxy-4-aminoazobenzene	3544-23-8		eat			60.2	2.4E+00	4.2E-02	11.1	2.6E-07	.	.	.	liv
378	2-Methoxy-3-aminodibenzofuran	5834-17-3		eat		29		1.2E+00	8.6E-02	11.1	5.4E-07	ezy kid ubl	ezy mgl ubl	.	.
379	8-Methoxypsoralen	298-81-7		gav	+	32.4		1.3E+00	7.7E-02	11.1	4.8E-07	ezy kid	.	.	.
380	Z-Methyl-O,N,N-azoxyethane	57497-34-4		wat		11.5		4.6E-01	2.2E-01	11.1	1.3E-06	kid liv	.	.	.
381	Methyl carbamate	598-55-0		gav	-	839		3.4E+01	3.0E-03	11.1	1.8E-08	liv	liv	.	.
382	Methyl clofenapate	21340-68-1		eat		9.17		3.7E-01	2.7E-01	11.1	1.7E-06	liv	.	.	
383	1-Methyl-1,4-dihydro-7-[2-(5-nitrofuryl)	---		eat			8.03	3.2E-01	3.1E-01	11.1	1.9E-06	.	.	hmo(B) lun(B)	hmo(B) lun(B
384	3'-Methyl-4-dimethylaminoazobenzene s	55-80-1		eat		3.28		1.3E-01	7.6E-01	11.1	4.7E-06	liv	.	.	.
385	N-Methyl-N,4-dinitrosoaniline	99-80-9		ipj		1.3		5.2E-02	1.9E+00	11.1	1.2E-05	per	.		
386	N-Methyl-N-formylhydrazine s	758-17-8		wat			1.37	5.5E-02	1.8E+00	11.1	1.1E-05	.	.	gal liv lun vsc	gal liv lun vsc
387	Methyl methanesulfonate	66-27-3		wat			31.8	1.3E+00	7.9E-02	11.1	4.9E-07	.	.	hmo lun	.
388	N-Methyl-N'-nitro-N-nitrosoguanidine s	70-25-7		wat	+	0.875		3.5E-02	2.9E+00	11.1	1.8E-05	eso smi sto	smi sto	.	.
389	2-Methyl-1-nitroanthraquinone	129-15-7		eat	+	84.8	1.56	3.4E+00	2.9E-02	11.1	1.8E-07	liv	liv	vsc	vsc
390	4-Methyl-1-[(5-nitrofurfurylidene)	21638-36-8		eat		5.34		2.1E-01	4.7E-01	11.1	2.9E-06	.	mgl		

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10b} [mg/kg-day]	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
391	4-(4-N-Methyl-N-nitrosaminostyryl)	16699-10-8		eat		0.699		2.8E-02	3.6E+00	11.1	2.2E-05	liv	liv	.	
392	N-Methyl-N-nitrosobenzamide	63412-06-6		wat		3.23		1.3E-01	7.7E-01	11.1	4.8E-06	sto	tba	.	
393	N-(N-Methyl-N-nitrosocarbamoyl)-l-ornithine	63642-17-1		ipj		0.787		3.1E-02	3.2E+00	11.1	2.0E-05	ezy kid pan ski	d mgl pan s	.	
394	R(-)-2-Methyl-N-nitrosopiperidine	14026-03-0		wat		20.4		8.2E-01	1.2E-01	11.1	7.6E-07	nrv(B)	nrv(B)	.	
395	S(+)-2-Methyl-N-nitrosopiperidine	36702-44-0		wat		13.2		5.3E-01	1.9E-01	11.1	1.2E-06	nrv(B)	nrv(B)	.	.
396	alpha-Methylbenzyl alcohol	98-85-1		gav	-	458		1.8E+01	5.5E-03	11.1	3.4E-08	kid	-	-	-
397	3-Methylbutanal methylformylhydrazone	---		gav			2.23	8.9E-02	1.1E+00	11.1	7.0E-06	.	.	gal liv lun pre	gal liv lun
398	3-Methylcholanthrene s	56-49-5		gav	+	0.491		2.0E-02	5.1E+00	11.1	3.2E-05	-	mgl		
399	4,4'-Methylene-bis(2-chloroaniline) s	101-14-4		eat	+	19.3		7.7E-01	1.3E-01	11.1	8.0E-07	ezy liv lun mgl	liv lun mgl	.	
400	4,4'-Methylene-bis(2-	64049-29-2		eat			66.6	2.7E+00	3.8E-02	11.1	2.3E-07	-		-	liv
401	4,4'-Methylene-bis(2-methylaniline)	838-88-0	HVP	eat		7.38		3.0E-01	3.4E-01	11.1	2.1E-06	liv mgl sub	liv	.	
402	**Methylene chloride**	75-09-2	HVP	inh		724	918	2.9E+01	3.5E-03	11.1	2.1E-08	mgl	mgl	liv lun	liv lun
403	**4,4'-Methylenebis(N,N-dimethyl)**	101-61-1		eat		16.4	207	6.6E-01	1.5E-01	11.1	9.5E-07	thy	thy	-	liv
404	4,4'-Methylenedianiline.2HCl	13552-44-8		wat	+	20	32.4	8.0E-01	1.3E-01	11.1	7.8E-07	liv thy	thy	adr liv thy	hmo liv thy
405	Methylhydrazine s	60-34-4		wat	-		7.55	3.0E-01	3.3E-01	11.1	2.1E-06		.	liv	liv lun
406	Methylhydrazine sulfate	302-15-8		wat			2.72	1.1E-01	9.2E-01	11.1	5.7E-06	.	.	lun	lun
407	Methylnitramine	598-57-2		gav		17.4		7.0E-01	1.4E-01	11.1	8.9E-07	nrv	nrv	.	
408	4-(Methylnitrosamino)-1-(3-pyrridyl)-1-butanol	---		wat		0.103		4.1E-03	2.4E+01	11.1	1.5E-04	lun pan		.	.
409	4-(Methylnitrosamino)-1-(3-pyrridyl)-1-(butanone)	64091-91-4		wat		0.182		7.3E-03	1.4E+01	11.1	8.5E-05	liv lun pan		.	.
410	(N-6)-(Methylnitroso)adenine	---		wat			18	7.2E-01	1.4E-01	11.1	8.6E-07	.		lun	-
411	(N-6)-(Methylnitroso)adenosine	21928-82-5		wat			18.3	7.3E-01	1.4E-01	11.1	8.5E-07			lun	lun mgl ute
412	Methylnitrosocyanamide	33868-17-6		wat		0.48		1.9E-02	5.2E+00	11.1	3.2E-05	.	sto		
413	N-Methylolacrylamide	924-42-5	HVP	gav	-		26.6	1.1E+00	9.4E-02	11.1	5.8E-07	-	-	hag liv lun	hag liv lun ov
414	Metronidazole	443-48-1		eat	+	542	506	2.2E+01	4.6E-03	11.1	2.9E-08	pit tes	liv mgl	lun	hmo lun
415	Michler's ketone	90-94-8		eat		5.64	84.1	2.3E-01	4.4E-01	11.1	2.8E-06	liv	liv	vsc	liv
416	Mirex	2385-85-5		eat	-	1.77	1.45	7.1E-02	1.4E+00	11.1	8.8E-06	adr kid liv	hmo liv	liv	liv
417	Mirex, photo	39801-14-4		eat		1.46		5.8E-02	1.7E+00	11.1	1.1E-05	thy	.		
418	Mitomycin-C	50-07-7		ipj		0.00102		4.1E-05	2.5E+03	11.1	1.5E-02	per	per	.	
419	Monoacetyl hydrazine	1068-57-1		gav			9.85	3.9E-01	2.5E-01	11.1	1.6E-06		.	lun	lun
420	Monocrotaline	315-22-0		gav		0.94		3.8E-02	2.7E+00	11.1	1.7E-05	liv	.	.	
421	4-Morpholino-2-(5-nitro-2-thienyl)	58139-48-3		eat		5.03		2.0E-01	5.0E-01	11.1	3.1E-06	.	tba		
422	[-5-Morpholinomethyl-3-[(5-nitrofurfurylidene)amino]-2-nitrofurfurylid	3031-51-4		eat		6.33		2.5E-01	3.9E-01	11.1	2.5E-06	.	uno kid mg	.	
423	Nafenopin	3771-19-5		eat		22.1		8.8E-01	1.1E-01	11.1	7.0E-07	liv	.	.	
424	Nalidixic acid	389-08-2		eat	-	201		8.0E+00	1.2E-02	11.1	7.7E-08	pre	cli	-	-
425	Naphthalene	91-20-3	HVP	inh	-		163	6.5E+00	1.5E-02	11.1	9.5E-08	.	.	-	lun
426	1,5-Naphthalenediamine	2243-62-1	HVP	eat	+	69.6	162	2.8E+00	3.6E-02	11.1	2.2E-07	-	cli ute	thy	liv lun thy
427	2-Naphthylamine s	91-59-8		gav	+	61.6	36.7	2.5E+00	4.1E-02	11.1	2.5E-07	B-	ubl	liv(B)	liv
428	Nicotinic acid hydrazide	553-53-7		wat			228	9.1E+00	1.1E-02	11.1	6.8E-08	.	.	lun	lun
429	Nithiazide	139-94-6		eat	+	131	758	5.2E+00	1.9E-02	11.1	1.2E-07	-	mgl	liv	-
430	Nitrilotriacetic acid	139-13-9		eat	-	1760	2660	7.0E+01	1.4E-03	11.1	8.8E-09	kid	kid ubl	kid	kid
431	Nitrilotriacetic acid, trisodium salt, monohydrate	18662-53-8		eat	-	370		1.5E+01	6.8E-03	11.1	4.2E-08	kid	kid ubl	-	-
432	Nitrite, sodium s	7632-00-0		eat		167		6.7E+00	1.5E-02	11.1	9.3E-08	hmo(B) liv	hmo(B) liv	-	-
433	3-Nitro-p-acetophenetide	1777-84-0		eat	+		2270	9.1E+01	1.1E-03	11.1	6.8E-09	-	-	liv	-
434	5-Nitro-o-anisidine	99-59-2		eat	+	53.9	3720	2.2E+00	4.6E-02	11.1	2.9E-07	ezy ski	cli ski	-	liv

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10b} [mg/kg-day]	$\beta_{ED10\text{-Exc}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
435	5-Nitro-2-furaldehyde semicarbazone	59-87-0		eat		6.98	30.8	2.8E-01	3.6E-01	11.1	2.2E-06	-	mgl	-	ova
436	3-(5-Nitro-2-furyl)-imidazo(1,2-alpha)pyridine	75198-31-1		eat		13.6	27	5.4E-01	1.8E-01	11.1	1.1E-06	eso kid sto	so kid mgl s	eso sto	eso sto
437	5-(5-Nitro-2-furyl)-1,3,4-oxadiazole-2-ol	2122-86-3		eat		8.61		3.4E-01	2.9E-01	11.1	1.8E-06		tba		
438	N-{[3-(5-Nitro-2-furyl)-1,2,4-oxadiazole-5-yl]-methyl}acetamide	36133-88-7		eat		59.6		2.4E+00	4.2E-02	11.1	2.6E-07		kid lun		
439	N-[5-(5-Nitro-2-furyl)-1,3,4-thiadiazol-2-yl]acetamide	2578-75-8		eat		8.84	6.74	3.5E-01	2.8E-01	11.1	1.8E-06		no kid lun s		sto
440	4-(5-Nitro-2-furyl)thiazole	53757-28-1		eat		7.68		3.1E-01	3.3E-01	11.1	2.0E-06		mgl sto		
441	N-[4-(5-Nitro-2-furyl)-2-thiazolyl]	531-82-8		eat		17.8		7.1E-01	1.4E-01	11.1	8.7E-07		mgl		
442	N-[4-(5-Nitro-2-furyl)-2-thiazolyl]	24554-26-5		eat	+	4.25	19.7	1.7E-01	5.9E-01	11.1	3.7E-06	ubl	ubl	ubl	lmo lun sto ub
443	N,N'-[6-(5-Nitro-2-furyl)-S-triazine-2,4-diyl]bisacetamide	51325-35-0		eat		14.1		5.6E-01	1.8E-01	11.1	1.1E-06		mgl		
444	3-Nitro-3-hexene	4812-22-0		inh		8.66	0.346	3.5E-01	2.9E-01	11.1	1.8E-06	lun(B)	lun(B)	lun(B)	lun(B)
445	2-Nitro-p-phenylenediamine	5307-14-2		eat	+		614	2.5E+01	4.1E-03	11.1	2.5E-08	-	-	-	liv
446	5-Nitro-o-toluidine	99-55-8		eat			277	1.1E+01	9.0E-03	11.1	5.6E-08	-	-	liv vsc	liv vsc
447	5-Nitroacenaphthene s	602-87-9		eat	+	8.67	45.8	3.5E-01	2.9E-01	11.1	1.8E-06	ezy lun	ı ezy lun m	-	liv ova
448	o-Nitroanisole	91-23-6	HVP	eat	+	15.6	178	6.2E-01	1.6E-01	11.1	9.9E-07	lmo kid lgi ubl	no kid lgi u	liv	liv
449	6-Nitrobenzimidazole	94-52-0		eat	+		372	1.5E+01	6.7E-03	11.1	4.2E-08	-	-	liv	liv
450	p-Nitrobenzoic acid	62-23-7	HVP	eat	+	287		1.1E+01	8.7E-03	11.1	5.4E-08	-	cli	-	-
451	Nitrofen	1836-75-5	HVP	eat	+	420	115	1.7E+01	6.0E-03	11.1	3.7E-08	-	pan	liv vsc	liv
452	1-[(5-Nitrofurfurylidene)amino]hydantoin	67-20-9		eat	+	163	1400	6.5E+00	1.5E-02	11.1	9.5E-08	kid	-	-	ova
453	1-[(5-Nitrofurfurylidene)amino]-2-imidazolidinone	555-84-0		eat		5.26		2.1E-01	4.8E-01	11.1	2.9E-06		lmo mgl		
454	Nitrogen mustard	51-75-2		ivj		0.0114		4.6E-04	2.2E+02	11.1	1.4E-03	tba			
455	Nitrogen mustard N-oxide	126-85-2		ivj		0.764		3.1E-02	3.3E+00	11.1	2.0E-05	tba			
456	8-Nitroquinoline	607-35-2		eat		9.82		3.9E-01	2.5E-01	11.1	1.6E-06	sto	sto		
457	Nitroso-Baygon	38777-13-8		gav		0.364		1.5E-02	6.9E+00	11.1	4.3E-05	sto			
458	N-Nitroso-bis-(4,4,4-trifluoro-N-butyl)	83335-32-4		gav		0.748		3.0E-02	3.3E+00	11.1	2.1E-05	liv lun	liv lun		
459	1-Nitroso-5,6-dihydrouracil	16813-36-8		wat		0.0983		3.9E-03	2.5E+01	11.1	1.6E-04	liv	liv		
460	N-Nitroso-2,3-dihydroxypropyl-2-hydroxypropylamine s	89911-79-5		gav		0.0535		2.1E-03	4.7E+01	11.1	2.9E-04		eso orc sto		
461	Nitroso-2,3-dihydroxypropyl-2-oxopropylamine s	92177-50-9		gav		0.0352		1.4E-03	7.1E+01	11.1	4.4E-04		eso orc sto		
462	N-Nitroso-2,3-dihydroxypropylethanolamine s	89911-78-4		wat		5.98		2.4E-01	4.2E-01	11.1	2.6E-06		liv		
463	1-Nitroso-3,5-dimethyl-4-benzoylpiperazine	61034-40-0		wat		9.66		3.9E-01	2.6E-01	11.1	1.6E-06		sto		
464	1-Nitroso-1-hydroxyethyl-3-chloroethylurea	96806-34-7		gav		0.229		9.2E-03	1.1E+01	11.1	6.8E-05	kid liv	kid liv		
465	1-Nitroso-1-(2-hydroxypropyl)-3- chloroethylurea	96806-35-8		gav		0.873		3.5E-02	2.9E+00	11.1	1.8E-05	liv	liv		
467	N-Nitroso-3-hydroxypyrrolidine	56222-35-6		wat		7.65		3.1E-01	3.3E-01	11.1	2.0E-06	tba(B)	tba(B)		
468	N-Nitroso-N-isobutylurea	760-60-1		wat		4.73		1.9E-01	5.3E-01	11.1	3.3E-06		smi		
469	N-Nitroso-N-methyl-N-dodecylamine	55090-44-3		gav		0.537		2.1E-02	4.7E+00	11.1	2.9E-05	liv lun sto ubl	ubl		
470	N-Nitroso-N-methyl-4-fluoroaniline	937-25-7		wat		0.255		1.0E-02	9.8E+00	11.1	6.1E-05	eso			
471	Nitroso-N-methyl-N-(2-phenyl)	13256-11-6		wat		0.00998		4.0E-04	2.5E+02	11.1	1.6E-03	eso hmo liv orc			
472	N-Nitroso-N-methyl-N-tetradecylamine	75881-20-8		gav		1.65		6.6E-02	1.5E+00	11.1	9.4E-06	lun ubl			
473	N-Nitroso-N-methyldecylamine	75881-22-0		gav		1.26		5.0E-02	2.0E+00	11.1	1.2E-05	liv lun nas sto			
474	N-Nitroso-N-methylurea s	684-93-5		eat		0.0927		3.7E-03	2.7E+01	11.1	1.7E-04	lun nrv sto			
475	3-Nitroso-2-oxazolidinone	38347-74-9		wat		0.385		1.5E-02	6.5E+00	11.1	4.0E-05	liv smi			
476	Nitroso-2-oxopropylethanolamine s	92177-49-6		gav		1.8		7.2E-02	1.4E+00	11.1	8.6E-06		liv		
477	di(N-Nitroso)-perhydropyrimidine	15973-99-6		ipj		0.166		6.6E-03	1.5E+01	11.1	9.3E-05	nas			
478	Nitroso-1,2,3,6-tetrahydropyridine	55556-92-8		wat		0.0601		2.4E-03	4.2E+01	11.1	2.6E-04		so liv sto vs		
479	N-Nitroso(2,2,2-trifluoroethyl)	82018-90-4		gav		2.52		1.0E-01	9.9E-01	11.1	6.2E-06	eso nas			

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-Extr.}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
480	N-Nitroso-2,2,4-trimethyl-1,2-dihydroquinoline polymer	29929-77-9		ipj		3.31		1.3E-01	7.6E-01	11.1	4.7E-06	per	.	.	.
481	1-Nitroso-3,4,5-trimethylpiperazine s	75881-18-4		gav		0.151		6.0E-03	1.7E+01	11.1	1.0E-04	.	nas	.	.
482	N-Nitrosoallyl-2,3-dihydroxypropylamine	88208-16-6		wat		0.825		3.3E-02	3.0E+00	11.1	1.9E-05	.	eso nas	.	.
483	N-Nitrosoallyl-2-hydroxypropylamine	91308-70-2		wat		0.877		3.5E-02	2.9E+00	11.1	1.8E-05	.	eso liv nas	.	.
484	N-Nitrosoallyl-2-oxopropylamine s	91308-71-3		gav		0.335		1.3E-02	7.5E+00	11.1	4.6E-05	.	eso liv	.	.
485	N-Nitrosoallylethanolamine	91308-69-9		wat		0.491		2.0E-02	5.1E+00	11.1	3.2E-05	.	liv nas	.	.
486	Nitrosoamylurethan	64005-62-5		wat		1.01		4.0E-02	2.5E+00	11.1	1.5E-05	.	eso orc	.	.
487	Nitrosoanabasine	1133-64-8		wat		11.9		4.8E-01	2.1E-01	11.1	1.3E-06	eso	eso	.	.
488	N-Nitrosobenzthiazuron	51542-33-7		gav		1.13		4.5E-02	2.2E+00	11.1	1.4E-05	sto(B)	sto(B)	.	.
489	N-Nitrosobis(2-hydroxypropyl)amine	53609-64-6		wat		0.846		3.4E-02	3.0E+00	11.1	1.8E-05	lun pro	eso nas	.	.
490	N-Nitrosobis(2-oxopropyl)amine	60599-38-4		gav		0.491		2.0E-02	5.1E+00	11.1	3.2E-05	lgi liv lun nas	liv lun vsc	.	.
491	Nitrosodibutylamine	924-16-3		gav		0.691	1.09	2.8E-02	3.6E+00	11.1	2.2E-05	liv lun sto ubl	.	eso liv lun sto	.
492	**N-Nitrosodiethanolamine**	1116-54-7		wat	+	3.17		1.3E-01	7.9E-01	11.1	4.9E-06	eso hmo kid livso	kid liv na	.	.
493	N-Nitrosodiethylamine s	55-18-5		wat	+	0.0237		9.5E-04	1.1E+02	11.1	6.5E-04	eso liv ubl	so liv orc st	.	.
494	N-Nitrosodimethylamine s	62-75-9		gav	+	0.124	0.189	5.0E-03	2.0E+01	11.1	1.3E-04	kid liv lun tes	liv vsc	liv nrv	lun nrv
495	N-Nitrosodiphenylamine	86-30-6		eat	-	167		6.7E+00	1.5E-02	11.1	9.3E-08	ubl	ubl	.	-
496	p-Nitrosodiphenylamine	156-10-5		eat	+w	201	340	8.0E+00	1.2E-02	11.1	7.7E-08	liv	-	liv	-
497	N-Nitrosodipropylamine s	621-64-7		ipj		0.186		7.4E-03	1.3E+01	11.1	8.3E-05	.	eso liv nas	.	.
498	Nitrosododecamethyleneimine	40580-89-0		gav		10.9		4.4E-01	2.3E-01	11.1	1.4E-06	liv	liv	.	.
499	N-Nitrosoephedrine	17608-59-2		gav		95.2		3.8E+00	2.6E-02	11.1	1.6E-07	liv lun sto	.	.	.
500	Nitrosoethylmethylamine	10595-95-6		gav		0.0503		2.0E-03	5.0E+01	11.1	3.1E-04	liv lun nas	-	.	.
501	Nitrosoethylurethan	614-95-9		wat		0.0904		3.6E-03	2.8E+01	11.1	1.7E-04	.	so orc sma st	.	.
502	Nitrosoheptamethyleneimine	20917-49-1		wat		0.0378		1.5E-03	6.6E+01	11.1	4.1E-04	eso liv orc	.	.	.
503	N-Nitrosohexamethyleneimine	932-83-2		wat			0.357	1.4E-02	7.0E+00	11.1	4.3E-05	.	.	eso liv orc sto	eso liv orc sto
504	1-Nitrosohydantoin	42579-28-2		wat		43.8		1.8E+00	5.7E-02	11.1	3.5E-07	orc	tba	.	.
505	N-Nitrosomethyl-2,3-dihydroxypropylamine s	86451-37-8		gav		0.646		2.6E-02	3.9E+00	11.1	2.4E-05	.	so liv lun na	.	.
506	N-Nitrosomethyl-(2-hydroxyethyl)amine	26921-68-6		gav		1.29		5.2E-02	1.9E+00	11.1	1.2E-05	liv nas	.	.	.
507	N-Nitrosomethyl-(3-hydroxypropyl)	70415-59-7		gav		1.66		6.6E-02	1.5E+00	11.1	9.3E-06	liv lun	liv lun	.	.
508	N-Nitrosomethyl-2-hydroxypropylamine	75411-83-5		wat		0.0463		1.9E-03	5.4E+01	11.1	3.4E-04	eso nas	eso nas	.	.
509	N-Nitrosomethyl(2-oxopropyl)amine	55984-51-5		gav		0.0172		6.9E-04	1.5E+02	11.1	9.0E-04	eso liv nas orc	so liv nas or	.	.
510	N-Nitrosomethyl-(2-tosyloxyethyl)	---		gav		4.8		1.9E-01	5.2E-01	11.1	3.2E-06	liv vsc	liv vsc	.	.
511	2-Nitrosomethylaminopyridine	16219-98-0		gav		0.214		8.6E-03	1.2E+01	11.1	7.3E-05	.	eso	.	.
512	Nitrosomethylaniline	614-00-6		wat		0.142		5.7E-03	1.8E+01	11.1	1.1E-04	eso	eso	.	.
513	Nitrosomethylundecylamine	68107-26-6		gav		2.37		9.5E-02	1.1E+00	11.1	6.5E-06	liv lun	.	.	.
514	N-Nitrosomorpholine s	59-89-2		wat		0.109		4.4E-03	2.3E+01	11.1	1.4E-04	.	liv vsc	.	.
515	N'-Nitrosonornicotine-1-N-oxide s	78246-24-9		wat		0.876		3.5E-02	2.9E+00	11.1	1.8E-05	eso nas	eso nas	.	.
516	N-Nitrosopiperazine	5632-47-3		wat		8.78		3.5E-01	2.8E-01	11.1	1.8E-06	tba	tba	.	.
517	N-Nitrosopiperidine s	100-75-4		wat	+	1.43	1.3	5.7E-02	1.7E+00	11.1	1.1E-05	eso(B) liv(B)	so(B) liv(B	liv lun sto	.
518	**N-Nitrosopyrrolidine s**	930-55-2		wat		0.799	0.679	3.2E-02	3.1E+00	11.1	1.9E-05	liv ubl	liv vsc	tba	.
519	N-Nitrosothialdine	81795-07-5		gav		0.483		1.9E-02	5.2E+00	11.1	3.2E-05	.	eso liv orc	.	.
520	N-Nitrosothiomorpholine	26541-51-5		wat		5.39		2.2E-01	4.6E-01	11.1	2.9E-06	eso	eso orc	.	.
521	o-Nitrosotoluene	611-23-4		eat		50.7		2.0E+00	4.9E-02	11.1	3.1E-07	liv spl sub ubl	.	.	.
522	Norlestrin s	01.12.15		gav		1.94	1.34	7.8E-02	1.3E+00	11.1	8.0E-06	liv(B) mgl(B)	iv(B) mgl(B	.	pit
523	Ochratoxin A	303-47-9		eat	-	0.103	6.41	4.1E-03	2.4E+01	11.1	1.5E-04	kid	kid mgl	kid	liv

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524	C.I. acid orange 3	6373-74-6		gav		1710		6.8E+01	1.5E-03	11.1	9.1E-09	-	kid	-	-
525	Oxazepam	604-75-1		eat			35.8	1.4E+00	7.0E-02	11.1	4.3E-07	.	.	liv	liv thy
526	N-(9-Oxo-2-fluorenyl)acetamide	3096-50-2		eat		6.17		2.5E-01	4.1E-01	11.1	2.5E-06	.	ezy liv mgl	.	.
527	4,4'-Oxydianiline	101-80-4	HVP	eat	+	9.51	33.6	3.8E-01	2.6E-01	11.1	1.6E-06	liv thy	liv thy	hag liv	hag liv thy
528	N-Oxydiethylene thiocarbamyl-N-oxydiethylene sulfenamide	13752-51-7	HVP	eat		90.8		3.6E+00	2.8E-02	11.1	1.7E-07	kid ubl	kid ubl	.	.
529	Ozone	10028-15-6		inh	+w		1.88	7.5E-02	1.3E+00	11.1	8.3E-06	-	-	-	lun
530	Pentachlorooanisole	1825-21-4		gav	+	24.8	68	9.9E-01	1.0E-01	11.1	6.3E-07	adr	-	adr vsc	-
531	Pentachloroethane	76-01-7		gav	-		57.3	2.3E+00	4.4E-02	11.1	2.7E-07	-	-	liv	liv
532	Pentachloronitrobenzene	82-68-8	HVP	orl	-		71.1	2.8E+00	3.5E-02	11.1	2.2E-07	-	-	liv	-
533	**2,3,4,5,6-Pentachlorophenol**	87-86-5		eat	-		24	9.6E-01	1.0E-01	11.1	6.5E-07	-	-	adr liv	adr liv vsc
534	2,3,4,5,6-Pentachlorophenol, technical	87-86-5		eat	-	13.1	23	5.2E-01	1.9E-01	11.1	1.2E-06	-	liv	adr liv	liv vsc
535	Pentanal methylformylhydrazone	57590-20-2		gav			3.42	1.4E-01	7.3E-01	11.1	4.5E-06	.	.	liv lun pre	liv lun
536	n-Pentylhydrazine.HCl	1119-68-2		wat			5.87	2.3E-01	4.3E-01	11.1	2.6E-06	.	.	-	lun vsc
537	Petasitenine	60102-37-6		wat		0.922		3.7E-02	2.7E+00	11.1	1.7E-05	liv vsc	liv vsc	.	.
538	Phenacetin	62-44-2		eat		1250	2140	5.0E+01	2.0E-03	11.1	1.2E-08	kid nas sto ubl	y mgl nas u	kid	ubl
539	Phenazone	60-80-0	HVP	eat		1230		4.9E+01	2.0E-03	11.1	1.3E-08	kid ubl	.	.	.
540	Phenazopyridine.HCl	136-40-3		eat	?	303	71.1	1.2E+01	8.3E-03	11.1	5.1E-08	lgi	lgi	-	liv
541	Phenesterin	09.10.46		gav	-	0.523	0.616	2.1E-02	4.8E+00	11.1	3.0E-05	-	mgl	hmo lun myc	hmo lun myc
542	Phenobarbital s	50-06-6		eat	+w		6.09	2.4E-01	4.1E-01	11.1	2.5E-06	-	-	liv	liv
543	Phenobarbital, sodium	57-30-7		wat		86	51.2	3.4E+00	2.9E-02	11.1	1.8E-07	liv	liv	liv	liv
544	Phenoxybenzamine.HCl	63-92-3		ipj	+	1.09	5.36	4.4E-02	2.3E+00	11.1	1.4E-05	per	per	per	per
545	1-Phenyl-3,3-dimethyltriazene	7227-91-0		gav		2.31		9.2E-02	1.1E+00	11.1	6.7E-06	nrv(B)	nrv(B)	.	
546	1-Phenylazo-2-naphthol	842-07-9		eat		29.4		1.2E+00	8.5E-02	11.1	5.3E-07	liv	liv	-	-
547	Phenylbutazone	50-33-9		gav	-	1160	353	4.6E+01	2.2E-03	11.1	1.3E-08	-	kid	liv	-
548	o-Phenylenediamine.2HCl	615-28-1		eat		248	735	9.9E+00	1.0E-02	11.1	6.3E-08	liv	.	liv	liv
549	Phenylethylhydrazine sulfate	156-51-4		wat			14.6	5.8E-01	1.7E-01	11.1	1.1E-06	.	.	-	lun vsc
550	Phenylglycidyl ether	122-60-1		inh	+	44		1.8E+00	5.7E-02	11.1	3.5E-07	nas	nas	.	.
551	Phenylhydrazine.HCl	59-88-1		gav			71.3	2.9E+00	3.5E-02	11.1	2.2E-07	.	.	vsc	vsc
552	o-Phenylphenate, sodium	132-27-4	HVP	eat		545		2.2E+01	4.6E-03	11.1	2.8E-08	kid ubl	ubl	.	.
553	o-Phenylphenol	90-43-7	HVP	eat	+w	232		9.3E+00	1.1E-02	11.1	6.7E-08	ubl	.	.	.
554	PhIP.HCl	---		eat		4.98	33.2	2.0E-01	5.0E-01	11.1	3.1E-06	hmo lgi	lgi mgl	hmo	hmo
555	Phorbol	17673-25-5		ipj			2.21	8.8E-02	1.1E+00	11.1	7.0E-06	.	.	.	hmo
556	Piperonyl sulfoxide	120-62-7		eat	-		62.2	2.5E+00	4.0E-02	11.1	2.5E-07	-	-	liv	-
557	Pivalolactone	1955-45-9		gav	+	211		8.4E+00	1.2E-02	11.1	7.4E-08	sto	sto	-	-
558	Polybrominated biphenyl mixture	67774-32-7		eat		0.322	0.332	1.3E-02	7.8E+00	11.1	4.8E-05	liv	liv	liv	liv
559	Prednimustine	29069-24-7		gav		19.2		7.7E-01	1.3E-01	11.1	8.1E-07	.	ezy	.	.
560	Prednisolone	50-24-8		wat		1.53		6.1E-02	1.6E+00	11.1	1.0E-05	liv	-	.	.
561	Probenecid	57-66-9		gav	-		540	2.2E+01	4.6E-03	11.1	2.9E-08	-	-	.	liv
562	Procarbazine	671-16-9		ivj		4.01		1.6E-01	6.2E-01	11.1	3.9E-06	tba	.	.	.
563	Procarbazine.HCl s	366-70-1		ipj	-	0.351	0.558	1.4E-02	7.1E+00	11.1	4.4E-05	hmo mgl nrv	mo mgl nrv	hmo lun nrv	mo lun nrv ut
564	Propane sultone	1120-71-4		gav		3.84		1.5E-01	6.5E-01	11.1	4.0E-06	hmo nrv smu	to mgl nrv s	.	.
565	beta-Propiolactone	57-57-8		gav	+	1.46	1.24	5.8E-02	1.7E+00	11.1	1.1E-05	.	sto	sto	sto
566	N-N'-Propyl-N-formylhydrazine	77337-54-3		wat			8.79	3.5E-01	2.8E-01	11.1	1.8E-06			lun pre	gal liv lun
567	N-Propyl-N'-nitro-N-nitrosoguanidine	13010-07-6		wat		1.31		5.2E-02	1.9E+00	11.1	1.2E-05	sto	.	.	.

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568	N-Propyl-N-nitrosourea	816-57-9		wat		3.77		1.5E-01	6.6E-01	11.1	4.1E-06	hmo	hmo	.	.
569	**1,2-Propylene oxide**	75-56-9	HVP	inh		74.4	912	3.0E+00	3.4E-02	11.1	2.1E-07	adr nas	mgl nas sto	nas	nas
570	Propylhydrazine.HCl	56795-66-5		wat			45.5	1.8E+00	5.5E-02	11.1	3.4E-07	.	.	lun	lun
571	Propylthiouracil	51-52-5		eat		13.7	409	5.5E-01	1.8E-01	11.1	1.1E-06	thy	thy	pit(B)	pit(B)
573	Pyrilamine maleate	59-33-6		eat		280		1.1E+01	8.9E-03	11.1	5.5E-08	liv	liv	.	.
574	Quercetin	117-39-5		eat	+	10.1		4.0E-01	2.5E-01	11.1	1.5E-06	kid smi ubl	smi ubl	.	.
575	p-Quinone dioxime	105-11-3		eat	+	106		4.2E+00	2.4E-02	11.1	1.5E-07	.	ubl	.	.
576	C.I. acid red 114	6459-94-5		wat		3.89		1.6E-01	6.4E-01	11.1	4.0E-06	ezy liv ski	ili ezy lgi liv	.	.
577	C.I. pigment red 3	2425-85-6		eat		1170	35500	4.7E+01	2.1E-03	11.1	1.3E-08	adr	liv	kid thy	.
578	D & C red no. 5	3761-53-3		eat		415	716	1.7E+01	6.0E-03	11.1	3.7E-08	liv	liv	liv	liv
579	D & C red no. 9	01.02.60		eat		146		5.8E+00	1.7E-02	11.1	1.1E-07	liv spl	.	.	.
580	FD & C red no. 1	08.09.64		eat		521		2.1E+01	4.8E-03	11.1	3.0E-08	liv	liv	.	.
581	FD & C red no. 2	915-67-3		eat		1470		5.9E+01	1.7E-03	11.1	1.1E-08	hmo(B)	hmo(B)	.	.
582	FD & C red no. 4 s	4548-53-2		eat		8110		3.2E+02	3.1E-04	11.1	1.9E-09	hmo(B)	hmo(B)	B-	B-
583	Reserpine	50-55-5		eat	-	0.306	5.02	1.2E-02	8.2E+00	11.1	5.1E-05	adr	.	tes	mgl
584	Rifampicin	13292-46-1		wat			33.6	1.3E+00	7.4E-02	11.1	4.6E-07	.	.	.	liv
585	Ripazepam	26308-28-1		eat			114	4.6E+00	2.2E-02	11.1	1.4E-07	.	.	liv	liv
586	p-Rosaniline.HCl s	569-61-9		eat		39.4	51.5	1.6E+00	6.3E-02	11.1	3.9E-07	ezy liv ski sub	ezy sub thy	liv	adr liv
587	Saccharin, sodium	128-44-9	HVP	eat		2140		8.6E+01	1.2E-03	11.1	7.3E-09	ubl	.	.	.
588	Safrole	94-59-7		eat	-	441	51.3	1.8E+01	5.7E-03	11.1	3.5E-08	liv	liv(B)	liv	liv
589	Salbutamol	18559-94-9		eat		40		1.6E+00	6.3E-02	11.1	3.9E-07	.	meo	.	.
590	Selenium diethyldithiocarbamate	5456-28-0		orl			1.49	6.0E-02	1.7E+00	11.1	1.0E-05	.	.	liv	.
591	Selenium sulfide	7446-34-6		gav	+	8.01	69.3	3.2E-01	3.1E-01	11.1	1.9E-06	liv	liv	.	liv lun
592	Senkirkine	2318-18-5		ipj		1.7		6.8E-02	1.5E+00	11.1	9.1E-06	liv	.	.	.
593	Sesamol	533-31-3		eat		1350	4490	5.4E+01	1.9E-03	11.1	1.1E-08	sto	sto	sto	sto
594	Sterigmatocystin s	10048-13-2		eat		0.152	0.908	6.1E-03	1.6E+01	11.1	1.0E-04	liv vsc	liv(B)	.	vsc
595	Streptozotocin	18883-66-4		ipj		0.963	0.272	3.9E-02	2.6E+00	11.1	1.6E-05	kid	kid	ktd lun	ktd lun
596	Strobane	8001-50-1		orl			0.884	3.5E-02	2.8E+00	11.1	1.8E-05	.	.	hmo liv	.
597	Styrene	100-42-5	HVP	inh	-	23.3		9.3E-01	1.1E-01	11.1	6.7E-07	.	mgl	.	.
598	Styrene oxide	96-09-3		gav	+	55.4	118	2.2E+00	4.5E-02	11.1	2.8E-07	sto	sto	sto	sto
599	Sulfallate	95-06-7		eat	+	26.1	42.2	1.0E+00	9.6E-02	11.1	5.9E-07	sto	mgl	lun	mgl
600	Sulfamethazine	57-68-1		eat	-		1510	6.0E+01	1.7E-03	11.1	1.0E-08	.	.	thy	thy
601	4,4'-Sulfonylbisacetanilide	77-46-3		eat		55.6		2.2E+00	4.5E-02	11.1	2.8E-07	.	mgl	.	.
602	Symphytine	22571-95-5		ipj		1.91		7.6E-02	1.3E+00	11.1	8.1E-06	liv vsc	.	.	.
603	Telone II	542-75-6	HVP	gav		94	49.6	3.8E+00	2.7E-02	11.1	1.7E-07	liv sto	sto	I	lun sto ubl
604	Terbutaline	23031-25-6		eat		410		1.6E+01	6.1E-03	11.1	3.8E-08	.	meo	.	.
605	3,3',4,4'-Tetraaminobiphenyl.4HCl	7411-49-6		eat		395	288	1.6E+01	6.3E-03	11.1	3.9E-08	liv	.	lun	.
606	2,3,7,8-Tetrachlorodibenzo-p-dioxin	1746-01-6		gav		0.0000457	0.000156	1.8E-06	5.5E+04	11.1	3.4E-01	orc thy	liv lun	liv	liv thy
607	**1,1,1,2-Tetrachloroethane**	630-20-6	HVP	gav	-		182	7.3E+00	1.4E-02	11.1	8.5E-08	.	.	liv	liv
608	**1,1,2,2-Tetrachloroethane**	79-34-5	HVP	gav	-		38.3	1.5E+00	6.5E-02	11.1	4.1E-07	.	.	liv	liv
609	Tetrachloroethylene	127-18-4	HVP	gav	-	101	126	4.0E+00	2.5E-02	11.1	1.5E-07	hmo kid	hmo	liv	liv
610	Tetrachlorvinphos	961-11-5		eat			228	9.1E+00	1.1E-02	11.1	6.8E-08	.	.	liv	.
611	Tetrafluoro-m-phenylenediamine.2HCl	63886-77-1		eat			86.3	3.5E+00	2.9E-02	11.1	1.8E-07	.	.	liv	.
612	Tetrahydro-2-nitroso-2H-1,2-oxazine	40548-68-3	HVP	wat		24.3		9.7E-01	1.0E-01	11.1	6.4E-07	tba(B)	tba(B)	.	.

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10th} [mg/kg-day]	$\beta_{ED10\text{-}Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
613	Tetranitromethane	509-14-8		inh	+	0.447	1.19	1.8E-02	5.6E+00	11.1	3.5E-05	lun	lun	lun	lun
614	Thio-TEPA	52-24-4		ipj		0.164	0.223	6.6E-03	1.5E+01	11.1	9.5E-05	ezy hmo ski	ezy	hmo pre ski	hmo
615	Thioacetamide	62-55-5		eat	-	11.5	8.81	4.6E-01	2.2E-01	11.1	1.3E-06	liv	.	liv	liv
616	4,4'-Thiodianiline	139-65-1		eat	+	3.71	33.2	1.5E-01	6.7E-01	11.1	4.2E-06	ezy lgi liv thy	ezy thy ute	liv thy	liv thy
617	beta-Thioguanine deoxyriboside	64039-27-6		ipj		2.1		8.4E-02	1.2E+00	11.1	7.4E-06	-	ezy	l	l
618	Thiouracil	141-90-2		eat		11.9	55	4.8E-01	2.1E-01	11.1	1.3E-06	thy	thy	liv	liv
619	Thiourea	62-56-6	HVP	wat	-	98.5		3.9E+00	2.5E-02	11.1	1.6E-07	ski	-	.	.
620	Toluene	108-88-3	HVP	gav	-	716		2.9E+01	3.5E-03	11.1	2.2E-08	tba	tba	.	.
621	Toluene diisocyanate, commercial grade	26471-62-5	HVP	gav	+	33.7	250	1.3E+00	7.4E-02	11.1	4.6E-07	pan sub	v mgl pan st	-	liv vsc
622	o-Toluenesulfonamide	88-19-7	HVP	gav		3960		1.6E+02	6.3E-04	11.1	3.9E-09	ubl(B)	ubl(B)		.
623	m-Toluidine.HCl	638-03-9		eat	-		1440	5.8E+01	1.7E-03	11.1	1.1E-08	-	.	liv	-
624	o-Toluidine.HCl	636-21-5		eat	+	43.6	840	1.7E+00	5.7E-02	11.1	3.6E-07	mgl per spl subn	mgl ubl v	vsc	liv vsc
625	p-Toluidine.HCl	540-23-8		eat	+w		83.5	3.3E+00	3.0E-02	11.1	1.9E-07	-	.	liv	liv
626	p-Tolylurea	622-51-5		eat	-		206	8.2E+00	1.2E-02	11.1	7.5E-08	-	-	hmo	-
627	**Toxaphene**	8001-35-2		eat	+		5.57	2.2E-01	4.5E-01	11.1	2.8E-06	-	-	liv	liv
628	Trenimon	68-76-8		ivj		0.00504		2.0E-04	5.0E+02	11.1	3.1E-03	tba	.		.
629	Triamcinolone acetonide	76-25-5		wat		0.053		2.1E-03	4.7E+01	11.1	2.9E-04	liv	.	.	.
630	Triamterene	396-01-0		eat	-		60.2	2.4E+00	4.2E-02	11.1	2.6E-07	-	-	liv	liv
631	**Tribromomethane**	75-25-2		gav		648		2.6E+01	3.9E-03	11.1	2.4E-08	lgi	lgi	-	-
632	2,4,6-Trichloroaniline	634-93-5		eat	-		259	1.0E+01	9.7E-03	11.1	6.0E-08	-	.	liv vsc	-
633	**1,1,2-Trichloroethane**	79-00-5	HVP	gav	-		55	2.2E+00	4.5E-02	11.1	2.8E-07	-	-	adr liv	adr liv
634	Trichloroethylene s	79-01-6	HVP	inh	-	668	1580	2.7E+01	3.7E-03	11.1	2.3E-08	tes	-	liv lun	liv lun
635	Trichloroethylene	79-01-6	HVP	gav	-		343	1.4E+01	7.3E-03	11.1	4.5E-08	-	-	liv	liv
636	**N-(Trichloromethylthio)phthalimide**	133-07-3		eat			1170	4.7E+01	2.1E-03	11.1	1.3E-08	.	.	smi	smi
637	**2,4,6-Trichlorophenol**	88-06-2	HVP	eat	-	405	1070	1.6E+01	6.2E-03	11.1	3.8E-08	hmo	-	liv	liv
638	1,2,3-Trichloropropane	96-18-4	HVP	gav	+	1.35	0.875	5.4E-02	1.9E+00	11.1	1.1E-05	ezy kid orc pani	ezy mgl ou	hag liv sto	hag liv orc sto
639	Triethanolamine	102-71-6	HVP	eat	-		100	4.0E+00	2.5E-02	11.1	1.6E-07	-	-	tba	tba
640	2,2,2-Trifluoro-N-[4-(5-nitro-2-furyl)-2-thiazolyl]acetamide	42011-48-3		eat		6.79	9.98	2.7E-01	3.7E-01	11.1	2.3E-06	.	mgl	.	sto
641	**Trifluralin, technical grade**	1582-09-8		eat	+		330	1.3E+01	7.6E-03	11.1	4.7E-08	-	-	-	liv lun sto
642	2,4,5-Trimethylaniline	137-17-7		eat	+	33.6	6.13	1.3E+00	7.4E-02	11.1	4.6E-07	liv	liv lun	-	liv
643	2,4,5-Trimethylaniline.HCl	21436-97-5		eat		98.5	45.5	3.9E+00	2.5E-02	11.1	1.6E-07	liv sub	.	liv lun vsc	liv lun
644	2,4,6-Trimethylaniline.HCl	08.11.34		eat		5.17	24.8	2.1E-01	4.8E-01	11.1	3.0E-06	liv lun sto	.	liv vsc	liv
645	Trimethylphosphate	512-56-1	HVP	gav	+		335	1.3E+01	7.5E-03	11.1	4.6E-08	-	-	-	ute
646	Trimethylthiourea	2489-77-2		eat	-	25.8		1.0E+00	9.7E-02	11.1	6.0E-07	-	thy	-	-
647	2,4,6-Trinitro-1,3-dimethyl-5-tert-butylbenzene	81-15-2	HVP	eat			127	5.1E+00	2.0E-02	11.1	1.2E-07	.	.	hag liv	liv
648	Trinitroglycerin	55-63-0	HVP	eat		264		1.1E+01	9.5E-03	11.1	5.9E-08	liv tes	liv	.	.
649	Tris(2-chloroethyl)phosphate	115-96-8	HVP	gav	-	86.7		3.5E+00	2.9E-02	11.1	1.8E-07	kid	kid	-	-
650	Tris-1,2,3-(chloromethoxy)propane	38571-73-2		ipj			3.44	1.4E-01	7.3E-01	11.1	4.5E-06	.			per
651	Tris(2,3-dibromopropyl)phosphate	126-72-7		eat	+	3.83	128	1.5E-01	6.5E-01	11.1	4.1E-06	kid lgi	kid	kid lun sto	liv lun sto
652	Tris(2-ethylhexyl)phosphate	78-42-2	HVP	gav	-		2560	1.0E+02	9.8E-04	11.1	6.1E-09	-	-	-	liv
653	Trp-P-1 acetate	75104-43-7		eat		0.575	40.7	2.3E-02	4.3E+00	11.1	2.7E-05	liv	liv	liv	liv
654	Trp-P-2 acetate	72254-58-1		eat		6.66	12.6	2.7E-01	3.8E-01	11.1	2.3E-06	liv mgl ubl	i hmo liv m	liv	liv
655	Uracil	66-22-8		eat		671	2750	2.7E+01	3.7E-03	11.1	2.3E-08	ubl	ubl	ubl	ubl
656	Urethane s	51-79-6	HVP	wat	+w	41.3	16.9	1.7E+00	6.1E-02	11.1	3.8E-07	tba(B)	tba(B)	hmo liv lun vsc	lun

	Chemical	CAS RN	Production [OECD, 1997]	Main route of exposure	Mutagenicity test	$TD_{50\text{-rats}}$ [mg/kg-day]	$TD_{50\text{-mice}}$ [mg/kg-day]	ED_{10th} [mg/kg-day]	$\beta_{ED10\text{-Ext.}}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]	Mouse target sites Male	Mouse target sites Female	Rats target sites Male	Rats target sites Female
657	Vinyl acetate	108-05-4	HVP	wat		201		8.0E+00	1.2E-02	11.1	7.7E-08	liv thy	liv thy ute		
658	Vinyl bromide	593-60-2		inh		18.5		7.4E-01	1.4E-01	11.1	8.4E-07	liv vsc	liv vsc		
659	Vinyl carbamate	15805-73-9		ipj			0.124	5.0E-03	2.0E+01	11.1	1.3E-04			liv vsc	liv vsc
660	Vinyl chloride s	75-01-4	HVP	inh		19.1	20.9	7.6E-01	1.3E-01	11.1	8.1E-07	ezy kid(B) liv	zy kid(B) li	lun(B) mgl	lun mgl vsc
661	4-Vinylcyclohexene	100-40-3	HVP	gav	-		106	4.2E+00	2.4E-02	11.1	1.5E-07	l	l	l	ova
662	**Vinylidene chloride**	75-35-4	HVP	inh	-		34.6	1.4E+00	7.2E-02	11.1	4.5E-07	-	-	kid lun	lun mgl vsc
663	FD & C violet no. 1	1694-09-3		eat		612		2.4E+01	4.1E-03	11.1	2.5E-08	-	mgl ski	-	-
664	Xylene mixture (m-xylene, o-xylene,	mixture		gav	-	524		2.1E+01	4.8E-03	11.1	3.0E-08	tba	tba	-	-
665	2,4-Xylidine.HCl	21436-96-4		eat			12.4	5.0E-01	2.0E-01	11.1	1.3E-06	-	-	-	lun
666	2,5-Xylidine.HCl	51786-53-9		eat		152	626	6.1E+00	1.6E-02	11.1	1.0E-07	sub	-	vsc	liv
667	C.I. disperse yellow 3	2832-40-8		eat		380	1020	1.5E+01	6.6E-03	11.1	4.1E-08	liv	-	-	liv
668	C.I. vat yellow 4	128-66-5		eat			10900	4.4E+02	2.3E-04	11.1	1.4E-09	-	-	bmo	-
669	Zearalenone	17924-92-4		eat	-		39	1.6E+00	6.4E-02	11.1	4.0E-07	-	-	pit	liv pit
670	Zinc dimethyldithiocarbamate	137-30-4	HVP	eat		40.7		1.6E+00	6.1E-02	11.1	3.8E-07	tba(B) thy	tba(B)	-	-
671	Zinc ethylenebisthiocarbamate	12122-67-7	HVP	gav		255		1.0E+01	9.8E-03	11.1	6.1E-08	tba(B)	tba(B)	-	-

Appendix 2.2 Slope factors β_{ED10} derived from the tumor dose TD_{50} provided by Gold and Zeiger [1997] (see equation (2.14)) and effect factors derived from the slope factor β_{ED10} and the Disability Adjusted Life Years per affected Person ($DALY_p$) using equation (2.19).

In bold: Substances studied in detail in chapter 2 (see section 2.3 and appendix 2.1).

In italic: heavy metals studied in detail in section 2.6.

HVP (High Volume Production) chemicals are compounds whose production or importation exceeds 1000 tonnes in at least one OECD country [OECD, 1997].

Target site: adr = adrenal gland; bon = bone; cli = clitoral gland; eso = esophagus; ezy = ear/Zymbal's gland; gal = gall bladder; hag = harderian gland; hmo = hematopoietic system; kid = kidney; lgi = large intestine; liv = liver; lun = lung; meo = mesovarium; mgl = mammary gland; mix = mixture; myc = myocardium; nas = nasal cavity (includes tissues of the nose, nasal turbinates, paranasal sinuses and trachea); nrv = nervous system; orc = oral cavity (includes tissues of the mouth, oropharynx, pharynx, and larynx); ova = ovary; pan = pancreas; per = peritoneal cavity; pit = pituitary gland; pre = preputial gland; pro = prostate; ski = skin; smi = small intestine; spl = spleen; sto = stomach; sub = subcutaneous tissue; tba = all tumor bearing animals; tes = testes; thy = thyroid gland; ubl = urinary bladder; ute = uterus; vag = vagina; vsc = vascular system.

Route of exposure: wat=water; eat=diet; gav=gavage; inh=inhalation;orl=gavage preweanling, followed by diet; ipj=intraperitoneal injection; ivj=intravenous injection.

Results for the Salmonella Mutagenicity Test (Ames Test) provided by Gold and Zeiger [1997]:

+ : positive result; +w : weak positive result; ? : equivocal result or disagreement among tests; - : negative result

APPENDICES CHAPTER 3

Appendix 3.1 Effect factors for criteria air pollutants

Exposure-response slopes (E-R slopes) reported by Pilkington et al. [1997] to quantify the impact of air pollutants on the respiratory system are listed in this appendix. The exposure-response slopes for mortality are given as percentage increases compared to the background mortality.
A background mortality rate of 0.84% was calculated by Hofstetter [1998]. The share of the different population groups used in epidemiological studies is listed for morbidity endpoints. The disabilities adjusted life years per affected Person ($DALY_p$) was evaluated by Hofstetter [1998] for the respiratory effects, as well as for the acute and chronic mortality. Among the $DALY_p$ calculated by Hofstetter [1998], we chose the $DALY_p$ determined without discounting and with no age-weighting, in order to be compatible with our calculations.
The effect factor was derived by Hofstetter [1998] by combining the exposure-response slopes, the $DALY_p$, the share of the population for morbidity endpoints and the baseline mortality for mortality. We expressed the effect factor in years lost per mg absorbed, since these are the units of the effect factor that we defined in section 2.8.1.

The assumptions to calculate the exposure-response slopes are presented by Pilkington et al. [1997]. It is assumed that the slopes are independent from the ambient concentration, and the slope at the ambient concentration in the studied region is taken as a proxy. Hofstetter [1998] justified that assumption by arguing that the results are dominated by mortality which shows little dependency on the background concentration. Criteria for causation, for instance the effects come after the exposure and the biological plausibility, are used to validate the exposure-response relations derived from epidemiological studies.
A detailed reasoning and a description of all the exposure-response slopes is provided by Donnan and Hurley [1997]. As an example, Hofstetter [1998] reported the determination of the exposure-response slope for respiratory hospital admission due to particles PM10. Dab et al. [1996] reported that the population in the study area (Paris) is of 6140000 people, and that 28835 hospital admissions for all respiratory causes are yearly reported. This results in an absolute risk of 0.0047 [Case/pers-yr] (28835/6140000). This baseline risk is increased by 0.044% through the exposure to an increase in the concentration of one additional ug/m3. This results in an individual risk of 2.07·10-6 [Case/pers-yr-ug/m3], as indicated in appendix 3.1.

Pollutant and endpoint	Affected population group	E-R slope [cases / yr-pers-ug/m3] [% increase / ug/m3] [Pilkington, 1997]	Share of population Baseline mortality [Hofstetter, 1998]	$DALY_p$ [yr lost/pers] [Hofstetter, 1998]	EF [yr lost / yr-pers-ug/m3] [Hofstetter, 1998]	EF [yr lost / mg absorbed] [This study]
Particles PM10 / Nitrates						
Bronchodilator usage	adult asthmatics	0.163	4.00%	2.7E-04	1.8E-06	2.4E-07
	asthm. children	0.078	1.00%	2.7E-04	2.1E-07	2.9E-08
Cough	adult asthmatics	0.168	4.00%	1.4E-04	9.4E-07	1.3E-07
	asthm. children	0.133	1.00%	1.4E-04	1.9E-07	2.6E-08
Lower respiratory symptoms (wheeze)	adult asthmatics	0.061	4.00%	1.4E-04	3.4E-07	4.7E-08
	asthm. children	0.103	1.00%	1.4E-04	1.4E-07	2.0E-08
Chronic bronchitis	children	1.61E-03	20%	2.5E-02	8.1E-06	1.1E-06
	adults	4.90E-05	80%	2.0E+00	7.8E-05	1.1E-05
Chronic cough	children	2.07E-03	20%	2.5E-02	1.0E-05	1.4E-06
Restricted activity days (RAD)	adults	0.025	80%	2.7E-04	5.4E-06	7.4E-07
Respiratory hospital admissions	all	**2.07E-06**	100%	1.1E-02	2.3E-08	3.1E-09
Acute Mortality (AM)	all	0.04%	0.00%	7.5E-01	0.0E+00	0.0E+00
Chronic Mortality (CM)	all	0.39%	0.81%	6.6E+00	2.1E-04	2.9E-05
Emergency Room Visits for COPD	all	7.20E-06	100%	8.2E-04	5.9E-09	8.1E-10
Emergency Room Visits for asthma	all	6.45E-06	100%	8.2E-04	5.3E-09	7.2E-10
Emergency Room Visits for croup	all	2.91E-05	100%	8.2E-04	2.4E-08	3.3E-09
Total PM10					3.1E-04	**4.3E-05**
Particles PM2.5 / Sulfates						
Bronchodilator usage	adult asthmatics	0.272	4.00%	2.7E-04	2.9E-06	4.0E-07
	asthm. children	0.129	1.00%	2.7E-04	3.5E-07	4.8E-08
Cough	adult asthmatics	0.28	4.00%	1.4E-04	1.6E-06	2.1E-07
	asthm. children	0.223	1.00%	1.4E-04	3.1E-07	4.3E-08
Lower respiratory symptoms (wheeze)	adult asthmatics	0.101	4.00%	1.4E-04	5.7E-07	7.7E-08
	asthm. children	0.172	1.00%	1.4E-04	2.4E-07	3.3E-08
Chronic bronchitis	children	2.69E-03	20%	2.5E-02	1.3E-05	1.8E-06
	adults	7.80E-05	80%	2.0E+00	1.2E-04	1.7E-05
Chronic cough	children	3.46E-03	20%	2.5E-02	1.7E-05	2.4E-06
Restricted activity days (RAD)	adults	0.042	80%	2.7E-04	9.1E-06	1.2E-06
Respiratory hospital admissions	all	3.46E-06	100%	1.1E-02	3.8E-08	5.2E-09
Acute Mortality (AM)	all	0.07%	0.00%	7.5E-01	0.0E+00	0.0E+00
Chronic Mortality (CM)	all	0.64%	0.81%	6.6E+00	3.4E-04	4.7E-05
Emergency Room Visits for COPD	all	1.20E-05	100%	8.2E-04	9.8E-09	1.3E-09
Emergency Room Visits for asthma	all	1.08E-05	100%	8.2E-04	8.9E-09	1.2E-09
Emergency Room Visits for croup	all	4.86E-05	100%	8.2E-04	4.0E-08	5.5E-09
Total PM2.5/Sulphates					5.1E-04	**7.0E-05**
Ozone						
Asthma attacks (AA)	all	4.29E-03	100%	2.7E-04	1.2E-06	1.6E-07
Minor restricted activity day (MRAD)	adults	9.76E-03	80%	1.4E-04	1.1E-06	1.5E-07
Respiratory hospital admissions	all	3.54E-06	100%	1.1E-02	3.9E-08	5.3E-09
Symptom days	all	0.033	100%	1.4E-04	4.6E-06	6.3E-07
Acute Mortality (AM)	all	0.06%	0.84%	7.5E-01	3.8E-06	5.2E-07
Emergency Room Visits for asthma	all	1.32E-05	100%	8.2E-04	1.1E-08	1.5E-09
Total Ozone					1.1E-05	**1.5E-06**
Sulfur dioxide						
Respiratory hospital admissions	all	2.04E-06	100%	1.1E-02	2.2E-08	3.1E-09
Acute Mortality (AM)	all	0.07%	0.84%	7.5E-01	4.4E-06	6.0E-07
Total SO2					4.4E-06	**6.1E-07**
Nitrogen oxide						
Acute Mortality (AM)	all	0.034%	0.84%	7.5E-01	2.1E-06	2.9E-07
Respiratory hospital admissions	all	1.40E-06	100%	1.1E-02	1.5E-08	2.1E-09
Total NOx					2.2E-06	**3.0E-07**
Carbon monoxide						
Acute Mortality (AM)	all	0.00145%	0.84%	7.5E-01	9.1E-08	1.3E-08
Total CO					9.1E-08	**1.3E-08**

Appendix 3.1 Calculations of the effect factor EF for air pollutants, by Hofstetter [1998].

$DALY_p$: Disability Adjusted Life Years per affected Person.

COPD: chronic obstructive pulmonary disease.

In italic: chronic endpoints.

Appendix 3.2 Detailed analysis for 11 chemicals

	Chemical	CASRN	Tested animal	Critical endpoint	Route of exposure	Groupe 1 Dose (concentration) [mg/kg-day] ([mg/m3])	Response	Groupe 2 Dose (concentration) [mg/kg-day] ([mg/m3])	Response	Groupe 3 Dose (concentration) [mg/kg-day] ([mg/m3])	Response	Groupe 4 Dose (concentration) [mg/kg-day] ([mg/m3])	Response	Groupe 5 Dose (concentration) [mg/kg-day] ([mg/m3])	Response
1	Beryllium	7440-41-7	Dogs	Small intestinal lesions	Oral	0	0/10	0.026	0/10	0.135	0/10	1.2	1/10	14.8	9/10
2	MDI	9016-87-9	Rats	Hyperplasia of the olfactory epithelium	Inhalation	0	14/60	0.036	13/60	0.18	26/60	1.1	32/60		
3	Methyl methacrylate	80-62-6	Rats	Degeneration of the olfactory epithelium	Inhalation	0	0/39	102	0/47	408	35/48	1621	38/38		

Appendix 3.2.1 Noncarcinogenic bioassay data reported in the IRIS database [EPA, 1998] for beryllium, MDI (Methylene Diphenyl Diisocyanate) and methyl methacrylate.

	Chemical	CAS RN	Formula [Chemfinder, 1999]	Production [OECD, 1997]	Route of exposure	Data type	Critical endpoint	$NOAEL_a$ [unit]	$ED(C)_{10a}$ [unit]	CFa->h [-]	$ED(C)_{10h}$ [unit]	$BMD(C)_{10h}$ [unit]	Unit	$NOAEL_a$ [mg/kg-day]	ED_{10h} [mg/kg-day]	CFsub->chr [-]	ED_{10h} (*) [mg/kg-day]	β_{ED10} [Risk / mg/kg-day]	$DALY_p$ [yr lost /pers]	EF [yr lost /mg absorbed]	LD_{50a} [mg/kg] [NIOSH, 1998]
Direct calculation of the ED_{10h}																					
1	Beryllium	7440-41-7	Be		oral	Dogs, 3.3 year	Small intestinal lesions	0.5	1.4	1.6	0.85	0.3	[mg/kg-day]	0.5	0.85	1	8.5E-01	1.2E-01	1.1	7.2E-08	0.496
2	Methyl methacrylate	80-62-6	C5H8O2	HPV	inh.	Rat, 2 years	Degeneration of the epithelium	102	178	3.5	8.9	7.2	[mg/m3]	64.1	2.54	1	2.5E+00	3.9E-02	1.1	2.4E-08	7872
3	MDI	101-68-8	C15H10N2O2	HPV	inh.	Rat, 2 years	Hyperplasia of the epithelium	0.2	1.21	2.3	0.094	0.08	[mg/m3]	0.126	0.027	1	2.7E-02	2.7E+00	1.1	2.3E-06	2200
4	Naphtalene	91-20-3	C10H8	HPV	oral	Rat, 3 months	Decrease in body weight	100	171	6	20	15	[mg/kg-day]	100	20	3.3	6.1E+00	1.7E-02	1.1	1.0E-08	490
5	Phosphoric acid	7664-38-2	H3O4P	HPV	inh.	Rat, 3 months	Bronchiolar fibrosis	50	150	1.6	5.1	3.4	[mg/m3]	31.43	1.46	3.3	4.4E-01	2.3E-01	1.1	1.4E-07	1530
6	Chromium(VI)	18540-29-9	Cr(VI)		inh.	Rat, 1 to 3 months	LDH in bronchoalveolar lavage flui	n.a.	0.18	2.1	0.036	0.016	[mg/m3]	n.a.	0.010	3	3.4E-03	2.9E+01	1.1	1.8E-05	n.a
ED_{10h} derived from the BMD_{10h} (Equation 3.4)																					
7	Antimony trioxide	1309-64-4	Sb2O3	HPV	inh.	Rats, 1 year	Interstitial inflammation	0.489	1.57	2.1	0.13	0.074	[mg/m3]	0.307	0.038	2	1.9E-02	5.3E+00	1.1	3.2E-06	20000
8	Carbon disulfide	75-15-0	CS2	HPV	inh.	Epidem. study-12 yrs	Nervous system disfunction	n.a.	n.a.	1	35.46	19.7	[mg/m3]	n.a.	10.13	3.3	3.1E+00	3.3E-02	1.1	2.0E-08	2780
9	Methylmercury	22967-92-6			oral	Epidem. study-2 yrs	Neurological abnormalities	n.a.	n.a.	1	0.002	0.001	[mg/kg-day]	n.a.	0.002	3	6.6E-04	3.0E+01	1.1	1.9E-05	n.a.
10	1,1,1,2 Tetrafluoroethane	811-97-2	C2H2F4	HPV	inh.	Rat, 2 years	Leydig cell hyperplasia	41800	82800	1	14760	8200	[mg/m3]	26274	4217	1	4.2E+03	2.4E-05	1.1	1.5E-11	2.20E+06
11	Tributyltin oxide	56-35-9	C24H54OSn2	HPV	oral	Rat, 2 years	Immunosupression	0.025	0.054	6	0.009	0.005	[mg/kg-day]	0.025	0.009	1	9.0E-03	1.1E+01	1.1	6.8E-06	87

Appendix 3.2.2 Main parameters of the studied chemicals: effect factors EF derived from the Disaility Adjusted Life Years per affected person ($DALY_p$) and the slope factor β_{ED10} (see equation (2.19)), benchmark dose BMD_{10h} and effect dose ED_{10h} for humans, conversion factors CF (see section 3.4.3 for their definition), no observable adverse effect level $NOAEL_a$ and lethal dose LD_{50a} for animals.

For chemicals 1 to 3, we used bioassay data available in the IRIS database [EPA, 1998] to calculate the effect dose, using the multistage model provided by Crouch [1985].

For chemicals 4 to 6, we used the effect dose provided in the IRIS database [EPA, 1998].

For chemicals 7 to 11, we extrapolated the effect dose from the benchmark dose provided in the IRIS database [EPA, 1998], using equation (3.4.1).

* : Values after the application of the conversion factor for a lifetime exposure.

HVC (High Volume Chemical) chemical are substances whose production/importation exceeds 1000 tonnes in at least one OECD country [OECD, 1997].

MDI: Methylene Diphenyl Diisocyanate; n.a.: not available

	Chemical	CASRN	MULTISTAGE MODEL		QUANTAL LINEAR MODEL		QUANTAL QUADRATIC MODEL		WEIBULL MODEL		LOGISTIC MODEL		Max value/Min.value of the ED_{10h}
			ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/kg-day]	ED_{10h} [mg/ kg-day]	β_{ED10} [Risk/ mg/kg-day]	
1	Beryllium	7440-41-7	8.5E-01	1.2E-01	4.8E-01	2.1E-01	1.9E+00	5.3E-02	8.2E-01	1.2E-01	2.8E+00	3.6E-02	5.8
2	Methyl methacrylate	80-62-6	2.5E+00	3.9E-02	6.0E-01	1.6E-01	1.8E+00	5.7E-02	3.9E+00	2.6E-02	5.0E+00	1.9E-02	8.3
3	MDI	101-68-8	2.7E-02	3.7E+00	3.7E-02	2.7E+00	8.0E-02	1.3E+00	3.7E-02	2.7E+00	5.1E-02	1.9E+00	3.0

Appendix 3.2.3.a) Effect dose ED_{10h} and slope factor β_{ED10} for beryllium, methyl methacrylate and methylene diphenyl diisocyanate (MDI), derived by applying five different curve-fitting models provided in the benchmark dose software [EPA, 1999].

	Chemical	CASRN	MULTISTAGE MODEL		QUANTAL LINEAR MODEL		QUANTAL QUADRATIC MODEL		WEIBULL MODEL		LOGISTIC MODEL		Max value/Min.value of the $ED_{0.001h}$
			$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	$ED_{0.001h}$ [mg/ kg-day]	$\beta_{ED0.001}$ [Risk/ mg/kg-day]	
1	Beryllium	7440-41-7	8.9E-05	1.1E-01	4.6E-05	2.2E-01	6.1E-03	1.6E-03	6.1E-04	1.6E-02	7.4E-04	1.4E-02	135
2	Methyl methacrylate	80-62-6	1.2E-01	8.7E-05	6.0E-05	1.7E-01	1.7E-02	5.8E-04	8.6E-01	1.2E-05	3.0E+00	3.3E-06	50200
3	MDI	101-68-8	3.6E-06	2.8E+00	3.6E-06	2.8E+00	8.0E-04	1.3E-02	3.6E-06	2.8E+00	5.8E-06	1.7E+00	222

Appendix 3.2.3.b) Effect dose $ED_{0.001h}$ and slope factor $\beta_{ED0.001}$ for beryllium, methyl methacrylate and methylene diphenyl diisocyanate (MDI), derived by applying five different curve-fitting models provided in the benchmark dose software [EPA, 1999].

›pendix 3.3 Slope factors and effect factors derived from the NOAEL

Chemical	CAS RN	Production (OECD, 1997)	$NOAEL_{ADJ}$ (mg/kg-day)	$NOEL_{ADJ}$ (mg/kg-day)	Animal	Critical endpoint	ED_{10a} (mg/kg-day)	CFa->h (-)	CFsub->chr (-)	ED_{10h} (mg/kg-day)	$\beta_{ED10\text{-}Ext}$ (Risk / mg/kg-day)	$DALY_p$ (yr lost / pers)	EF (yr lost / mg absorb
Acenaphthene	83-32-9	HPV	175		Mouse	Hepatotoxicity	2.8E+02	13	3.3	6.5E+00	1.5E-02	1.1	9.4E-09
Acetochlor	34256-82-1		2		Dog	Salivation, decreased blood glucose levels	3.2E+00	1.6	1	2.0E+00	5.0E-02	1.1	3.1E-08
Acetone	67-64-1	HPV		100	Rat	Increased liver and kidney weight	1.6E+02	6	3.3	8.1E+00	1.2E-02	1.1	7.6E-09
Acetonitrile	75-05-8	HPV	19.3		Mouse	Decreased RBC (erythrocytes) counts	3.1E+01	13	1	2.4E+00	4.2E-02	1.1	2.6E-08
Acetophenone	98-86-2	HPV	423		Rat	General toxicity	6.8E+02	6	3.3	3.4E+01	2.9E-03	1.1	1.8E-09
Acifluorfen sodium	62476-59-9			1.25	Rat	Mortality and kidney lesions	2.0E+00	6	1	3.3E-01	3.0E-01	1.1	1.8E-07
Acrylamide	79-06-1	HPV		0.2	Rat	Nerve damage	3.2E-01	6	3.3	1.6E-02	6.2E+00	1.1	3.8E-06
Acrylic acid	79-10-7	HPV	53		Rat	Reduced pupils weight	8.5E+01	6	1	1.4E+01	7.1E-03	1.1	4.4E-09
Alachlor	15972-60-8		1		Dog	Hemosiderosis	1.6E+00	1.6	1	1.0E+00	1.0E-01	1.1	6.2E-08
Alar	1596-84-5			15	Rat	No adverse effects	2.4E+01	6	1	4.0E+00	2.5E-02	1.1	1.5E-08
Aldicarb	116-06-3			0.01	Human	Sweating	1.6E-02	1	1	1.6E-02	6.3E+00	0.11	3.8E-07
Aldicarb sulfone	1646-88-4		0.11		Dog	Brain cholinesterase inhibition in females	1.8E-01	1.6	1	1.1E-01	9.1E-01	1.1	5.6E-07
Ally	74223-64-6			25	Rat	Decreased body weight	4.0E+01	6	1	6.7E+00	1.5E-02	1.1	9.2E-09
Ally alcohol	107-18-6	HPV		4.8	Rat	Impaired renal function, increased liver and kidneys weight	7.7E+00	6	3.3	3.9E-01	2.6E-01	1.1	1.6E-07
Aluminium phosphide	20859-73-8		0.043		Rat	Body weight	6.9E-02	6	1	1.1E-02	8.7E+00	1.1	5.4E-06
Amdro	67485-29-4			0.33	Dog	Increased organ weight	5.3E-01	1.6	3.3	1.0E-01	1.0E+00	1.1	6.2E-07
Ametryn	834-12-8	HPV		8.6	Rat	Liver toxicity	1.4E+01	6	3.3	6.9E-01	1.4E-01	1.1	8.9E-08
Amitraz	33089-61-1			0.25	Dog	Increased mean blood sugar concentration	4.0E-01	1.6	1	2.5E-01	4.0E-01	1.1	2.5E-07
Ammonium sulfamate	7773-06-0	HPV		214.3	Rat	Decrease in body weights	3.4E+02	6	3.3	1.7E+01	5.8E-03	1.1	3.6E-09
Anthracene	120-12-7	HPV		1000	Mice	No observed effects	1.6E+03	13	3.3	3.7E+01	2.7E-03	1.1	1.6E-09
Apollo	74115-24-5			1.25	Dog	Liver effects; organ weight change	2.0E+00	1.6	1	1.3E+00	8.0E-02	1.1	4.9E-08
Aroclor 1016	12674-11-2		0.007		Monkey	Reduced birth weight	1.1E-02	1.8	3.3	1.9E-03	5.3E+01	1.1	3.3E-05
Arsenic inorganic	7440-38-2		0.0008		Human	Hyperpigmentation, keratosis	1.3E-03	1	1	1.3E-03	7.8E+01	1.1	4.8E-05
Assure	76578-14-8		1.1		Rat	Liver cell enlargement	1.8E+00	6	1	2.9E-01	3.4E-01	1.1	2.1E-07
Atrazine	1912-24-9	HPV	3.5		Rat	Decreased body weight gain	5.6E+00	6	1	9.3E-01	1.1E-01	1.1	6.6E-08
Barium and compounds	7440-39-3		0.21		Human	Hypertension	3.4E-01	1	1	3.4E-01	3.0E-01	1.1	1.8E-07
Bayleton	43121-43-3	HPV		2.5	Rat	Decreased body weight	4.0E+00	6	1	6.7E-01	1.5E-01	1.1	9.2E-08
Baythroid	68359-37-5			2.5	Rat	Decreased body weight	4.0E+00	6	1	6.7E-01	1.5E-01	1.1	9.2E-08
Benefin	1861-40-1		25		Dog	Depressed erythrocyte counts	4.0E+01	1.6	1	2.5E+01	4.0E-03	1.1	2.5E-09
Bentazon	25057-89-0		3.2		Dog	Blood loss into the gastrointestinal tract	5.1E+00	1.6	1	3.2E+00	3.1E-02	1.1	1.9E-08
Benzaldehyde	100-52-7	HPV		143	Rat	Forestomach lesions, kidney toxicity	2.3E+02	6	3.3	1.2E+01	8.7E-03	1.1	5.3E-09
Benzoic acid	65-85-0	HPV	34		Human	No adverse effects	5.4E+01	1	1	5.4E+01	1.8E-03	0.11	1.1E-10
beta-Chloronaphthalene	91-58-7		250		Mouse	Dyspnea, abnormal appearance, liver enlargement	4.0E+02	13	3.3	9.3E+00	1.1E-02	1.1	6.6E-09
Bidrin	141-66-2			0.1	Rat	Decreased pupils survival	1.6E-01	6	3.3	8.1E-03	1.2E+01	1.1	7.6E-06
Biphenthrin	82657-04-3			1.5	Dog	Tremors	2.4E+00	1.6	1	1.5E+00	6.7E-02	1.1	4.1E-08
1,1-Biphenyl	92-52-4	HPV	50		Rat	Kidney damage	8.0E+01	6	1	1.3E+01	7.5E-03	1.1	4.6E-09
Bis(2-chloroisopropyl) ether	39638-32-9		35.8		Mouse	Decrease in hemoglobin	5.7E+01	13	1	4.4E+00	2.3E-02	1.1	1.4E-08
Boron (Boron and Borates only)	7440-42-8		8.8		Dog	Testicular atrophy, spermatogenic arrest	1.4E+01	1.6	1	8.8E+00	1.1E-02	1.1	7.0E-09
Bromoform	75-25-2			17.9	Rat	Hepatic lesions	2.9E+01	6	3.3	1.4E+00	6.9E-02	1.1	4.3E-08
Bromomethane	74-83-9	HPV	1.4		Rat	Epithelial hyperplasia of the forestomach	2.2E+00	6	3.3	1.1E-01	8.8E-01	1.1	5.4E-07
Bromoxynil	1689-84-5			5	Rat	No adverse effects	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
Bromoxynil octanoate	1689-99-2	HPV		7.3	Rat	No effects	1.2E+01	6	1	1.9E+00	5.1E-02	1.1	3.2E-08

	Chemical	CAS RN	Production [OECD, 1997]	$NOAEL_{w(ADJ)}$ [mg/kg-day]	$NOEL_{w(ADJ)}$ [mg/kg-day]	Animal	Critical endpoint	ED_{10a} [mg/kg-day]	CFa-sh [-]	CFsub-sch [-]	ED_{10h} [mg/kg-day]	$\beta_{ED10-Ener}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg abse
3	n-Butanol	71-36-3	HPV	125		Rat	Hypoactivity and ataxia	2.0E+02	6	3.3	1.0E+01	9.9E-03	1.1	6.1E-09
4	Butyl benzyl phthalate	85-68-7	HPV	159		Rat	Significantly increased liver-to-body weight and liver-to-brain weight ratios	2.5E+02	6	3.3	1.3E+01	7.8E-03	1.1	4.8E-09
5	Butylate	2008-41-5		5		Dog	Increased relative liver weight in male dogs	8.0E+00	1.6	1	5.0E+00	2.0E-02	1.1	1.2E-08
6	Butylphthalyl butylglycolate	85-70-1			1000	Rat	No adverse effect	1.6E+03	6	1	2.7E+02	3.8E-04	1.1	2.3E-10
7	*Cadmium*	7440-43-9	HPV	0.01		Human	Proteinuria	1.6E-02	1	1	1.6E-02	6.3E+00	0.11	3.8E-07
8	Calcium cyanide	592-01-8		19.1		Rat	Weight loss, thyroid effects and myelin degeneration	3.1E+01	6	1	5.1E+00	2.0E-02	1.1	1.2E-08
9	Caprolactam	105-60-2	HPV	50		Rat	Reduced offspring body weight	8.0E+01	6	1	1.3E+01	7.5E-03	1.1	4.6E-09
0	Captan	133-06-2			12.5	Rat	Decreased mean body weights	2.0E+01	6	1	3.3E+00	3.0E-02	1.1	1.8E-08
1	Carbaryl	63-25-2		9.6		Rat	Kidney and liver toxicity	1.5E+01	6	1	2.6E+00	3.9E-02	1.1	2.4E-08
2	Carbofuran	1563-66-2	HPV		0.5	Dog	RBC (erythrocytes) and plasma cholinesterase inhibition	8.0E-01	1.6	1	5.0E-01	2.0E-01	1.1	1.2E-07
3	Carbon disulfide	75-15-0	HPV		11	Rabbit	Fetal toxicity-malformation	1.8E+01	6	1	2.9E+00	3.4E-02	1.1	2.1E-08
4	Carbon tetrachloride	56-23-5	HPV	0.7		Rat	Liver lesions	1.1E+00	6	3.3	5.7E-02	1.8E+00	1.1	1.1E-06
5	Carbosulfan	55285-14-8			1	Rat	Decreased body weight	1.6E+00	6	1	2.7E-01	3.8E-01	1.1	2.3E-07
6	Carboxin	5234-68-4	HPV		10	Rat	Reduced weight gain, organ weight changes, increased mortality	1.6E+01	6	3.3	8.1E-01	1.2E-01	1.1	7.6E-08
7	Chlordane	12789-03-6		0.15		Mouse	Hepatic Necrosis	2.4E-01	13	1	1.8E-02	5.4E+00	1.1	3.3E-06
8	Chlorimuron-ethyl	90982-32-4			6.25	Dog	Increase in WBC (leukocytes), decreased in RBC (erythrocytes) in females	1.0E+01	1.6	1	6.3E+00	1.6E-02	1.1	9.8E-09
9	Chlorine	7782-50-5	HPV	14.4		Rat	No observed adverse effects	2.3E+01	6	1	3.8E+00	2.6E-02	1.1	1.6E-08
0	Chlorine cyanide	506-77-4		25.3		Rat	Weight loss, thyroid effects and myelin degeneration	4.0E+01	6	1	6.7E+00	1.5E-02	1.1	9.1E-09
1	Chlorobenzene	108-90-7	HPV	19		Dog	Histopathologic changes in liver	3.0E+01	1.6	3.3	5.8E+00	1.7E-02	1.1	1.1E-08
2	Chlorobenzilate	510-15-6			5	Rabbit	Decreased stool quantity, food consumption and body weight gains	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
3	2-Chlorophenol	95-57-8	HPV	5		Rat	Reproductive effects	8.0E+00	6	3.3	4.0E-01	2.5E-01	1.1	1.5E-07
4	Chlorothalonil	1897-45-6			1.5	Dog	Renal tubular epithelial vacuolation	2.4E+00	1.6	1	1.5E+00	6.7E-02	1.1	4.1E-08
5	o-Chlorotoluene	95-49-8	HPV	20		Rat	Decrease in body weight	3.2E+01	6	3.3	1.6E+00	6.2E-02	1.1	3.8E-08
6	Chlorpropham	101-21-3			50	Rat	Kidney, spleen, liver and bone marrow toxicity	8.0E+01	6	1	1.3E+01	7.5E-03	1.1	4.6E-09
7	Chlorpyrifos	2921-88-2			0.03	Human	Decreased plasma cholinesterase activity	4.8E-02	1	1	4.8E-02	2.1E+00	0.11	1.3E-07
8	Chlorsulfuron	64902-72-3			5	Rat	Decreased body weight	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
9	*Chromium(III), insoluble salts*	16065-83-1		1468		Rat	No effects observed	*2.3E+03*	6	1	*3.9E+02*	*2.6E-04*	*1.1*	*1.6E-10*
0	*Chromium(VI)*	18540-29-9		2.5		Rat	None reported	4.0E+00	6	1	6.7E-01	1.5E-01	1.1	9.2E-08
1	Copper cyanide	544-92-3		5		Rat	Decreased body and organ weights, histopathologic alterations in liver	8.0E+00	6	3.3	4.0E-01	2.5E-01	1.1	1.5E-07
2	Cumene	98-82-8	HPV	110		Rat	Increased average kidney weight in female rats	1.8E+02	6	3.3	8.9E+00	1.1E-02	1.1	6.9E-09
3	Cyanide, free	57-12-5		10.8		Rat	Weight loss, thyroid effects and myelin degeneration degeneration	1.7E+01	6	1	2.9E+00	3.5E-02	1.1	2.1E-08
4	Cyanogen	460-19-5		21.6		Rat	No adverse effects	3.5E+01	6	1	5.8E+00	1.7E-02	1.1	1.1E-08
5	Cyanogen bromide	506-68-3		44		Rat	Weight loss, thyroid effects and myelin degeneration degeneration	7.0E+01	6	1	1.2E+01	8.5E-03	1.1	5.2E-09
6	Cyclohexanone	108-94-1	HPV	462		Rat	Body weight depression	7.4E+02	6	1	1.2E+02	8.1E-04	1.1	5.0E-10
7	Cyclohexylamine	108-91-8	HPV	18		Rat	Testicular damage	2.9E+01	6	1	4.8E+00	2.1E-02	1.1	1.3E-08
8	Cyhalothrin/Karate	68085-85-8			0.5	Rat	Reduced body weight gain preceding pregnancy; reduced body weight gain	8.0E-01	6	1	1.3E-01	7.5E-01	1.1	4.6E-07
9	Cypermethrin	52315-07-8			1	Dog	G.I. (gastroin(estinal) tract disturbances	1.6E+00	1.6	1	1.0E+00	1.0E-01	1.1	6.2E-08
0	Cyromazine	66215-27-8			0.75	Dog	Hematologic effects	1.2E+00	1.6	1	7.5E-01	1.3E-01	1.1	8.2E-08
1	Dacthal	1861-32-1		1		Rat	Effects on the lungs liver, kidney, thyroid	1.6E+00	6	1	2.7E-01	3.8E-01	1.1	2.3E-07
2	Dalapon, sodium salt	75-99-0			8.45	Rat	Increased kidney body weight ratio	1.4E+01	6	1	2.3E+00	4.4E-02	1.1	2.7E-08
3	Dantoi	39515-41-8		2.5		Dog	Tremors	4.0E+00	1.6	1	2.5E+00	4.0E-02	1.1	2.5E-08
4	Decabromodiphenyl ether (DBDPE)	1163-19-5	HPV		1	Rat	No adverse effects observed	1.6E+00	6	1	2.7E-01	3.8E-01	1.1	2.3E-07
5	Di(2-ethylhexyl)adipate	103-23-1	HPV	170		Rat	Changes in body weight and liver weight, increased liver weight, etc	2.7E+02	6	1	4.5E+01	2.2E-03	1.1	1.4E-09
6	1,4-Dibromobenzene	106-37-6		10		Rat	Liver/body weight ratio and hepatic microsomal enzyme induction	1.6E+01	6	3.3	8.1E-01	1.2E-01	1.1	7.6E-08
7	Dibromochloromethane	124-48-1			21.4	Rat	Hepatic lesions	3.4E+01	6	3.3	1.7E+00	5.8E-02	1.1	3.6E-08
8	Dibutyl phthalate	84-74-2	HPV	125		Rat	Increased mortality	2.0E+02	6	3.3	1.0E+01	9.9E-03	1.1	6.1E-09
9	Dicamba	1918-00-9			3	Rabbit	Maternal and fetal toxicity	4.8E+00	6	1	8.0E-01	1.3E-01	1.1	7.7E-08

Chemical	CAS RN	Production [OECD, 1997]	$NOAEL_{s(ADI)}$ [mg/kg-day]	$NOEL_{s(ADI)}$ [mg/kg-day]	Animal	Critical endpoint	ED_{10s} [mg/kg-day]	CFa->h [-]	CFsub->chr [-]	ED_{10h} [mg/kg-day]	$\beta_{ED10hExp}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg abse
1,2-Dichlorobenzene	95-50-1	HPV	85.7		Rat	No adverse effects observed	1.4E+02	6	3.3	6.9E+00	1.4E-02	1.1	8.9E-09
Dichlorodifluoromethane	75-71-8	HPV	15		Rat	Reduced body weight	2.4E+01	6	1	4.0E+00	2.5E-02	1.1	1.5E-08
p,p'-Dichlorodiphenyltrichloroethane (DDT)	50-29-3	HPV		0.05	Rat	Liver lesions	8.0E-02	6	1	1.3E-02	7.5E+00	1.1	4.6E-06
trans-1,2-Dichloroethylene	156-60-5	HPV	17		Mouse	Increased serum alkaline phosphatase in male mice	2.7E+01	12	3.3	6.3E-01	1.6E-01	1.1	9.7E-08
Dichloromethane	75-09-2	HPV	5.85		Rat	Liver toxicity	9.4E+00	6	1	1.6E+00	6.4E-02	1.1	3.9E-08
2,4-Dichlorophenol	120-83-2	HPV		0.3	Rat	Decreased delayed hypersensitivity response	4.8E-01	6	1	8.0E-02	1.3E+00	1.1	7.7E-07
4-(2,4-Dichlorophenoxy)butyric acid	94-82-6		8		Dog	Internal hemorrhage, mortality	1.3E+01	1.6	3.3	2.4E+00	4.1E-02	1.1	2.5E-08
2,4-Dichlorophenoxyacetic acid (2,4-D)	94-75-7	HPV	1		Rat	Hematologic, hepatic and renal toxicity	1.6E+00	6	1	2.7E-01	3.8E-01	1.1	2.3E-07
2,3-Dichloropropanol	616-23-9	HPV	10		Rat	Myocardial degeneration, hepatotoxicity and nephrotoxicity	1.6E+01	6	3.3	8.1E-01	1.2E-01	1.1	7.6E-08
1,3-Dichloropropene	542-75-6	HPV		3	Rats	Increased organ weights	4.8E+00	6	3.3	2.4E-01	4.1E-01	1.1	2.5E-07
Dichlorvos	62-73-7	HPV	0.05		Dog	Plasma and RBC (erythrocytes), cholinesterase inhibition	8.0E-02	1.6	1	5.0E-02	2.0E+00	1.1	1.2E-06
Dieldrin	60-57-1		0.005		Rat	Liver lesions	8.0E-03	6	1	1.3E-03	7.5E+01	1.1	4.6E-05
Diethyl phthalate	84-66-2	HPV	750		Rat	Decreased growth rate, food consumption and altered organ weights	1.2E+03	6	3.3	6.1E+01	1.7E-03	1.1	1.0E-09
Difenzoquat	43222-48-6			25	Rat	Decreased body weight	4.0E+01	6	1	6.7E+00	1.5E-02	1.1	9.2E-09
Diflubenzuron	35367-38-5			2	Dog	Methemoglobin and sulfhemoglobin formation	3.2E+00	1.6	1	2.0E+00	5.0E-02	1.1	3.1E-08
Dissopropyl methylphosphonate (DIMP)	1445-75-6			75	Dog	No effects related to treatment	1.2E+02	1.6	3.3	2.3E+01	4.4E-03	1.1	2.7E-09
Dimethipin	55290-64-7			2	Rat	Increased absolute and relative liver weight	3.2E+00	6	1	5.3E-01	1.9E-01	1.1	1.2E-07
Dimethoate	60-51-5	HPV		0.05	Rat	Brain cholinesterase inhibition	8.0E-02	6	1	1.3E-02	7.5E+00	1.1	4.6E-06
2,4-Dimethylphenol	105-67-9	HPV	50		Mouse	Clinical signs (lethargy, prostration, and ataxia) and hematological changes	8.0E+01	13	3.3	1.9E+00	5.4E-02	1.1	3.3E-08
2,6-Dimethylphenol	576-26-1	HPV		0.6	Rat	Body weight changes and histopathological changes of internal organs	9.6E-01	6	3.3	4.8E-02	2.1E+00	1.1	1.3E-06
3,4-Dimethylphenol	95-65-8	HPV		1.4	Rat	Changes in blood pressure and body weight; Changes in liver, kidney and spleen	2.2E+00	6	3.3	1.1E-01	8.8E-01	1.1	5.4E-07
m-Dinitrobenzene	99-65-0	HPV	0.4		Rat	Increased splenic weight	6.4E-01	6	3.3	3.2E-02	3.1E+00	1.1	1.9E-06
2,4-Dinitrotoluene	121-14-2	HPV	0.2		Dog	Neurotoxicity, Heinz bodies and biliary tract hyperplasia	3.2E-01	1.6	1	2.0E-01	5.0E-01	1.1	3.1E-07
Diphenamid	957-51-7			3	Dog	Liver toxicity	4.8E+00	1.6	1	3.0E+00	3.3E-02	1.1	2.1E-08
Diphenylamine	122-39-4	HPV		2.5	Dog	Decreased body weight gain, and increased liver and kidney weights	4.0E+00	1.6	1	2.5E+00	4.0E-02	1.1	2.5E-08
Diquat	85-00-7			0.22	Rat	Minimal lens opacity and cataracts	3.5E-01	6	1	5.9E-02	1.7E+00	1.1	1.0E-06
Diuron	330-54-1	HPV		0.625	Dog	Abnormal pigments in blood	1.0E+00	1.6	1	6.3E-01	1.6E-01	1.1	9.8E-08
Dodine	02.10.35			1.25	Dog	Thyroid toxicity	2.0E+00	1.6	1	1.3E+00	8.0E-02	1.1	4.9E-08
Endosulfan	115-29-7	HPV	0.6		Rat	Reduced body weight gain	9.6E-01	6	1	1.6E-01	6.3E-01	1.1	3.8E-07
Endothall	145-73-3			2	Dog	Increased absolute and relative weights of stomach and small intestine	3.2E+00	1.6	1	2.0E+00	5.0E-02	1.1	3.1E-08
Endrin	72-20-8			0.025	Dog	Mild histological lesions in liver, occasional convulsions	4.0E-02	1.6	1	2.5E-02	4.0E+00	1.1	2.5E-06
Ethion	563-12-2			0.05	Human	Plasma cholinesterase inhibition	8.0E-02	1	1	8.0E-02	1.3E+00	0.11	7.7E-08
Ethyl acetate	141-78-6	HPV		900	Rat	Mortality and body weight loss	1.4E+03	6	3.3	7.3E+01	1.4E-03	1.1	8.5E-10
S-Ethyl dipropylthiocarbamate (EPTC)	759-94-4			2.5	Rat	Degenerative cardiomyopathy	4.0E+00	6	1	6.7E-01	1.5E-01	1.1	9.2E-08
Ethyl ether	60-29-7	HPV	500		Rat	Depressed body weights	8.0E+02	6	3.3	4.0E+01	2.5E-03	1.1	1.5E-09
Ethyl p-nitrophenyl phenylphosphorothioate	2104-64-5			0.01	Hen	Neurotoxicity	1.6E-02	6	3.3	8.1E-04	1.2E+02	1.1	7.6E-05
Ethylbenzene	100-41-4	HPV		97.1	Rat	Liver and kidney toxicity	1.6E+02	6	3.3	7.8E+00	1.3E-02	1.1	7.8E-09
Ethylene glycol	107-21-1	HPV	200		Rat	Kidney toxicity	3.2E+02	6	1	5.3E+01	1.9E-03	1.1	1.2E-09
Ethylphthalyl ethylglycolate (EPEG)	84-72-0			250	Rat	Kidney damage and reduced lifespan	4.0E+02	6	1	6.7E+01	1.5E-03	1.1	9.2E-10
Express	101200-48-0			0.79	Dog	Elevated serum bilirubin and AST (aspartate aminotransferase) levels	1.3E+00	1.6	1	7.9E-01	1.3E-01	1.1	7.8E-08
Fenamiphos	22224-92-6	HPV		0.025	Dog	Cholinesterase inhibition	4.0E-02	1.6	1	2.5E-02	4.0E+00	1.1	2.5E-06
Fluometuron	2164-17-2		12.5		Rat	No adverse effects	2.0E+01	6	3.3	1.0E+00	9.9E-02	1.1	6.1E-08
Fluoranthene	206-44-0		125		Mouse	Nephropathy, increased liver weights, hematological alterations, and clinical effects	2.0E+02	13	3.3	4.7E+00	2.1E-02	1.1	1.3E-08
Fluorene	86-73-7		125		Mouse	Decreased RBC (erythrocytes) , packed cell volume and hemoglobin	2.0E+02	13	3.3	4.7E+00	2.1E-02	1.1	1.3E-08
Fluorine (soluble fluoride)	7782-41-4	HPV	0.06		Human	Objectionable dental fluorosis, a cosmetic effect	9.6E-02	1	1	9.6E-02	1.0E+00	0.11	6.4E-08
Fluridone	59756-60-4			8	Rat	Glomerulonephritis, atrophic testes, eye keratitis; decreased body weight	1.3E+01	6	1	2.1E+00	4.7E-02	1.1	2.9E-08
Flurprimidol	56425-91-3			1.8	Rat	Increased incidence of hepatocellular changes including fatty change and vacuolation.	2.9E+00	6	1	4.8E-01	2.1E-01	1.1	1.3E-07

Chemical	CAS RN	Production [OECD, 1997]	$NOAEL_{w(ADJ)}$ [mg/kg-day]	$NOEL_{w(ADJ)}$ [mg/kg-day]	Animal	Critical endpoint	ED_{10a} [mg/kg-day]	CFa->h [-]	CFsub->chr [-]	ED_{10b} [mg/kg-day]	$\beta_{ED10\text{-}Exc}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorb
Fluvalinate	69409-94-5			1	Rat	Decreases in body weight gain; increase in plantar ulcer (females)	1.6E+00	6	1	2.7E-01	3.8E-01	1.1	2.3E-07
Folpet	133-07-3			10	Dog	Decreased body weight gain, altered serum chemistry parameters	1.6E+01	1.6	1	1.0E+01	1.0E-02	1.1	6.2E-09
Fonofos	944-22-9			0.2	Dog	Cholinesterase inhibition, cholinergic symptoms, and increased liver weight	3.2E-01	1.6	1	2.0E-01	5.0E-01	1.1	3.1E-07
Formaldehyde	50-00-0	HPV	15		Rat	Reduced weight gain, histopathology in rats	2.4E+01	6	1	4.0E+00	2.5E-02	1.1	1.5E-08
Fosetyl-al	39148-24-8	HPV		250	Dog	Slight testicular degeneration	4.0E+02	1.6	1	2.5E+02	4.0E-04	1.1	2.5E-10
Furan	110-00-9		1.4		Mouse	Hepatic lesions	2.2E+00	13	3.3	5.2E-02	1.9E+00	1.1	1.2E-06
Glufosinate-ammonium	77182-82-2	HPV		0.4	Rat	Increased absolute and relative kidney weights in males	6.4E-01	6	3.3	3.2E-02	3.1E+00	1.1	1.9E-06
Glycidaldehyde	765-34-4		1.09		Rat	Weight gain retardation, enlarged adrenals, hydropic renal pelvis	1.7E+00	6	3.3	8.8E-02	1.1E+00	1.1	7.0E-07
Glyphosate	1071-83-6	HPV		10	Rat	Increased incidence of renal tubular dilation in F3b offspring.	1.6E+01	6	1	2.7E+00	3.8E-02	1.1	2.3E-08
Haloxyfop-methyl	69806-40-2			0.005	Rat	Reduced relative kidney weights; Reduced fertility in the F1/F2b generation	8.0E-03	6	1	1.3E-03	7.5E-01	1.1	4.6E-05
Harmony	79277-27-3			1.25	Rat	Reduced body weight gains in males, reduced serum sodium in males and females	2.0E+00	6	1	3.3E-01	3.0E-01	1.1	1.8E-07
Heptachlor	76-44-8			0.15	Rat	Liver weight increases increases in males	2.4E-01	6	1	4.0E-02	2.5E+00	1.1	1.5E-06
Hexabromobenzene	87-82-1		2		Rat	Induced serum carboxylesterase activity	3.2E+00	6	3.3	1.6E-01	6.2E-01	1.1	3.8E-07
Hexachlorobenzene	118-74-1	HPV	0.08		Rat	Liver effects	1.3E-01	6	1	2.1E-02	4.7E+00	1.1	2.9E-06
gamma-Hexachlorocyclohexane	58-89-9	HPV	0.33		Rat	Liver and kidney toxicity	5.3E-01	6	3.3	2.7E-02	3.8E+00	1.1	2.3E-06
Hexachlorocyclopentadiene (HCCPD)	77-47-4	HPV	7		Rat	Stomach lesions	1.1E+01	6	3.3	5.7E-01	1.8E-01	1.1	1.1E-07
Hexachloroethane	67-72-1		1		Rat	Atrophy and degeneration of the renal tubules	1.6E+00	6	3.3	8.1E-02	1.2E+00	1.1	7.6E-07
Hexahydro-1,3,5-trinitro-1,3,5-triazine	121-82-4	HPV		0.3	Rat	Inflammation of the prostate	4.8E-01	6	1	8.0E-02	1.3E+00	1.1	7.7E-07
Hexazinone	51235-04-2			10	Rat	Decreased body weight	1.6E+01	6	1	2.7E+00	3.8E-02	1.1	2.3E-08
Hydrogen cyanide	74-90-8	HPV	11.2		Rat	Weight loss, thyroid effects, and myelin degeneration	1.8E+01	6	1	3.0E+00	3.3E-02	1.1	2.1E-08
Hydrogen sulfide	7783-06-4	HPV	3.1		Pig	GI gastrointestinal disturbance	5.0E+00	4	3.3	3.8E-01	2.7E-01	1.1	1.6E-07
Imazalil	35554-44-0			1.25	Dog	Decreased body weight gain	2.0E+00	1.6	1	1.3E+00	8.0E-02	1.1	4.9E-08
Imazaquin	81335-37-7			25	Dog	Decreased body weight gain, skeletal myopathy, slight anemia, bone marrow hyperplasia.	4.0E+01	1.6	1	2.5E+01	4.0E-03	1.1	2.5E-09
Iprodione	36734-19-7	HPV		4.2	Dog	Increased RBC (erythrocytes) Heinz bodies; decreased prostate weight	6.7E+00	1.6	1	4.2E+00	2.4E-02	1.1	1.5E-08
Isobutyl alcohol	78-83-1	HPV		316	Rat	Hyperactivity and ataxia	5.1E+02	6	3.3	2.6E+01	3.9E-03	1.1	2.4E-09
Isophorone	78-59-1	HPV		150	Dog	No observed effects	2.4E+02	1.6	3.3	4.5E+01	2.2E-03	1.1	1.4E-09
Isopropalin	33820-53-0			15	Rat	Reduced hemoglobin concentration, lowered hematocrits, and altered organ weights	2.4E+01	6	3.3	1.2E+00	8.3E-02	1.1	5.1E-08
Isopropyl methyl phosphonic acid (IMPA)	1832-54-8		279		Rat	No adverse effects observed	4.5E+02	6	3.3	2.3E+01	4.4E-03	1.1	2.7E-09
Isoxaben	82558-50-7			5	Rat	Decreased serum AP (alkaline phosphatase) and AST (aspartate aminotransferase)	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
Londax	83055-99-6			19.9	Dog	Liver effects	3.2E+01	1.6	1	2.0E+01	5.0E-03	1.1	3.1E-09
Malathion	121-75-5	HPV		0.23	Human	Depression in plasma and RBC (erythrocytes) cholinesterase activity	3.7E-01	1	1	3.7E-01	2.7E-01	0.11	1.7E-08
Maleic anhydride	108-31-6	HPV	10		Rat	No adverse effects	1.6E+01	6	1	2.7E+00	3.8E-02	1.1	2.3E-08
Maneb	12427-38-2	HPV		5	Monkey	Increased thyroid weight	8.0E+00	1.8	3.3	1.3E+00	7.4E-02	1.1	4.6E-08
Manganese	7439-96-5		0.14		Human	CNS effects	2.2E-01	1	1	2.2E-01	4.3E-01	1.1	2.7E-07
Mepiquat chloride	24307-26-4			25	Dog	Sedation and tonic/clonic spasms; decreased food intake and body weights	4.0E+01	1.6	3.3	7.6E+00	1.3E-02	1.1	8.1E-09
Merphos	150-50-5	HPV		0.1	Hen	Ataxia, delayed neurotoxicity and weight loss	1.6E-01	6	3.3	8.1E-03	1.2E+01	1.1	7.6E-06
Merphos oxide	78-48-8			0.1	Hen	Ataxia, delayed neurotoxicity and weight loss	1.6E-01	6	3.3	8.1E-03	1.2E+01	1.1	7.6E-06
Metalaxyl	57837-19-1			6.25	Dog	Increased serum alkaline phosphatase levels and increased liver-to-brain weight ratio	1.0E+01	1.6	1	6.3E+00	1.5E-02	1.1	9.8E-09
Methacrylonitrile	126-98-7	HPV	0.34		Dog	Increased SGOT and SGPT levels	5.4E-01	1.6	3.3	1.0E-01	9.7E-01	1.1	6.0E-07
Methanol	67-56-1	HPV		500	Rat	Increased SAP (serum alcaline phosphatase) and SGPT, and decreased brain weight	8.0E+02	6	3.3	4.0E+01	2.5E-03	1.1	1.5E-09
Methidathion	950-37-8	HPV		0.1	Dog	Liver toxicity	1.6E-01	1.6	1	1.0E-01	1.0E+00	1.1	6.2E-07
Methomyl	16752-77-5			2.5	Dog	Kidney and Spleen Pathology	4.0E+00	1.6	1	2.5E+00	4.0E-02	1.1	2.5E-08
Methoxychlor	72-43-5			5.01	Rabbit	Excessive loss of litters	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
Methyl ethyl ketone (MEK)	78-93-3	HPV	1771		Rat	Decreased fetal birth weight	2.8E+03	6	3.3	1.4E+02	7.0E-04	1.1	4.3E-10
Methyl methacrylate	80-62-6	HPV	136		Rat	None	2.2E+02	6	3.3	1.1E+01	9.1E-03	1.1	5.6E-09
Methyl parathion	298-00-0	HPV		0.025	Rat	RBC (erythrocytes), Cholinesterase inhibition; reduced hemoglobin, hematocrit and RBCs	4.0E-02	6	1	6.7E-03	1.5E+01	1.1	9.2E-06
4-(2-Methyl-4-chlorophenoxy) butyric acid	94-81-5			12	Dog	Male reproductive toxicity and other effects	1.9E+01	1.6	3.3	3.6E+00	2.8E-02	1.1	1.7E-08

Chemical	CAS RN	Production [OECD, 1997]	$NOAEL_{w(ADJ)}$ [mg/kg-day]	$NOEL_{w(ADJ)}$ [mg/kg-day]	Animal	Critical endpoint	ED_{10a} [mg/kg-day]	CFa->h [-]	CFsub->chr [-]	ED_{10h} [mg/kg-day]	$\beta_{ED10\text{-}Exp.}$ [Risk / mg/kg-day]	$DALY_E$ [yr lost / pers]	EF [yr lost / mg absorb
2-(2-Methyl-4-chlorophenoxy)propionic acid	93-65-2	HPV		3	Rat	Increased absolute and relative kidney weights	4.8E+00	6	3.3	2.4E-01	4.1E-01	1.1	2.5E-07
2-Methyl-4-chlorophenoxyacetic acid	94-74-6	HPV		0.15	Dog	Kidney and liver toxicity	2.4E-01	1.6	1	1.5E-01	6.7E-01	1.1	4.1E-07
2-Methylphenol	95-48-7	HPV	50		Rat	Decreased body weights and neurotoxicity	8.0E+01	6	3.3	4.0E+00	2.5E-02	1.1	1.5E-08
3-Methylphenol	108-39-4	HPV	50		Rat	Decreased body weights and neurotoxicity	8.0E+01	6	3.3	4.0E+00	2.5E-02	1.1	1.5E-08
Metolachlor	51218-45-2			15	Rat	Decreased body weight gain	2.4E+01	6	1	4.0E+00	2.5E-02	1.1	1.5E-08
Metribuzin	21087-64-9			2.5	Dog	Liver and kidney effects, decreased body weight, mortality	4.0E+00	1.6	1	2.5E+00	4.0E-02	1.1	2.5E-08
Mirex	2385-85-5		0.07		Rat	Liver cytomegaly, fatty metamorphosis, angiectasis; thyroid cystic follicles	1.1E-01	6	1	1.9E-02	5.4E+00	1.1	3.3E-06
Molinate	2212-67-1			0.2	Rat	Reproductive toxicity	3.2E-01	6	1	5.3E-02	1.9E+00	1.1	1.2E-06
Monochloramine	10599-90-3		9.5		Rat	No observed effects	1.5E+01	6	1	2.5E+00	3.9E-02	1.1	2.4E-08
Naled	300-76-5			0.2	Rat	Brain Cholinesterase inhibition	3.2E-01	6	1	5.3E-02	1.9E+00	1.1	1.2E-06
Naphthalene	91-20-3	HPV	71		Rat	Decreased mean terminal body weight in males	1.1E+02	6	3.3	5.7E+00	1.7E-02	1.1	1.1E-08
Napropamide	15299-99-7			30	Rat	Decreased body weight gain in parental animals and pupils	4.8E+01	6	1	8.0E+00	1.3E-02	1.1	7.7E-09
Nickel, soluble salts	Various		5		Rat	Decreased body and organ weights	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
Nitrate	14797-55-8		1.6		Human	Early clinical signs of methemoglobinemia in excess of 10%	2.6E+00	1	1	2.6E+00	3.9E-02	1.11	2.4E-08
Nitrite	147975-0			1	Human	Methemoglobinemia	1.6E+00	1	1	1.6E+00	6.3E-02	1.11	3.9E-08
Nitroguanidine	556-88-7	HPV	316		Rat	Reduced weight gain in female rats, maternal/feral toxicity in rats	5.1E+02	6	3.3	2.6E+01	3.9E-03	1.1	2.4E-09
Norflurazon	27314-13-2			3.75	Dog	Liver and thyroid effects	6.0E+00	1.6	1	3.8E+00	2.7E-02	1.1	1.6E-08
NuStar	85509-19-9			0.2	Dog	Liver cell enlargement	3.2E-01	1.6	1	2.0E-01	5.0E-01	1.1	3.1E-07
Octabromodiphenyl ether	32536-52-0	HPV	2.51		Rat	Induction of hepatic enzymes; liver histopathology	4.0E+00	6	3.3	2.0E-01	4.9E-01	1.1	3.0E-07
Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	2691-41-0	HPV	50		Rat	Hepatic lesions	8.0E+01	6	3.3	4.0E+00	2.5E-02	1.1	1.5E-08
Oryzalin	19044-88-3			5	Dog	Increases in serum cholesterol, alkaline phosphatase, and relative liver and kidney weights	8.0E+00	1.6	1	5.0E+00	2.0E-02	1.1	1.2E-08
Oxadiazon	19666-30-9			0.5	Rat	Increased levels of serum proteins and increased liver weights	8.0E-01	6	1	1.3E-01	7.5E-01	1.1	4.6E-07
Oxamyl	23135-22-0			2.5	Rat	Decreased body weight gain and food consumption	4.0E+00	6	1	6.7E-01	1.5E-01	1.1	9.2E-08
Oxyfluorfen	42874-03-3			0.3	Mouse	Increased absolute liver weight and nonneoplastic lesions	4.8E-01	13	1	3.7E-02	2.7E+00	1.1	1.7E-06
Paclobutrazol	76738-62-0			12.5	Rat	Elevated liver weights, serum cholesterol, hepatic aminopyrine N-demethylase activity	2.0E+01	6	3.3	1.0E+00	9.9E-02	1.1	6.1E-08
Paraquat	1910-42-5			0.45	Dog	Chronic pneumonitis	7.2E-01	1.6	1	4.5E-01	2.2E-01	1.1	1.4E-07
Pendimethalin	40487-42-1			12.5	Dog	Increase in serum alkaline phosphatase and liver weight, and hepatic lesions	2.0E+01	1.6	1	1.3E+01	8.0E-03	1.1	4.9E-09
Pentabromodiphenyl ether	32534-81-9	HPV	1.77		Rat	Induction of hepatic enzymes	2.8E+00	6	3.3	1.4E-01	7.0E-01	1.1	4.3E-07
Pentachloronitrobenzene (PCNB)	82-68-8	HPV		0.75	Dog	Liver toxicity	1.2E+00	1.6	1	7.5E-01	1.3E-01	1.1	8.2E-08
Pentachlorophenol	87-86-5		3		Rat	Liver and kidney pathology	4.8E+00	6	1	8.0E-01	1.3E-01	1.1	7.7E-08
Permethrin	52645-53-1			5	Rat	Increased liver weights	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
Phenmedipham	13684-63-4	HPV	25		Rat	No adverse effects	4.0E+01	6	1	6.7E+00	1.5E-02	1.1	9.2E-09
Phenol	108-95-2	HPV	60		Rat	Reduced fetal body weight in rats	9.6E+01	6	1	1.6E+01	6.3E-03	1.1	3.8E-09
m-Phenylenediamine	108-45-2	HPV		6	Rat	Increased relative and absolute liver weights and degenerative liver lesions	9.6E+00	6	3.3	4.8E-01	2.1E-01	1.1	1.3E-07
Phenylmercuric acetate	62-38-4		0.0084		Rat	Renal damage	1.3E-02	6	1	2.2E-03	4.5E+01	1.1	2.7E-05
Phosmet	732-11-6			2	Rat	Reduced body weight (males), liver cell vacuolation, cholinerase inhibition	3.2E+00	6	1	5.3E-01	1.9E-01	1.1	1.2E-07
Phosphine	7803-51-2			0.026	Rat	Body weight and clinical parameters	4.2E-02	6	1	6.9E-03	1.4E+01	1.1	8.9E-06
Picloram	31.01.14			7	Dog	Increased liver weights	1.1E+01	1.6	1	7.0E+00	1.4E-02	1.1	8.8E-09
Pirimiphos-methyl	29232-93-7			0.25	Human	Transient plasm, cholinesterase depression	4.0E-01	1	1	4.0E-01	2.5E-01	0.11	1.5E-08
Potassium cyanide	151-50-8	HPV	27		Rat	Weight loss, thyroid effects and myelin degeneration	4.3E+01	6	1	7.2E+00	1.4E-02	1.1	8.5E-09
Potassium silver cyanide	506-61-6		82.7		Rat	Weight loss, thyroid effects and myelin degeneration	1.3E+02	6	1	2.2E+01	4.5E-03	1.1	2.8E-09
Prochloraz	67747-09-5	HPV		0.9	Dog	Increase in SAP (serum alcaline phosphatase) and liver weigths, liver histopathology	1.4E+00	1.6	1	9.0E-01	1.1E-01	1.1	6.8E-08
Prometon	1610-18-0		15		Rat	No treatment related effects observed	2.4E+01	6	3.3	1.2E+00	8.3E-02	1.1	5.1E-08
Prometryn	7287-19-6			3.75	Dog	Liver and kidney degeneration and bone marrow atrophy	6.0E+00	1.6	1	3.8E+00	2.7E-02	1.1	1.6E-08
Pronamide	23950-58-5			7.5	Dog	No effects	1.2E+01	1.6	1	7.5E+00	1.3E-02	1.1	8.2E-09
Propachlor	1918-16-7			13.3	Dog	Decreased weight gain, food consumption; increased relative liver weights.	2.1E+01	1.6	3.3	4.0E+00	2.5E-02	1.1	1.5E-08
Propanil	709-98-8	HPV		5	Rat	Increased relative spleen weight in females	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08

	Chemical	CAS RN	Production (OECD, 1997)	$NOAEL_{H(ADJ)}$ (mg/kg-day)	$NOEL_{H(ADJ)}$ (mg/kg-day)	Animal	Critical endpoint	ED_{10a} (mg/kg-day)	CFa->h [-]	CFsub->chr [-]	ED_{10h} (mg/kg-day)	$\beta_{ED10\text{-}Ext}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absor
1	Propargite	2312-35-8	HPV		22.5	Dog	No adverse effects observed	3.6E+01	1.6	1	2.3E+01	4.4E-03	1.1	2.7E-09
2	Propargyl alcohol	107-19-7		5		Rat	Renal and hepatotoxicity	8.0E+00	6	3.3	4.0E-01	2.5E-01	1.1	1.5E-07
3	Propazine	139-40-2	HPV		5	Rat	Decreased in body weight	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
4	Propham	122-42-9			50	Rat	Increase in male spleen weight and cholinesterase depression in females	8.0E+01	6	3.3	4.0E+00	2.5E-02	1.1	1.5E-08
5	Propiconazole	60207-90-1			1.25	Dog	Gastric mucosal irritation	2.0E+00	1.6	1	1.3E+00	8.0E-02	1.1	4.9E-08
6	Pursuit	81335-77-5			25	Dog	Hemoglobin, erythrocytes in females, decreased packed cell volume,	4.0E+01	1.6	1	2.5E+01	4.0E-03	1.1	2.5E-09
7	Pydrin	51630-58-1			2.5	Rat	Neurological dysfunction	4.0E+00	6	1	6.7E-01	1.5E-01	1.1	9.2E-08
8	Pyrene	129-00-0		75		Mouse	Kidney effects (renal tubular pathology, decreased kidney weights)	1.2E+02	13	3.3	2.8E+00	3.6E-02	1.1	2.2E-08
9	Pyridine	110-86-1	HPV	1		Rat	Increased liver weight	1.6E+00	6	3.3	8.1E-02	1.2E+00	1.1	7.6E-07
0	Quinalphos	13593-03-8			0.05	Dog	No adverse effects reported	8.0E-02	1.6	1	5.0E-02	2.0E+00	1.1	1.2E-06
1	Rotenone	83-79-4			0.38	Rat	Reduced pupils weight	6.1E-01	6	1	1.0E-01	9.9E-01	1.1	6.1E-07
2	Savey	78587-05-0			2.5	Dog	Hypertrophy of adrenal cortex (both sexes); hematologic effects (males)	4.0E+00	1.6	1	2.5E+00	4.0E-02	1.1	2.5E-08
3	Selenious acid	7783-00-8		0.015		Human	Clinical selenosis	2.4E-02	1	1	2.4E-02	4.2E+00	0.11	2.6E-07
4	Selenium and Compounds	7782-49-2		0.015		Human	Clinical selenosis	2.4E-02	1	1	2.4E-02	4.2E+00	0.11	2.6E-07
5	Sethoxydim	74051-80-2			8.86	Dog	Mild anemia in males	1.4E+01	1.6	1	8.9E+00	1.1E-02	1.1	6.9E-09
6	Silver cyanide	506-64-9		55.7		Rat	Weight loss, thyroid effects and myelin degeneration	8.9E+01	6	1	1.5E+01	6.7E-03	1.1	4.1E-09
7	Simazine	122-34-9	HPV	0.52		Rat	Reduction in weight gains; hematological changes in females	8.3E-01	6	1	1.4E-01	7.2E-01	1.1	4.4E-07
8	Sodium azide	26628-22-8		3.57		Rat	Clinical signs (e.g., hunched postures) and reduced body weight	5.7E+00	6	3.3	2.9E-01	3.5E-01	1.1	2.1E-07
9	Sodium cyanide	143-33-9	HPV	20.4		Rat	Weight loss, thyroid effects and myelin degeneration	3.5E+01	6	1	5.4E+00	1.8E-02	1.1	1.1E-08
0	Sodium diethyldithiocarbamate	148-18-5			30	Rat	Reduced body weight	4.8E+01	6	3.3	2.4E+00	4.1E-02	1.1	2.5E-08
1	Sodium fluoroacetate	62-74-8		0.05		Rat	Increased heart weight in females and males, decreased testis weight in males	8.0E-02	6	3.3	4.0E-03	2.5E+01	1.1	1.5E-05
2	Strontium	7440-24-6		190		Rat	Rachitic bone	3.0E+02	6	1	5.1E+01	2.0E-03	1.1	1.2E-09
3	Styrene	100-42-5	HPV	200		Dog	Red blood cell and liver effects	3.2E+02	1.6	3.3	6.1E+01	1.7E-03	1.1	1.0E-09
4	Systhane	88671-89-0			2.49	Rat	Testicular atrophy	4.0E+00	6	1	6.8E-01	1.5E-01	1.1	9.3E-08
5	Tebuthiuron	34014-18-1			7	Rat	Depressed body weight gain in F1 females	1.1E+01	6	1	1.9E+00	5.4E-02	1.1	3.3E-08
6	Terbacil	5902-51-2			1.25	Dog	Increase in thyroid/body weight ratio; slight increase in liver weights	2.0E+00	1.6	1	1.3E+00	8.0E-02	1.1	4.9E-08
7	Terbutryn	886-50-0			0.1	Rat	Hematologic effects in females	1.6E-01	6	1	2.7E-02	3.8E+00	1.1	2.3E-06
8	1,2,4,5-Tetrachlorobenzene	95-94-3	HPV	0.34		Rat	Kidney lesions	5.4E-01	6	3.3	2.7E-02	3.6E+00	1.1	2.2E-06
9	Tetrachloroethylene	127-18-4	HPV	14		Mouse	Hepatotoxicity in mice, weight gain in rats	2.2E+01	13	3.3	5.2E-01	1.9E-01	1.1	1.2E-07
0	2,3,4,6-Tetrachlorophenol	58-90-2		25		Rat	Increased liver weights and centrilobular hypertrophy	4.0E+01	6	3.3	2.0E+00	5.0E-02	1.1	3.0E-08
1	Tetrachlorvinphos	961-11-5			3.13	Dog	Reduced body weight gain, increased liver and kidney weights, and RBC (erythrocytes)	5.0E+00	1.6	1	3.1E+00	3.2E-02	1.1	2.0E-08
2	Tetraethyldithiopyrophosphate	3689-24-5			0.5	Rat	Depressed RBC (erythrocytes) and plasma cholinesterase activity	8.0E-01	6	3.3	4.0E-02	2.5E+00	1.1	1.5E-06
3	Thallium acetate	563-68-8		0.26		Rat	Increased levels of SGOT and LDH	4.2E-01	6	3.3	2.1E-02	4.8E+00	1.1	2.9E-06
4	Thallium carbonate	6533-73-9		0.23		Rat	Increased levels of SGOT and LDH	3.7E-01	6	3.3	1.9E-02	5.4E+00	1.1	3.3E-06
5	Thallium chloride	7791-12-0		0.23		Rat	Increased levels of SGOT and LDH	3.7E-01	6	3.3	1.9E-02	5.4E+00	1.1	3.3E-06
6	Thallium nitrate	10102-45-1		0.26		Rat	Increased levels of SGOT and LDH	4.2E-01	6	3.3	2.1E-02	4.8E+00	1.1	2.9E-06
7	Thallium(I) sulfate	7446-18-6		0.25		Rat	No adverse effects	4.0E-01	6	3.3	2.0E-02	5.0E+00	1.1	3.0E-06
8	Thiobencarb	28249-77-6			1	Rat	Decrease in body weight, increase in BUN	1.6E+00	6	1	2.7E-01	3.8E-01	1.1	2.3E-07
9	Thiophanate-methyl	23564-05-8			8	Rat	Decreased body weight, decreased spermatogenesis, and evidence of hyperthyroidism	1.3E+01	6	1	2.1E+00	4.7E-02	1.1	2.9E-08
0	Thiram	137-26-8	HPV		5	Rat	Neurotoxicity	8.0E+00	6	1	1.3E+00	7.5E-02	1.1	4.6E-08
1	Toluene	108-88-3	HPV	223		Rat	Changes in liver and kidney weights	3.6E+02	6	1	5.9E+01	1.7E-03	1.1	1.0E-09
2	Tralomethrin	66841-25-6			0.75	Rat	Decreased body weight gain in males; increased food and water consumption	1.2E+00	6	1	2.0E-01	5.0E-01	1.1	3.1E-07
3	Triallate	2303-17-5	HPV	1.275		Dog	Increased hemosiderin deposition, serum alkaline phosphatase, and liver weight in females	2.0E+00	1.6	1	1.3E+00	7.8E-02	1.1	4.8E-08
4	Triasulfuron	82097-50-5			1.2	Mouse	Centrilobular hepatocytomegaly in males	1.9E+00	13	1	1.5E-01	6.8E-01	1.1	4.2E-07
5	1,2,4-Tribromobenzene	615-54-3		5		Rat	Increased liver-to-body weight ratio and hepatic microsomal enzyme induction	8.0E+00	6	3.3	4.0E-01	2.5E-01	1.1	1.5E-07
6	1,1,2-Trichloro-1,2,2-trifluoroethane (CFC-113)	76-13-1	HPV	273		Human	Psychomotor impairment	4.4E+02	1	1	4.4E+02	2.3E-04	0.11	1.4E-11
7	1,2,4-Trichlorobenzene	120-82-1	HPV	14.8		Rat	Increased adrenal weights; vacuolization of zona fasciculata in the cortex	2.4E+01	6	3.3	1.2E+00	8.4E-02	1.1	5.1E-08

Chemical	CAS RN	Production [OECD, 1997]	$NOAEL_{a(ADJ)}$ [mg/kg-day]	$NOEL_{a(ADJ)}$ [mg/kg-day]	Animal	Critical endpoint	ED_{10a} [mg/kg-day]	CFa->h [-]	CFsub->chr [-]	ED_{10h} [mg/kg-day]	$\beta_{ED10\ Extr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorb
1,1,2-Trichloroethane	79-00-5	HPV	3.9		Mouse	Clinical serum chemistry	6.2E+00	13	3.3	1.5E-01	6.9E-01	1.1	4.2E-07
2,4,5-Trichlorophenol	95-95-4			100	Rat	Liver and kidney pathology	1.6E+02	6	3.3	8.1E+00	1.2E-02	1.1	7.6E-09
2 (2,4,5-Trichlorophenoxy) propionic acid	93-72-1			0.75	Dog	Histopathological changes in the liver	1.2E+00	1.6	1	7.5E-01	1.3E-01	1.1	8.2E-08
2,4,5-Trichlorophenoxyacetic acid (2,4,5-T)	93-76-5		3		Rat	Increased urinary coproporphyrins	4.8E+00	6	1	8.0E-01	1.3E-01	1.1	7.7E-08
1,1,2-Trichloropropane	598-77-6			15	Rat	Mild lesions in liver, kidney and thyroid	2.4E+01	6	3.3	1.2E+00	8.3E-02	1.1	5.1E-08
1,2,3-Trichloropropane	96-18-4	HPV	5.71		Rat	Alterations in clinical chemistry and reduction in red cell mass	9.1E+00	6	3.3	4.6E-01	2.2E-01	1.1	1.3E-07
Tridiphane	58138-08-2			0.33	Rat	Decreased fertility index and depressed body weight of dams	5.3E-01	6	1	8.8E-02	1.1E+00	1.1	7.0E-07
Trifluralin	1582-09-8			0.75	Dog	Increased liver weights; increase in methemoglobin	1.2E+00	1.6	1	7.5E-01	1.3E-01	1.1	8.2E-08
1,3,5-Trinitrobenzene	99-35-4		2.68		Rat	Methemoglobinemia and spleen-erythroid cell hyperplasia	4.3E+00	6	1	7.1E-01	1.4E-01	1.1	8.6E-08
Vanadium pentoxide	1314-62-1	HPV	0.89		Rat	Decreased hair cystine	1.4E+00	6	1	2.4E-01	4.2E-01	1.1	2.6E-07
Vernam	1929-77-7			1	Rat	Decreased body weight	1.6E+00	6	3.3	8.1E-02	1.2E+00	1.1	7.6E-07
Vinclozolin	50471-44-8	HPV		2.5	Dog	Organ weight changes	4.0E+00	1.6	1	2.5E+00	4.0E-02	1.1	2.5E-08
White phosphorus	7723-14-0	HPV	0.015		Rat	Parturition mortality; forelimb hair loss	2.4E-02	6	3.3	1.2E-03	8.3E+01	1.1	5.1E-05
Xylenes	1330-20-7	HPV	179		Rat	Hyperactivity, decreased body weight and increased mortality (males)	2.9E+02	6	1	4.8E+01	2.1E-03	1.1	1.3E-09
Zinc cyanide	557-21-1		24.3		Rat	Weight loss, thyroid effects and myelin degeneration	3.9E+01	6	1	6.5E+00	1.5E-02	1.1	9.5E-09

ɪendix 3.3.a) Slopes factors β_{ED10} derived with equation (3.9) from the No Observable Adverse Effect Level (NOAEL) or No Observable Effect Level (NOEL) provided in the IRIS database [EPA, 1998], and
ɔt factors EF derived from the slope factor $\beta_{ED10}$and the Disability Adjusted Life Years per affected Person (DALYp) (see equation (2.19)).
critical endpoint associated with each compound, as well as the conversion factors (see section 3.4.3 for their definition) used to derive the lifetime human effet dose ED_{10h} from the animal dose ED_{10a} are also listed.
te of exposure: oral.
' (High Production Volume) chemicals are chemicals with an annual production and/or importation volumes above 1000 tonnes per year in at least one OECD country [OECD, 1997].
alic: metals studied in details in section 3.6.

	Chemical	CAS RN	Production [OECD, 1997]	$NOAEL_{a(ADJ)}$ [mg/m3]	$NOAEL_{a(ADJ)}$ [mg/kg-day]	Animal	Critical endpoint	ED_{10a} [mg/kg-day]	CFa->h [-]	CFsub->chr [-]	ED_{10h} [mg/kg-day]	$\beta_{ED10-Eadr}$ [Risk / mg/kg-day]	$DALY_p$ [yr lost / pers]	EF [yr lost / mg absorbed]
1	Acetaldehyde	75-07-0	HPV	48.75	3.1E+01	Rat	Degeneration of olfactory epithelium	4.9E+01	5.6	3.3	2.7E+00	3.8E-02	1.1	2.3E-08
2	Allyl chloride	107-05-1	HPV	3.6	2.3E+00	Rabbit	Functional neurotoxicity	3.6E+00	1	3.3	1.1E+00	9.1E-02	1.1	5.6E-08
3	Ammonia	7664-41-7	HPV	2.3	6.6E-01	Occupational Study	Pulmonary function	1.1E+00	1	1	1.1E+00	9.5E-02	1.1	5.8E-08
4	Aniline	62-53-3	HPV	3.4	2.1E+00	Rat, guinea pigs	Lack of toxicity	3.4E+00	1	3.3	1.0E+00	9.7E-02	1.1	5.9E-08
5	Arsine	7784-42-1		0.014	8.8E-03	Rat, mouse	Increased hemolysis, abnormal RBC morphology	1.4E-02	1	1	1.4E-02	7.1E+00	1.1	4.4E-06
6	*Beryllium*	7440-41-7		0.0001	2.9E-05	Human	Chronic beryllium disease	4.6E-05	1	1	4.6E-05	2.2E+03	1.1	1.3E-03
7	1-Chloro-1,1-difluoroethane	75-68-3	HPV	14710	9.2E+03	Rat	No adverse effects	1.5E+04	1	1	1.5E+04	6.8E-06	1.1	4.2E-12
8	Chlorodifluoromethane	75-45-6	HPV	5260	3.3E+03	Rat	Increased kidney, adrenal and pituitary weights	5.3E+03	1	3.3	1.6E+03	6.2E-05	1.1	3.8E-11
9	1,2-Dibromo-3-chloropropane (DBC	96-12-8		0.17	1.1E-01	Rabbit	Testicular effects	1.7E-01	1	3.3	5.2E-02	1.9E+00	1.1	1.2E-06
10	1,4-Dichlorobenzene	106-46-7	HPV	75	4.7E+01	Rat	Increased liver weights	7.5E+01	1	1	7.5E+01	1.3E-03	1.1	8.2E-10
11	Diesel engine emissions			0.46	2.9E-01	Rat	Histological changes in the lung	4.6E-01	3	1	1.6E-01	6.4E-01	1.1	3.9E-07
12	1,1-Difluoroethane	75-37-6	HPV	12051	7.6E+03	Rats	No adverse effects observed	1.2E+04	1	1	1.2E+04	8.3E-06	1.1	5.1E-12
13	Epichlorohydrin	106-89-8	HPV	3.4	2.1E+00	Rat and mouse	Changes in the nasal turbinates	3.4E+00	9.4	3.3	1.1E-01	9.1E-01	1.1	5.6E-07
14	2-Ethoxyethanol	110-80-5	HPV	68	4.3E+01	Rabbit	Decreased testis weight and decreased hemoglobin	6.8E+01	1	3.3	2.1E+01	4.8E-03	1.1	3.0E-09
15	Ethyl chloride	75-00-3	HPV	4000	2.5E+03	Mouse	Delayed fetal ossification	4.0E+03	1	1	4.0E+03	2.5E-05	1.1	1.5E-11
16	1,6-Hexamethylene diisocyanate	822-06-0	HPV	0.006	3.8E-03	Rat	Degeneration of olfactory epithelium	6.0E-03	6	1	1.0E-03	9.9E+01	1.1	6.1E-05
17	n-Hexane	110-54-3	HPV	315	2.0E+02	Mouse	Epithelial lesions in the nasal cavity	3.2E+02	8.3	3.3	1.2E+01	8.6E-03	1.1	5.3E-09
18	2-Methoxyethanol	109-86-4	HPV	17	1.1E+01	Rabbits	Testicular effects	1.7E+01	1	3.3	5.2E+00	1.9E-02	1.1	1.2E-08
19	Methyl tert-butyl ether (MTBE)	1634-04-4	HPV	258	1.6E+02	Rat	Increased liver and kidney weights	2.6E+02	1	1	2.6E+02	3.8E-04	1.1	2.4E-10
20	Propylene glycol monomethyl ether	107-98-2	HPV	658	4.1E+02	Rat and rabbit	Mild reversible sedation	6.6E+02	1	3.3	2.0E+02	5.0E-04	1.1	3.1E-10
21	2,4-/2,6-Toluene diisocyanate mixtu	26471-62-5	HPV	0.006	1.7E-03	Occupational Study	Chronic lung-function decline	2.7E-03	3	1	9.1E-04	1.1E+02	1.1	6.7E-05
22	Triethylamine	121-44-8	HPV	182.5	1.1E+02	Rat	No observed adverse effects	1.8E+02	9.4	3.3	5.9E+00	1.7E-02	1.1	1.0E-08
23	Vinyl acetate	108-05-4	HPV	31	1.9E+01	Rat	Nasal epithelial lesions	3.1E+01	6.2	1	5.0E+00	2.0E-02	1.1	1.2E-08

Appendix 3.3.b) Slopes factors β_{ED10} derived with equation (3.9) from the No Observable Adverse Effect Level (NOAEL) or No Observable Effect Level (NOEL) provided in the IRIS database [EPA, 1998], and effect factors EF derived from the slope factor and the Disability Adjusted Life Years per affected Person ($DALY_p$) (see equation (2.19)).

The critical endpoint associated with each compound, as well as the conversion factors (see section 3.4.3 for their definition) used to derive the lifetime human effet dose ED_{10h} from the animal dose ED10a are also listed.

Route of exposure: inhalation.

HPV (High Production Volume) chemicals are chemicals with an annual production and/or importation volumes above 1000 tonnes per year in at least one OECD country [OECD, 1997].

Appendix 3.4 Disability Adjusted Life Years per affected Person

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
1. Infectious and parasitic diseases	**Tuberculosis**							
	HIV sero-negative cases	0.294	2.1	0.62	34304000	1960000	17.5	18.1
	HIV sero-positive cases	0.294	0.99	0.29	34304000	1960000	17.5	17.8
	Syphilis							
	congenital syphilis	0.315	3	0.95	5852000	204000	28.7	29.6
	low birth weight	0	0.5	0.00	5852000	204000	28.7	28.7
	primary	0.015	0.05	0.00	5852000	204000	28.7	28.7
	secondary	0.048	0.09	0.00	5852000	204000	28.7	28.7
	tertiary -- cardiovascular	0.196	10	1.96	5852000	204000	28.7	30.6
	tertiary -- gummas	0.102	2	0.20	5852000	204000	28.7	28.9
	tertiary -- neurologic	0.283	10	2.83	5852000	204000	28.7	31.5
	Chlamydia							
	Ophthalmia neonatorum	0.18	0.04	0.01	463000	16000	28.9	28.9
	low birth weight	0	0.5	0.00	463000	16000	28.9	28.9
	corneal scar -- blindness	0.493	32.3	15.92	463000	16000	28.9	44.9
	corneal scar -- low vision	0.245	14.1	3.45	463000	16000	28.9	32.4
	cervicitis	0.049	0.05	0.00	463000	16000	28.9	28.9
	neonatal pneumonia	0.28	0.5	0.14	463000	16000	28.9	29.1
	pelvic inflammatory disease	0.169	0.03	0.01	463000	16000	28.9	28.9
	ectopic pregnancy	0.549	0.08	0.04	463000	16000	28.9	29.0
	tubo-ovarian abscess	0.549	0.08	0.04	463000	16000	28.9	29.0
	chronic pelvic pain	0.122	3	0.37	463000	16000	28.9	29.3
	infertility	0.18	16.8	3.02	463000	16000	28.9	32.0
	symptomatic urethritis	0.067	0.04	0.00	463000	16000	28.9	28.9
	epididymitis	0.167	0.06	0.01	463000	16000	28.9	28.9
	stricture	0.151	2.1	0.32	463000	16000	28.9	29.3
	Gonorrhoea							
	Ophthalmia neonatorum	0.18	0.04	0.01	263000	9000	29.2	29.2
	low birth weight	0	0.5	0.00	263000	9000	29.2	29.2
	corneal scar -- blindness	0.6	31	18.60	263000	9000	29.2	47.8
	corneal scar -- low vision	0.245	21.8	5.34	263000	9000	29.2	34.6

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
	cervicitis	0.049	0.05	0.00	263000	9000	29.2	29.2
	pelvic inflammatory disease	0.169	0.03	0.01	263000	9000	29.2	29.2
	ectopic pregnancy	0.549	0.08	0.04	263000	9000	29.2	29.3
	tubo-ovarian abscess	0.549	0.08	0.04	263000	9000	29.2	29.3
	chronic pelvic pain	0.122	3	0.37	263000	9000	29.2	29.6
	infertility	0.18	16.1	2.90	263000	9000	29.2	32.1
	symptomatic urethritis	0.067	0.04	0.00	263000	9000	29.2	29.2
	epididymitis	0.167	0.06	0.01	263000	9000	29.2	29.2
	stricture	0.151	2.1	0.32	263000	9000	29.2	29.5
	HIV							
	cases	0.136	6.9	0.94	8832000	312000	28.3	29.2
	AIDS	0.505	1.09	0.55	8832000	312000	28.3	28.9
	Diarrhoeal diseases -- episodes	0.094	0.02	0.00	94434000	2946000	32.1	32.1
	Pertussis							
	episodes	0	0.08	0.00	11878000	347000	34.2	34.2
	mental retardation	0.451	59.1	26.65	11878000	347000	34.2	60.9
	Poliomyelitis -- lameness	0.369	59	21.77	909000	27000	33.7	55.4
	Diphteria							
	episodes	0.231	0.04	0.01	360000	11000	32.7	32.7
	neurological complications	0.078	0.17	0.01	360000	11000	32.7	32.7
	myocarditis	0.323	0.25	0.08	360000	11000	32.7	32.8
	Measles -- episodes	0.152	0.04	0.01	36450000	1058000	34.5	34.5
	Tetanus -- episodes	0.64	0.04	0.03	17508000	542000	32.3	32.3
	Bacterial meningitis, meningococcaemia							
	episodes	0.616	0.08	0.05	4532000	180000	25.2	25.2
	haemophilus influenzae -- episodes	0.616	0.08	0.05	4532000	180000	25.2	25.2
	neisseria meningitidis -- episodes	0.616	0.08	0.05	4532000	180000	25.2	25.2
	meningococcaemia without meningitis -- episodes	0.152	0.08	0.01	4532000	180000	25.2	25.2
	deafness	0.175	55.2	9.66	4532000	180000	25.2	34.8
	seizure disorder	0.065	55.1	3.58	4532000	180000	25.2	28.8
	motor deficit	0.39	55.1	21.49	4532000	180000	25.2	46.7
	mental retardation	0.451	55.1	24.85	4532000	180000	25.2	50.0
	Hepatitis B and hepatitis C -- Episodes	0.209	0.17	0.04	2072000	108000	19.2	19.2
	Malaria							
	episodes	0.195	0.01	0.00	28038000	856000	32.8	32.8
	anaemia	0.012	n.a.	n.a.	28038000	856000	32.8	n.a.
	neurological sequelae	0.436	52.2	22.76	28038000	856000	32.8	55.5

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
	Trypanosomiasis -- episodes	0.35	5	1.75	1346000	47000	28.6	30.4
	Chaga Disease							
	infection	0	33.7	0.00	300000	19000	15.8	15.8
	cardiomyopathy without congestive heart failure	0.062	28.4	1.76	300000	19000	15.8	17.6
	cardiomyopathy with congestive heart failure	0.171	28.4	4.86	300000	19000	15.8	20.6
	megaviscera	0.24	31.1	7.46	300000	19000	15.8	23.3
	Schistosomiasis -- infection	0.006	n.a.	n.a.	156000	8000	19.5	19.5
	Leishmaniasis							
	visceral	0.243	3.4	0.83	1628000	50000	32.6	33.4
	cutaneous	0.023	1.8	0.04	1628000	50000	32.6	32.6
	Lymphatic filariasis							
	hydrocele > 15 cm	0.075	41.7	3.13	n.a.	n.a.	n.a.	n.a.
	bancroftian lymphoedema	0.113	41.6	4.70	n.a.	n.a.	n.a.	n.a.
	brugian lymphoedema	0.113	33.3	3.76	n.a.	n.a.	n.a.	n.a.
	Onchocerciasis							
	blindness	0.488	11	5.37	n.a.	n.a.	n.a.	n.a.
	itching	0.068	5	0.34	n.a.	n.a.	n.a.	n.a.
	low vision	0.245	7.9	1.94	n.a.	n.a.	n.a.	n.a.
	Leprosy							
	cases	0	5.2	0.00	46000	3000	15.3	15.3
	disabling leprosy	0.153	43.1	6.59	46000	3000	15.3	21.9
	Dengue							
	dengue haemorrhagic fever	0.195	0.08	0.02	743000	21000	35.4	35.4
	Japanese encephalitis							
	episodes	0.616	0.5	0.31	163000	5000	32.6	32.9
	cognitive impairment	0.451	60.5	27.29	163000	5000	32.6	59.9
	neurological sequelae	0.337	60.5	20.39	163000	5000	32.6	53.0
	Trachoma							
	blindness	0.493	8.7	4.29	n.a.	n.a.	n.a.	n.a.
	low vision	0.245	6.1	1.49	n.a.	n.a.	n.a.	n.a.
	Ascariasis							
	high intensity infection	0	n.a.	n.a	406000	11000	36.9	36.9
	cotemporaneous cognitive deficit	0.006	1	0.01	406000	11000	36.9	36.9
	cognitive impairment	0.463	59.4	27.50	406000	11000	36.9	64.4
	intestinal obstruction	0.024	0.06	0.00	406000	11000	36.9	36.9
	Trichuriasis							
	high intensity infection	0	n.a.	n.a	269000	7000	38.4	38.4

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
	cotemporaneous cognitive deficit	0.006	n.a.	n.a	269000	7000	38.4	38.4
	massive dysentery syndrome	0.129	1	0.13	269000	7000	38.4	38.6
	cognitive impairment	0.024	59.2	1.42	269000	7000	38.4	39.8
	Ancylostomiasis and necatoriasis							
	high intensity infection	0	n.a.	n.a	78000	4000	19.5	19.5
	anaemia	0.024	n.a.	n.a	78000	4000	19.5	19.5
	cognitive impairment	0.024	57.4	1.38	78000	4000	19.5	20.9
2. Respiratory infections	**Lower respiratory infections**							
	episodes	0.28	0.03	0.01	108601000	4299000	25.3	25.3
	chronic sequelae	0.099	61.1	6.05	108601000	4299000	25.3	31.3
	Upper respiratory infections							
	episodes	0	0.01	0.00	1114000	43000	25.9	25.9
	pharyngitis	0.07	0.01	0.00	1114000	43000	25.9	25.9
	Otitis media							
	episodes	0.023	0.08	0.00	952000	28000	34.0	34.0
	deafness	0.175	60	10.50	952000	28000	34.0	44.5
3. Maternal conditions	**Maternal haemorrhage**							
	episodes	0	30.3	0.00	3327000	114000	29.2	29.2
	sheehan syndrome	0.065	42.4	2.76	3327000	114000	29.2	31.9
	severe anaemia	0.093	1.3	0.12	3327000	114000	29.2	29.3
	Maternal sepsis							
	episodes	0	n.a.	n.a	1976000	68000	29.1	29.1
	infertility	0.18	15	2.70	1976000	68000	29.1	31.8
	Hypertensive disorders of pregnancy							
	episodes	0	n.a.	n.a	1656000	57000	29.1	29.1
	neurological sequelae	0.397	42.1	16.71	1656000	57000	29.1	45.8
	Obstructed labour							
	episodes	0	n.a.	n.a	1004000	34000	29.5	29.5
	stress incontinence	0.025	42.5	1.06	1004000	34000	29.5	30.6
	rectovaginal fistula	0.43	10.7	4.60	1004000	34000	29.5	34.1
	Abortion							
	episodes	0	n.a.	n.a	1794000	61000	29.4	29.4
	infertility	0.18	15	2.70	1794000	61000	29.4	32.1
4. Perinatal conditions	**Low birth weight** -- all sequelae	0.256	63.5	16.26	35092000	1036000	33.9	50.1
	birth asphyxia and birth trauma -- all sequelae	0.334	63.5	21.21	26049	770000	0.0	21.2
5. Nutrional deficiencies	**Protein-energy malnutrition**							
	wasting	0.053	n.a.	n.a	11080000	372000	29.8	29.8

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
	stunting	0.002	n.a.	n.a	11080000	372000	29.8	29.8
	developmental disability	0.024	58.7	1.41	11080000	372000	29.8	31.2
	Iodine deficiency							
	goitre -- grade 0	0	n.a.	n.a	795000	23000	34.6	34.6
	goitre -- grade 1	0.001	n.a.	n.a	795000	23000	34.6	34.6
	goitre -- grade 2	0.025	n.a.	n.a	795000	23000	34.6	34.6
	mild developmental disability	0.006	62.1	0.37	795000	23000	34.6	34.9
	cretinoidism	0.255	62.1	15.84	795000	23000	34.6	50.4
	cretinism	0.804	10	8.04	795000	23000	34.6	42.6
	Vitamin A deficiency							
	xerophthalmia	0	58.5	0.00	3722000	106000	35.1	35.1
	corneal scar	0.282	4.7	1.33	3722000	106000	35.1	36.4
	Iron-deficiency anaemia							
	mild	0	n.a.	n.a	2627000	129000	20.4	20.4
	moderate	0.011	n.a.	n.a	2627000	129000	20.4	20.4
	severe	0.087	n.a.	n.a	2627000	129000	20.4	20.4
	very severe	0.255	n.a.	n.a	2627000	129000	20.4	20.4
	cognitive impairment	0.024	61.1	1.47	2627000	129000	20.4	21.8
6. Malignant neoplasms	**Cancers** -- preterminal							
	mouth and oropharynx	0.145	4.3	0.62	3247000	286000	11.4	12.0
	oesophagus	0.217	1.7	0.37	3375000	358000	9.4	9.8
	stomach	0.217	2.9	0.63	6984000	752000	9.3	9.9
	colon and rectum	0.217	3.7	0.80	3926000	472000	8.3	9.1
	liver	0.239	1.59	0.38	6333000	501000	12.6	13.0
	pancreas	0.301	1.24	0.37	1483000	183000	8.1	8.5
	Trachea, bronchis, lung cancer	0.146	1.8	0.26	8303000	945000	8.8	9.0
	melanoma and other skin	0.045	4.2	0.19	508000	48000	10.6	10.8
	breast	0.069	4.2	0.29	3785000	322000	11.8	12.0
	cervix uteri	0.075	3.8	0.29	2661000	200000	13.3	13.6
	corpus uteri	0.066	4.5	0.30	576000	64000	9.0	9.3
	ovary	0.081	3.4	0.28	1309000	107000	12.2	12.5
	prostate	0.113	4.2	0.47	1055000	193000	5.5	5.9
	bladder	0.085	4.2	0.36	976000	131000	7.5	7.8
	lymphomas and multiple myeloma	0.089	3.5	0.31	2953000	214000	13.8	14.1
	leukaemia	0.112	3.1	0.35	4422000	226000	19.6	19.9
	Cancers -- terminal	0.809	n.a.	n.a	12941000	1023000	12.7	12.7
7. Diabetes mellitus	cases	0.033	15.9	0.52	5769000	571000	10.1	10.6

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
	diabetic foot	0.129	0.17	0.02	5769000	571000	10.1	10.1
	neuropathy	0.064	n.a.	n.a	5769000	571000	10.1	10.1
	retinopathy -- blindness	0.493	12.8	6.31	5769000	571000	10.1	16.4
	amputation	0.068	15.9	1.08	5769000	571000	10.1	11.2
8. Neuro-psychiatric conditions	**Unipolar major depression** -- episodes	0.302	0.61	0.18	n.a.	n.a.	n.a.	n.a.
	Bipolar disorder -- cases	0.383	1.4	0.54	116000	15000	7.7	8.3
	Schizophrenia -- cases	0.351	53	18.60	615000	51000	12.1	30.7
	Epilepsy -- cases	0.065	3.8	0.25	1641000	68000	24.1	24.4
	Alcohol use --							
	alcohol dependance syndrome	0.18	1.6	0.29	890000	56000	15.9	16.2
	Dementia -- cases	0.627	7.9	4.95	1435000	203000	7.1	12.0
	Parkinson disease -- cases	0.316	13.4	4.23	241000	58000	4.2	8.4
	Multiple sclerosis -- cases	0.42	32.5	13.65	352000	25000	14.1	27.7
	Drug uses -- dysfunctional and harmful drug uses	0.252	n.a.	n.a	299000	11000	27.2	27.2
	Post-traumatic stress disorder -- cases	0.108	2.5	0.27	n.f.	n.f.	n.f.	n.f.
	Obsessive-compulsive disorders -- cases	0.08	1.6	0.13	n.f.	n.f.	n.f.	n.f.
	Panic disorder -- cases	0.091	0.75	0.07	n.f.	n.f.	n.f.	n.f.
9. Sense organ disease	**Glaucoma** -- blindness	0.6	9.4	5.64	75000	6000	12.5	18.1
	Cataracts -- blindness	0.493	1.9	0.94	72000	6000	12.0	12.9
10. Cardiovascular disease	**Rheumatic heart disease** -- congestive heart failu	0.171	5.08	0.87	5527000	340000	16.3	17.1
	Ischaemic heart disease							
	acute myocardial infarction	0.395	0.06	0.02	41595000	6260000	6.6	6.7
	angina pectoris	0.095	n.a.	n.a.	41595000	6260000	6.6	6.6
	congestive heart failure	0.171	2.8	0.48	41595000	6260000	6.6	7.1
	Cerebrovascular disease -- first-ever stroke	0.224	5.2	1.16	32115000	4381000	7.3	8.5
	Inflammatory heart diseases							
	myocarditis	0.171	3.7	0.63	8347000	495000	16.9	17.5
	pericarditis	0.171	0.09	0.02	8347000	495000	16.9	16.9
	endocarditis	0.171	2.7	0.46	8347000	495000	16.9	17.3
	cardiomyopathy	0.171	3.4	0.58	8347000	495000	16.9	17.4
11. Respiratory disease	**COPD** -- symptomatic cases	0.388	7.8	3.03	14444000	2211000	6.5	9.6
	Asthma -- cases	0.059	5.4	0.32	1665000	137000	12.2	12.5
12. Digestive disease	**Peptic ulcer** -- cases	0.003	5.5	0.02	1789000	175000	10.2	10.2
	Cirrhosis of the liver -- symptomatic cases	0.33	7.8	2.57	10549000	779000	13.5	16.1
	Appendicitis -- episodes	0.463	0.04	0.02	1676000	56000	29.9	29.9
13. Genito-urinary disease	**Nephritis and nephrosis**							
	acute glomerulonephritis	0.107	1.41	0.15	7837000	536000	14.6	14.8

Disease class	Health outcome	Disability			Death			Disability and death
		Disability weight W (treated form) [-]	Duration of the disease D [yr disability/pers]	$YLD_p = W*D$ [yr lost/pers]	Total number of YLL Li [yr lost]	Total number of death N [pers]	$YLL_p = Li/N$ [yr lost/pers]	$DALY_p = YLD_p + YLL_p$ [yr lost/pers]
	end-stage renal disease	0.107	7.83	0.84	7837000	536000	14.6	15.5
	Benign prostatic hypertrophy --							
	symptomatic cases	0.038	8.6	0.33	162000	32000	5.1	5.4
14. Musculo-skeletal diseas	**Rheumatoid arthritis --** cases	0.174	6.8	1.18	118000	16000	7.4	8.6
	Osteoarthritis							
	hip	0.108	20.1	2.17	850000	81000	10.5	12.7
	knee	0.108	21.7	2.34	850000	81000	10.5	12.8
15. Congenital anomalies	**Congenital anomalies**							
	abdominal wall defect -- cases	0.85	0.01	0.01	174000	5000	34.8	34.8
	anencephaly -- cases	0.85	0.01	0.01	4993000	148000	33.7	33.7
	anorectal atresia -- cases	0.85	0.24	0.20	61000	2000	30.5	30.7
	cleft lip -- cases	0.016	63.3	1.01	171000	5000	34.2	35.2
	cleft palate -- cases	0.015	63.7	0.96	137000	4000	34.3	35.2
	oesophageal atresia -- cases	0.85	0.01	0.01	103000	3000	34.3	34.3
	renal agenesis -- cases	0.85	0.01	0.01	394000	12000	32.8	32.8
	down syndrome -- cases	0.593	61.4	36.41	1855000	57000	32.5	69.0
	congenital heart anomalies -- cases	0.323	62.1	20.06	6654000	207000	32.1	52.2
	spina bifida -- cases	0.593	63.9	37.89	1995000	59000	33.8	71.7

Appendix 3.4 Disability Adjusted Life Years per affected Person ($DALY_p$) for over 200 health outcomes, classified in 15 disease classes by Murray and Lopez [1996] (not all classes are relevant from an environmental point of view).

YLD_p: Years of Life lived with a Disability, per affected Person; YLL_p: Years of Life Lost, per affected Person.

Appendix 3.5 Nonlinear and damage-oriented approach

Different LCIA methods for characterizing the toxic effect of compounds have been reviewed in section 3.1.2. Damage-oriented methods, using a nonlinear dose-response function, appeared to be the more sophisticated. We mentioned that such methods are presently not available in LCIA. A framework for these methods is presented in this section. Arguments justifying why we did not implement such a method in this thesis are also put forward.

a) Procedure

As explained in section 2.1.4, curve-fitting models have been developed for extrapolating the risk from high to low doses. Using one of these models, the predicted dose-response curve can be obtained (see figure A.2). In the case of a nonlinear dose-response function, the frequency of exposure to a given dose has to be introduced to quantify the risk, since the slope of the dose-response curve varies with the exposure dose. A probability density function PDF(d) is introduced to express the distribution of exposure across people. An average slope factor β_{av} is gained by combining the probability density function with the dose-response function. This slope factor is derived by summing up the risk over the range of exposure and reporting this average risk to the total exposure dose, as stated in equation (A.0).

$$\beta_{av} = \frac{\int_0^\infty R(d) \cdot PDF(d) \cdot \partial d}{\int_0^\infty d \cdot PDF(d) \cdot \partial d} \qquad \text{Equation (A.0)}$$

where:

β_{av}: Average slope factor $[\frac{Risk}{mg/kg\text{-}day}]$

R(d): Response at dose d [Risk]

d: Dose [mg/kg-day]

PDF(d): Probability Density Function at dose d [-]

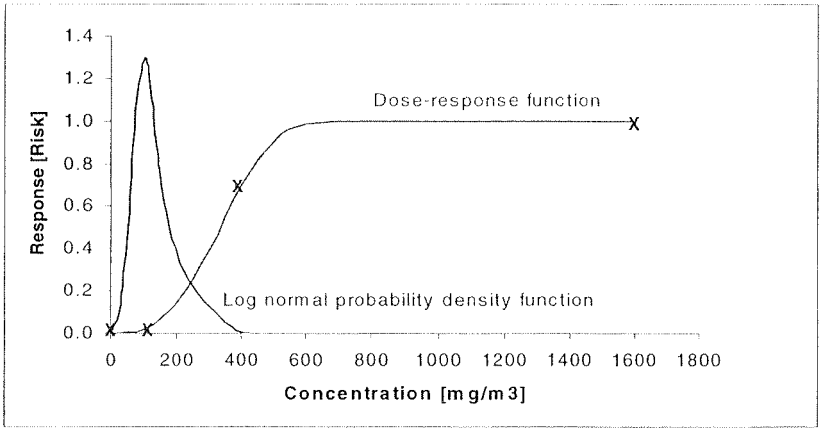

Figure A.2 Combining the dose-response function with a log-normal probability density function. X : Dose-response values observed in a rats bioassay, reported for methyl methacrylate in the Integrated Risk Information Service database [EPA, 1998]; the probability density function is not based on actual values and is presented only for illustrative purposes.

b) Application

Equation (A-0) provides a framework to include a chemical's background concentration and the nonlinearity of its dose-response curve. Slope factors which are dependent on the ambient concentration could be derived from that framework; effect factors for urban and rural regions could therefore be distinguished, leading to a site-specific evaluation.

However, in spite of these advantages, this procedure is not practical. The assessment of the background level for each chemical and each site of release is hardly feasible within a regular LCA. Furthermore, dose-response modeling using curve-fitting models is subject to controversy. While models fit well to the observed data, they vary by many orders of magnitude for low doses [NRC, 1983; Gray, 1998]. The average slope factor would thus depend on the selected model.

APPENDICES CHAPTER 4

Appendix 4.1 Fate factor and exposure efficiency in air

4.1.1 Fate factor

The mass balance of a substance i contained in a single box can be written as:
Mass variation = Input – Output
= Emission flow - (Degradation + Deposition + Advection flow).
Since the mass of the substance is given by the product of its concentration and the volume, the mass balance can be rewritten as:

$$\frac{d(dC_i^a \cdot V_i^a)}{dt} = \frac{M_i^a}{A} - \left(\frac{dC_i^a \cdot V_i^a}{\tau_i^a}\right) \qquad \text{Equation (A.1)}$$

where

dC_i^a: Concentration increase due to an emission flow M_i^a [mg/m^3]

V_i^a: Volume of dilution of substance i in air, per unit surface [m^3/m^2]

M_i^a: Emission flow of substance i into air [kg/yr]

A: Area over which the emission occurs [m^2]

τ_i^a: Residence time of substance i in air [yr]

The residence time of substance i in air accounts for the degradation, the deposition and the advection rate characterizing the substance i, as indicated in equation (A.2).

$$\tau_i^a = \frac{1}{\frac{1}{\tau_{degr}} + \frac{1}{\tau_{dep}} + \frac{V_i^{adv}}{V_i^a}} \qquad \text{Equation (A.2)}$$

where:

τ_{degr}: Degradation time of substance i [yr]

τ_{dep}: Deposition time of substance i [yr]

V_i^{adv}: Advection flow per unit area [m^3/m^2-yr]

Assuming a steady state, equation (A.1) can be rewritten as equation (A.3):

$$\frac{M_i^a}{A} - \left(\frac{dC_i^a \cdot V_i^a}{\tau_i^a}\right) = 0 \qquad \text{Equation (A.3)}$$

that is:

$$dC_i^a = \frac{M_i^a}{A} \cdot \frac{\tau_i^a}{V_i^a} \qquad \text{Equation (A.4)}$$

By definition, the fate factor links the emission to the concentration increase. Therefore, equation (A.5) can be derived from equation (A.4):

$$F_i^{aa} = \frac{dC_i^a}{M_i^a/A} = \frac{\tau_i^a}{V_i^a}$$ Equation (A.5)

where:

F_i^{aa}: Fate factor of substance i released into air (a), reaching humans by inhalation (a) [yr-m^2/m^3]

Equation (A.5) indicates that the fate factor accounts for the degradation, deposition and advection processes (via the residence time) and for the dilution. The fate of air pollutants can therefore be described as the ratio of a pollutant's residence time divided by its volume of dilution per unit area. This corresponds to the intuitive principle "the higher the residence time and the lower the volume of dilution, the greater the concentration increase at the earth surface".
In the mass balance, the transfer from the single box to another environmental compartment is not considered. Intermedia transfer coefficients can be used to link the different boxes together.

From equation (A.5), equation (A.6) expressing the equivalent volume of dilution can be derived. The equivalent volume of dilution is based on the assumption that the substance is uniformly distributed within the mixing column, with the concentration at the earth surface as the uniform concentration. This is why this volume is also referred to as the equivalent height of dilution.

$$V_i^a = \frac{\tau_i^a}{F_i^{aa}}$$ Equation (A.6)

4.1.2 Exposure efficiency

By definition, the exposure efficiency EE_i^{aa} represents the fraction of an atmospheric emission which is absorbed by inhalation:

$$EE_i^{aa} = \frac{M_{i\text{-abs}}^a}{M_i^a}$$ Equation (4.1)

where:

EE_i^{aa}: Exposure efficiency of substance i released into air (a), reaching humans by inhalation (a) [$mg_{absorbed}$/ mg_{emited}]

M_i^a: Emission flow of substance i into air (a) [kg/yr]

$M_{i\text{-abs}}^a$: Mass of substance i which is absorbed by inhalation (a), after the emission flow M_i^a [kg/yr]

The absorbed mass is proportional to the concentration increase induced by the emission, to the volume of inhaled air and to the population density. Therefore, equation (4.1) can be rewritten as equation (A.7):

$$EE_i^{aa} = \frac{\int_{t=o}^{\infty} \iint_{x\text{-}y} dC_i^a(x,y,z=0,t) \cdot dx dy dt \cdot \left[V^{in} \cdot \rho(x,y) \cdot N_{365} \right] dx \cdot dy \cdot dt}{M_i^a}$$ Equation (A.7)

where:

N_{365}: Number of days per year [days/year]

$\rho(x,y)$: Population density [pers/m^2]

V^{in}: Volume of air inhaled by humans [m^3/pers-day]

Assuming that both the concentration of substance i and the population density are uniformly distributed over the surface A, equation (A.7) becomes:

$$EE_i^{aa} = \frac{dC_i^a}{M_i^a/A} \cdot (V^{in} \cdot \rho \cdot N_{365})$$ Equation (A.8)

Combining equations (A.5) with (A.8) leads to equation (A.9):

$$EE_i^{aa} = \frac{\tau_i^a}{V_i^a} \cdot (V^{in} \cdot \rho \cdot N_{365})$$ Equation (A.9)

Appendix 4.2 Review of ambient air concentrations

4.2.1 Background concentration

a) Fines particles

Concentations of typical submicrometer-particules summarized by the Intergovernmental Panel on Climate Change [IPCC, 1995] are: 5-50 [$\mu g/m^3$] for polluted continental air (rural area), 1-10 [$\mu g/m^3$] for clean continental air (desert areas) and 1-5 [$\mu g/m^3$] for clean marine air. Additional data found in the literature are in accordance with these estimates: the concentrations of particles from nine rural sites were reported by the Organization for Economic Cooperation and Development [OECD, 1993] and an average background concentration of 15 [$\mu g/m^3$] can be derived. According to Charlson [1988], sub-micrometer particle mass concentration at Barrow and Samoa (Polylnesia) vary around a few $\mu g/m^3$. Final values for the marine, rural and desert concentrations are listed in the table below.

b) Sulfure dioxide

On the 1978 GAMETAG flight (Global Atmospheric Measurements Experiments of Tropospheric Aerosols and Gases), about two hundreds measurements of the SO_2 concentration were made over a latitude ranging from 57°S to 70°N [Maroulis et al., 1980]. The sampled area included the Pacific Ocean and the western section of North America. In the boundary layer, the mean SO_2 marine value was 54 ppt. Another study was conducted by Cuong et al. [1973] over Antarctic and Subantarctic areas. Sulfur dioxide concentrations ranging from 15 to 346 ppt were measured. Other measurements, made during an Atlantic expedition, estimated the oceanic SO_2 level for large areas of the earth's surface to be around 288 ppt [Georgi, 1970]. We derived from these data an average marine concentration C_m around 175 ppt = 0.5 [$\mu g/m^3$].

Rural concentrations of SO_2 ranging from 0.1 μg [S/m^3] to 14.8 [$\mu gS/m^3$] were reported in the statistics of the European Monitoring and Evaluation Programme [EMEP, 1992]. We derived from these data an average concentration for inhabited rural areas C_r of 8 [$\mu gSO_2/m^3$]. This value is in accordance with the concentrations ranging from 5 [$\mu g/m^3$] to 25 [$\mu g/m^3$] reported for most rural areas of Europe by the World Health Organization [WHO, 1987]. It is used as a default value for clean continental air (desert area).

c) Nitrogen oxide

Fehsenfeld et al. [1998] reviewed different measurements of NO_X that have been made in the non-urban troposphere for many years. In isolated inland sites and in coastal inflow sites, NO_X values ranged from 0.2 to 1.7 ppb and from 0.14 to 0.4 ppb respectively. In maritime areas, NO_X concentrations ranging from 0.01 to 0.05 ppb were reported. From these values, we derived an average background concentration for desert regions C_d of 0.7 ppb = 1.3 [$\mu g/m^3$] and an average marine concentration C_m of 0.025 ppb = 0.05 [$\mu g/m^3$].

For rural areas, the National Research Council [NRC, 1991] reported concentrations ranging from 0.2 to 10 ppb. We chose an average value of 5 ppb = 9 [$\mu g/m^3$].

d) Carbon monoxide

From 1979 to 1988, Khalil and Rasmussen [1988] took systematic measurements of carbon monoxide at six remote sites (the Arctic Circle, Oregon, Hawaii, Samoa, Tasmania and the South Pole). The site-by-site data were used to form average monthly concentrations representative of each hemisphere. Measurements indicated that there is more CO in the Northern Hemisphere than in the Southern Hemisphere. An average concentration for the remote sites of 75 ppb = 85 [$\mu g/m^3$] was reported. We used this concentration as an indicator of the average concentration for desert regions C_d and for marine regions C_m.

Seinfeld and Pandis [1998] reported concentrations for nonurban regions ranging from 40 to 200 ppb. We used the upper value of 200 ppb = 225 [$\mu g/m^3$] as an estimate of the average concentration in inhabited rural areas.

4.2.2 Urban concentration

A relatively large number of measurements of urban air pollution is available in the literature. A report from the United Nation Environmental Program [UNEP, WHO, 1988] provided current levels of SO_2, NO_2, CO and fine particles in many urban areas throughout the world. We derived an average urban concentration from these data. For instance, an interval of concentrations ranging from 70 to 400 [ug/ m^3] was reported for fine particles and we chose an average value of 200 [ug/ m^3].

Substance	C_m [ug/m^3]	C_d [ug/m^3]	C_r [ug/m^3]	C_u [ug/m^3]	C_g [ug/m^3]	C_c [ug/m^3]
NOx	0.05	1.3	9	71	1.3	15.2
SO2	0.5	< 8	8	50	3.0	12.2
Fine particles	2	10	15	200	5.8	33.5
CO	< 85	85	225	3030	111.1	505.5

Appendix 4.2.1 Concentrations in marine (C_m), desert (C_d), inhabited rural (C_r), urban (C_u), global (C_g) and continental (C_c) regions, based on measurements reported in the literature and equations (4.5) and (4.8) for the global and continental concentrations.

APPENDICES CHAPTER 5: EXAMPLE OF CALCULATION

The calculations of the exposure efficiencies, the effect factors and the damage factors for cadmium are presented in this appendix as an example.

5.1.1 Outdoor air emission of cadmium

a) Exposure path: inhalation

- Exposure efficiency

The exposure efficiency of cadmium released into air is assumed to be equal to the exposure efficiency of particles (see section 4.4.2). This efficiency is calculated using equation (4.9):

$$EE^{aa}_{Particles} = \frac{C_u \cdot P_u + C_r \cdot P_r}{M^a_{Particles}} \cdot V^{in} \cdot N_{365}$$

$$= \frac{200\frac{\mu g}{m^3} \cdot 2.7 \cdot 10^9 \text{ pers} + 15\frac{\mu g}{m^3} \cdot 3.3 \cdot 10^9 \text{ pers}}{447 \cdot 10^6 \frac{\text{ton}}{\text{yr}}} \cdot 20\frac{m^3}{\text{pers-day}} \cdot 365\frac{\text{day}}{\text{yr}} \qquad \text{Equation (4.9}$$

$$= 9.6 \cdot 10^{-6} \frac{mg_{absorbed}}{mg_{emitted}}$$

- Effect analysis, carcinogenic endpoints

The effect factor for the appearance of a lung cancer after inhalation of cadmium is calculated using equation (2.19), based on the slope factor estimated in section 2.6.1 and the disability adjusted life year of 9 [year lost/pers] associated with lung cancer (see table 2.3):

$$EF^a_{Cd} = \beta_{ED10\text{-}Cd} \cdot \frac{1}{BW} \cdot \frac{1}{LT_h} \cdot \frac{1}{N_{365}} \cdot DALY_p$$

$$= 6.1 \frac{\text{Risk}}{\text{mg/kg-day}} \cdot \frac{1}{70}\frac{\text{pers}}{\text{kg}} \cdot \frac{1}{70}\frac{1}{\text{yr}} \cdot \frac{1}{365}\frac{\text{yr}}{\text{day}} \cdot 9\frac{\text{yrlost}}{\text{pers}} \qquad \text{Equation (2.1}$$

$$= 3.1 \cdot 10^{-5} \frac{\text{yrlost}}{mg_{absorbed}}$$

- Human damage factor, for carcinogenic endpoint

The human damage factor is derived by combining the exposure efficiency with the effe factor:

$$HDF^{aa}_{Cd} = EE^{aa}_{Cd} \cdot EF^a_{Cd}$$

$$= 9.6 \cdot 10^{-6} \frac{mg_{absorbed}}{mg_{emitted}} \cdot 3.1 \cdot 10^{-5} \frac{\text{yrlost}}{mg_{absorbed}} \qquad \text{Equation (5.1}$$

$$= 3 \cdot 10^{-10} \frac{\text{yrlost}}{mg_{emitted}}$$

b) Exposure path: atmospheric deposition and food transfer

- Exposure efficiency

The exposure efficiency for an atmospheric release of cadmium and a transfer into food products after deposition on an agricultural soil is calculated by applying equation (4.10), using the soil to food transfer coefficient assessed in section 4.4.4 with the USES 2.0 model.

$$EE_{Cd}^{af} = f^{as} \cdot EE_{Cd}^{sf}$$

$$= 0.115 \cdot 3.2 \cdot 10^{-3} \frac{mg_{absorbed}}{mg_{emitted}} = 3.6 \cdot 10^{-4} \frac{mg_{absorbed}}{mg_{emitted}} \qquad \text{Equation (4.10)}$$

- Effect analysis, noncarcinogenic endpoints

The effect factor after oral exposure for the critical endpoint "proteinuria" associated with proteinurea is calculated using equation (2.19), based on the slope factor estimated in section 3.6.1 and a $DALY_p$ of 0.11 [yr lost/pers] (see section 3.7.2.d)):

$$EF_{Cd}^{f} = \beta_{ED10-Cd} \cdot \frac{1}{BW} \cdot \frac{1}{LT_h} \cdot \frac{1}{N_{365}} \cdot DALYp$$

$$= 41.5 \frac{Risk}{mg/kg\text{-}day} \cdot \frac{1}{70} \frac{pers}{kg} \cdot \frac{1}{70} \frac{1}{yr} \cdot \frac{1}{365} \frac{yr}{day} \cdot 0.11 \frac{yrlost}{pers}$$

$$= 2.5 \cdot 10^{-6} \frac{yrlost}{mg_{absorbed}} \qquad \text{Equation (2.19)}$$

- Human damage factor, for noncarcinogenic endpoint

The human damage factor is derived by combining the exposure efficiency with the effec factor:

$$HDF_{Cd}^{af} = EE_{Cd}^{af} \cdot EF_{Cd}^{f}$$

$$= 3.6 \cdot 10^{-4} \frac{mg_{absorbed}}{mg_{emitted}} \cdot 2.5 \cdot 10^{-6} \frac{yrlost}{mg_{absorbed}} \qquad \text{Equation (A.10)}$$

$$= 9 \cdot 10^{-10} \frac{yrlost}{mg_{emitted}}$$

c) Total exposure

Finally, the overall damage factor including both direct and indirect impact of cadmium released into air can be assessed using equation (5.2).

For the noncarcinogenic effect, we get:

$$HDF_{Cd}^{a} = HDF_{Cd}^{aa} + HDF_{Cd}^{af} = 9 \cdot 10^{-10} \frac{yrlost}{mg_{emitted}} \qquad \text{Equation(5.2)}$$

For the carcinogenic effect, we get:

$$HDF_{Cd}^{a} = HDF_{Cd}^{aa} + HDF_{Cd}^{af} = 3 \cdot 10^{-10} \frac{yrlost}{mg_{emitted}} \qquad \text{Equation(5.2)}$$

5.1.2 Indoor air emission of cadmium

The exposure efficiency for an indoor air release is calculated by using equation (4.4):

$$EE^{aa}_{Cd\text{-}indoor} = \frac{\tau^a}{V^a} \cdot V^{in} \cdot \rho_p \cdot N_{365}$$

$$= \frac{3.4 \cdot 10^{-4}\ yr}{3\ m^3/m^2} \cdot 20 \frac{m^3}{pers\text{-}day} \cdot 10^{-2} \frac{pers}{m^2} \cdot 365 \frac{day}{yr} \qquad \text{Equation (4.4)}$$

$$= 9.1 \cdot 10^{-3} \frac{mg_{absorbed}}{mg_{emitted}}$$

5.1.3 Emission of cadmium on an agricultural soil

The human damage factor is given by equation (5.3):

$$HDF^{sf}_{Cd} = EE^{sf}_{Cd} \cdot EF^{f}_{Cd}$$

$$= 3.2 \cdot 10^{-3} \frac{mg_{absorbed}}{mg_{emitted}} \cdot 2.5 \cdot 10^{-6} \frac{yrlost}{mg_{absorbed}} \qquad \text{Equation (5.3)}$$

$$= 8 \cdot 10^{-9} \frac{yrlost}{mg_{emitted}}$$

APPENDICES CHAPTER 6

Appendix 6.1 Participants

The Cyclaupe study was sponsored by the Swiss Agency for the Environment, Forests and Landscape (BUWAL). For its execution, we collaborated with the consulting office RWB SA, which was responsible for determining the input flows for the inventory and for the economic analysis. As required by the Society of Environmental Toxicity and Chemistry's code of practice [Consoli et al., 1993], two peer-reviewers had the responsibility to validate the different steps of the Life Cycle Assessment. A group of experts on water management was also constituted to define the scenarios and to get data and feedbacks. Members of this group and other participants are listed in table appendix 6.1.

Actors	Office	Name	Address
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	OEKAG	Morandini	Bodenhof Terrasse 13A, 6005 Luzerne
	CREM	C. Matas	Rue Morasse 5, CP256, Martigny

Appendix 6.1 Participants of the Cyclaupe study.

Appendix 6.2 Water quality

6.2.1 Rainwater and water flowing from the roof

Values measured by Mottier [1995] near Zürich are presented in this appendix as an evaluation of the rainwater quality and of the quality of water flowing from roofs.

- The quantity of water flowing from the roof varies from 0 to 26% of the rainfalls for a gravel roof, from 66 to 87% for a roof made of tiles and from 56 to 100% for a polyester roof. A roof made of tiles is assumed in the Cyclaupe study, since this type of roof is the most frequent.
- Rainwater quality is different from the quality of water flowing from roofs (see the below table). Due to the high pollution level of the sampling area located near Zürich, these values represent high estimates for Switzerland. Since the concentration of pollutants varies from one rain event to another and during a rain event, these estimates are average values of 4 rain events Mottier [1995].

	Unit	Rainwater Mottier, 1995]	Roof made of tiles [Mottier, 1995]	PE roof [Mottier, 1995]	Gravel roof [Mottier, 1995]
Ionic compounds					
Cl	mg/l	0.3	0.3	0.4	0.7
SO4	mg/l	1.6	2.4	2.9	6.7
SiO4	mg/l	0.1	0.4	0.3	1.8
NO3	mg N/l	0.1	0.4	0.7	3.2
NO2	mg N/l		0.06	0.06	0.12
Ntot	mg N/l	1	1.7	2.7	4.2
PO4	ug P/l	5.1	13.8	13.8	9.9
Ptot	ug P/l	27.9	133.2	133.2	35.3
NH4	mg N/l	0.42	0.44	0.76	0.05
Ca	mg/l	0.6	2.4	1.6	20.4
Heavy metals					
Mg	mg/l	0.2	0.65	0.17	0.82
Na	mg/l	0.16	0.2	0.11	0.31
Cr	ug/l	0.47	0.75	0.49	0.53
Mn	ug/l	1	6.4	11.7	4.1
Fe	ug/l	33.4	98.5	174.2	77.9
Cu	ug/l	3	125	324.1	19.7
Zn	ug/l	14.6	21.2	62.8	7.5
Cd	ug/l	0.09	0.2	0.14	0.07
Pb	ug/l	2.8	20.3	10.6	2.6

Appendix 6.2.1 Concentration of pollutants in rainwater and water flowing from different types of roof [Mottier, 1995].

6.2.2 Drinking water

- Metals

The contamination of drinking water by metals is evaluated here. Concentrations of metals measured 4 times a year at the drinking water treatment plant of Lutry (VD) are selected. Average values derived from measurements [Truffer, 1997] are: 0.14 [ug/l] for cadmium, 0.66 [ug/l] for copper, 1.68 [ug/l] for lead and 15 [ug/l] for zinc. In addition, a manganese concentration of 10 [ugMn/l] is reported by the Swiss Agency for the Environment, Forests and Landscape [BUWAL, 1993].

- P, N and S pollution

Average concentrations in phosphore, nitrate, nitrite and sulfate, measured each month at the drinking water treatment plant of Lutry (VD), are presented below [Truffer, 1997].

Substance	unit	Concentration [unit/l]	unit	Concentration [unit/l]
Phosphore total	mg P	0.032	mg P	0.03
Nitrate	mg N	0.93	mg NO3	4.1
Nitrite	mg N	0.00030	mg NO2	0.001
Sulfate	mg S	15.67	mg SO4	47

Appendix 6.2.2 P, N and S pollution in drinking water, at the drinking water treatment plant of Lutry (VD), according to [Truffer, 1997].

Appendix 6.3 Transfer of pollutants contained in water

Emissions linked to the transfer of pollutants contained in rainwater and drinking water are presented here.

6.3.1. Conventional scenarios

a) Infiltration

Rainwater is infiltrated around the house in the conventional scenarios; pollutants contained in rainwater are therefore transferred into the infiltration soil. Emissions into the infiltration soil per m^3 and per functional unit (for normal toilets) are presented here as an example.

Substances	Release into the infiltration soil [kg/m^3]	Release into the infiltration soil [kg/FPD]
Mn	6.4E-06	3.5E-07
Zn	2.1E-05	1.1E-06
Cr	7.5E-07	4.1E-08
Cu	1.3E-04	6.8E-06
C d	2.0E-07	1.1E-08
Pb	2.0E-05	1.1E-06
Fe	9.9E-05	5.3E-06
Mg	6.5E-04	3.5E-05
Na	2.0E-04	1.1E-05

Appendix 6.3.1.a) Emissions into the infiltration soil per m^3, and per FPD (Flushing of a toilet for one Person during one Day) for conventional toilets.

b) Transfer at the wastewater treatment plant

Pollutants contained in drinking water are transferred toward the wastewater treatment plan, where a transfer into air, water and soil occurs. Resulting emissions are listed below, using data from Zimmermann et al. [1996] for the transfer at the wastewater treatment plant.

Polluants	Concentration of the water entering the WTP [kg/m^3]	Air emissions [kg/m^3]	Water emissions [kg/m^3]	Soil emissions [kg/m^3]
Mn	1.0E-05	7.1E-10	5.2E-06	2.3E-06
Zn	1.5E-05	1.1E-08	6.2E-06	4.8E-06
Cr	n.a.	n.a.	n.a.	n.a.
Cu	6.6E-07	2.0E-10	2.3E-07	2.3E-07
C d	1.4E-07	3.3E-10	8.6E-08	3.4E-08
Pb	1.7E-06	1.1E-09	2.4E-07	7.0E-07
Fe	n.a.	n.a.	n.a.	n.a
Mg	n.a.	n.a.	n.a.	n.a
Na	n.a.	n.a.	n.a.	n.a

Appendix 6.3.1.b) Emissions resulting from the transfer occurring at the wastewater treatment plant (WTP), when drinking water is used for the flushing; n.a.: not available.

6.3.2 Recuperation scenarios

Pollutants contained in rainwater are transferred toward the wastewater treatment plant. Emissions resulting from their transfer at the wastewater plant are listed below, using data from Zimmermann et al. [1996]. We assumed that all emissions on soil occur on an agricultural soil, after application of the sludges from the wastewater treatment plant.

An infiltration of rainwater occurs only when the storage tank is full, whereas drinking water is used for the flushing only when the storage tank is empty.

Pollutants	Concentration of water entering the WTP [kg/m^3]	Air emissions [kg/m^3]	Water emissions [kg/m^3]	Soil emissions [kg/m^3]
Mn	6.4E-06	4.5E-10	3.3E-06	1.5E-06
Zn	2.1E-05	1.5E-08	8.7E-06	6.8E-06
Cr	7.5E-07	9.7E-11	4.0E-07	1.7E-07
Cu	1.3E-04	3.8E-08	4.4E-05	4.3E-05
C d	2.0E-07	4.7E-10	1.2E-07	4.9E-08
Pb	2.0E-05	1.3E-08	2.9E-06	8.5E-06
Fe	9.9E-05	n.a.	n.a.	n.a.
Mg	6.5E-04	n.a.	n.a.	n.a.
Na	2.0E-04	n.a.	n.a.	n.a.

Appendix 6.3.2 Emissions resulting from the transfer occurring at the wastewater treatment plant (WTP), when rainwater is used for the flushing; n.a.: not available.

Appendix 6.4 Calorific losses

The temperature of the flushing water entering in the house is lower than the ambient temperature inside the house. The water temperature therefore increases between two uses of the toilets. We carried out some measurements to evaluate the calorific losses associated with that temperature increase for an individual house. A temperature increase of 3 ^{o}C has been found [Crettaz et al., 1998]. It consists of an increase of 1.5 ^{o}C in the pipes between the entry of the house and the toilets, and in an increase of 1.5 ^{o}C in the flushing tank.

A calorific loss of 4.16 [MJ/m^3-^{o}C] is derived from the calorific coefficient of water (4.16 [J/g] of water). A loss of 12.5 [MJuseful/m^3] is derived for a temperature increase of 3 ^{o}C, that is a calorific loss of 7.2 [MJuseful/m^3] (=12.5 MJ/m^3 · 210/365) for a heating period of 210 days per year in Switzerland. Applying a heating yield of 0.85, a calorific loss of 8.45 [MJfinal/m^3] is obtained. Therefore, for a house of 16 persons, the calorific loss due to the flushing is of 2700 [Mjfinal/house-yr] (=8.45 MJf/m^3 · 0.054 m^3/pers-day · 16 pers/house · 365 day/yr).

Appendix 6.5 Full inventory

Substances and medium of release	Unit	CONV [unit/FPD]	REC10 [unit/FPD]	CONVeco [unit/FPD]	REC10eco [unit/FPD]	REC100% [unit/FPD]
AIR						
benzo[a]pyrene	µg	0.3	**0.4**	0.1	**0.2**	0.2
Cd	µg	2.4	**3.7**	0.9	2.3	**2.8**
CO	mg	107.0	**157.0**	41.1	91.1	**116.8**
CO2	g	61.0	**69.0**	23.4	31.9	**35.3**
Cr	µg	5.1	**6.4**	2.0	3.3	**3.6**
Cu	µg	43.3	**68.9**	16.1	**41.9**	39.3
H2S	µg	175.0	**228.0**	67.1	**121.9**	119.4
HCl	mg	1.2	**1.7**	0.5	1.0	**1.1**
HF	µg	191.0	**271.0**	74.6	159.4	**173.0**
Hg	µg	1.1	**1.3**	0.4	0.7	**0.8**
methane	mg	104.1	**130.2**	39.8	67.7	**81.1**
Mn	µg	134.2	**152.0**	51.7	**70.4**	68.4
N2O	mg	**1.9**	1.6	0.7	0.6	**0.7**
NH3	µg	68.2	**696.1**	25.9	444.4	**458.3**
Ni	µg	66.8	**103.9**	25.2	64.3	**73.9**
NMHC	mg	124.1	**205.6**	48.3	130.1	**197.8**
NOx	mg	102.5	**125.0**	39.1	62.9	**72.1**
P	µg	3.6	**5.8**	1.4	3.2	**3.4**
particles	mg	41.5	**53.3**	15.8	27.9	**28.5**
Pb	µg	36.1	**44.6**	14.0	22.8	**22.9**
SOx	mg	278.5	**440.7**	108.0	273.3	**274.2**
V	µg	103.6	**186.9**	39.1	125.0	**170.9**
Zn	µg	201.1	**220.7**	78.0	**98.2**	93.1
WATER						
Ag	µg	0.6	**0.7**	0.2	0.4	**0.5**
Al	mg	9.9	**12.0**	3.8	**6.2**	6.2
As	µg	19.7	**24.4**	7.7	**12.8**	**12.8**
Ba	mg	2.5	**3.1**	1.0	1.6	**2.0**
BOD	µg	409.8	**514.8**	159.4	266.9	**312.0**
Cd	µg	8.3	**9.8**	3.2	4.4	**4.6**
chloride	mg	455.8	**568.8**	177.3	293.2	**370.9**
Cl-	µg	0.3	**0.4**	0.1	**0.2**	**0.2**
Co	µg	19.0	**23.7**	7.4	**12.4**	12.3
COD	mg	2.8	**19.5**	1.1	12.7	**14.2**
Cr+3	µg	112.9	**155.0**	44.7	84.9	**85.4**
Cr+6	µg	5.28E-03	**7.70E-03**	2.05E-03	4.60E-03	**5.06E-03**
Cu	mg	0.1	**1.4**	0.025	0.9	**1.0**
cyanide	µg	15.1	**20.1**	5.9	10.9	**11.3**
F	µg	602.5	**741.2**	234.2	377.1	**383.0**
Fe	mg	5.2	**6.8**	2.0	3.7	**4.2**
Hg	µg	0.3	**0.3**	0.1	**0.2**	**0.2**

Substances and medium of release	Unit	CONV [unit/FPD]	REC10 [unit/FPD]	CONVeco [unit/FPD]	REC10eco [unit/FPD]	REC100% [unit/FPD]
hydrocarbons	µg	7.8	6.8	3.0	**2.6**	**2.6**
Mn	µg	565.4	544.2	220.2	229.1	**236.6**
NH3	mg	1.1	**18.9**	0.4	12.3	**12.9**
Ni	µg	55.0	**68.9**	21.4	**36.4**	36.3
nitrate **	mg	606.6	192.1	**235.8**	155.6	149.3
oil	mg	13.2	**16.8**	5.1	8.8	**11.7**
Pb	µg	131.0	**227.5**	49.0	**121.9**	123.1
phenol	µg	97.5	**513.5**	37.9	454.2	**835.3**
phosphate	mg	0.8	**1.3**	0.3	**0.7**	**0.7**
Se	µg	149.7	**161.1**	57.5	**71.3**	58.5
sulfide	µg	17.8	**24.0**	6.9	13.2	**18.0**
TBT	µg	0.9	**1.2**	0.4	0.6	**0.8**
Zn	µg	4839.1	**600.9**	186.3	279.7	**284.6**
INFILTRATION SOIL						
As	µg	**n.a.**	n.a.	**n.a.**	n.a.	n.a.
Cd	µg	**10.8**	0.4	**4.2**	2.5	2.4
Co	µg	**n.a.**	n.a.	**n.a.**	n.a.	n.a.
Cr	µg	**40.5**	1.7	**15.7**	9.5	8.9
Cu	mg	**6.75**	0.3	**2.6**	1.6	1.5
Fe	mg	**5.32**	0.2	**2.1**	1.2	1.2
Hg	µg	**n.a.**	n.a.	**n.a.**	n.a.	n.a.
Mg	mg	**35.1**	1.4	**13.6**	8.2	7.7
Mn	µg	**346**	14.0	**134.0**	81	76
Ni	µg	**n.a.**	n.a.	**n.a.**	n.a.	n.a.
Pb	mg	**1.1**	0.0	**0.43**	0.26	0.24
Zn	mg	**1.14**	0.0	**0.45**	0.27	0.25
AGRICULTURAL SOIL						
As	µg	0.35	**0.44**	0.14	0.22	**0.29**
Cd	µg	1.85	**2.31**	0.72	1.02	**1.03**
Co	µg	0.019	**0.024**	0.007	0.012	**0.016**
Cr	µg	4.41	**10.82**	1.72	6.31	**7.25**
Cu	mg	0.01	**1.34**	0.0048	0.88	**0.91**
Fe	mg	1.77	**2.20**	0.69	1.12	**1.46**
Hg	µg	0.0026	**0.0034**	0.0010	0.0018	**0.0023**
Mn	µg	159.55	**142.39**	**62.05**	53.82	60.01
Ni	µg	0.138	**0.176**	0.05	0.09	**0.12**
Pb	µg	38.33	**279.48**	14.907	173.80	**178.54**
Zn	µg	274.99	**340.14**	106.94	151.05	**154.95**

Appendix 6.5 Full inventory of substances emitted into air, water, infiltration soil and agricultural soil, for the 5 scenarios.
In bold: highest value among the scenarios.
n.a.: not available.

Appendix 6.6 Economic study

The cost for the equipment maintenance, the cost for 1 m^3 of drinking and wastewater, and the additional expenses for recuperation have been evaluated by Orlando and Cuanillon [1997]. The mortgage and the pay-off have been considered in these calculations. A summary of the results are presented in this appendix.
Economic toilets lead to a significant reduction of the expenses, equal to 50 [$/pers-yr] for a conventional water supply. Recuperation scenarios appear to be economically unfavourable. Compared to the scenario CONVeco, the extra cost is 51 [$/pers-yr] for the scenario REC10eco, a 160% increase. The scenario REC10eco becomes favourable only for a drinking water price of 9 [$/$m^3$], without consideration of the wastewater treatment. The scenario REC100% does not appear to be economically feasible.

	CONV max	CONV Eco	REC10 max	REC10 eco	REC10 eco Society cost	REC100% max
Installation cost	0	0	11633	12700	12700	2200
Mortage + paying off			700	762	762	1318
Maintenance cost			267	293	293	267
Total expenses			965	1055	1055	1585
Number of persons	16	16	16	16	16	16
Total cost per pers (fixed cost)	0	0	60	66	66	99
Flushing water consumption (m3)	315	123	315	123	123	315
Flushing water consum. (m3/pers)	19.7	7.7	19.7	7.7	7.7	19.7
Recovery fraction	0	0	0.57	0.97	0.97	0.57
m3 of recycled water to pump	0	0	11.2	7.5	7.5	11.2
Cost for the pumping electricity $/pers-yr	0	0	0.16	0.11	0.11	0.16
Drinking water cons. m3/pers	19.7	7.7	8.5	0.2	0.2	8.5
Total cost of 1 m3 of drink. water $/m3	2	2	2	2	2	2
Contribution of fixed cost (90%)					1.8	
Contribution of variable cost (10%)					0.2	
Cost for drinking water ($/yr)	39	15	17	0.5	0.5	17
Cost drinking water, equiv. fixed cost					13	
Cost for waste water treatment ($/yr) (2.1 $/m3)	42	17	42	17	17	42
Annual total cost ($/pers)	82	32	120	83	96	158
%	256	100	375	260	300	494
Annual extra cost per family of 4 pers	199	0	351	205	258	505

Appendix 6.6 Economic comparison of the scenarios, by Orlando and Cuanillon [1997].