Corner: UNEP/SETAC Life Cycle Initiative

Dose-Response Modeling for Life Cycle Impact Assessment

Findings of the Portland Review Workshop

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With contributions of the workshop participants[5]

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Introduction

The United Nations Environment Program (UNEP)/SETAC Life Cycle Initiative aims at putting life cycle thinking into practice and at improving the supporting tools for this process through better data and indicators. The initiative has thus launched three programs with associated working groups (http://www.uneptie.org/pc/sustain/lcinitiative/). The *Task Force on Toxic Impacts* was established under the Life Cycle Impact Assessment (LCIA) program to establish recommended practice and guidance for use in human toxicity, ecosystem toxicity, and related categories with direct effects on human health and ecosystem health.

During the 2004 SETAC Europe meeting in Prague, an international group of LCIA practitioners initiated activities of the LCIA Task Force 3 (TF3) to address exposure and toxicity with the goal of establishing guidance for LCIA. As an adjunct activity of the 2004 SETAC World Congress in Portland, Oregon, TF3 members organized a workshop to review existing proposals on human toxicity indicators for LCIA. The particular focus of this workshop was on options regarding dose-effect response and severity. The review workshop consisted of formal presentations of approaches followed by a review discussion performed by a panel of internationally recognized dose-response modeling experts. This workshop was organized by Thomas McKone of the University of California, Berkeley and Michael Hauschild and Stig Irving Olsen from the Danish Technical University in Denmark. Amy Kyle of the University of California, Berkeley, facilitated the workshop. This workshop involved several internationally recognized dose-response modeling experts as well as LCIA specialists (see footnote for the full list). The product of this workshop is a set of short recommendations that are being transmitted via this report.

Workshop Format

The workshop consisted of three elements:

(A) Presentations summarizing (1) the goals of the LCIA Task Force (2) historical approaches to exposure and toxic impacts in LCIA (3) current alternative proposals for addressing human health impacts. Viewgraphs from two of these presentations are provided in Appendix B to this report.

(B) Discussion among a panel of experts about the scientific defensibility of these historical and proposed approaches in the context of the goals of the LCIA Task Force 3 on toxicity impacts.

(C) Development of the recommendations to the LCIA program and working group for optimum short- and long-term strategies for addressing human health impacts in LCA.

Background and Key References

Life cycle assessment (LCA) is a framework for comparing products (or product-related emissions) according to their total estimated environmental impact summed over all chemical emissions and activities associated with the product's life cycle. To assess human toxicity impact, the LCIA practitioner considers for each chemical involved the cumulative exposure associated with the mass released to a defined (indoor, urban, regional, etc.) environment by multiplying the release amount by a measure of toxic impact to characterize the likelihood of health effects and their potential consequences.

[5] Besides the authors, other workshop participants were: Lois Swirsky Gold, University of California, Berkeley, CA USA, Lorenz Rhomberg, Reviewer, Gradient Corporation, Cambridge, MA USA, Glenn Suter, US Environmental Protection Agency, Cincinnati, OH, USA, Jane Bare, US Environmental Protection Agency, Thomas Gloria, Five Winds International, Stefanie Hellweg, Swiss Federal Institute of Technology (ETH), Zürich, Switzerland, Allan Astrup Jensen, Force Technology, Denmark, Randy Maddalena, Lawrence Berkeley National Laboratory, Guido Sonnemann, Division of Technology, Industry & Economics, United Nations Environment Programme, Paris, France, Dik van de Meent, Member, RIVM Laboratory for Ecological Risk Assessment, Bilthoven, The Netherlands.

Table 1: Questions addressed by the review workshop

1.	**General issues**
	What is the scientific evidence for classifying any substance as a human carcinogen?
	What is the scientific evidence for classifying any substance as inducing some type of non-cancer disease impact such as neurotoxicity, reproductive toxicity, respiratory irritation, developmental delay, asthma, autoimmune diseases, etc.?
	What is the validity and utility of using non-threshold linear dose-response models for assessing either cancer or non-cancer population disease burden?
	Are disability adjusted life years (DALYs) an appropriate endpoint measure of disease burden for life-cycle impact?
	Are there alternatives to DALYs that should be considered?
	Should we consider individual or population (collective) risk as a measure of impact in life-cycle assessment?
	When combining the effects from exposures to multiple harmful substances, should we consider effect additivity, risk additivity, or cumulative disease burden in a measure of human health impact for LCA?
2.	**Measures of potency**
	What is the basis for the potency measure (e.g. critical effect, most severe effect, etc.)?
	Should carcinogens and non-carcinogens be separated when calculating health impact midpoints and/or health impact endpoints?
	For non-cancer outcomes should the midpoint and/or endpoint measure of disease burden make use of no adverse/lowest adverse effect (NOAEL/LOAEL) doses or benchmark doses (e.g. TD50, ED10)?
	For cancer outcomes should the midpoint and/or endpoint be based on slope factors or other potency measures such as benchmark dose?
3.	**Species and population extrapolation**
	In developing dose-response and disease burden models, should we apply extrapolation factors to account for differences between animals and humans, between sensitive subpopulations, etc.?
	If we use extrapolation factors, how should the extrapolation factors be derived, e.g. probabilistic methods or some set of default assumptions?
4.	**Measures of severity**
	Should and how can LCIA models of toxicity include the severity of the effect?
	Should severity assessment be qualitative (indicator-based), semi-quantitative, or quantitative?
	If the measure of severity is quantitative: should the model include full damage modeling, that is both morbidity and mortality, and how should mortality and morbidity be aggregated?
	Should the model include partial damage modeling (e.g. only mortality)?
	What methods of damage modeling should be used?
	If the measure of severity is semi-quantitative or qualitative, what approach should be used to categorize and/or classify severity?
5.	**Data quality and availability**
	Can and how should data quality for human health impact and disease burden be quality assured?
	Are both experimental data and derived 'safe' levels such as allowable daily intake (ADI) and reference dose (RfD) from the EPA IRIS database etc. available for a broad set of chemicals?
	What is the minimum level of data availability required to establish the lethal dose for 50% of a population (LD50), NOAEL, and/or benchmark doses from chronic studies?

The SETAC Life Cycle Impact Assessment (LCIA) Working Group on Human Toxicity (Krewitt et al. 2002) have classified measures of toxic impact into two broad categories: (1) potency-based characterization factors that are used to assess the likelihood of a disease or effect (cancer, death, reproductive failure, etc.) and (2) severity-based characterization factors or damage factors that, in addition to the qualitative or quantitative likelihood of disease, reflect population consequences of the disease in terms of years of life loss or some other measure of societal impact. But rather than indicating the likelihood of disease, potency mainly indicates a dose that has an effect (the effect dose or ED) or the lower confidence on the ED (Gold et al. 2003). Recently, Crettaz et al. (2002) and Pennington et al. (2002) have proposed for both cancer and non-cancer health impacts in LCIA alternative approaches that include elements of both the potency and severity impact measures note above. For carcinogens, Crettaz et al. (2002) based their approach on the maximum likelihood estimate of the dose inducing a 10% response over background (the ED10) and derive from this a linear low-dose extrapolation using the slope 0.1/ED10. They obtain the ED10 values by using the US EPA Integrated Risk Information System (IRIS), the medium tumor dose rate (TD50) from the Cancer Potency database of Gold et al. (2006), or data on median single lethal dose (LD50). Potential consequences and severity are addressed by combining the low-dose slope with a measure of disability adjusted life years lost due to cancer to obtain a aggregate number of disability adjusted life years (DALYs) attributable to a specified chemical release. For non-carcinogens Pennington et al. (2002) follow an approach similar to that of Crettaz et al. (2002), but made use of the benchmark dose to obtain a low-dose slope factor for non-cancer diseases.

Review Questions

The workshop organizers provided a set of review questions in advance to both the experts and other workshop participants. With regard to dose-response modeling in LCIA, the workshop organizers structured these review questions into five categories (**Table 1**): general issues, measures of potency, species and population extrapolation, measures of severity, and data quality and availability.

Workshop Findings

The workshop findings are organized into three categories – overarching issues, measures of potency, and measures of severity.

Overarching Issues

In concurrence with other workshop participants, the dose-response experts concluded that it is appropriate to include human toxicity in the LCIA process. The basis for this recommendation is that, in the absence of a toxicity metric, many LCIA practitioners will continue to rely on emissions magnitude as a measure of emissions impact. But, because of the significant differences among chemicals in the dose levels that are toxic, it is essential to consider human toxicity in comparing releases of different toxic chemicals.

There is an overarching concern that the LCIA process should address toxicity but limit the level of detail in the analysis to information that provides benefits or value to the overall LCIA. Too much detail can reduce the transparency and reliability of the LCIA. However, there may be cases where more analysis matters. That is, cases where exposure is below a threshold of effect and for which more details on the distribution of population exposure will impact estimates of disease burden.

Measures of Potency

The expert panel recommended the use of a hierarchy of toxicity values in LCIA with priorities assigned so that LCIA assessors can evaluate the relative advantages of different toxicity metrics. The goal is to allow LCIA assessors to determine which metrics would be scientifically defensible and informative as well as identifying methods that are transparent and easy to use. With regard to measures of potency, the workshop participants made the following specific recommendations.

a) **Human preference:** Relevant and applicable human data should be given priority wherever such data are available.

b) **Preference for benchmark measures:** The review panel preferred the use of benchmark measures of effect as a means of scaling relative toxicity, rather than a no observed adverse effect level (NOAEL), lowest observed adverse effect level (LOAEL) or Reference Dose (RfD), which is derived from NOAEL or LOAEL. Benchmark measures include the ED10, the dose that results in a toxic effect to 10% of the exposed population, and the ED50, the dose that results in a toxic effect to 50% of the exposed population. The basis for this recommendation is the frequent dependence of the NOAEL or LOAEL on the limitations of study design. However, the experts expressed the view that it would be better to use the NOAEL or LOAEL rather than no measure at all, as a basis to estimate ED10 or ED50. Given the overall uncertainties, there are large differences between these alternate approaches in ranking chemicals in LCIA. RfD values are obtained from NOAELs or LOAELs using safety or uncertainty factors that reflect differing degrees of precaution or protection. As a result, it is not clear whether the RfD, which was developed to provide an adequate margin of safety, can provide the consistent measure of harm needed in LCIA. Thus, when an RfD is used in chemical ranking, the panel recommended that the uncertainty measures used and the corresponding NOAEL or LOEL should be separated out from the RfD and reported along with the RfD.

As a follow-up issue, the panel identified the need to come to a conclusion about whether an ED10 value, an ED50 value, some other benchmark (ED25), or some approach that combines these benchmark doses would be best suited to LCIA. The ED50 is at the median of the range of doses that produce significant results. The advantages of the ED50 are that it is a more stable measure and represents the point most comparable among biological species. The ED10 is usually within the dose range tested for statistically significant results. The advantage of the ED10 is that the information about slope or dose-response that is most chemical specific is between the ED50 and ED10 range, and this is better captured in the ED10. But the use of ED10 will not automatically reduce the level of uncertainty for low dose extrapolation. If a practitioner believes that 'slope' values from animal studies predict human values, this would argue for using the ED10. But this is a question that requires further research and for which we do not yet know the answer.

A related need is to determine how to make use of combinations of ED50 and ED10 and possibly LOAEL and NOAEL in life-cycle impact rankings. The experts recognized that when these different measures are combined there is a need for correction factors to make them consistent, to correct for data from different species, and to correct for differences in duration of the experimental exposures. The correction factors should be used to steer all values to best estimates as opposed to the most health protective values. It is important to avoid introducing bias even with methods that are consistent. There is a need to include a larger number of chemicals in studies of correlation among the different measures of toxicity that were discussed at the workshop.

c) **Complexity of multi-chemical comparison and low dose extrapolation:** The complexities of the analysis make it somewhat difficult to understand how the various dose-response methods might compare with respect to the value of information they provide to an LCIA. This problem derives in large part from differences among the methods of low dose extrapolation. LCIA involves comparisons among the life cycles of products not comparisons among the life cycle of chemicals. But even though this leads to comparisons among chemicals, LCIA is more complicated than single chemical comparisons. Moreover, the problem is one of multi-dimensional optimization. This means that one input depends on others. In LCIA we need a way to compare processes and activities that are not always comparable. The need to confront and inform tradeoffs requires the ability to express relative preferences.

d) **Normalization:** Normalization is a critical issue. It is important to determine what to use as normalizing factor. There are differences between normalizing to manmade changes and to natural background. Global warming provides a cautionary example. The discussion of the relative importance of environmental exposure as a cause of human health impacts and hence the relevance to address human toxic impacts in life cycle impact assessment lead to identification of a need for normalization against other types of impact.

Measures of Severity

With regard to measures of severity, the workshop participants made the following specific recommendations.

a) **Relation between severity and potency:** The expert panel noted the value of taking severity into account but hesitated to recommend specific methods to characterize severity. They took this position because the way that potency is addressed will bear on severity but is not yet fully decided in the LCIA literature. In other words, it is necessary and acceptable to address severity, but we need to work out the specifics of potency issues to decide how. The panel recognized that not using some measure of severity is the same as treating all outcomes as having equal severity. When confronting severity, there may be some simple methods that are more applicable in some cases, such as distinguishing between carcinogens and non-carcinogens, but, such approaches will also mask real differences in some or many cases. On the other hand, the panel expressed concern that explicitly treating severity may imply that we know more than we do and that we can estimate severity better than is actually feasible. We want to avoid this situation.

b) **Multiple effects:** It may be appropriate to look at more than one outcome. Similar to other approaches, the RfD approach looks for the critical effect, which is the one that may occur at the lowest dose. The panel noted that this involves toxicity testing that is carried out to find the lowest level that produces an effect rather than completing a whole battery of tests at higher doses. This is appropriate when looking for a 'safe' dose but may not be appropriate when trying to characterize representative impacts or the DALY burden on a population. More severe or more common outcomes that are not the ones that occur at the lowest dose may also be important. With only critical effects testing it is not possible to obtain information on more severe outcomes that occur at higher doses. It may be very important to include a very common but not very severe outcome or a rare but very severe outcome. Thus, there is a need to develop methods to address these concerns.

c) **Aggregation:** There are aspects of toxic impacts that should be aggregated and other aspects that should be kept disaggregated. There could be elements of severity that fit both. In contrast to policy assessors, modeling/methods experts may have different needs in regard to the issue of aggregation.

If we are going to put a valuation on an endpoint, it is important to be transparent. The experts expressed concerns about DALYs because they represent one judgment about the significance of various health outcomes but these judgments may not be those of the target audience and may not have an established empirical basis. Thus, along with DALYs the analyst should report separately intermediate results such as Years of Life Lost (YOL) or years of life disabled. Additional weighting coefficients should be reported in a transparent way.

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Supporting Information: Dose-Response Workshop, Appendix B. Presentations from Olivier Jolliet and Lorenz Rhomberg. Online only <DOI: http://dx.doi.org/10.1065/lca2006.005.1>

The findings of the Portland Review Workshop 'Dose-Response Modeling for Life Cycle Impact Assessment' (November 2004) have likewise been summarized for Int J LCA. The Workshop Report (Thomas E. McKone, Amy D. Kyle, Olivier Jolliet, Stig Irving Olsen and Michael Hauschild) will be published in Int J LCA No. 4 (July issue). It is available in OnlineFirst and can be accessed at <http://dx.doi.org/10.1065/lca2006.02.005.1>.

Supporting Information: DOI: http://dx.doi.org/10.1065/lca2006.02.005.01

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Dealing with toxic impacts in life cycle assessment

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with contributions from David Pennington, Pierre Crettaz, Geneviève Perrenoud and Simon-Pierre Keller

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Portland dose-response workshop, 14 November 2004

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Emission to damage

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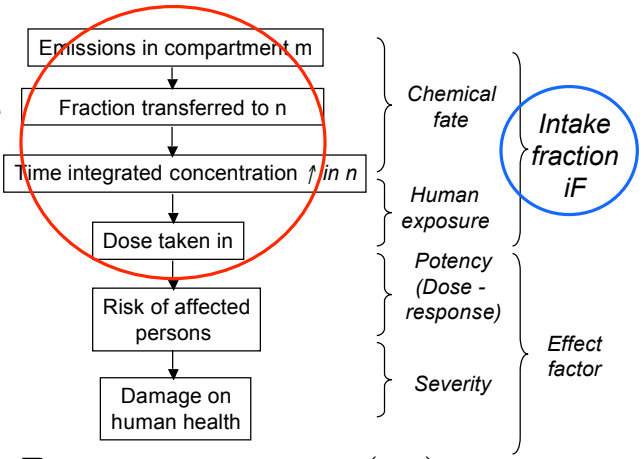
Fate side



$$iF = \frac{\sum_{people,\,time} \text{intake of pollutant by an individual } (mass)}{\text{mass released into the environment } (mass)}$$

(ES&T, 2002)

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Ranges in intake fraction outdoor air emissions

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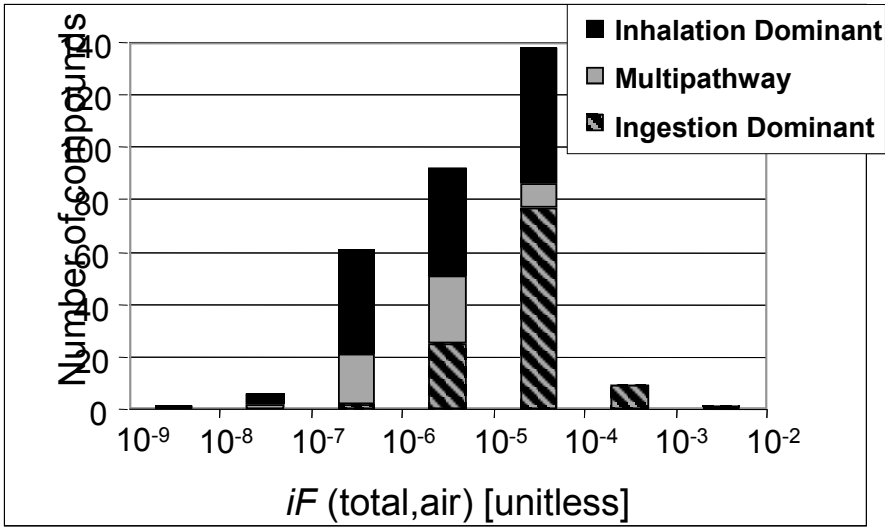

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Human health framework

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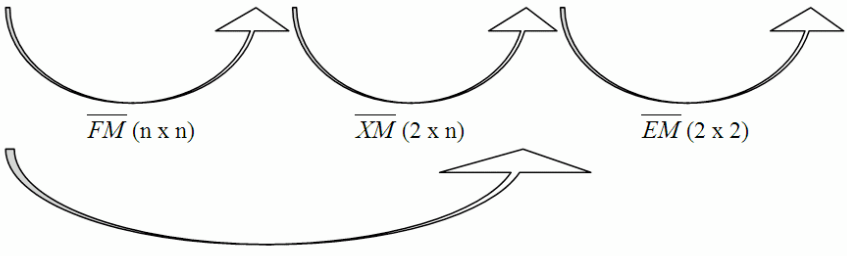
$\vec{S}$ Source (n) [kg/day]	$\vec{M}$ Mass (n) [kg]	$\vec{I}$ Intake flow (2) [kg/day]	$\vec{N}$ Impact flow (2) [No. of cases/day]
$\vec{S}$ Mass emitted [kg]	$\int \vec{M} dt$ Time integr. mass [kg-day]	$\vec{I}$ Mass intake [kg]	$\vec{N}$ Impact [No. of cases]



$\overline{FM}$ (n x n) $\overline{XM}$ (2 x n) $\overline{EM}$ (2 x 2)

$$\overline{iF} = \overline{XM} \cdot \overline{FM} \quad (2 \text{ x } n)$$

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Emission to damage a) Human health

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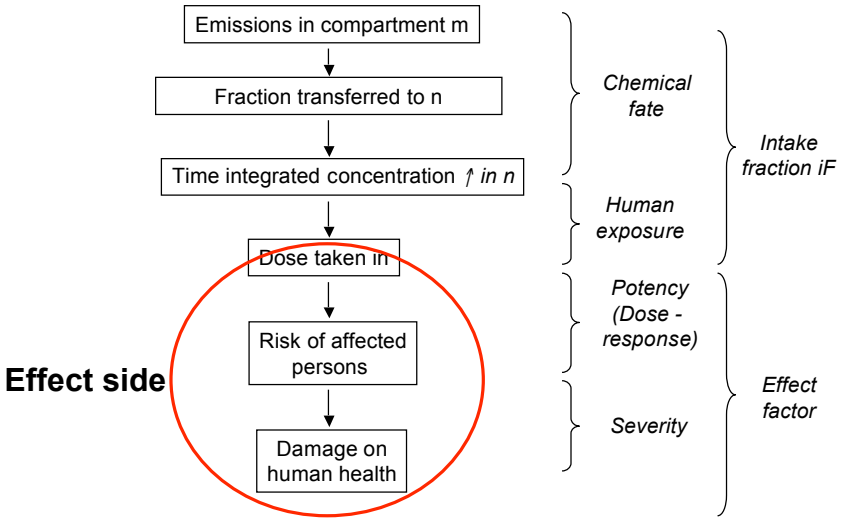

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ILSII panel 95: Limitations of RfD for an application to LCIA

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Burke et al., 1996 (ILSII panel) recommended to use the NOAEL or response doses rather than RfD,

since the comparison of toxic releases based on their RfD can be biased, because:

- **The UFs applied to derive the RfD are conservative.**
- **The response level associated with the No Observable Adverse Effect Level (NOAEL) can change.**
- **The RfD is dependent on the experimental design.**

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ILSI Panel
Severity: Burke et al., 1996

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Subcategory 1 (Irreversible/life-shortening effects)	*Subcategory 2* (Maybe reversible /maybe life-shortening)	*Subcategory 3* (Generally reversible/generally not life-shortening)
Cancer Reproductive effects Teratogenic effects Acute fatal or acute severe and irreversible effects (i.e. fatal poisoning) Mutagenicity	Immunotoxicity Neurotoxicity Kidney damage Liver damage Heart disease Pulmonary (i.e. asthma)	Irritation Sensitization Reversible acute organ effects (i.e. GI inflammation)

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Dose - response / potency
SETAC-EU WGIA2

(working group on impact assessment)

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Type of indicator	Key Advantages	Key Issues	LCIA application
Regulatory potency measures, ADIs, RFDs, RFCs	Widely adopted risk assessment	Inconsistent conservatism, adverse risk rather than low-dose risk	Hertwich Huijbregts Goedkopp and Spriensma, partly Hauschild et al.
Slope factors based on benchmark doses, such as βED10	Introduced to provide a consistent basis for low-dose risk response carcinogens and non-carcinogens	Not widely adopted yet while implicit in most measures for non-carcinogenic effects	(Crettaz et al., 2001a, b) 1000 substances
Acute toxicity data, such as LD_{50}s and LC_{50}s	Widely available data.	Relative acute to chronic importance is unlikely to be consistent across chemical emissions.	Partly used in (Hauschild et al., 1997). Extrapolations acute to chronic data are widely adopted.

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Severity based indicators SETAC-EU WGIA2

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Type of indicators	Key Advantages	Key Issues	LCIA application
Qualitative indicators			
ILSI classification: Health endpoints allocated to 3 categories (Burke et al., 1996)	Somewhat homogeneous group of health effects with different levels of severity.	3 categories allows rough severity ranking only. Weighting requires value judgement.	Demonstrated by Owens (2000) and adapted by Crettaz et al. (2001b)
Quantitative indicators			
Disability Adjusted Life Years (DALY), based on (Murray and Lopez, 1996), supported by WHO, World Bank	Allows aggregation of mortality and morbidity) on a single cardinal scale.	No final consensus on weighting factors for different health effects. DALY not always possible	(Hofstetter), Eco-indicator '99 (Goedkopp and Spriensma (Crettaz et al. 2001a, b) present data for over 1000 chemicals.
Quality Adjusted Life Years (QALY) (e.g. Rosser, 1987)	(similar to DALY)	(similar to DALY)	not currently used in LCIA but in RA
Years Of Life Lost (YOLL)	aggregation of different mortality effects	Giving the same value to any life year:a value choice not cover non-fatal effects.	key indicator in ExternE-type applications (European Commission, 1999)

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Human toxicity recommendations A stepwise procedure (SETAC-EU WGIA2)

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1. Toxicological potency indicators such as ED10 as a minimum default

- While methods in their infancy, it is encouraged to take into account relative severity,

--> 2. YOLL 3. DALY/QALY

Key tasks:

- Lack of toxicity data

- Population density

- Aggregation linked to severity authorised by international body

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Points to be adressed

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- How to derive dose-response information for a large number of chemicals (eventually screening and advanced approaches) ?
- Relevance: How to relate the animal endpoint to human endpoints and eventually YLL, YLD ?
- How to make enpoints comparable, using e.g. DALY's ?

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Points to be raised

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- Extrapolations chemical with acute, QSAR: shows that restricted !!
- Severity: as soon as impact scores are added, a weighting is performes with equal severity. If all endpoints are kept separate → OK
- Interesting to come to DALY because: upper limit, put into perpective to observed damages
- Always come back to initial goal of comparison → kg equ substance to communicate
- The way it can be used in practice: BMW

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Carcinogens (EPFL&Harvard) The ED10 approach

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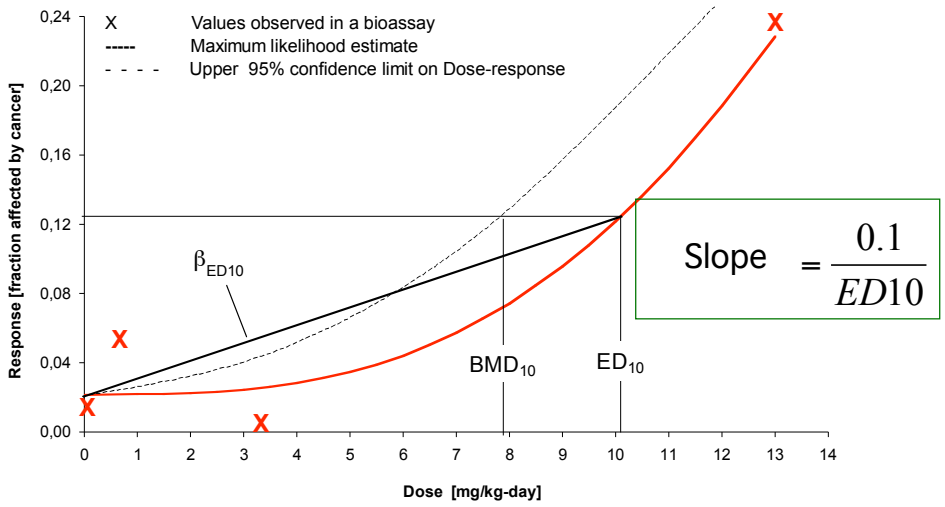
For comparative assessment: *Effect Dose 10% over background*



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Linearity at low doses ?

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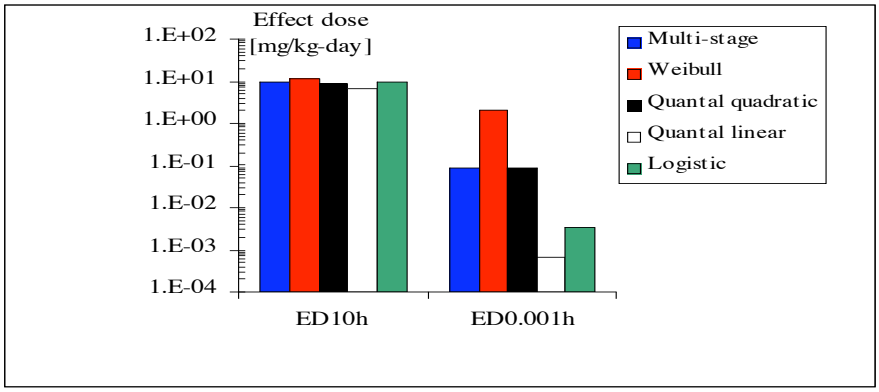

Below 10% effect, the answer depends only on the model retained ! Impossible to predict (non-) linearity on the basis of bioassays !

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EVALUATION from the tumor dose TD_{50a}

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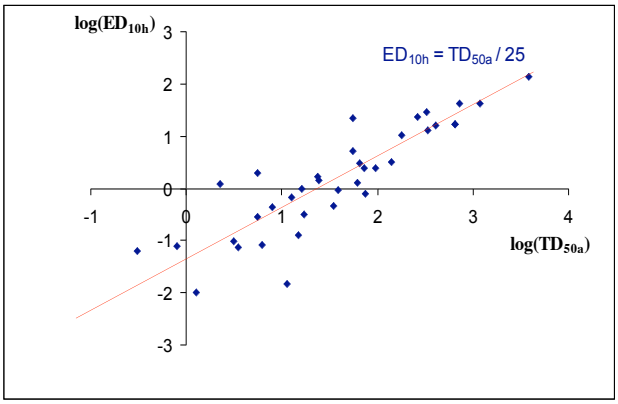
• The TD_{50s} - ED_{10s} correlation is relatively high (n=37; R^2=0.75)

IRIS



GOLD

• Apply to 671 substances with a TD_{50a} in the CPDB [Gold and Zeiger, 1997]
==> Slope factors: 10^{-4} ---> 10^{4} [Risk/ mg/kg-day]: Factor 100 million !

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Correlation ED10 - TD50 data provided for 670 carcinogens

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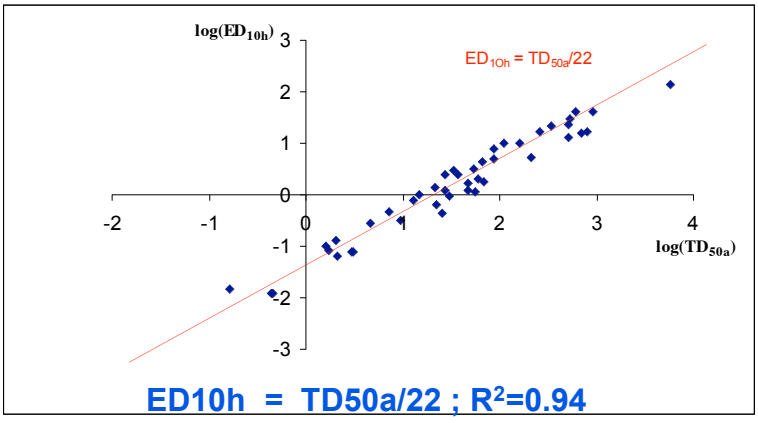
IRIS



IRIS

Dose-response: 80% variation between databases, against 20% between TD50 and ED10. Use the best database for TD50.

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Correlation β(ED10) - q1*

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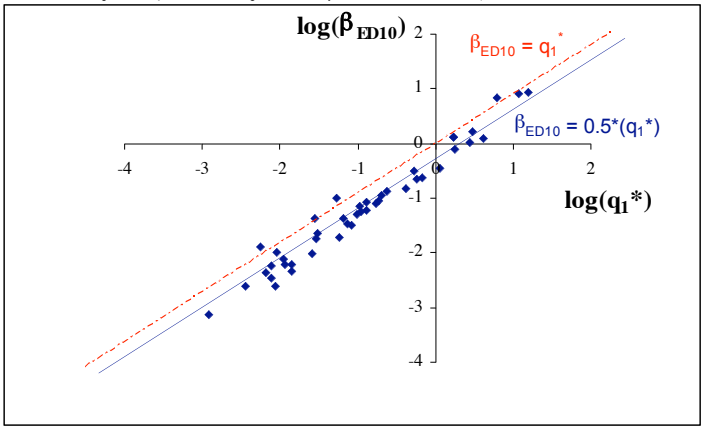
q_1^* and β_{ED10} are strongly correlated (R^2 = 0.94): q1* reflects a linear assumption !!

On average, q_1^* is higher by a factor 2 (no more than a factor 10)



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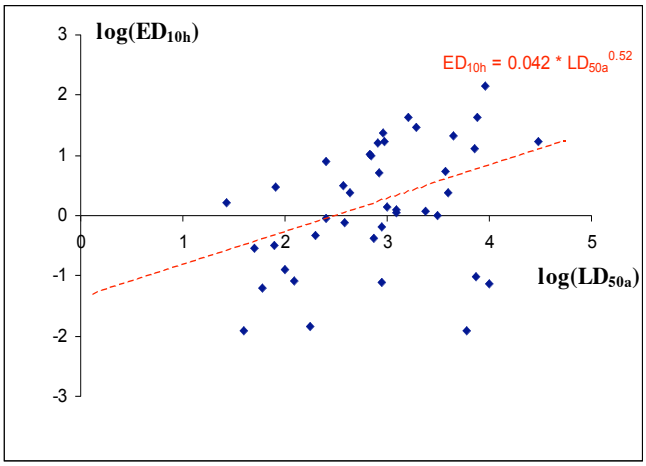
EXTRAPOLATION from the lethal dose LD_{50a} (cancer)

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

The LD50s - ED10s correlation is rejected (n=41; R^2=0.14)
==> No assessment of data-poor substances is provided!



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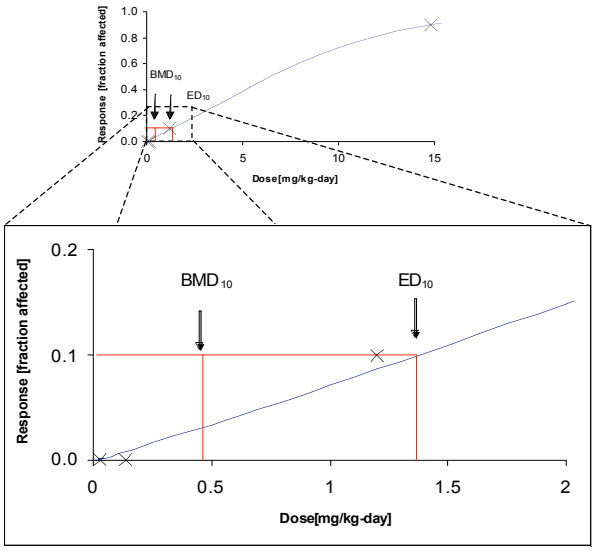
Evaluation of non cancer

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE



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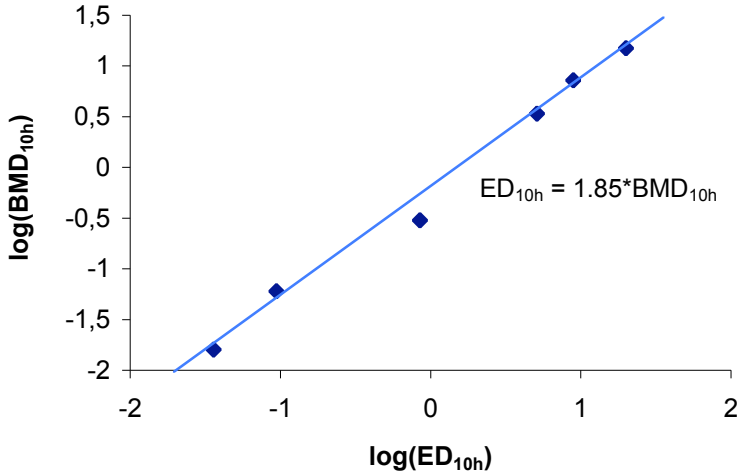
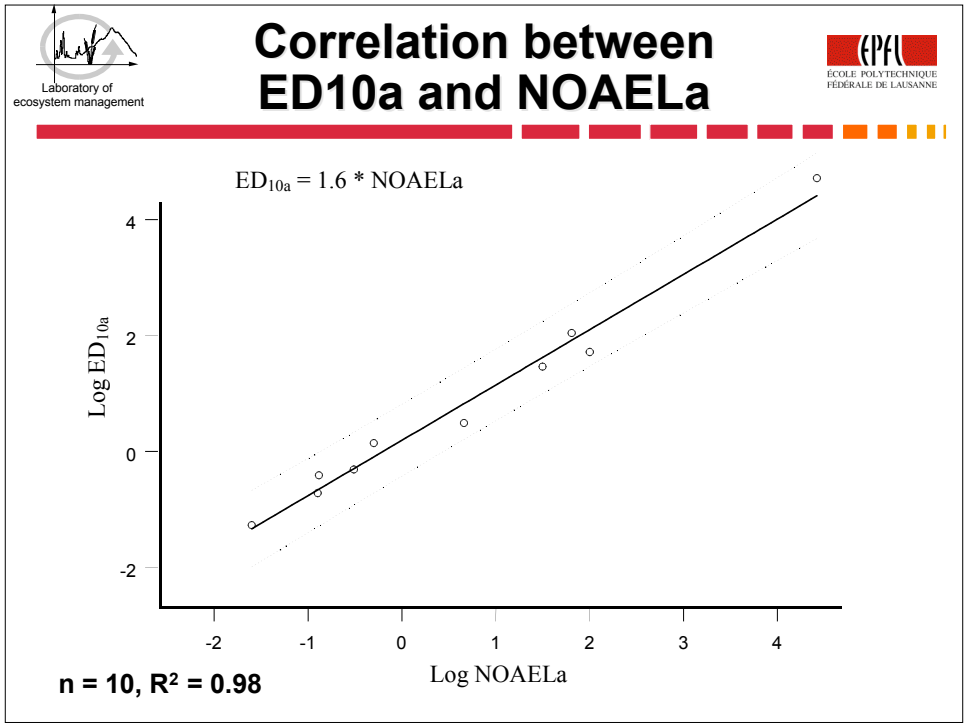
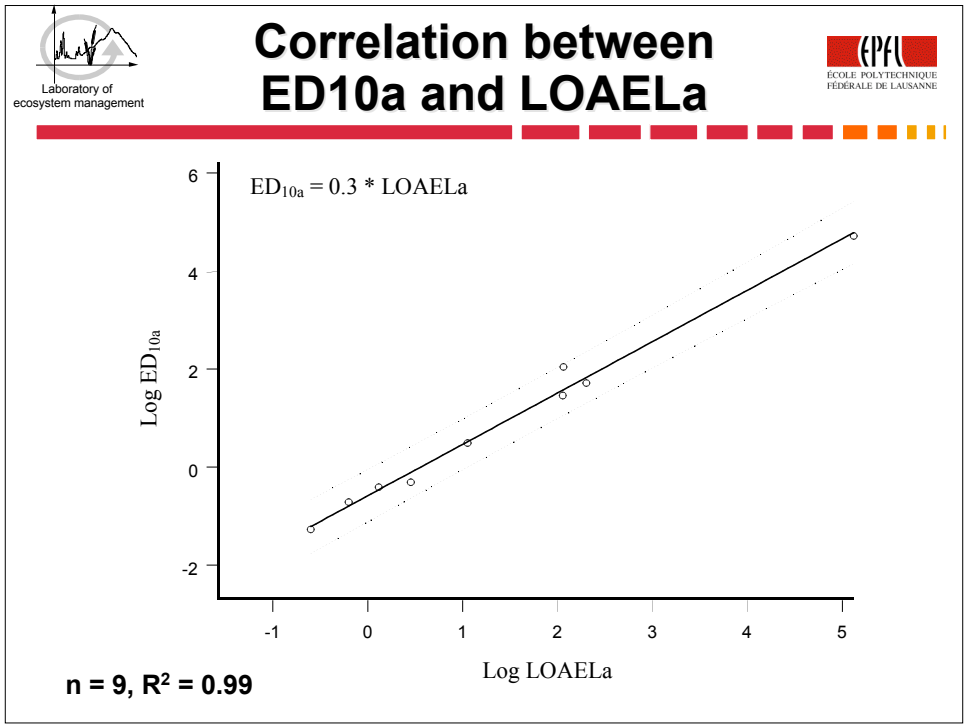
Comparison of ED10h and benchmark dose BMD10h

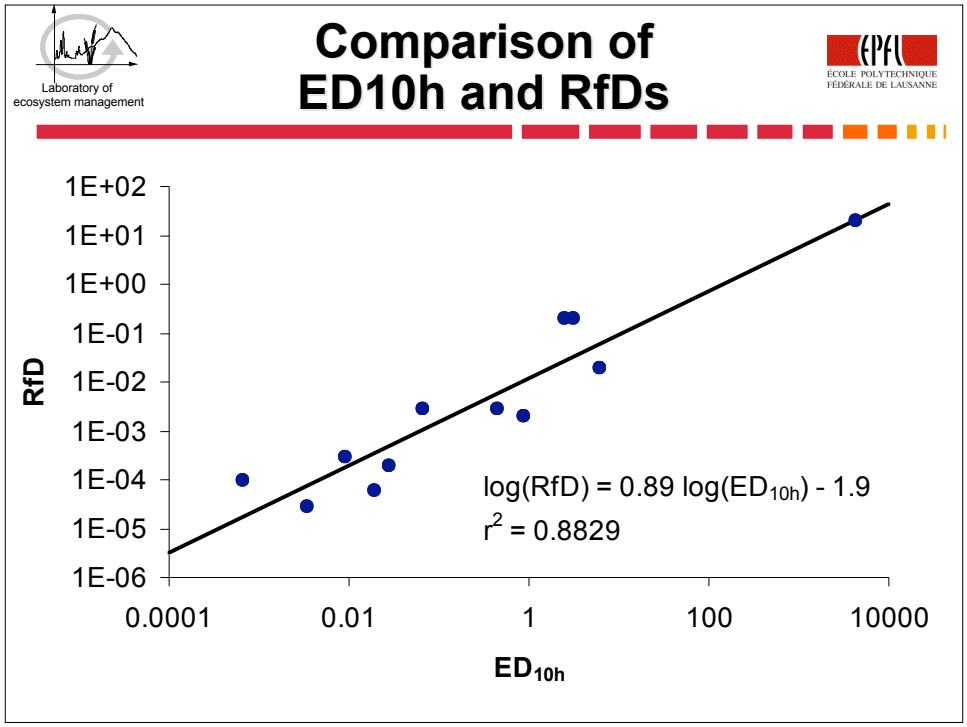
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

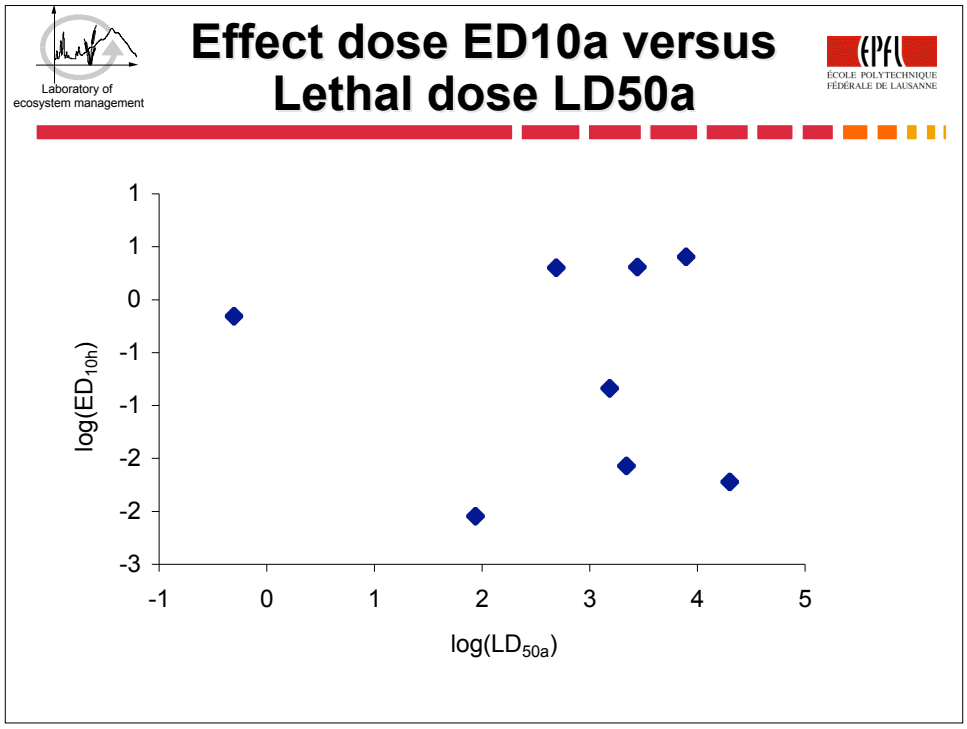


(n = 6; R^2 = 0.98)


Laboratory of ecosystem management
Correlation between ED10a and NOAELa
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
ED10a = 1.6 * NOAELa
Log ED10a
Log NOAELa
4
2
0
-2
-2
-1
0
1
2
3
4
n = 10, R² = 0.98


Laboratory of ecosystem management
Correlation between ED10a and LOAELa
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
ED10a = 0.3 * LOAELa
Log ED10a
Log LOAELa
6
4
2
0
-2
-1
0
1
2
3
4
5
n = 9, R² = 0.99


Laboratory of ecosystem management
Comparison of ED10h and RfDs
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
1E+02
1E+01
1E+00
1E-01
1E-02
1E-03
1E-04
1E-05
1E-06
RfD
0.0001
0.01
1
100
10000
ED10h
log(RfD) = 0.89 log(ED10h) - 1.9
r2 = 0.8829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Effect dose ED10a versus Lethal dose LD50a
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
1
1
0
-1
-1
-2
-2
-3
log(ED10h)
-1
0
1
2
3
4
5
log(LD50a)

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Compatibility between approaches

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Unit risks versus epidemiologic approaches !

Impacts of particles:

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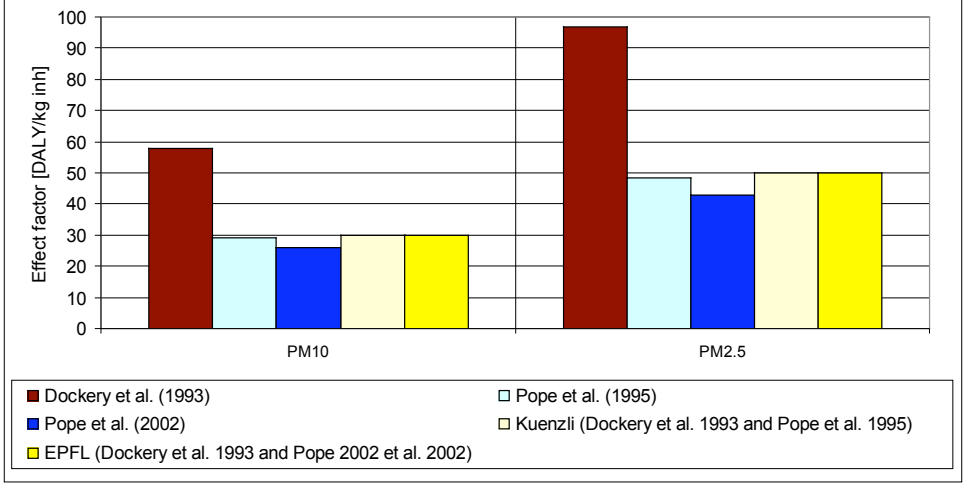
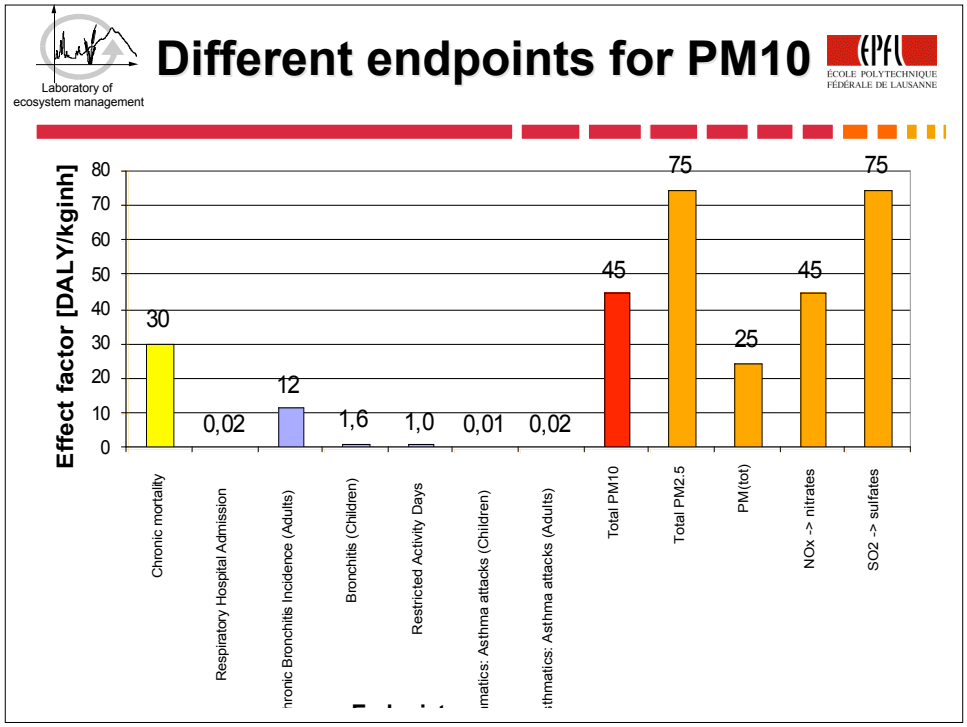
Effect factors: Particles

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

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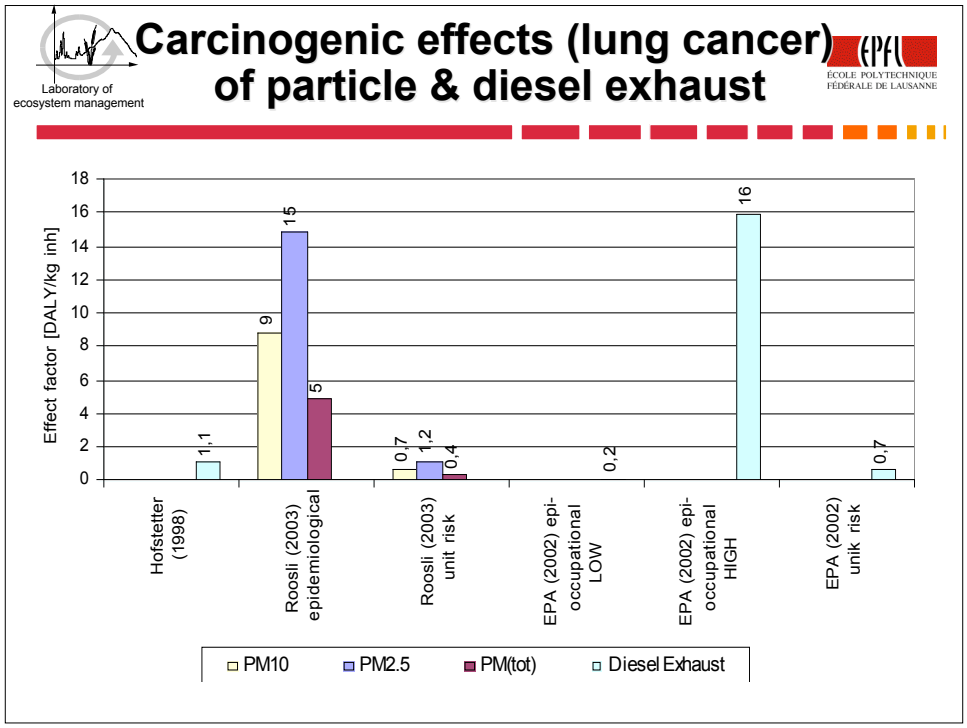
Different endpoints for PM10
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
Effect factor [DALY/kginh]
80
70
60
50
40
30
20
10
0
30
0,02
12
1,6
1,0
0,01
0,02
45
75
25
45
75
Chronic mortality
Respiratory Hospital Admission
Bronchitis (Children)
Restricted Activity Days
Total PM10
Total PM2.5
PM(tot)
NOx -> nitrates
SO2 -> sulfates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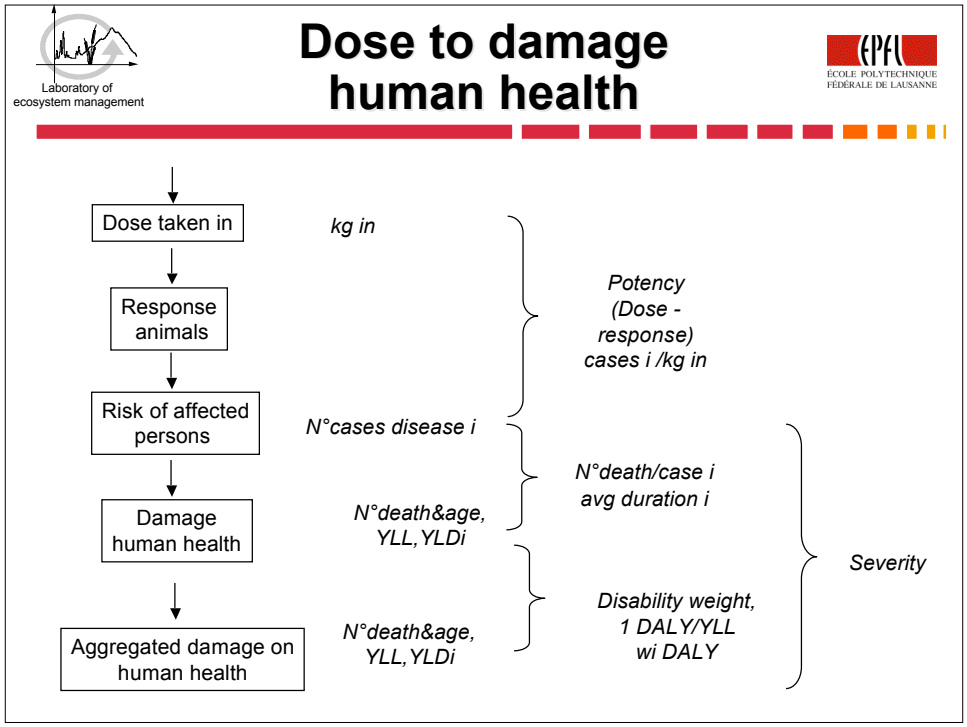
Carcinogenic effects (lung cancer) of particle & diesel exhaust
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
Effect factor [DALY/kg inh]
18
16
14
12
10
8
6
4
2
0
1,1
9
15
5
0,7
1,2
0,4
0,2
16
0,7
Hofstetter (1998)
Roosli (2003) epidemiological
Roosli (2003) unit risk
EPA (2002) epi-occupational LOW
EPA (2002) epi-occupational HIGH
EPA (2002) unik risk
PM10
PM2.5
PM(tot)
Diesel Exhaust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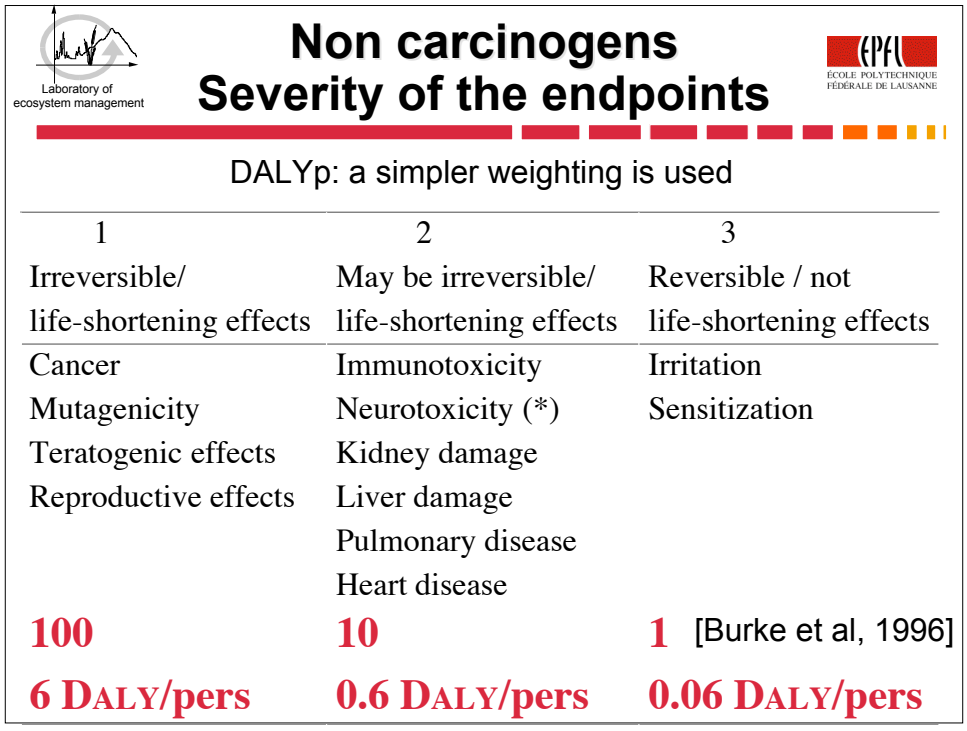
Dose to damage human health
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
Dose taken in
Response animals
Risk of affected persons
Damage human health
Aggregated damage on human health
kg in
N°cases disease i
N°death&age, YLL, YLDi
N°death&age, YLL, YLDi
Potency (Dose - response) cases i /kg in
N°death/case i avg duration i
Disability weight, 1 DALY/YLL wi DALY
Severity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Non carcinogens
Severity of the endpoints
ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE
DALYp: a simpler weighting is used
1
Irreversible/ life-shortening effects
Cancer
Mutagenicity
Teratogenic effects
Reproductive effects
100
6 DALY/pers
2
May be irreversible/ life-shortening effects
Immunotoxicity
Neurotoxicity (*)
Kidney damage
Liver damage
Pulmonary disease
Heart disease
10
0.6 DALY/pers
3
Reversible / not life-shortening effects
Irritation
Sensitization
1 [Burke et al, 1996]
0.06 DALY/pers

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Cancers severity

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Type of Cancer	Disability			Death			Disability + Death
	W [-]	D [yr. lost/inc.]	$YLD_p = W \cdot D$ [yr lost/inc.]	L [yr. lost]	N [inc.]	$YLL_p = L/N$ [yr. lost/inc.]	$DALY_p = YLD_p + YLL_p$ [yr. lost/inc.]
Mouth and oropharynx	0.145	4.3	0.62	3.2E+06	1.1E+06	2.9	3.5
Oesophagus	0.217	1.7	0.37	3.4E+06	3.8E+05	8.9	9.3
Stomach	0.217	2.9	0.63	7.0E+06	1.1E+06	6.5	7.2
Colon and rectum	0.217	3.7	0.80	3.9E+06	9.9E+05	3.9	4.7
Liver	0.239	1.6	0.38	6.3E+06	5.4E+05	11.6	12.0
Pancreas	0.301	1.2	0.37	1.5E+06	1.9E+05	7.9	8.3
Trachea, bronchus, lung	0.146	1.8	0.26	8.3E+06	1.1E+06	7.9	8.2
Melanoma	0.045	4.2	0.19	5.1E+05	1.7E+05	3.1	3.2
Breast	0.069	4.2	0.29	3.8E+06	1.1E+06	3.6	3.9
Cervix uteri	0.066	3.8	0.25	2.7E+06	4.5E+05	6.0	6.2
Corpus uteri	0.066	4.5	0.30	5.8E+05	3.1E+05	1.9	2.2
Ovary	0.081	3.4	0.28	1.3E+06	2.0E+05	6.4	6.7
Prostate	0.113	4.2	0.47	1.1E+06	6.8E+05	1.6	2.1
Bladder	0.085	4.2	0.36	9.8E+05	4.6E+05	2.1	2.5
Lymphomas and myeloma	0.089	3.5	0.31	3.0E+06	4.2E+05	7.2	7.5
Leukemia	0.112	3.1	0.35	4.4E+06	3.1E+05	14.3	14.6
Other cancers*	0.809	n.a.		1.3E+07	1.0E+06	13.0	13.0
Average							6.7

Due to difficulty to determine human endpoint, taken the average for all cancers

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Severity

ÉCOLE POLYTECHNIQUE FÉDÉRALE DE LAUSANNE

Main challenges:

- Dose-response for animal → human endpoints

- No severity = (Implicit) weighting in LCA, when summing up accross substances assume equal severity !! Not ISO compatible

- Report death, N°cases, YLL, YLD separately

- Disability weight optionals, new approaches to establish them

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Relationship animal endpoint - human

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Alternatives

- Stay at separate endpoints for animals (Owens)

- Endpoint animals = endpoint humans ? No !

- Start from human evidences and link it back to or use animal dose-response.

a) If similar endpoints human-animals = lower uncertainty

b) If different endpoints human-animals = high uncertainty in dose-response

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Example carbon tetrachloride

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Strong humans evidences	YLL/incidence years	Duration years	Disability weight	YLD	DALY
Cirrhosis	17	7.8	0.33	2.6	19.6
Hepatitis	2.14	0.17	0.20	0.04	2.18

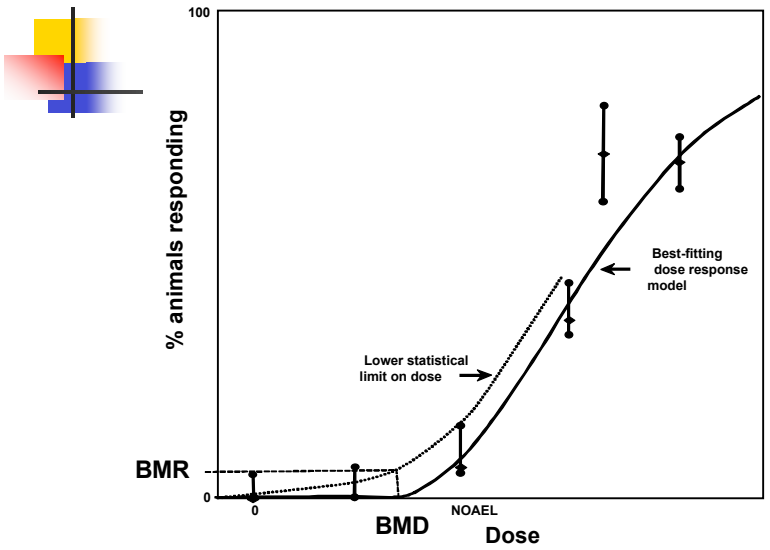
Some Comments on LCIA for Noncancer Effects

Lorenz Rhomberg, Ph.D.
Gradient Corporation
Cambridge, MA
lrhomberg@gradientcorp.com

$$IMPACT = \left[\begin{matrix} Pop'n. \\ Exposed \end{matrix}\right] \times \left[\begin{matrix} Avg. \\ Exposure \end{matrix}\right] \times \left[\begin{matrix} Risk\ per \\ person-unit\ Exposure \end{matrix}\right]$$

$$\frac{IMPACT}{unit\ emission} = \left[\frac{[\text{Pop'n. Exposed}] \times [\text{Avg. Exposure}]}{\text{unit emission}}\right] \times [Risk\ per\ person-unit\ Exposure]$$

Risk must be a linear function of Exposure
(in the range of interest)



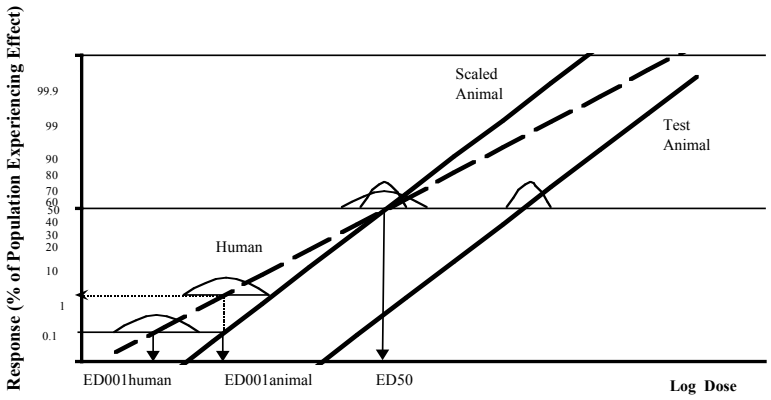
Source: US EPA, 1995. The use of the benchmark dose approach in health risk assessment. Risk Assessment Forum,
Office of Research and Development, Washington, DC. EPA/630/R-94/007.

For Noncancer Effects

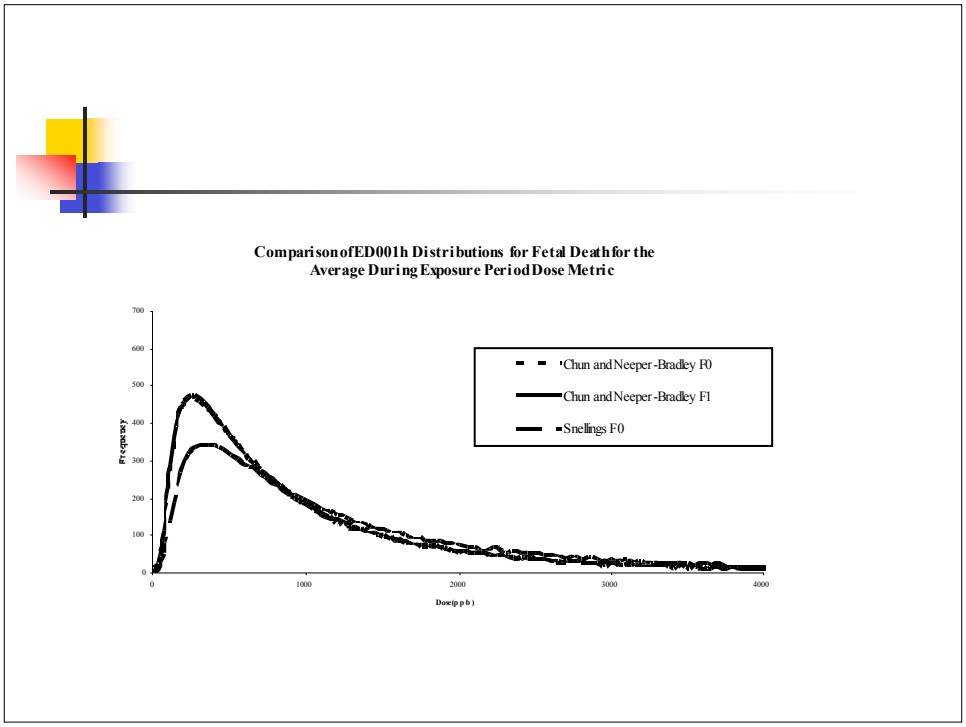
- Threshold effects; nonlinear dose-response
- Traditional approach focuses on identifying a dose-rate likely to be "safe" (and not on dose-response)

LCIA Needs for Assessing Noncancer Effects

1. An approach to nonlinear dose-response in humans
2. Estimates of the numbers of people exposed at different levels

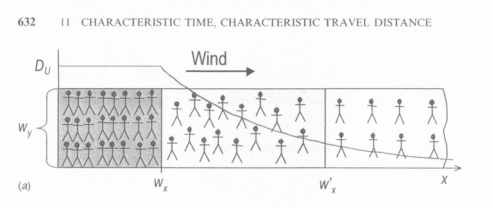


Source: SJS Baird *et al.*, SRA, 2000



The challenge for exposure analysis:
to express the population distribution of exposure
(per unit of emissions, without specific times and places).

Air Emissions



$$\text{Population-based potential dose} = \iint P(x, y) \times \text{ADD}(x, y)\, dx\, dy \qquad (11.8)$$

where P is the population density (persons/m^2) and ADD is the dose per person (mg/kg-d). In this equation, both the dose per person and the population density can vary spatially.

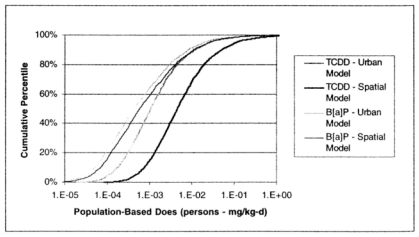
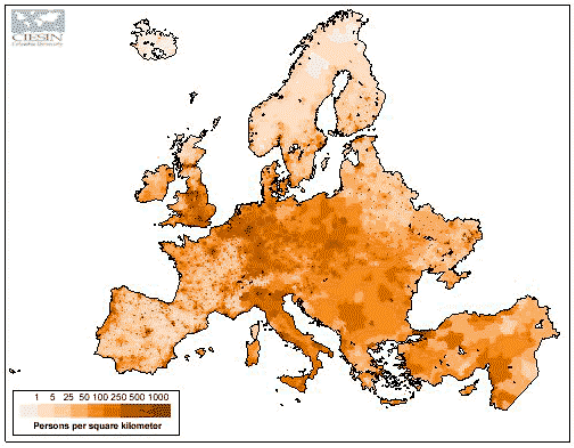


Figure 11.8 Cumulative percentile distribution of population-based potential dose for each calculation method for TCDD (a chemical with a long characteristic travel distance, CTD).

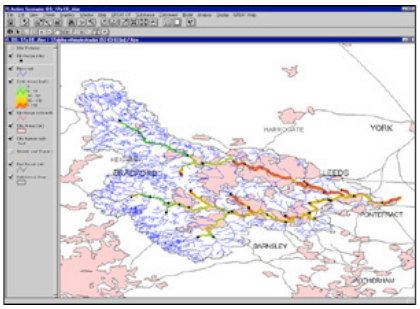
Source: Bennett, DH; McKone, TE; Kastenberg, WE. 2002. Characteristic time, characteristic travel distance, and population-based potential dose in a multimedia environment: A case study. Human and Ecological Risk Assessment: Theory and Practice (Ed.: Paustenbach, DJ). John Wiley & Sons, Inc.

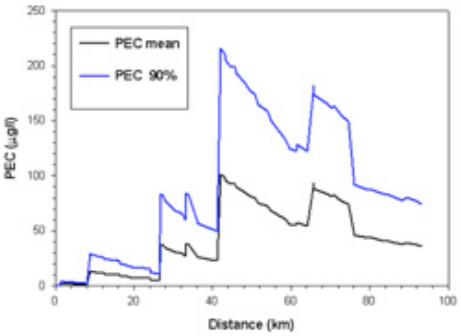
Europe Population Density, 1995



Source: http://sedac.ciesin.columbia.edu/plue/gpw/europe.html

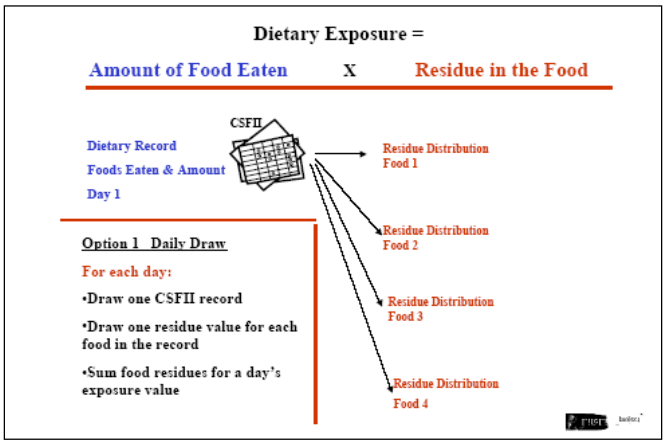
Surface Water Emissions





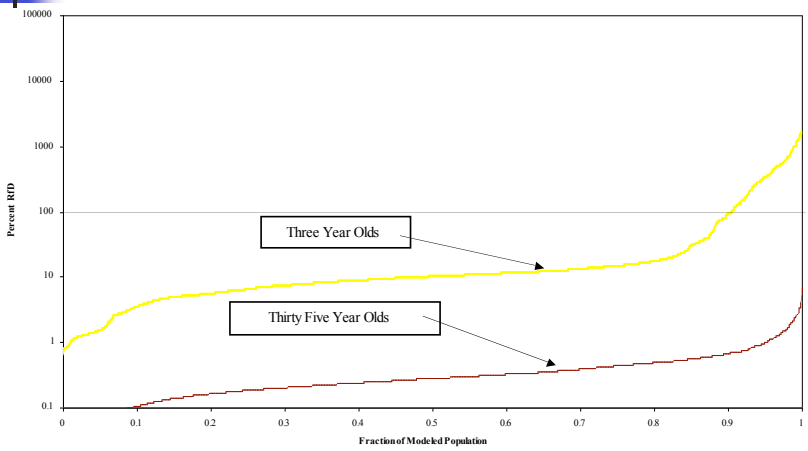
Source: www.great-er.org

Dietary Exposures



Source: The Lifeline Group

Distribution of %RfD Associated with Alpha Exposure at Two Ages



Source: The Lifeline Group

Combining Risk and Exposure Distributions