Workshop: DMEL and risks in occ.exposure to carcinogenic compounds
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Room Document

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"Derived Minimal Effect Levels" (DMEL) in ECHA Guidance Documents

Problems and Steps to be taken

Introduction

The REACH regulation, laying down general provisions for assessing substances and preparing chemical safety reports, in annex I, para 6.5, stipulates that "for those human effects [...] for which it was not possible to determine a DNEL [...], a qualitative assessment of the likelihood that effects are avoided when implementing the exposure scenario shall be carried out."

In order to make this concept more precise ECHA develops the concept of Derived Minimal Effect Levels (DMEL) within the guidance document on IR & CSA Chapter R.8 "Characterisation of dose [concentration]-response for human health". On page 6 of this document DMELs are characterised as "a risk-related reference value that should be used to better target risk management measures" for substances for which no DNEL can be derived, namely for non-threshold mutagens/carcinogens.

In cases where a safe level of exposure cannot be determined, we endorse a risk-based approach for the protection of human health, **provided** that all possible efforts are made to achieve minimisation and substitution. ECHA supports a risk-based approach in Guidance Chapter R.8, but is missing an essential component.

When deriving a risk-related reference value of exposure, two data sets are needed:

(1) an exposure-risk function – essentially a result of scientific evaluation of available data
(2) an acceptable risk level – essentially a political decision

Based on these two data sets, an exposure level can be determined which corresponds to this politically consented risk level.

We conclude that without an acceptable risk level, a DMEL cannot be determined. It is necessary that such a risk level is the result of a political debate.

Nevertheless, it is to be expected that DMEL values will be submitted in applications for authorisation and DMEL values have already been submitted within registration

dossiers. In the near future, the risk assessment committee as well as MS CAs in the course of substance evaluation will be confronted with DMELs. Furthermore, many registrants may believe that they are obliged to communicate a DMEL in the safety data sheet (SDS) and will do so.

(i) No DMEL without acceptable cancer risk

(ii) Political agreement is needed on an EU wide acceptable risk level

Risk-based exposure limits, such as DMEL values, must be based on a specified reference cancer risk (***acceptable cancer risk level***). This decision is a question of societal concern, and a consensus has to be reached on political level [1]. The ECHA Guidance Documents do not state which acceptable cancer risk should be used in DMEL derivation. It is unacceptable that this decision is shifted to single companies.

It has to be avoided that future SDSs will communicate DMELs associated with completely different, arbitrary cancer risks [2] which were not revealed in the SDS.

The acceptable risk level consented in the German traffic light model as of 2018 (4:100,000/life time) provides a good proposal for laying down this EU wide risk level.
This proposal is in sound accordance with the decision-making approach of the Health & Safety Executive (UK): "HSE believes that an individual risk of death of one in a million per annum for both workers and the public corresponds to a very low level of risk and should be used as a guideline for the boundary between the broadly acceptable and tolerable regions" [3].
It is also consistent with the Swiss guideline for cancer risk acceptance (maximum additional risk 1:1.000.000 per year).

The steps forward:

In longer perspective:

- **Initiate a discussion of the Council and the Parliament with the aim to lay down a general EU wide acceptable risk level for additional cancer cases due to anthropogenic causes in the environment, including the working environment.**

[1] The authors of Guidance R.8 obviously share the point of view that determining the acceptable risk level is a political decision when writing "[...] the establishment of a reference risk level for the DMEL clearly is of societal concern and needs policy guidance" (p.6).

[2] This can be demonstrated by some DMEL values from the registration dossiers already submitted to ECHA. The values were extracted from the publicly available ECHA dissemination website. Examples: Ethylenoxide: DMEL "Long term, inhalation" 1,6 mg/m³ on ECHA webpage versus Traffic Light Model derived Exposure Limit (lifetime risk 4:100,000) 0,02 mg/m³. — Trichloroethene: DMEL "Long term, inhalation" 54,7 mg/m³ versus Traffic Light Model derived Exposure Limit (risk 4:100,000) 3,3 mg/m³. — 1,3-Butadiene: DMEL "Long term, inhalation" 2,21 mg/m³ versus Traffic Light Model derived Exposure Limit (risk 4:100,000) 0,05 mg/m³.

[3] Reducing risks – protecting people (HSE's decision-making process); http://www.hse.gov.uk/risk/theory/r2p2.pdf. An annual risk of one in a million corresponds to a lifetime risk of 4:100,000 assuming a working life of 40 years.

Transitional measure [4]***:***

- **For the period until a harmonised acceptable risk level is determined it is proposed to follow a conservative (precautionary) approach by using the ratio of 4:100.000 as a benchmark for the lifetime risk** (e.g. when DMELs have to be evaluated in the course of substance evaluation or the authorisation procedure).

As accompanying measures:

- **Invite ECHA and MS CAs to assess whether the first set of registrations shows a consistent picture of the application of the DMEL concept by registrants. Should this not be the case, invite CARACAL to revise Guidance Chapter R.8 appropriately.**
- **ECHA should request that registrants communicate, in addition to the DMEL value, the risk level on which the DMEL is based.**

Inappropriate Methodology

As shown above, for deriving a risk based exposure limit, two data sets are needed, namely the exposure-risk relationship and the (politically consented) acceptable risk level. In Guidance Chapter R.8, ECHA proposes two different approaches, the "Linearised" approach and the "Large Assessment Factor" approach. In contrast to the "Linearised" approach the "Large Assessment Factor" approach does not take into account an explicit acceptable risk level. Instead, this approach, which was originally developed by EFSA for application within a different context, uses a fixed set of assessment factors [5] which does not necessarily cover the carcinogenic potency of the specific substance.

We are of the opinion that an approach which does not explicitly take into account an acceptable risk level should not be used for the derivation of DMEL values.

Moreover, the "Large Assessment Factor" approach has been developed with a totally different aim in mind. The EFSA Scientific Committee states that their approach "can be applied in cases where carcinogenic substances have been found in food, irrespective of their origin, for giving guidance on risk management measures"; they do not endorse adding such substances to food deliberately. They point out that the

[4] Guidance R.8 states: "**Should such EU legislation for setting the 'tolerable' risk level for carcinogens [in society] be developed in future, then DMELs need to be derived on that basis**" (Footnote 26). This can be understood as a confirmation that there is no duty to derive a DMEL until the mentioned EU legislation will come into force. However, as DMELs are already generated, an acceptable risk level is already needed now.

[5] The German Committee on Hazardous Substances (AGS) comments on the 'Large Assessment Factor' approach: "There are currently no supportive statistical data or regulations for the levels of the safety factors used in the modified EFSA procedure" and concluded: "Society would have to agree on conventions used (1% risk for sensitive persons notified)" (BekGS 910)

assessment factors suggested have to be societally consented prior to using them. The authors describe their approach as a tool for setting priorities for action, and emphasise minimisation as the major task.

The step to be taken

- **The "Large Assessment Factor" approach should be removed from the guidance document.**
- Guidance Chapter R.8 should be adapted in order to include a more specific description on how to apply the "Linearised" approach, providing an unambiguous method for DMEL derivation.[6]

Minimisation Principle is lacking

The minimisation principle is not sufficiently underlined in the guidance documents so far. According to the DMEL concept, there is no need for further action, if the DMEL is met. It does not request to minimise the exposure as far as possible – although there is a cancer risk remaining at DMEL level.

Of course, REACH as well as the guidance documents refer to the Chemical Agents Directive (CAD) and the Chemicals & Mutagens Directive (CMD) and the minimisation principle contained in these directives, but in practice this knowledge is not present in the majority of companies. It is deemed necessary to emphasise these minimisation duties also in the guidance documents to alert the people responsible for the derivation of Exposure Scenarios and SDS.

The steps to be taken:

- **The relevant guidance should be revised to emphasise the minimisation principle.** [7]

  Futhermore, the TOP principle (Technical measures > Organisational measures > Personal measures, eg PPE) should be strengthened in the guidance.

[6] The current version of the guidance R.8 supports the application e.g. of different dose descriptors leading to the possibility that diverging DMEL values could be derived based on the same data for a given substance.

[7] It should be noted that neither REACH nor the guidance documents support the minimisation principle with regard to the general public, although considerable concentrations of carcinogens are allowed to be present (up to 0.1%) in mixtures available to the public.

Severe Ethical Fault

To cite ECHA Guidance: *"cancer risk levels of 10^{-5} and 10^{-6} could be seen as indicative tolerable risks levels when setting DMELs for workers and the general population, respectively"*.

This statement brings out that the Guidance seems to support the objective that a 10-fold higher risk level is imposed on workers compared to the population at large. This would imply, as a rule-making strategy, different levels of acceptable cancer risks for workers on the one hand, and for the general population on the other hand.

Splitting up humans into two groups (i) one with a high level of protection [which has the right of a lower acceptable cancer risk] and (ii) one for which a higher risk is consciously accepted (e.g. a 10-fold higher cancer risk), would contradict the unconditional values of equity and respect for human life and dignity.

This approach would constitute an infringement on inalienable human rights [8]. We assume that this was not the authors' intention. We conclude that the authors confused a different level of susceptibility of the groups with a different risk level or with a risk level associated with empirical exposures. It should be made unequivocally clear that the acceptable risk level is the **same** for each and every human being.

In contrast to acceptable risk levels, differences between acceptable **exposure** levels (e.g. concentration limits) for different groups can result from different exposure times, from different susceptibility, and from other inter-group differences [9]. In any case these factors have to be well established to justify a differentiation of exposure limits.

Steps to be taken:

- **Make clear that a different acceptable risk level for workers and for the population at large is not acceptable on ethical grounds. As a minimum, any reference or suggestion on a divided acceptable cancer risk for different groups of humans must be deleted from the guidance.**

→ **The acceptable risk level must be non-discriminating and impose the same acceptable risk on workers as on the population at large.**

[8] "Everyone is equal before the law" (Article 20 of the Charter of Fundamental Rights of the EU). Discrimination between *a-priori* risk levels for persons who are at work versus the "general population" conflicts also with other provisions of the Charter of Fundamental Rights, and is a violation of human rights. The Charta states: *"Human **dignity** is inviolable. It must be respected and protected."* (Article 1) and *"Every worker has the right to working conditions which respect his or her health, safety and **dignity**"* (Article 31).

[9] Please note: In DNEL derivation, differences between "workers" and "general population", as the case may be, are based exclusively on scientific evidence and are subject to scientific exploration (and *not* to political discussion).

Further reading: http://www.auva.at/mediaDB/703789_DMEL-Position_EN.pdf
http://www.auva.at/mediaDB/703790_DMELs_Problematisches_Konzept.pdf