„Real DMELs“ - What do they look like ?

An analysis of DMELs in some REACH-registration dossiers

Dr. Aart Rouw, May 17th 2011

Contents

- Why /How of analysis
- Results
- What did we learn

17.05.2011

Why this presentation ?

- *Underlying fear/suspicion in discussion*:
  Registrants will use risk levels for DMELs that fit them best (and are much higher than those in German model) – and consider this to be “safe”
- If true, this would put models like the German Traffic model in trouble, as they may be overtaken by generally accepted practice. (esp. if ECHA accepts this)
- ***Questions to answer :***
  - ***How have REACH registrants dealt with DMELs ?***
  - ***How do risk levels compare to traffic light model ?***

17.05.2011

The data

- In our CARACAL presentation we announced our plan to analyze DMELS as used in REACH Registration dossiers.
- *Data source :* REACH Registrations dossiers contain everything you always wanted to know..… (including DMELs)
- One database query and done….
- Registration Dossiers difficult to access (IT Problems, confidentiality) - no query possible (yet)

17.05.2011

Searching DMELs – dead or alive…..

What is a „good“ DMEL ?

- Clear link to tox data
- Formally correct
  (non-threshold carcinogenic effects)
- Transparent calculation
  (or link to a published calculation)
- Indication residual risk level
- Used in ES /RCRs
- Reference to political framework
  (pre-setting risk level)

How to get Data – some creativity required

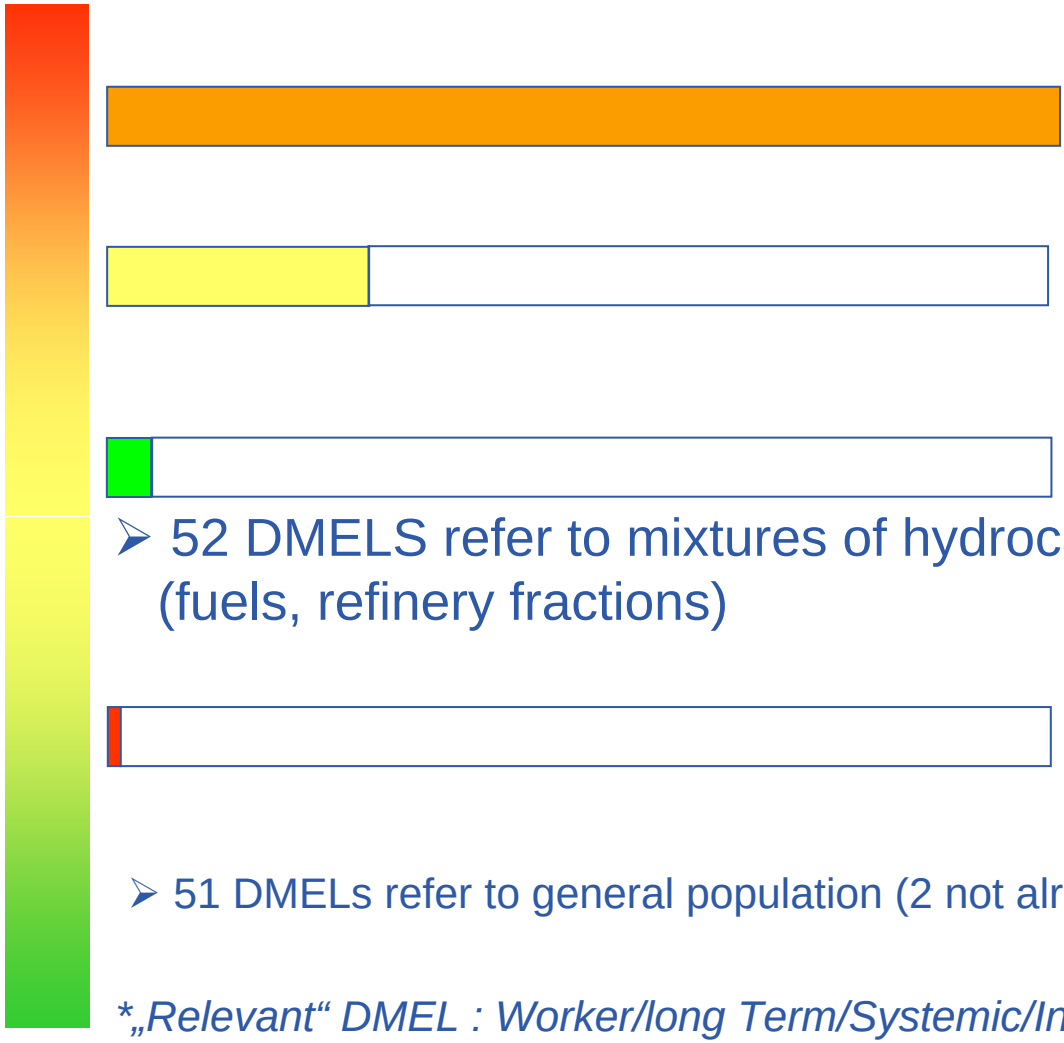
➢Find alternative ways to select :

1. Hand-pick dossiers of substances where Germany has already established an exposition-risk relationship (ERBs)
   → *Requested 12 substances (17 dossiers)*

2. Use of ECHA EXCEL spreadsheet as a „light version“ of listed data – (to fill IT gap for MSCAs.)
   Allows to select all Substances with a DMEL in IUCLID dossier (Section 7)
   → *Requested 15 substances (16 dossiers)*

17.05.2011

Selection process



ECHA : 23122 Registrations

ECHA EXCEL:
4808 Substances (CAS Nr)
(lead Reg. Dossiers)

Relevant* DMEL : 86

- 52 DMELS refer to mixtures of hydrocarbons (fuels, refinery fractions)

DMEL for Mono- or multiconstituent substances: 34

- 51 DMELs refer to general population (2 not already covered) – not analyzed

„Relevant“ DMEL : Worker/long Term/Systemic/Inhalation (carcinogenic endpoint)

17.05.2011

Hidden and disguised DMELs

Selection process – all found ?

- Not all IUCLID files have DMELs entered correctly
  (Some in CSR, not in Section 7; some in Text box in Section 7)
- Only text of Chemical Safety Report (CSR) explains why and how in sufficient detail.
- Some substances have a very high number of registrations. Usually we only looked at the lead registrant (and may miss others if they derived own DMELs – however this seems to be the exception)
- *Probably there are more DMELs, in the system, but we think we have selected a representative sample.*

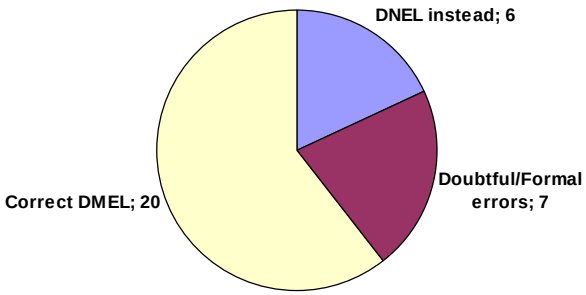
Some caution….

- Because of confidentiality: reference to substances and companies will be only indirect (details upon request)
  (DMEL values in public IUCLID files on ECHA website)

- We will only comment the derivation process of DMELs, *not* the quality of underlying toxicological data.

Results (N_Dossiers=33, 27 substances) :

- Correct reference to tox studies (company or literature) : 100% ☺
- Correct derivation of DMELs : 20/33 = 61% 😐



DNEL instead :
Acc. to German ERB “No threshold”
- but registrants differ in opinion:
In 2 out of 3 cases where a direct comparison is possible the DNELs are in the yellow/red transisition zone of the traffic light model → may need action!

17.05.201

Creative & doubtful interpretations (N= 7)

- Statement :

„No DNEL/DMELs are proposed for chronic exposures to xxxxx, due to its possible carcinogenity” (3)

- DMEL in IUCLID, but DNEL in CSR (Typing error?) (1)
- 2 Dossiers for same substance : 1x DMEL, 1 DNEL using same value & reference
- Derivation of “short term, no cancer DMEL”, but nothing for long term. (2) *– same consultant ?*
- OEL, BOELV, TLV or STEL taken as DMEL. (4)

3 for the same substance

Claimed to be acceptable under ECHA rules (?)

– In Guidance R8 only for DNELs.

17.05.2011

DMEL Transparancy of calculation & Risk

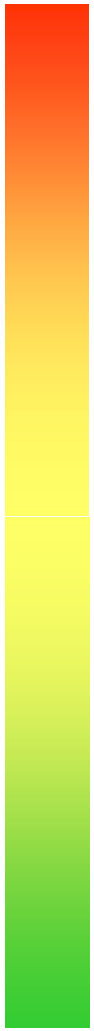
(N_Dossiers=25 with DMEL; = *22 substances*)

- Transparent calculation : 20 (=80%) 😐
- DMEL calculation :
  *Linear extrapolation to low dose (or via Models) : 13 (15)**
  Use of "assessment factors" (AF) : 9 (7) 😐
  OEL taken as DMEL 3
- No indication of residual risk levels : 7
  (4 via AF method, 3OEL cases). ☹
  (Risk may still be estimated if AF data well presented.)
- Most AFs do not correspond to
  those listed in Guidance Doc. R8 ☹ ☹

** : List AF, but in reality a linear extrapolation to 1:1E5 risk for workers*

17.05.2011

Risk levels (N=23 with some kind of risk)



Risk level as range groups

Includes AF cases that mention risk levels

2 OEL cases taken as the same risk as estimated for same substance in other dossier

N.B. All refer to life time risk (cancer cases /40 yrs of working life)

😐	1-5 / 1000	: 7 *(9 with. 2 doubtful AF cases)*
☺	1-5 / 10.000	: 2 *(4 with AF cases)*
☺	1-5 / 100.000	: 9
	1 / 1.000.000	: 1

Targeting German risk levels : 4 (3x Tol, 1x Acc)

17.05.2011

Use in Exposure Scenarios / RCRs

- Exposure scenarios : Model calculations
  (many closed systems etc., where “real exposure” is questionable)

No CSR (while intermediate): 2

☺ Use DMELs in „Risk characterization ratio“ (RCR) : 12

☹ *RCR>1 for one scenario: Risk ad-hoc adjusted :* 1

DMEL not used in RCR : 8

☺ “*Only imported in form of Polymer, No ES necessary* “: 4

Other explanations why not necessary : 4

☹ *„Inherently safe, while in closed system“ :* *1*

„Exposure is prevented“ : *3*

"Exposure is kept to minimum and always below DMEL“

→ But no data/calculation/ rationalization

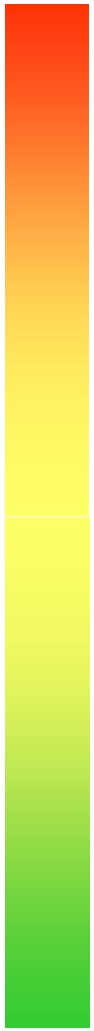
17.05.2011

What does this tell us about DMELs?

- There is ongoing scientific debate (and confusion) on threshold / non-threshold carcinogenic effects and where D**M**ELs or D**N**ELs should be derived
- The basic idea of the DMEL concept as a tool to evaluate residual risks for non-threshold carcinogens is not understood equally well by everyone
- The methods to derive DMELs are sometimes questionable (esp. in AF calc, use of OEL)
  Useful enough for rational decisions on risks ?

- *There seems to exist a fruitful working field for dossier and substance evaluations !*

What does this tell us about risks ?



- Most registrants have derived (some kind of) risk level.
- Most risk levels have been calculated in a transparent way.
- A majority of the registrants uses a (kind of) “linear extrapolation” method (clear risk level)
- Despite the variation in calculations, a considerable part of the risk levels fits the “acceptability” limit as used in DE/NL (even if not explicitly mentioned)
- Consequent use of DMELs in Exposure Scenarios is open for improvement (when to have ES, how to describe risks in RCR)

17.05.2011

Thank you for your attention !

Dr. Aart Rouw

Federal Institute for Occupational Safety and Health, Germany (BAUA)

Division 4 - Hazardous substances and biological agents
REACH – Assessment unit safety and health protection of employees

Friedrich - Henkel-Weg 1-25
44149 Dortmund; Germany

Tel. 0231/9071-2511
Fax 0231/9071-2611
rouw.aart@baua.bund.de

www.baua.de

17.05.2011