

DNELs and IH

Jimmy Perkins, PhD, CIH
University of Texas School of
Public Health
San Antonio Regional Campuses



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Need for OELs – Number of Hazardous Substances

- USA –TSCA reporting
 - ~80,000 chemicals in commerce
 - ~2,800 are High Production Volume (HPV) Chemicals
 - (>1 million pounds/year) - excluding polymers
- Organisation for Economic Co-operation and Development (OECD)
 - 4638 HPV chemicals compiled in 2007
 - Annual production volume >1,000 metric tons in more than one economically developed country



U.S. Based OEL Standards/Guidelines

- Standards
 - OSHA PELs – 447, all but 28 from late 60s
 - State specific PELs
 - California - 747
 - Minnesota
 - Michigan
 - Washington
 - Other?
 - Foreign standards (EU about 700)
- Guidelines
 - 2008 TLVs® /BEIs® ~700
 - 2008 WEELs – 113
 - Company guidelines
 - NIOSH RELs



OELs...Current developments

- Globally Harmonized System (GHS) for classification and labeling of chemicals
- Control Banding – focus on exposure controls rather than quantitative risk assessment via OEL
- REACh (Registration Evaluation and Control of Chemicals) – producer/manufacturer required to demonstrate absence or acceptability of risks associated for every aspect of chemical use before marketing



REACH Schedule

- Registration phase-in depending on tonnages
- Pre-registration for all substances manufactured/ imported quantities >1 ton/year
 - Pre-registration ended November 2008
 - >130,000 substances pre-registered by >300,000 entities
- Full registration by December 12, 2010
 - Chemical Safety Report (CSR)
 - Chemical Safety Assessment (CSA)
 - >1000 tons per year
 - >1 ton if carcinogenic, mutagenic, reproductive effects



REACH DNELs and DMELs

- DNEL
 - Level of exposure above which humans should not be exposed.
- DMEL
 - Derived Minimum Effect Level (DMEL), based on some concept of acceptable or negligible risk
 - Continued question: “Should such materials automatically be banned because they cannot be adequately controlled?”



REACH –DNEELS

- Derived No-Effect Levels (DNEELS)
- if chemical used >10 t/yr, manufacturers /importers must include DNEELS in
 - CSA
 - CSR to the EU
 - Haz Comm
 - SDS (Safety Data Sheet)
- DNEEL used in risk characterization of CSA



DNEL-based risk characterisation

Exposure
by Inhalation

Dermal
Exposure

+

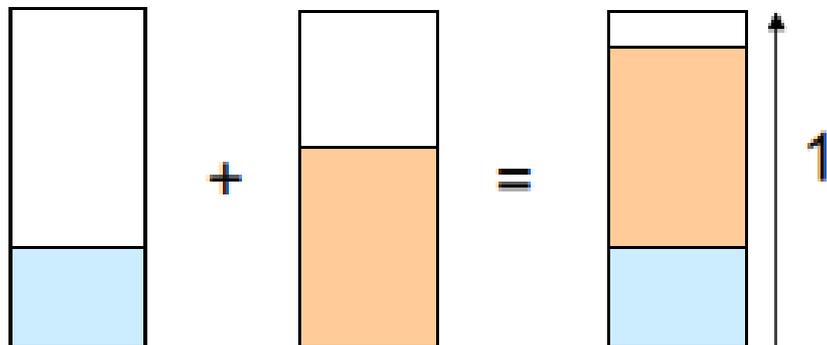
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RCR

DNEL
(inhalation)

DNEL
(dermal)

(combined
exposure)



Risk is
adequately controlled
if
RCR is less than "1"



REACH DNEL Derivation

- Gather all available (DD) dose descriptors...NOAEL, LOAEL, BMDL₁₀
- Decide on the mode of action (threshold or non-threshold)
- Select DD(s) for “critical” health endpoint; modify as necessary (route-to-route extrapolation, exposure time differences, etc.)
- Apply relevant Assessment Factors (AF)

$$DNEL = \frac{\text{modified Dose Descriptor}}{AF_1 \times AF_2 \times AF_3 \times AF_4}$$

$$\text{Risk Characterization Ratio (RCR)} = \frac{\text{known or modeled Exposure}}{DNEL}$$

- If Exposure < DNEL, risk is adequately controlled (RCR <1)
- If Exposure > DNEL, risk is not adequately controlled (RCR > 1)



Allometric scaling

Assessment (fudge) factors

Assessment factor – accounting for differences in:		Default value systemic effects	Default value local effects
Interspecies	- correction for differences in metabolic rate per body weight	AS ^{a, b}	–
	- remaining differences	2.5	1 ^f 2.5 ^g
Intraspecies	- worker	5	5
	- general population	10 ^c	10 ^c
Exposure duration	- subacute to sub-chronic	3	3 ^h
	- sub-chronic to chronic	2	2 ^h
	- subacute to chronic	6	6 ^h
Dose-response	- issues related to reliability of the dose-response, incl. LOAEL/NAEL extrapolation and severity of effect	1 ^d	1 ^d
Quality of whole database	- issues related to completeness and consistency of the available data	1 ^d 1 ^e	1 ^d 1 ^e
	- issues related to reliability of the alternative data		

Where do the data come from?

Lead example

- Consortium members are
 - EU lead substance producers
 - Importers of lead substances to the EU
 - EU-based traders
 - Users of lead (companies or associations)
- Currently 90 companies (legal entities)



EU OEL use in setting DNELs

- Indicative Occupational Exposure Limits
IOEL- health-based, non-binding values, with measurement techniques.
 - May use an IOEL for a DNEL, if documented in CSR
- Binding Occupational Exposure Limit (BOEL)
reflect socio-economic, technical feasibility
...4 substances
 - registrant cannot use as DNEL without eliminating technical and socio-economic feasibility.
- Member States may set national OELs
 - These may be used as above



Use of other OELs

- Currently, companies are prohibited from using
 - Company internal OELs
 - OELs from non EU organizations (e.g. TLV, MAK, DECOS, etc.)
 - new created OELs (e.g. by consultative group)
- Above OELs can not be used
 - even when using the same methodologies as IOELs,
 - even when the toxicological bases are current



Example DNEL for Worker- Inhalation-Long-term-Systemic

- Step 1: NOAEL Dose Descriptor
 - Rat 90-d inh. NOAEL=350 mg/m³ @ 6 hr/d; liver tox
- Step 2: Non-carcinogenic Mode of Action
- Step 3&4: DD Modification and Apply AFs
 - 2.5 (interspecies)

$$350 \frac{\text{mg}}{\text{m}^3} \times \frac{6 \text{ hr}}{8 \text{ hr}} \times \frac{6.7 \text{ m}^3}{10 \text{ m}^3} \begin{matrix} -5 \text{ (worker; intraspecies)} \\ -2 \text{ (subchronic to chronic)} \end{matrix}$$

$$\times 2.5 \times 5 \times 2 = 7 \frac{\text{mg}}{\text{m}^3}$$



Examples of OELs and DNEL estimates (ppm, unless noted)

Chemical	Health-Based OEL	EU IOEL	National OEL	DNEL ~
Chemical S	1	---	5	0.1
A Glycol Ether	5	---	2	1.6
Chemical MA	200	---	200	10
Chemical PP	50	---	20-25	5
Chemical M	200	200	200	55
A Ketone mg/m3	---	---	---	20
A Glycol	---	20	10 and 20	30
An Acetate	10	---	5	4
A Glycol Ether	---	---	10	0.5
Chemical A	25	20	10 and 20	2
An Acrylate mg/m3	37.5	---	---	8

Robert Roy, Update for Hazard Communicators: Coexistence REACH DNELs and Health-Based OELs for Occupational Exposures, 3M Medical Department, Presented at: SCHC Spring 2009 Meeting, April 7, 2009



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Comparison of OELs to DNEELs for Two Chemical Examples (mg/m³)

Chemical	OSHA	ACGIH	AIHA	IOEL	DNEL
Cyclohexane 110-82-7	1050	350		700	15
Isooctyl Acrylate 29590-42-9			37.5		8
Nickel (NIOSH15x10 ⁻³)	1	0.2-1.5			8x10 ⁻⁶

Roy et al, "The Use of Health-Based Occupational Exposure Limits As REACH Derived No Effect Levels." Poster presented at SOT Meeting, Seattle Wa 2008



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OEL/DNEL Differences

- Safety factors
 - OEL (TLV) safety factors based on expert judgment
 - DNELs have default value safety factors
- Toxicological Criteria
 - differ especially for local effects, skin, and the respiratory system, which cause some of the major occupational health problems
- Epidemiological data & biological monitoring used in OELs
- DNELs likely to use QSARs...reduce animal testing; used for OELs as last resort
- OELs are set for priority substances (# workers exposed and levels, effects, etc.) For DNELs -the amount of the substance produced/marketed/imported.
- DNELs for all exposure routes, OELs mainly for inhalation exposure, notifications for sensitization and skin permeability.



Perspective on REACH – 3M

- The use of defensible, health-based OEL as DNEL would decrease time and effort in complying with REACH
- DNELs could replace OELs (considered appealing to some, as they will be more stringent)
- OELs generally involve peer review and consensus
- Having both a DNEL and a health-based OEL may cause confusion

Roy et al, “The Use of Health-Based Occupational Exposure Limits As REACH Derived No Effect Levels.”
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Other DNEL Concerns

- May impact substance/product distribution/use
 - EU
 - non-EU countries and states
- Users still required to comply with legal OELs
- His may be faced with contradictory OEVs
- There is a potential in the future for DNELs to supplant OELs, either in practice or force



The future

- Some stress differences in OELs and DNEs arguing that both types of values have their own role and should be used in parallel.
- For others it seems confusing to be faced with these two values, e.g., in the safety data sheet, without a clear understanding of the difference.

