

REACH.

differences.

DNELs/DMELs

carcinogens)

• Durations of exposure include "acute" and long-term

Set for protection of worker health and safety

DNELs/DMELs and Their Relationship to Health-Based OELs Adam Bettmann, Ann Johnson, Robert Roy, Christian Thorvaldson and Josie Walton Medical Department, 3M Company, St. Paul, Minnesota, USA



DNEL/DMEL Derivation Process Health-Based OEL Derivation Process Introduction The safety factor approach is most common in establishing OELs **Derived No Effect Levels (DNELs) and Derived Minimal Effect** Levels (DMELs) are defined as "...the level of exposure above which humans should not be exposed." DNELs and DMELs are required to NOAEL, LOAEL, BMDL, T25 from all available studies NOAEL, LOAEL, BMDL, T25 from all available studies Sources may include human data, animal data, in vitro studies, and/or modeling be prepared and be present on the REACH-compliant SDS (section 8.1) Sources may include human data, animal data, in vitro studies, and/or modeling Gather results Gather results for any hazardous substance manufactured in, or imported into, the Relevant Data Relevant Data European Union at a volume of greater than or equal to 10 tons per year. They are typically derived from a No Observed Adverse Effect Level (NOAEL), Lowest Observed Adverse Effect Level (LOAEL), or Generally, there will be more then one "adverse effect" to select from the data Bench Mark Dose (BMD) from experimental animal studies. The Based on the data above, determine the chemical's mode of action (MoA) process to derive DNELs and DMELs has been outlined in guidance • ECHA provides guidance for making this determination (Chapter R.8) Need toxicological expertise and professional judgement to select the appropriate provided by the European Chemicals Agency (ECHA). They are • Threshold \rightarrow DNEL Derived Determine Establish and sensitive endpoint that will provide the basis for the health-based OEL ultimately used in the risk characterization process of the Chemical Non-threshold → DMEL Derived calculation Mode of Actio Critical Effect Safety Report (CSR) when registering a hazardous substance for Safety factors (SFs) should be applied to account for uncertainties in the data set This poster is designed to provide a brief overview of how It may be necessary to modify the relevant dose descriptors for each endpoint and the extrapolation procedures (oral \rightarrow dermal, animals \rightarrow humans, etc.) DNELs/DMELs that are set for inhalation in the occupational setting Generally, 5 areas of uncertainty, each ranging from 1-10 each Assessment Factors (AFs) are applied to account for uncertainties in the data set compare to the chemical's health-based Occupational Exposure and the extrapolation procedures • There are: reference level, animal to human, human to human, duration of Modify Data Limit(s) (OELs), and emphasize that although the processes of Apply SFs exposure, severety of response • ECHA provides guidance on these processes (Chapter R.8) and Apply AFs derivation are in some ways similar, there exist key significant $DNEL = \frac{(modified)Dose Descriptor}{Total AF}$ Inhalation Exposure Study $OEL = \frac{NOAEL \text{ or } LOAEL}{Total SF}$ **Example DNEL Derivation** Worker-Inhalation-Long-Term-Systemic Used in REACH risk characterization Data: Example Health-Based OEL Derivation •Established for workers, consumers, and the general public Rat 90-day inhalation NOAEL = 350 mg/m³ @ 6 hrs/day Data: Rat 90-day inhalation NOAEL = 350 mg/m³ @ 6 hrs/day • Routes of exposure include inhalation, dermal, and ingestion Mode of action: Increase in cell size, not numbers for 1/10 0 • Durations of exposure include acute and long-term Non-carcinogenic mode of action • No weight or histopathology changes in examining organs 0 Health effects include systemic and local effects No centrilobular hepatic necrosis (based on histopathology) 0 Modify data per ECHA guidance: •DNELs are "threshold" chemicals (corrected)Inhalation NOAEL = $350mg/m^3 \times \frac{6hrs}{day} \times \frac{6.7 m^3}{10 m^3} = 175 mg/m^3$ Modify data for 8 hr work shift: •DMELs are for "non-threshold" chemicals (mutagens or (corrected)Inhalation NOAEL = $350mg/m^3 \times \frac{6hrs/day}{8hrs/day} = 263 mg/m^3$ Need 8 hr/day for human-worker Drive the selection of appropriate Risk Management Measures Need 8 hr/day for human-worker 6.7 m^3 = worker respiration rate at rest • (RMMs) and Operation Conditions of Use (OCs) Apply safety factors (these are considered "typical" default SFs): 10 m^3 = worker respiration rate during light activity NOAEL used = 1 Animal \rightarrow Human = 1 Apply Assessment Factors per ECHA guidance: Human \rightarrow Human = 3 (default for workers) Health-Based OELs Interspecies = 2.5Duration of exposure = 2 (subchronic study) Worker Interspecies = 5Severity of Response = 3 (adaptive change – default) •Used in hazard determination, hazard communication, exposure Sub-chronic to Chronic = 2Total $SF = 1 \times 1 \times 3 \times 2 \times 3 = 18$ Total AF = 2.5 x 5 x 2 = 25 reduction, regulatory compliance, and risk assessment. $OEL = 263 mg/m^3 \div 18 = 14.6 mg/m^3$ Established for workers only $DNEL = 175 mg/m^3 \div 25 = 7.0 mg/m^3$ Route of exposure is inhalation only

Even though the same NOAEL was used to derive both the DNEL and health-based OEL, the processes of deriving each are much different. Due to the fact that both of these values may be present in section 8 of the REACH-compliant SDS, it is imperative that the hazard communication professional know what each are used for and why the values are not the same.