Binning as a Screening Process for the Universe to the PCCL

Report for the NDWAC CCL Work Group

Plenary Meeting

September 17-18, 2003

Overview

- **Where we were in screening – In July**
  - ❑ Qualitative – Open Gate Approach
  - ❑ Quantitative – Risk Calculation Approach
- **WHY Binning approach may be useful:**
  - ❑ Consistent with with NRC approach-Its Simple
  - ❑ Can be used as a coarse screen to PCCL
  - ❑ Consistent with adverse health effect and occurrence attribute and developing the CCL
- **The Workgroup asked:**
  - ❑ Can we test the Risk Approximation Approach (Binning)
  - ❑ Can we use a 2x3 matrix of high, medium, and low for toxicity and occurrence to screen contaminants for the PCCL?
  - ❑ Does the binning matrix need to have more separation among contaminants?

Overview

- Objective: evaluate potential of binning (semi-quantitative/Risk Approximation approach) to screen chemicals from the Universe to the PCCL
  - "Binned" QSAR data and empirical (measured) data
    - High, medium, low (3 bins)
  - Parameters Evaluated:
    - Lowest Observable Adverse Effect Level (LOAEL)
    - Water solubility
    - Biodegradation (little empirical data located)
  - After creating bins, compared binning results for health effects and occurrence measures
  - Compared binning of measured data to binned QSAR data

Screening Data and Sources

- ## LOAELs
  - Measured: Registry of Toxic Effects of Chemical Substances (RTECS) (cumulative dose/duration)
  - Modeled: TOPKAT QSAR model

- ## Solubility
  - Measured: SRC CHEMFATE database; HSDB; NTP; MacKay et al., (1999); IPCS
 - Modeled: WSKOWWIN QSAR model from EPI Suite

- ## Half-Life
 - Modeled: BIOWIN QSAR model from EPI Suite

Bin Analysis

- Chemicals in each of the bins were compared across data types (e.g., LOAEL to Water Solubility) to identify PCCL candidates
  - Measured LOAELs (RTECS) were compared to measured solubility
  - Modeled LOAELs (TOPKAT) were compared to Model estimated solubility (EPIWIN)

- Compared results from binning by percentages to results binned by value (e.g. Top 33% of LOAELs versus LOAELs 0.1 - 9.9)

Distribution of Measured and Modeled LOAEL Values
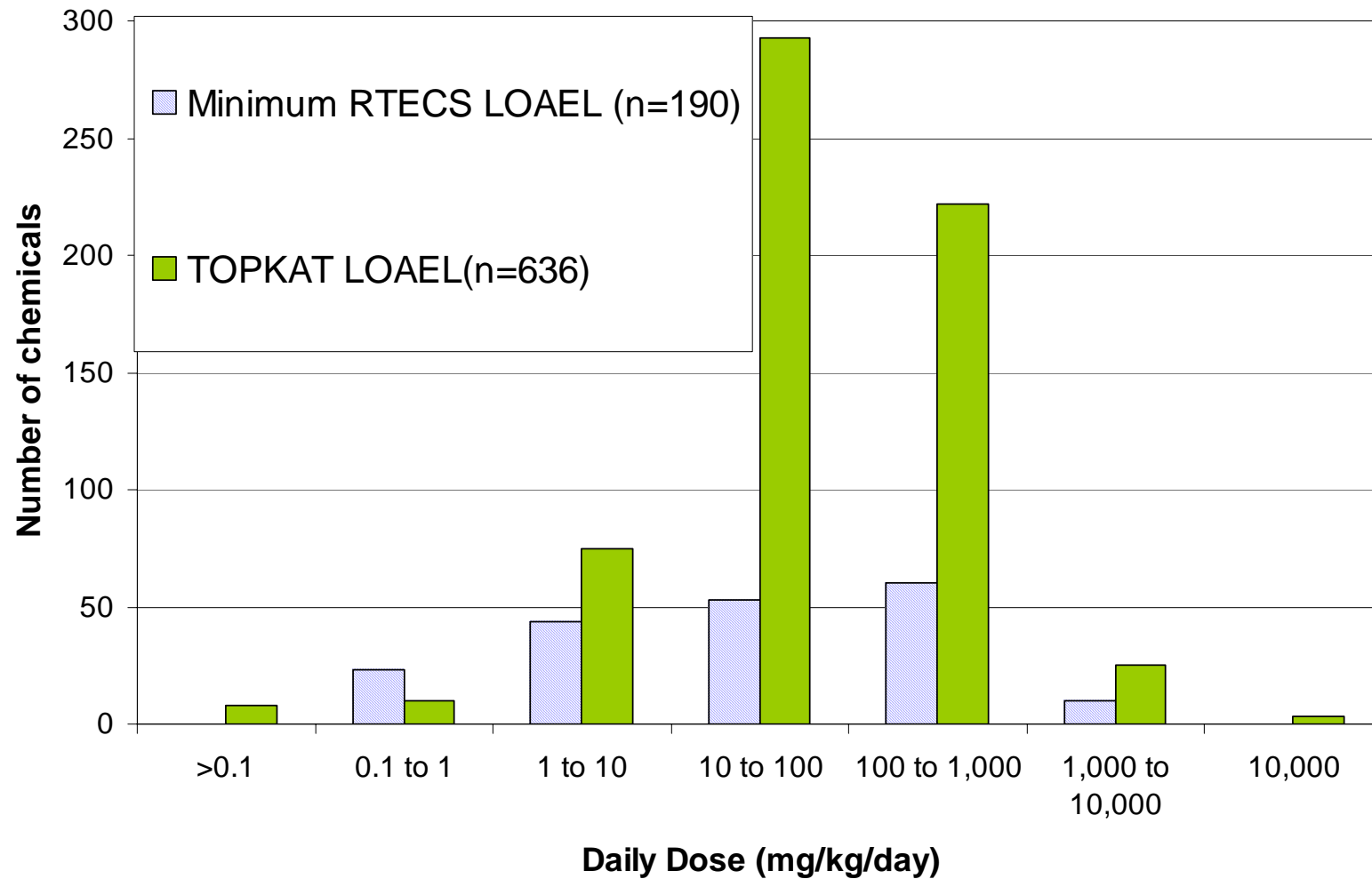
Distribution of Measured and Modeled Solubility Values
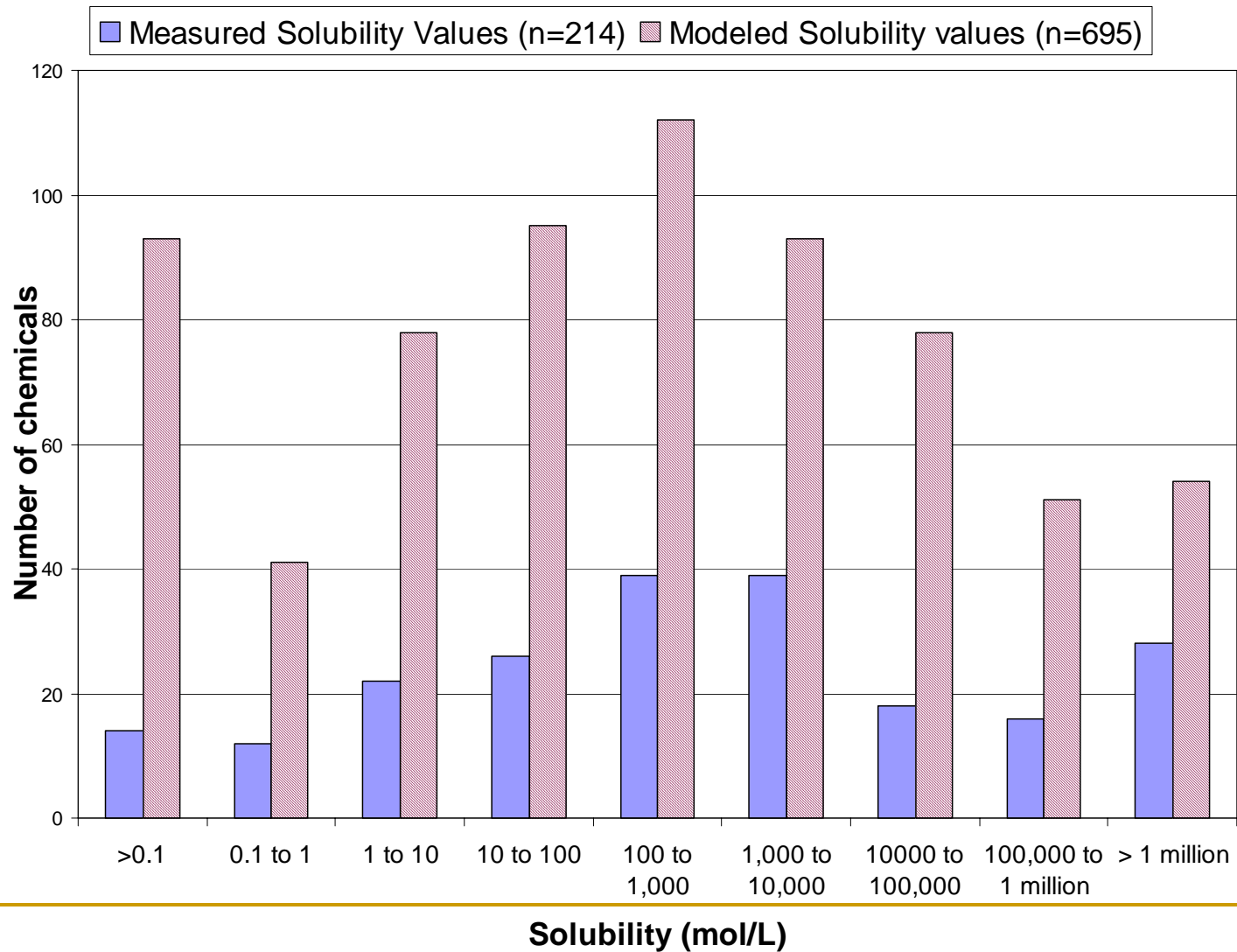
LOAEL Values (mg/kg-day) in Equal Percentage Bins

Bin #	RTECS Minimum LOAEL	n	TOPKAT LOAEL	n
1	0 - 7	63	0 - 31.9	213
2	8 - 125	65	32 - 156.9	211
3	126 - 3000	62	157 - 10000	212

Range of Values in Bins Varies by Binning Approach

	BINNED BY VALUE			BINNED BY PERCENTAGE		
	HIGH (1)	MED (2)	LOW (3)	HIGH (1)	MED (2)	LOW (3)
RTECS LOAEL (mg/kg/d)	0 - 9.9	10 - 99.9	100 - Max	0 - 7	8 - 125	126 - 3,000
# Chemical in Bin	67	53	70	63	65	62
Measured Solubility	>1,000	0.1 - 1,000	<0.1	5,000 - 9.31E6	66 - 4,900	1.16E-6 - 65
#Chemical in Bin	98	102	14	71	71	72

Intersections of LOAELs and Solubility in Bins

Bin Intersections

- **High Toxicity [most potent/lowest LOAEL] High solubility (1:1)**

- **High Toxicity [most potent LOAEL] Medium solubility (1:2)**

- **Medium LOAEL High solubility (2:1)**

- **Sum of above** **1:1; 1:2; 2:1**

Toxicity

Occurrence

LOAEL

Solubility

HIGH (1)		HIGH (1)
MED (2)		MED (2)
LOW (3)		LOW (3)
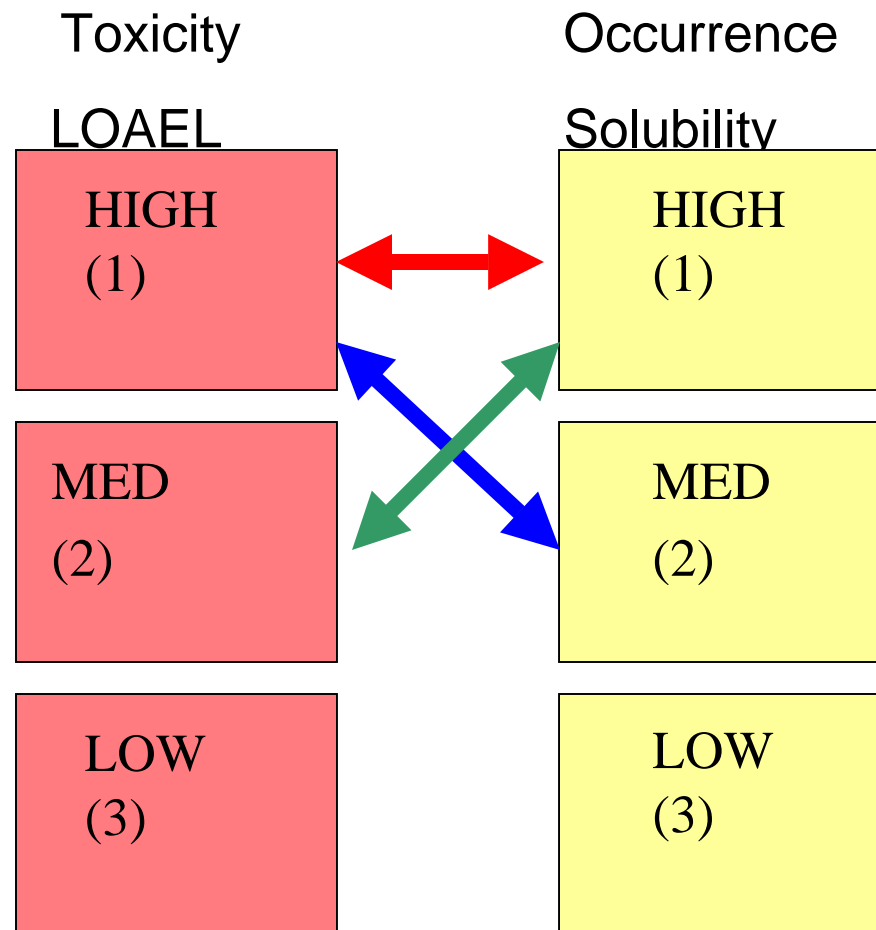
Measured LOAEL to Measured Solubility – Bins by Value

Minimum LOAEL — Solubility

HIGH (1) n=67	1-1 17 (18%)	HIGH (1) n=98
	1-2 21 (22%)	
MED (2) n=67	2-1 11 (12%) Sum= 49 (52%)	MED (2) n=102
LOW (3) n=56		LOW (3) n=14

Measured LOAEL to Measured Solubility - Bins by Equal Percentage (N=94)

Minimum LOAEL   Solubility

HIGH (1) n=63	**1-1 13 (13.8%)**	HIGH (1) n=71
MED (2) n=65	**1-2 12 (12.8%)** **2-1 6 (6.4%)** **Sum= 31 (33%)**	MED (2) n=71
LOW (3) n=62		LOW (3) n=72

QSAR Estimated LOAEL to QSAR Estimated Solubility (N=636)

Minimum LOAEL

Solubility

HIGH (1) n=213	1-1 47 (12.1%)	HIGH (1) n=232
	1-2 40 (10.3%)	
	2-1 34 (8.8%)	
MED (2) n=211	Sum= 121 (31%)	MED (2) n=232
LOW (3) n=212		LOW (3) n=232

Percentage Results by Binning Approach

	HIGH (1-1) %	High Plus High/Med (%)	N
Measured By Value	18	52	49
Measured By Equal %	14	33	31
QSAR Estimated by Equal %	12	31	121

Initial Findings

- Binning approach is straightforward

- Generally see similar results in bins, but get more contaminants if segregate by value

- QSAR estimated values produce similar percentages to measured values

- Can bin by Percentage or Values to select candidates

Next Steps

- Bin subset of chemicals with both empirical and QSAR-modeled data

- Bin larger data set of empirical data set supplemented with QSAR results

- Add third binning parameter
      (half-life - persistence)

- Bin by quintiles