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

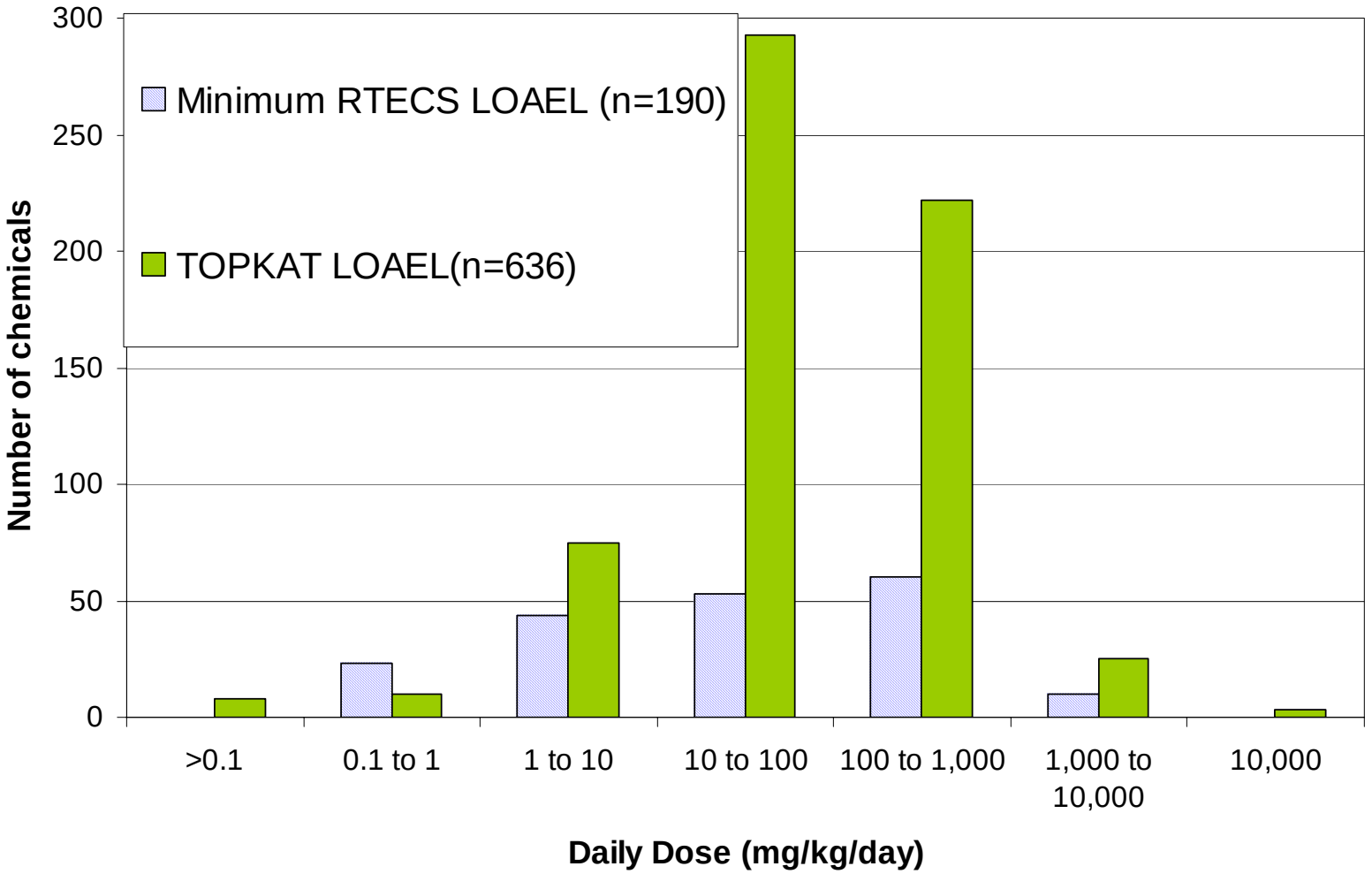
Screening Data and Sources

- 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

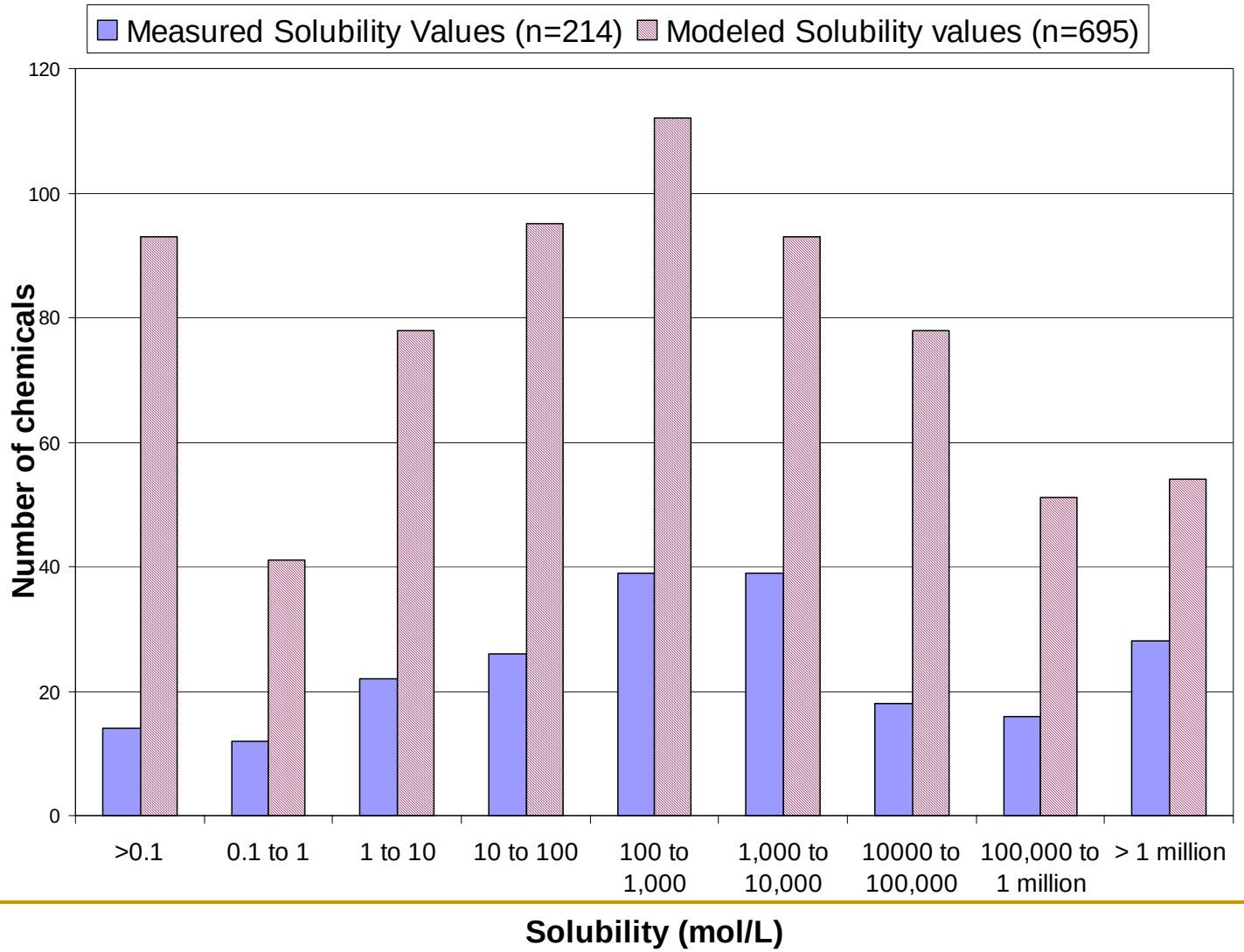
Bin Analysis

- 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

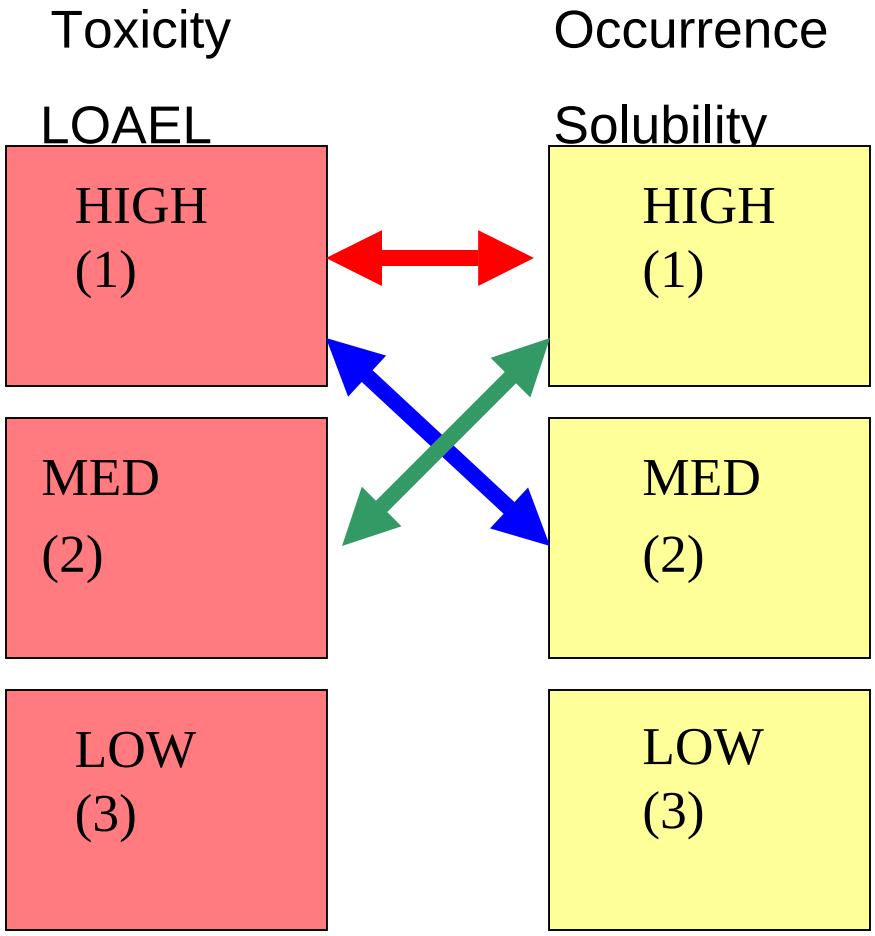
Range of Values in Bins Varies by Binning Approach

	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

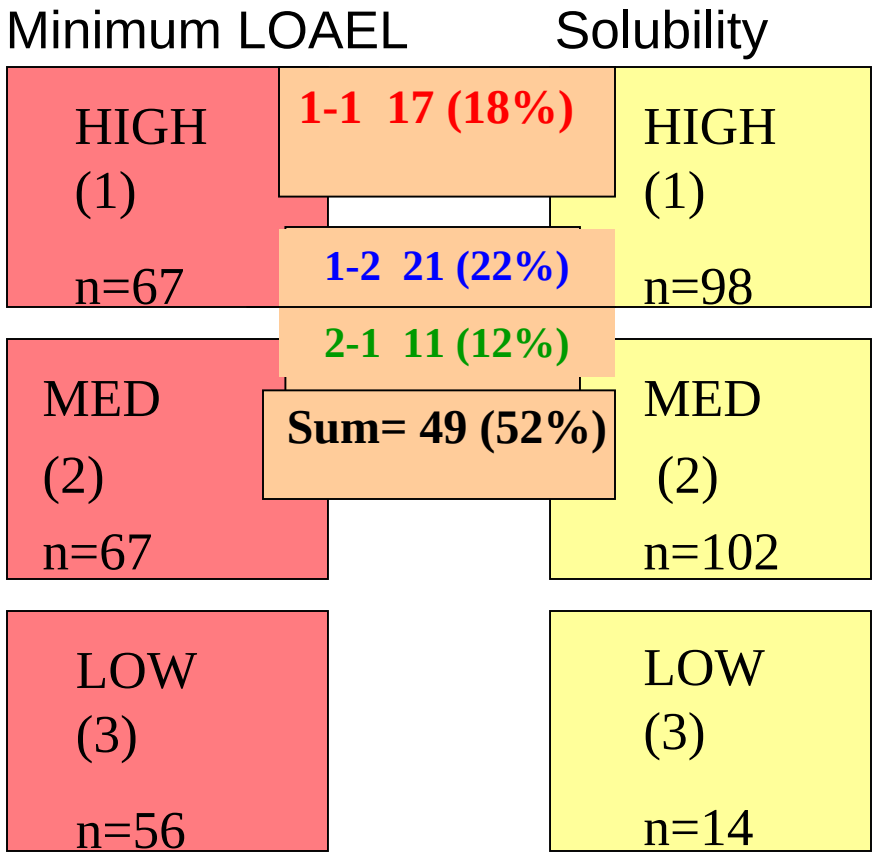
Intersections of LOAELs and Solubility in Bins

Bin Intersections

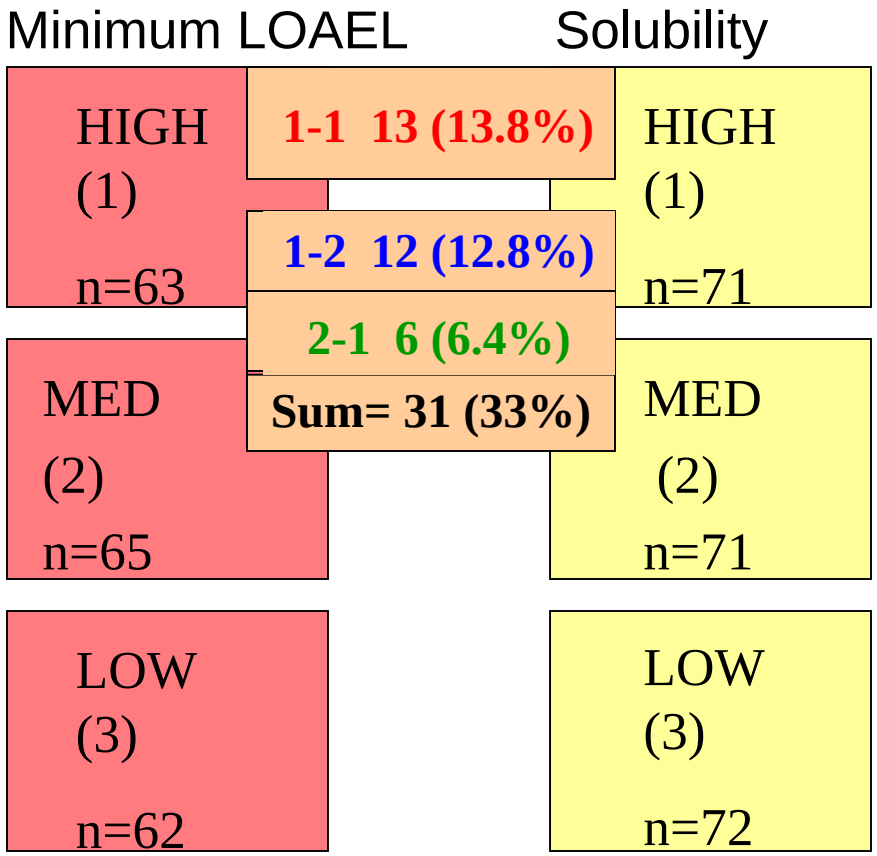
- **High Toxicity [most potent/lowest LOAEL] High solubility (1:1)**
- **High Toxicity [most potent LOAEL] Medium solubility (1:2)**
- **Medium LOAEL High solubility (2:1)**
- **Sum of above** **1:1; 1:2; 2:1**



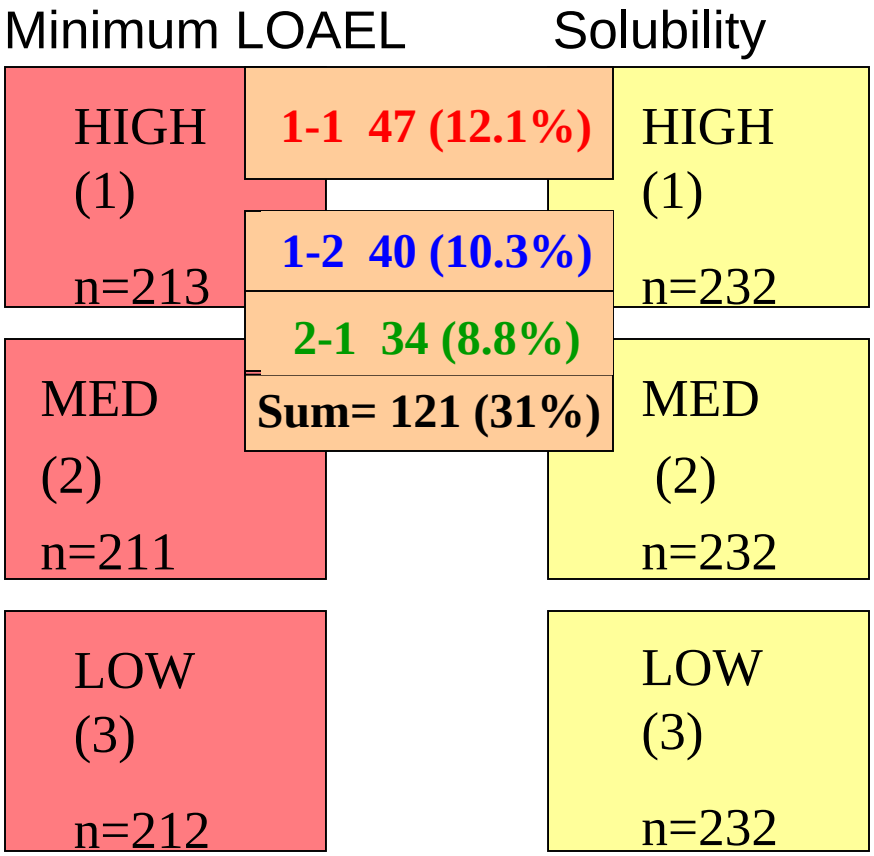
Measured LOAEL to Measured Solubility – Bins by Value



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



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



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