
Predicting Exposure Potential

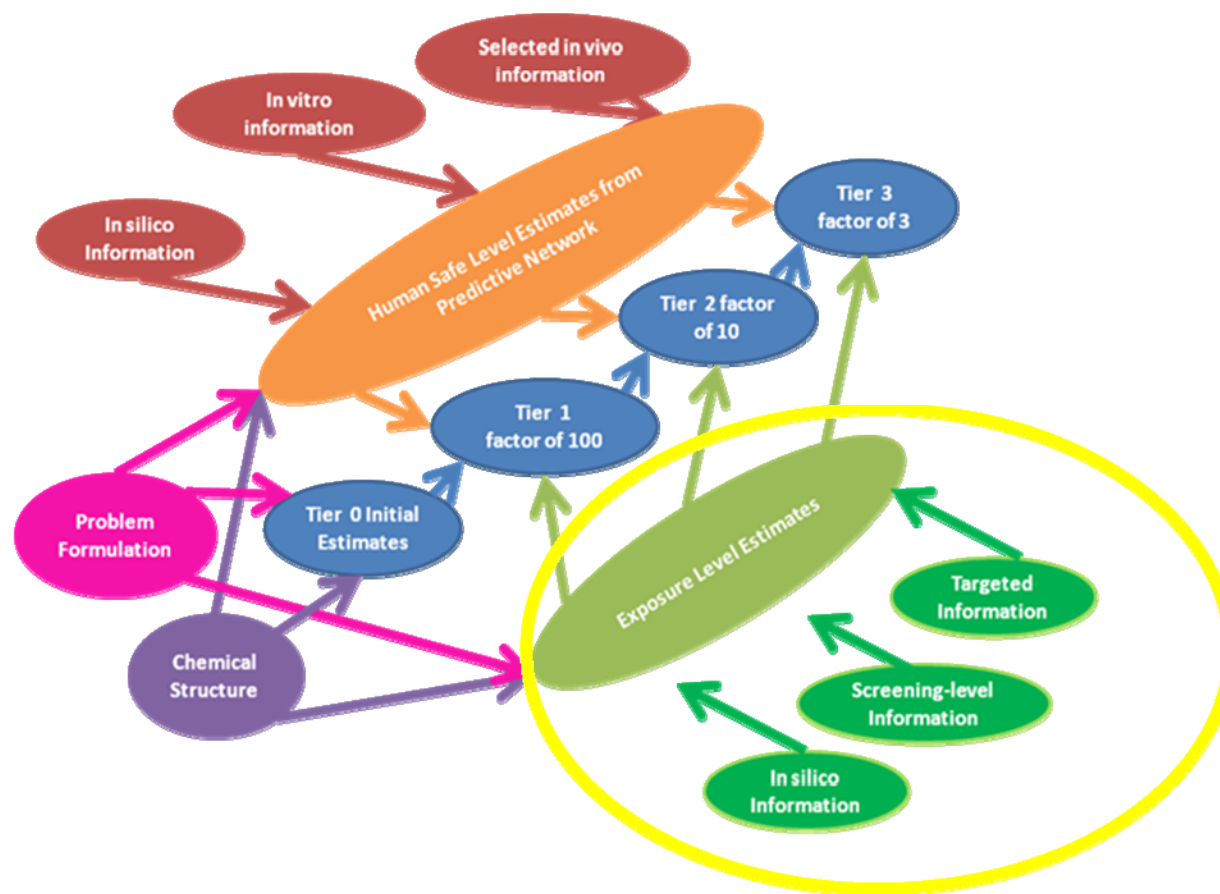
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RISK 21 Exposure Data Framework

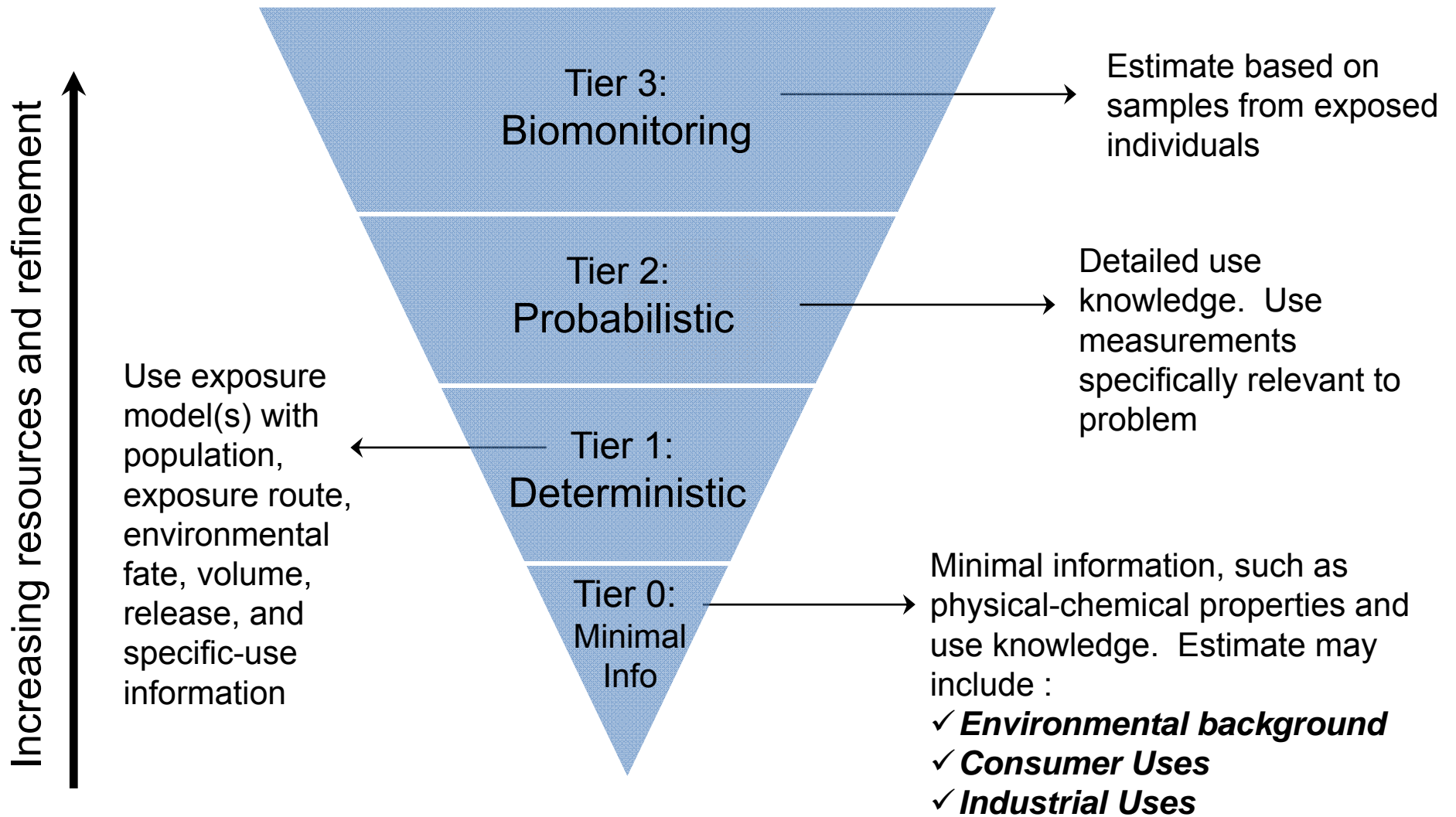


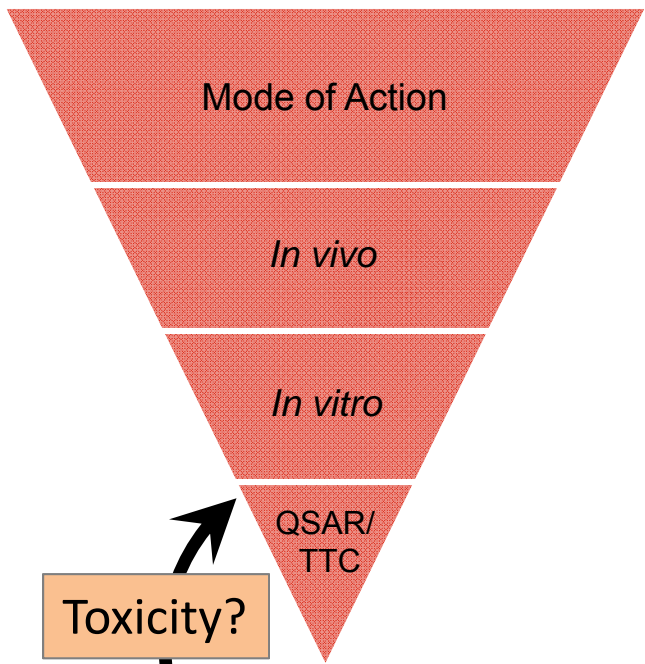
Early Use of Exposure Data



- Guides the amount and type of toxicity data necessary for a risk assessment.
- If the exposure estimate is low, then less precision and a lower-tier toxicity estimate may be adequate to assess acceptable level of safety.
- Exposure estimates can be used to prioritize chemicals for further exposure and toxicity testing.

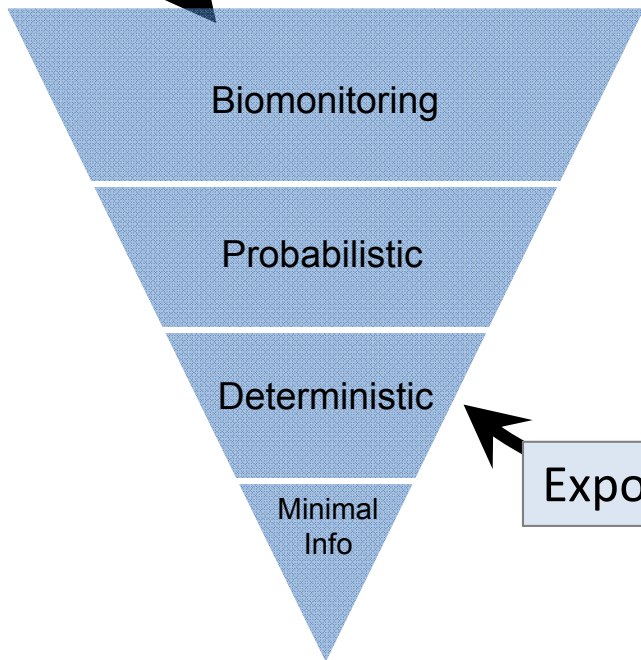
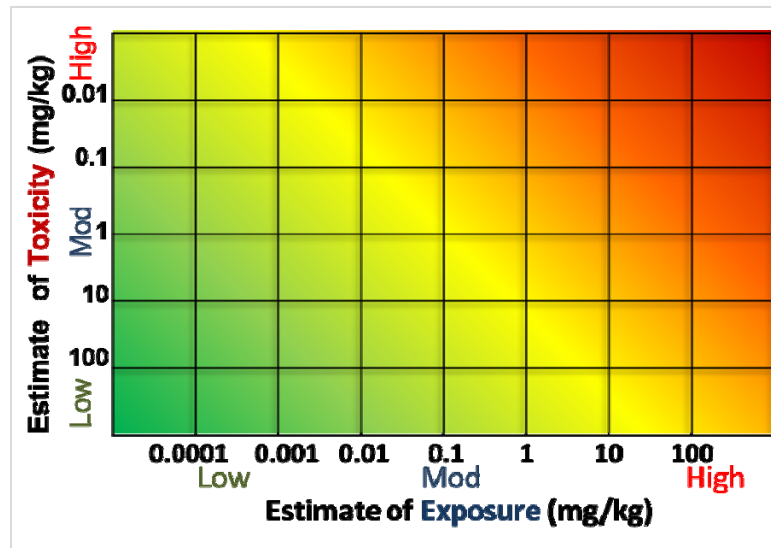
Tiered Approach for Exposure Estimate





Toxicity?

Risk? Safety?



Exposure?

Problem Formulation

Conclude

Sources of Information for Exposure Tiers



Tier	Description	Examples of tools/models/data
Tier 0	Limited substance and/or specific use knowledge. Use of physical-chemical properties.	EPI Suite, look-up tables from various models, monitoring databases, physical-chemical properties, etc.
Tier 1	Limited use knowledge. Models with population, exposure route, environmental fate, volume, release, and specific-use information; geometric mean monitoring values.	ECETOC TRA, USETox, ConsExpo, EUSES, etc.
Tier 2	Detailed use knowledge. Specific contaminant monitoring and measurement data for use in probabilistic modeling.	PRZM-EXAMS, SHEDS, full distribution of monitoring data, etc.
Tier 3	Extensive knowledge. Internal dose, biomonitoring information, specific contaminant monitoring and measurement data.	National Report on Human Exposure to Environmental Chemicals, NHANES, etc.

Exposure Bands in RISK21



- How can we quickly develop screening level exposure estimates?
 - Banding-based models come to mind
 - Potential way to develop exposure look-up tables
- Exposure tools developed to meet EU REACH regulation: ECETOC TRA, EGRET
 - Intentionally conservative, useful for screening
 - Utilized banding concept
 - Environmental bands available based upon EUSES (basis of TRA environmental module)
 - Public tools (no cost, transparent)

Occupational Exposure Banding



- Based upon ECETOC TRA
- Exposure estimates by Process Category (PROC), bands based upon fugacity (vapor pressure and/or dustiness)
- Inhalation and dermal contact exposure estimates
- Tables of distinct estimates for industrial workers and professional workers
- Tables for non-solids and solids

Consumer Exposure Banding



- Based on ECETOC TRA and EGRET
- Exposure estimates by product codes, bands based upon vapor pressure
- Inhalation, dermal and oral exposure estimates
 - Dermal and oral unchanged by physicochemical properties
- Acute (day of use) values for TRA for non-article products and articles
- Acute and chronic values for EGRET for non-article products

Problem Formulation: The Starting Point



Define Boundaries for assessment:

1. What is the substance?
 2. How, where and by whom is it used?
 3. What do we already know (physicochemical properties, toxicity, and exposure)? and
 4. What else do we need to know?
1. Pyrethroid
 2. Use description
 - a. The populations of interest – children, 6-12 years and adult workers (children consumers sleeping under the bed net and adult workers manufacturing the nets)
 - b. Route of exposure – inhalation and dermal (oral not significant).
 3. Already known – Existing World Health Organization (WHO) document on treating bed nets to protect against malaria using deltamethrin, which is a common pyrethroid
 4. Need to know – use and material preparation data to estimate exposure

Tier 0: Exposure Assessment



Stage 1: Physicochemical data

Property	Value *
Molecular Formula	$C_{22}H_{19}Br_2NO_3$
Molecular Weight (g/mole)	505.21
Solubility in Water (mg/L) at 20°C	0.002
Vapor Pressure (Pa) at 25°C	2.00E-06
Melting Point (°C)	98°C
Boiling Point (°C)	300°C
Log Kow	4.6

- Deltamethrin is a solid at room temperature with low vapor pressure
- not readily soluble in water
- can purchase as a solid or as dispersed in water
- by purchasing aqueous solutions reduce material preparation and inhalation exposure

Stage 2: Banding based look-up tables

- Worker Scenario - Loading (PROC 8a) and Dipping (PROC 13).
- Consumer Scenario - Fabrics, textiles and apparel (AC5).
- Humans via the environment - water solubility as worst case estimate
(0.002 mg/L x 3L/80 kg = 7E-05 mg/kg/day)

Stage 3: Compare the exposure estimates with Threshold of Toxicological Concern (TTC)

Tier 0 Worker Exposure Look Up Table



Industrial Worker Exposure Look-up Table from ECETOC TRA v.3. Model

Process Category (PROC)		•Industrial Workers •Non-solids and Solids •All Fugacity Levels •No Local Exhaust		Negligible VP < 0.01 Pa
		Long-term Dermal mg/kg-day	Long-term Local Dermal µg/cm ²	Long-term Inhalation ppm volatiles
4	Use in batch and other process (synthesis) where opportunity for exposure arises	6.86	1000	0.1
5	Mixing or blending in batch processes (multistage and/or significant contact)	13.71	2000	0.1
6	Calendering operations	27.43	2000	0.1
7	Industrial spraying – Non-solids inhalation sentinel	42.86	2000	100
8a	Transfer of chemicals from/to vessels/ large containers at non dedicated facilities	13.71	1000	0.1
9	Transfer of chemicals into small containers (dedicated filling line)	6.86	1000	0.1
10	Roller application or brushing	27.43	2000	10
12	Use of blow agents for foam production	0.34	100	2
13	Treatment of articles by dipping and pouring	13.71	2000	0.1

Identified worker dermal exposure to be 14 mg/kg/day
For both transfer and dipping

Total dermal exposure = 28 mg/kg/day

Total inhalation exposure = 0.1ppm or 2 mg/m³ x 10 m³/day = 0.3 mg/kg/day

Tier 0 Consumer Exposure Look-Up Table



Tier 0 Consumer Exposure (ECETOC TRA v3), Acute (day of use) exposure estimates

Descriptor	Product Subcategory	Total Predicted Exposure (mg/kg/d)		
		< 0.1 Pa	0.1 - <1 Pa	1 - < 10 Pa
AC5: Fabrics, textiles and apparel	Clothing (all kind of materials), towel	1031	1031	1034
	Bedding, mattress	28	28	63
	Toys (cuddly toy)	57	57	57
	Car seat, chair, flooring	148	148	171
AC6: Leather articles	Purse, wallet, covering steering wheel (car)	0.7	0.7	1.0
	Footwear (shoes, boots)	3.6	3.6	4.7
	Furniture (sofa)	16	16	28
AC8: Paper articles	Diapers	56	56	56
	Sanitary towels	7.1	7.1	7.1
	Tissues, paper towels, wet tissues, toilet paper	29	29	29
	Printed paper (papers, magazines, books)	4.2	4.2	8.4
AC10: Rubber articles	Rubber handles, tyres	6.1	6.1	54.5
	Flooring	6.0	6.0	28.7
	Footwear (shoes, boots)	3.6	3.6	4.7
	Rubber toys	2.3	2.3	2.3
AC11: Wood articles	Furniture (chair)	14.8	14.8	16.3
	Walls and flooring (also applicable to non-wood materials)	5.9	5.9	27.2
	Small toys (car, train)	2.3	2.3	2.3
	Toys, outdoor equipment	6.6	6.6	6.6

Identified bedding contact as best match to sleeping with bed netting.

Exposure = 28 mg/kg/day (based on 10% substance in the article)

For 1% substance in the bed netting,
Total exposure = 2.8 mg/kg/day

Tier 1: Exposure Assessment



Stage 1: Additional exposure information

Parameter	Worker
Hours spent transferring from large container to tank (hr.)	15 min -1 hr.
Actual time workers might contact solution in dipping tank (hrs.)	15 min -1 hr.
Deltamethrin Concentration in plastic container (wt. %)	5-25
Deltamethrin Concentration in dipping tank (wt. %)	No more than 1
Wear chemically protective gloves (APF = 10)	Yes
Bed nets treatment at plant (days/year)	20
Total nets produced per year	200

Stage 2: Direct estimates from tools

- Worker – ECETOC-TRA worker module - PROC 8a & PROC 13
- Consumer – WHO defaults (30% surface body area touches & target dose is 25 mg/m²), consider dermal and oral exposure (via hand to mouth)

Stage 3: Compare the exposure estimates with POD hazard estimate

Conclusions



- Proof of concept demonstrated that exposure estimates from look up tables can be applied more widely for use in exposure assessments but more work is needed to verify reliability.
- Look-up tables suggest potential utility for tiers 0 and 1 but further research is needed to test tier 2 and 3 data.
- Application of the RISK 21 approach can be enhanced by:
 - Refining and standardizing default values
 - Adding scenarios of interest
 - Adjusting weight fractions by functional purpose (consumer)
 - Investigating additional physicochemical properties

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