Chemical Exposure Priority Setting Tool (CEPST)

Presented by:

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October 7, 2008

Brief History

- Born in 2004 under the name ComET (**Com**plex **E**xposure **T**ool) in work done for Health Canada under the leadership of Bette Meek.
- It is now fully formed as a working construct and demonstrated in a Excel Spreadsheet beta version (CEPSTbeta.xls). http://www.thelifelinegroup.org/CEPTS/index.htm

Somewhat Misunderstood

- It is NOT: just an exposure risk ranking tool BUT it does do risk ranking.
- It is NOT a “full-blown” exposure/risk modeling tool BUT it does provide a quantitative estimate of exposure/risk.
- It IS a **Hybrid** of the two general types of models.

CEPST Provides

- Initial (first tier) quantitative estimates of exposure and risk for:
  - Each and any number of chemical substances (CAS numbers) up to a practical limit of about 500
- A “first look” Hazard Index for each material under consideration.
- A ranking order of “worst things first” based on the information at hand.

So what exactly is **CEPST**?

- **C**hemical **E**xposure **P**riority **S**etting **T**ool
- Modeling Construct that uses all available information and peer-reviewed technology to **quantitatively** estimate the exposure potential of Any Number of Substances starting only with the Identity (CAS number) of the substances of concern.

Uses for CEPST Output

- Quantitative EXPOSURE Assessment done by
  - Age (Children, adults, and the elderly)
  - Individual routes of exposure or systemic dose
  - Acute (1 day), short term (90 days), or long term (365.25 days) exposure
- Readily LINKED to Toxicological Benchmarks to estimate/rank Risk for the substances under consideration – for “worst things first” ranking.

Why Develop a New Model?

- Existing Ranking Model do not provide quantitative estimates.
- Existing Quantitative Estimating Models are predominantly Compound-Centric *i.e.,* designed to estimate the exposure/risk of a single compound, or to compare risk from a few compounds
- New Regulatory Mandates require a Tool to Serve their Mandates and allow for:
  - Handling a potentially "blinding number" of substances
  - Ranking to potentially identify and declare *de minimus* exposure and risk
  - Identification of exposure/toxicity data needs
  - The rank ordering of "worst things first"

6 Objectives for the Design of CEPST

1. Assure that Approach and Assumptions are completely transparent.
2. Use all data available to provide a QUANTIATIVE estimate of exposure.
3. Be reasonably conservative (protective).
4. Identify (Flag) those substances and estimates for which there are limited data (i.e., explicitly identify elements of uncertainty)
5. Allow the use of multiple criteria:
   - Adult or child exposures
   - Chronic, Subchronic or Acute
6. **Evergreen refinement of estimates as better data and technology become available**

Exposure Assessment Assumptions

- As a start, critical substance use (**Sentinel Product(s)**) are determined based on publicly available description of products. **Internet Search Protocol** – supplemented OR totally provided by **Stakeholders**
- Use-Frequency based on published studies
- Physical-chemical values for substances from available sources
- Values on physiology, dietary consumption, from available regulatory guidance documents
- **Gaps** filled in with "**best professional judgment**" – pending scientific peer-review

Definitions

- Sentinel Product **(SP)**: A product that is judged to cause the plausible upper bound individual human exposure to the substance of interest within the product
- Sentinel Product Function **(SPF)**: The general functional category to which the SP belongs
- Sentinel Product Scenario **(SPS)**: Explicit exposure circumstance translated into specific exposure predicting algorithms and parameters for each relevant route

Multiple Doses are Determined for each Use Scenario

- Route-specific dose
  - Oral, Dermal, Inhalation, and Systemic (Total)
- Six age groups
  - <0.5, 0.5-4, 5-11, 12-19, 20-59, and >60
- Duration
  - Short term = 1 day
  - Intermediate = 90 day
  - Chronic = 1 year

Source Characteristics

- Dermal (external/absorbed dose)
- Inhalation of respirable particles, soluble particles and released vapors
- Oral: dietary, water, non-dietary oral, and inspired particles that are ingested

Age Specific Anatomical, Physiological, and Dietary Parameters

- Body Weight;
- Total Surface Area;
- Inhalation Rate;
- Surface Areas of trunk, arms, legs, hands, and feet
- Ingestion rates for water and food
- Inadvertent soil ingestion rates

CESPT TOOLS

- Inclusive Library of Sentinel Products Functions (SPF) and, under each SPF, at least one Sentinel Product (SP) described with one or more Sentinel Product Exposure Scenario(s) (SPS)
- Evergreen Collection of Exposure Estimating Algorithms for Oral, Dermal and Inhalation Exposures Matched as needed for each SPF/SP/SPS.

Step by Step Through CEPST

Step 1: Identify "Sentinel" Products

- For each substance under consideration:
  - **Match the substance to at least one high exposure (Sentinel) product (SP) related to its use.**
  - **Every SP exists in a "Library" organized under its Sentinel Product Function (SPF).**
  - **Each SPF/SP has at least one Sentinel Product Scenario (SPS) that quantitatively describes the exposure potential by relevant route with oral, dermal or inhalation algorithms.**
- For each SPF/SP/SPS matched to the substance:
  - **Scenario specific variables exist within the library as defaults in separate dose models for each age, route, and exposure duration**
  - **The User supplies documented scenario-specific and substance/scenario specific information for the algorithms.**

Example SPF/SP/SPS Hierarchy

- SPF – Surface Coating (non-aq base)
- SP – Interior Wall Paint
- SPS – Painted Walls Small Bedroom
  - Scenario 2.1a: Applicator Exposure
    - Dermal Algorithm
    - Inhalation Algorithm
  - Scenario 2.1p - Post Applicator Exposure
    - Inhalation Algorithm

Prerequisites for Assigning Sentinel Product(s)

- Reliable outputs from either an Internet Search or verifiable sales and marketing information.
- A coordinated/interacting TEAM of Experts with demonstrated professional experience/judgment in the realm of human health exposure assessment from consumer products – especially modeling
- Subject to Validated Stakeholder Input

SOME SPECIFIC VARIABLES (VARYING SP/SPS) USED IN CEPST EXPOSURE CALCULATION ALGORITHMS

- **FQacute** = NUMBER OF EVENTS PER DAY (1/DAY)
- **FQchronic** = NUMBER OF DAYS PER YEAR USED (DAY/YEAR)
- **ED** = EXPOSURE DURATION TIME PER EVENT (HOURS/EVENT)
- **AMT** = AMOUNT PER EVENT (GRAMS)
- **SA** = SURFACE AREA OF SKIN CONTACT (CM2)
- **ppmF** = PERCENTAGE IN FOOD (PPM w/w)
- **RF** = RESPIRABLE MASS FRACTION (ACGIH DEFINITION) IN **AMT** (unit less)
- **IF** = INHALABLE MASS FRACTION (ACGIH DEFINITION) OF **AMT** (unit less)
- **EV** = THE EFFECTED VOLUME AROUND THE BREATHING ZONE FOR EACH EVENT (M3)
- **AREA** = SURFACE AREA OF VAPORIZING SOURCE (CM2)
- **PC** = PROPORTION BY WEIGHT IN PRODUCT OR ARTICLE (0-1)
- **DR** = DISLODGEABLE RESIDUE (MG/CM2)
- **PT** = PROPORTION TRANSFERRED ON DERMAL CONTACT (unit less 0 to 1)
- **TEMP** = TEMPERATURE OF THE PRODUCT (C)

SOME COMPOUND-SPECIFIC VARIABLES

- **KowPRED = EPI PREDICTED LOG Kow**
- **KowEXP= EPI EXPERIMENTAL LOG Kow**
- **BPPRED = EPI PREDICTED NORMAL PRESSURE BOILING POINT (C)**
- **VP = EPI PREDICTED VAPOR PRESSURE (mmHG)**
- **SOLPRED = EPI PREDICTED WATER SOLUBILITY AT 25C (MG/L)**
- **SOLPRED = EPI EXPERIMENTAL WATER SOLUBILITY (MG/L)**
- **HLCPRED = EPI PREDICTED HENRY'S LAW CONSTANT (BOND METHOD) (atm-m3/mole)**
- **MW = MOLECULAR WEIGHT (GRAMS/MOLE)**
- **INHALATIONPOT = ABILITY OR OPPORTUNITY TO BECOME AIRBORNE AND THUS ENTER THE BODY THROUGH INHALATION SYSTEMICALLY ABSORBED BY DERMAL ROUTE. A UNITLESS QUANTITY BETWEEN 0 AND 1 .**
- **DERMPOT = ABILITY TO BE SYSTEMICALLY ABSORBED BY DERMAL ROUTE (0 TO 1).**
- **ORALPOT = ABILITY TO BE SYSTEMICALLY ABSORBED BY ORAL ROUTE (0 TO 1).**

Step 2: Check and Refine CEPST Model Input

- Apply and document the inputs for the entire universe of substances under consideration
- Be certain to include situations where a substance can occur in more than one sentinel product (SP); then decide on either:
  - The sum of the estimates, or
  - The highest estimate for that substance to be used in the exposure estimation.

Step 3: Viewing the “Answers”

- Example Spreadsheet (CEPSTbeta.xls) provides values for any of the 72 different types of dose:
  - Acute, short term, or long term;
  - Any of the six age groups;
  - Any of the three route specific estimates or the total estimate; and
  - Applied and/or Absorbed Dose

Step 3: Viewing the Answers, (cont.)

- For those substances that have multiple products the exposure estimate can be based on:
  - the highest estimate of any of the products evaluated or
  - the sum of the products
- Various viewing options will allow the user to determine the potential relevance of the estimate for different ages of concern, or for shorter-term and long-term exposures
- These exposure estimates will allow:
  - Comparison of compounds based only on exposure
  - Provide exposure input for comparison with hazard values

Distinguishing Between Data and Derived Information Inputs

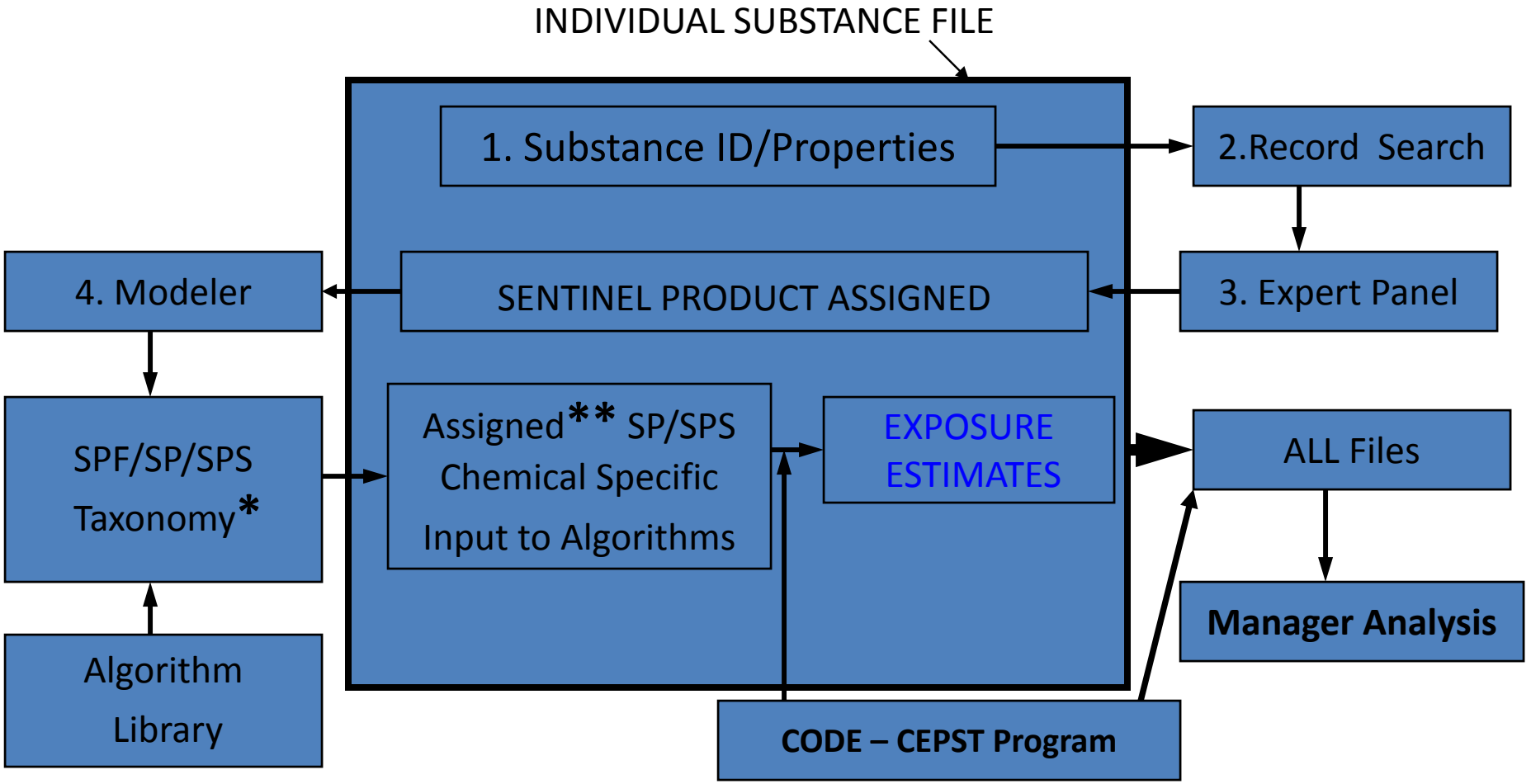
Objective:

- Transparency
- Identifying those exposure estimates that are largely based on assumptions that are not well documented
- Sensitivity to input parameters
- Determine areas for additional or improved data

Approach: "Talley of Derived Data"
Possible Approaches:

- Determine the levels of documentation associated with each parameter used in each exposure calculation
- For each estimate total the number of highly professional judgment parameters that are used in deriving the dose
- Display this "Count" with each exposure calculation

CEPST *EXPOSURE* ASSESSMENT PROCESS DIAGRAM



* Modeler Identifies relevant algorithms from Library or generates new ones

** Modeler Identifies Sentinel Product/Sentinel Product State sets from the Taxonomy then assigns substance/scenario specific input variables.

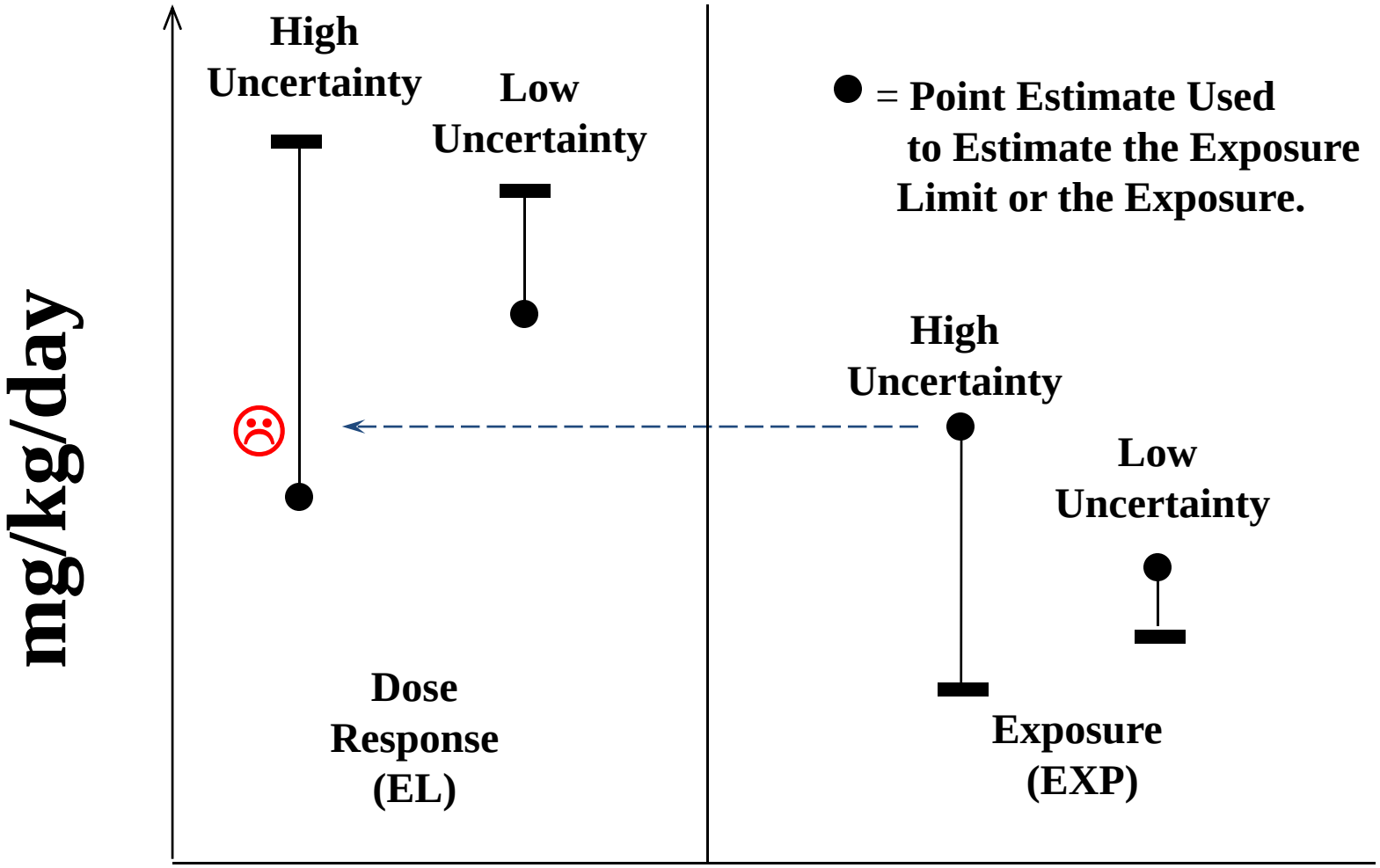
Tiered Approach

- Going from simple (over-estimating) to more complicated (less conservative) models
- Advantages:
  - Less information-less resource needed.
  - May get you "home" ☺
- Disadvantage: It may not.
- Allows for a reasoned approach to trade conservatism for data ($).

In Risk Assessment you get two "bites at the apple"

- You can lower the uncertainty around and estimated level of exposure.
- OR you can lower the uncertainty around the toxicological benchmark (e.g., DNEL).
- Both require resources but it is often more cost-effective to work on the exposure side of the ratio.

Levels of Confidence in Exposure and Dose-Response Assessments



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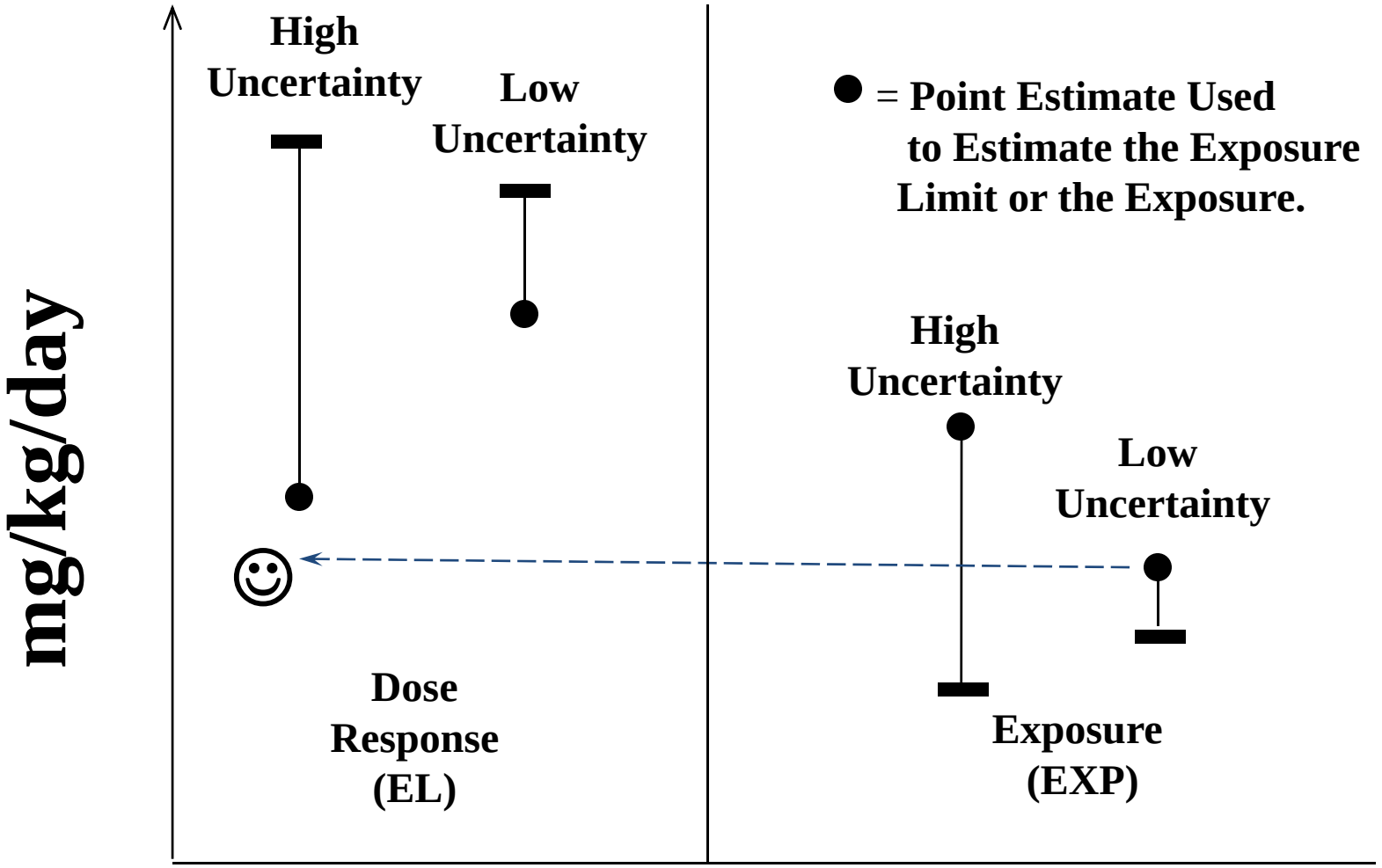

CEPST compared to ECETOC TRA

- No “wired” set-asides or risk management judgments.
  - *e.g.,* the embedded logic in Tier 0 of ECETOC automatically declares a 10 MT/year, “dusty” substance, with wide-dispersive use, and NO toxicity data as “No Immediate Concern”.
- CEPST basically combines Tier 0 and Tier 1 in that it quantitative describes (and ranks) the Hazard Indices of many substance while leaving the assessor to make the call.

Journal of Exposure Science and Environmental Epidemiology (2008) 00, 1–10

www.nature.com/jes

Using publicly available information to create exposure and risk-based ranking of chemicals used in the workplace and consumer products

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