CANADIAN BIOACCUMULATION EXPERIENCE FROM THE ASSESSMENT OF SUBSTANCES UNDER CEPA

ILSI-HESI / JRC / SETAC Workshop on Bioaccumulation Assessment

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Presentation Objectives

There are 2 goals of this presentation:

- To relate to workshop participants how bioaccumulation information (modeled and empirical) was used in PB(i)T Categorization and how it can and will be used in CEPA substance screening level ERA
  - PBTs, PiTs and BiTs going to SLERA
  - New substances
- Lessons learned from Categorization and SLERA

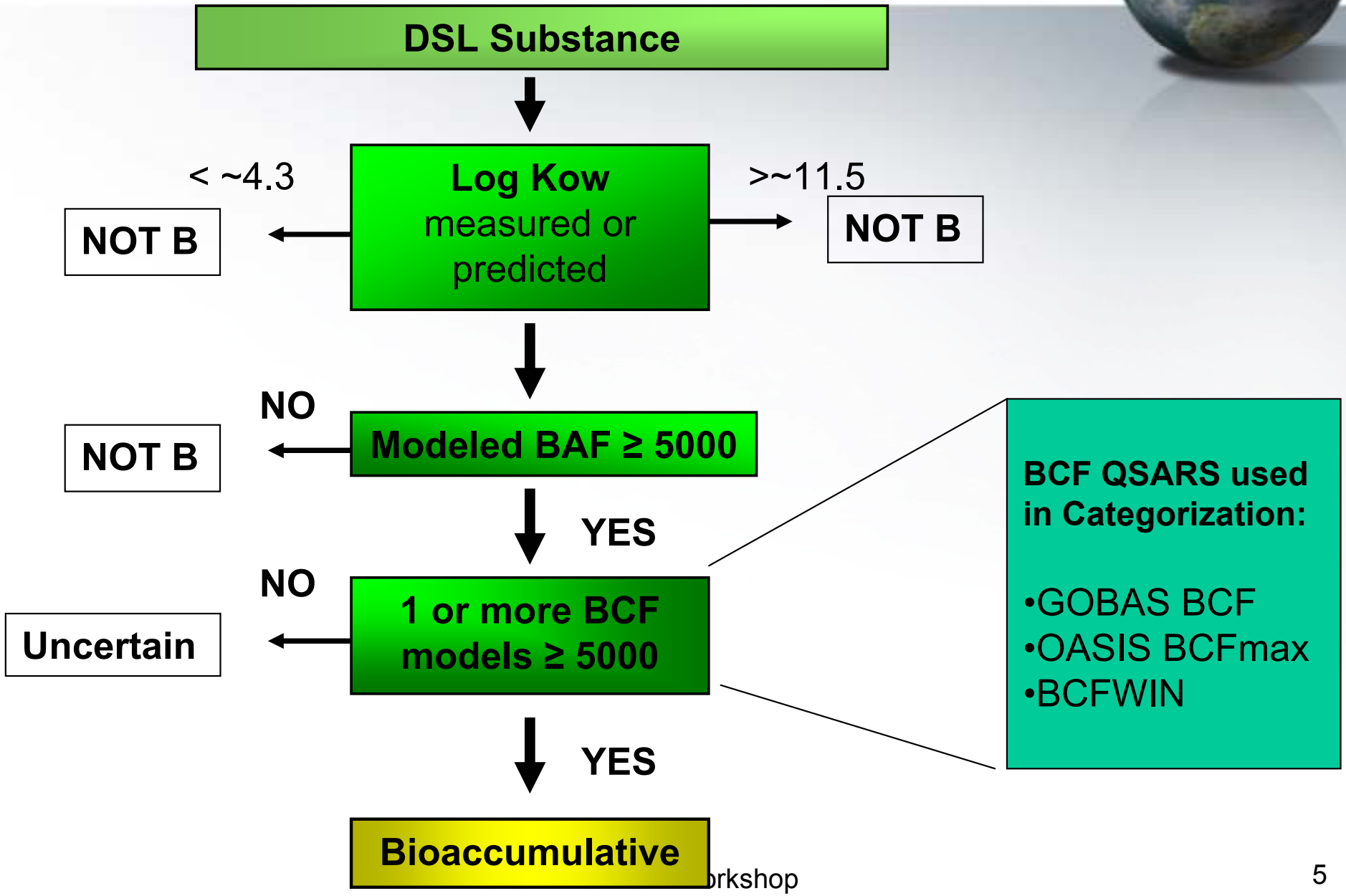
Status of Bioaccumulation Assessment

Issues:

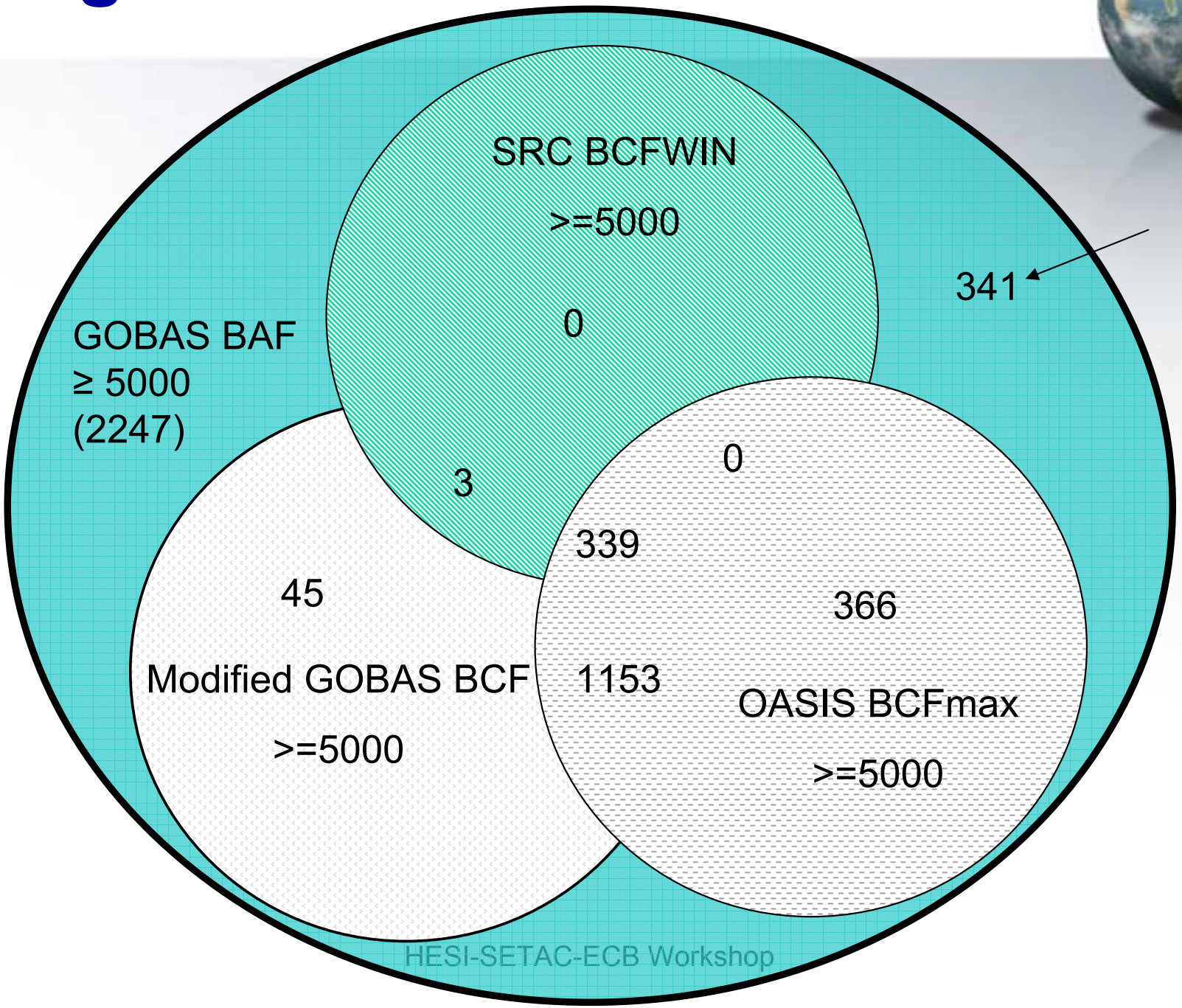
- Global regulatory attention on bioaccumulation (B) because of PBT and vPvB programs as well as ERA
- Considerable activity, but limited harmonisation. Each country has it‘s own approach for B assessment.
- Current approaches have shortcomings:
  - Bioaccumulation models and read across approaches are limited to well studied chemical classes and can lead to false negatives and positives.

Categorization for Bioaccumulation

"Weight of Evidence" to Using B Models



Putting Numbers to Wt. of Ev.



Exception to Bioaccumulation: Evidence for Biotransformation

- Available evidence for biotransformation considered in making the B determination
- Biotransformation is either “off” by default in models or is not considered at all
- So categorization acknowledges a certain degree of over-conservatism in the approach
- Generally, tendency has been for industry/stakeholders to provide categorization section with documentation/evidence and submit this info as an “industry submission”
- The decision on if the chemical(s) meet the criteria for B would then be pending the outcome of our review of these submissions.

Experience from B Categorization

Experience: Experimental B Data

- Studies undertaken for DSL and non-DSL organics by Frank Gobas and Jon Arnot found a paucity of experimental B data
  - For example: 11,400 discrete organics on the DSL
    - 2,672 BCFs in fish for 415 DSL chemicals (3.6%)
    - 223 BAFs in fish for 38 DSL chemicals (0.3%)
    - 2,895 empirical BCF and BAF values from 81 fish species for 423 DSL chemicals (3.7%)
  - Above studies not screened for quality
- Limited read-across potential (legacy chemicals)

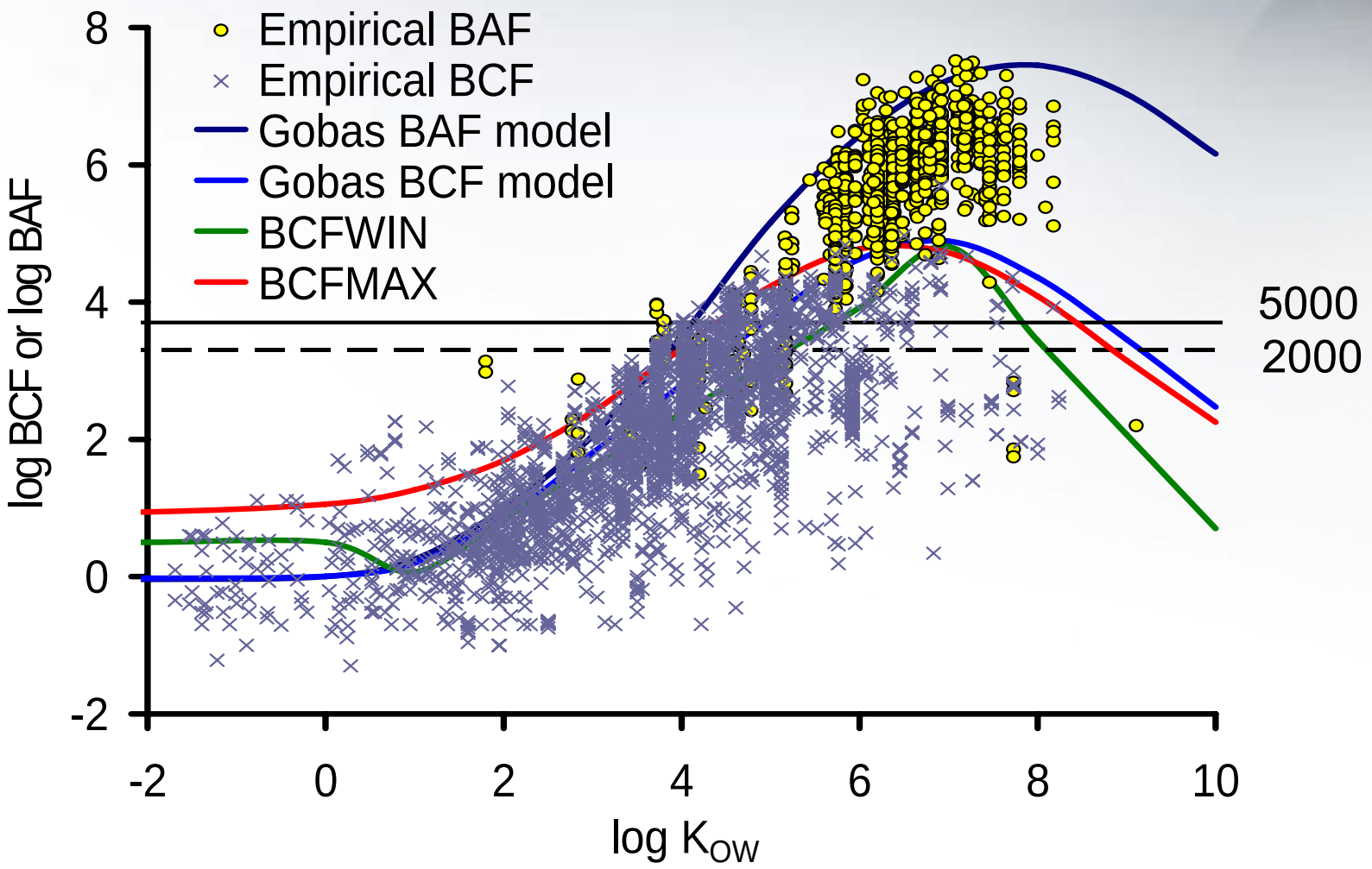
Experience: Quality Experimental B Data

- Environment Canada's DSL acceptable 'B' database
  - 1,441 BCFs in fish for 344 DSL chemicals (3.0%)
  - 130 BAFs in fish for 23 DSL chemicals (0.2%)
  - 1,571 empirical BCF and BAF values for 350 DSL chemicals (3.1%)

Experiences: Modeling

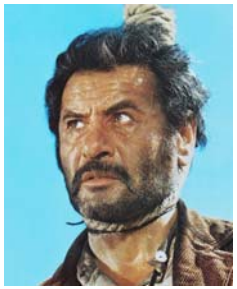
- Heavy reliance on B models
- ~97% ‘B’ categorizations rely on predictions by 4 models (BCFWIN, BCFMAX, Gobas BCF and Gobas BAF)
  - Individual models estimate between 400 and 2300 organics to be 'B' (July 2005)
  - Type II errors can be as high as 72% using a BCF model alone for categorization, i.e., potential for missing B chemicals
  - Gobas BAF model calibrated to selected ‘tolerable’ level of uncertainty (e.g., 5%)
  - To help counter some of the weaknesses of the B models (real or perceived) EC developed a weight of evidence approach to use of B models

Empirical Data and the 4 Models



From Arnot and Gobas 2006

Experiences: Modeling (The Good, Bad and Ugly Faces of 'B' Models)



- 'B' models work well when chemical queried is in the model training set or domain (the good)
- Practical, easily understood, can be transparent, open to analogue searching, act as databases (the good)
- 'B' models are starting to account for absorption, distribution, metabolism and excretion processes (the good)
- We don't have a good understanding of what the rates for ADME processes should be for fish (the bad)
- QSAR training set domains are limited (the bad)
- 'B' models requiring $\log K_{ow}$ as input will transfer the error associated with the $\log K_{ow}$ (the bad)
- Models are only as good as the data used to build them or garbage in = garbage out (the ugly)
- Most work on passive diffusion principle and cannot be used to explain bioaccumulation based on different mechanisms (e.g., perfluro substances) (the ugly)

Experiences: Other Considerations

- The W of E approach is quite conservative, and essentially $logK_{ow}$ driven
- Substances with a certain $logk_{ow}$, and assuming metabolic potential is not known, will always be predicted as B by the BAF model (e.g. between 4 and ~10)
- Other factors which affect bioaccumulation are not considered by categorization (i.e. ADME, bioavailability, trophic dilution, etc)
- Quality of data generated in experimental studies, even for those for which we have accepted through the RSS process, must be used with caution

Experience: Main Point to Consider

It is simply practical to have <u>tiers of reliable alternative methods</u> to evaluate 'B', meet regulatory deadlines, **reduce animal testing,** and avoid the inhibitory cost of *in vivo* OECD 305 bioconcentration tests **on hundreds of substances**.

Bioaccumulation in CEPA Ecological Risk Assessment

Ecological Risk Assessment

Primary use of bioaccumulation information in ERA is to:

1. Assess the potential for exposure and effects to ecological receptors as well as their food chains
2. To determine stand alone B for P&B and PBT purposes in risk assessment (new and existing) → P+B+CEPA "Toxic" = targeted for "virtual elimination"