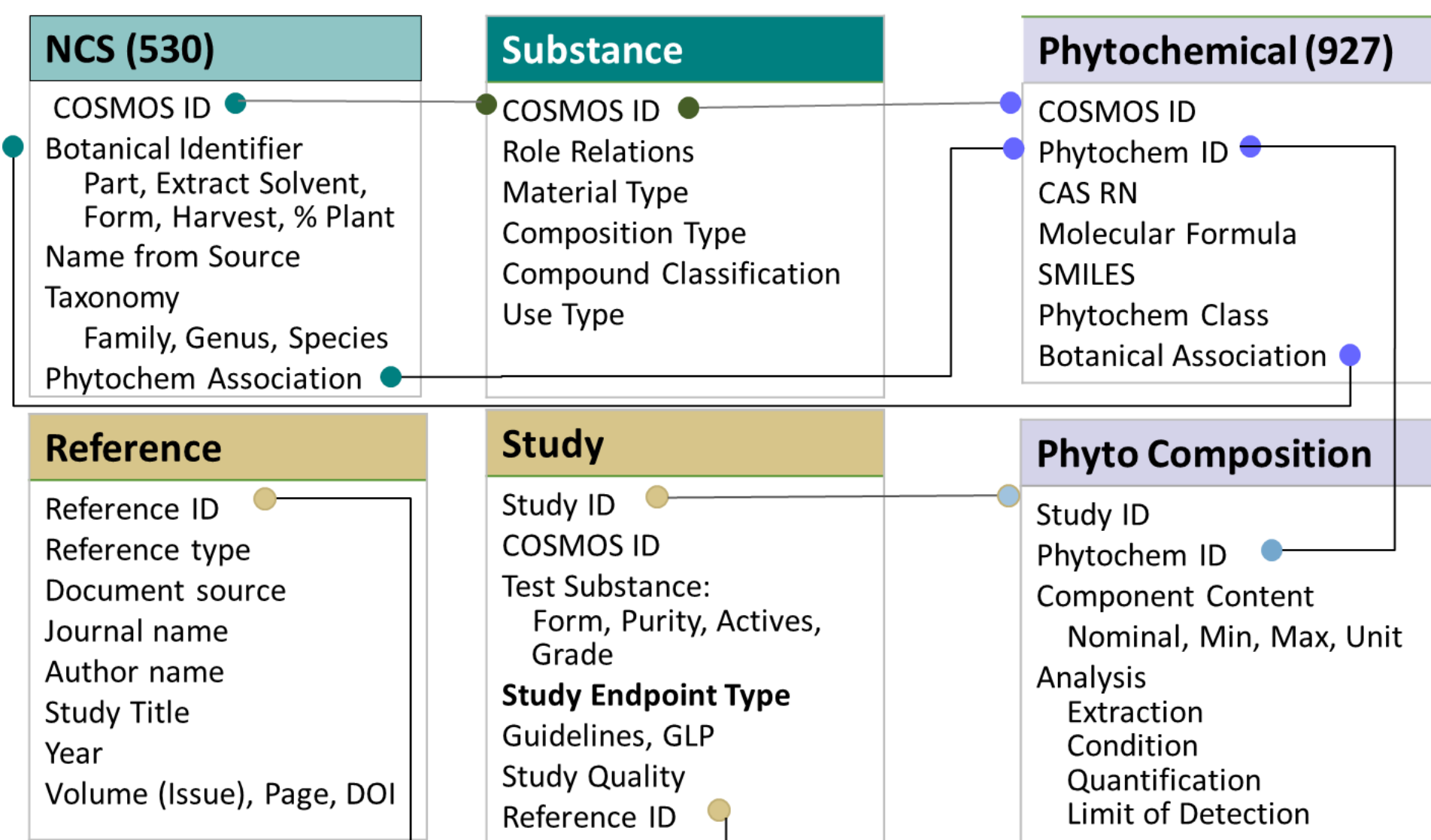




# An Integrated Approach to Threshold of Toxicological Concern for Botanical Substances

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## COSMOS BOTANICAL DATABASE



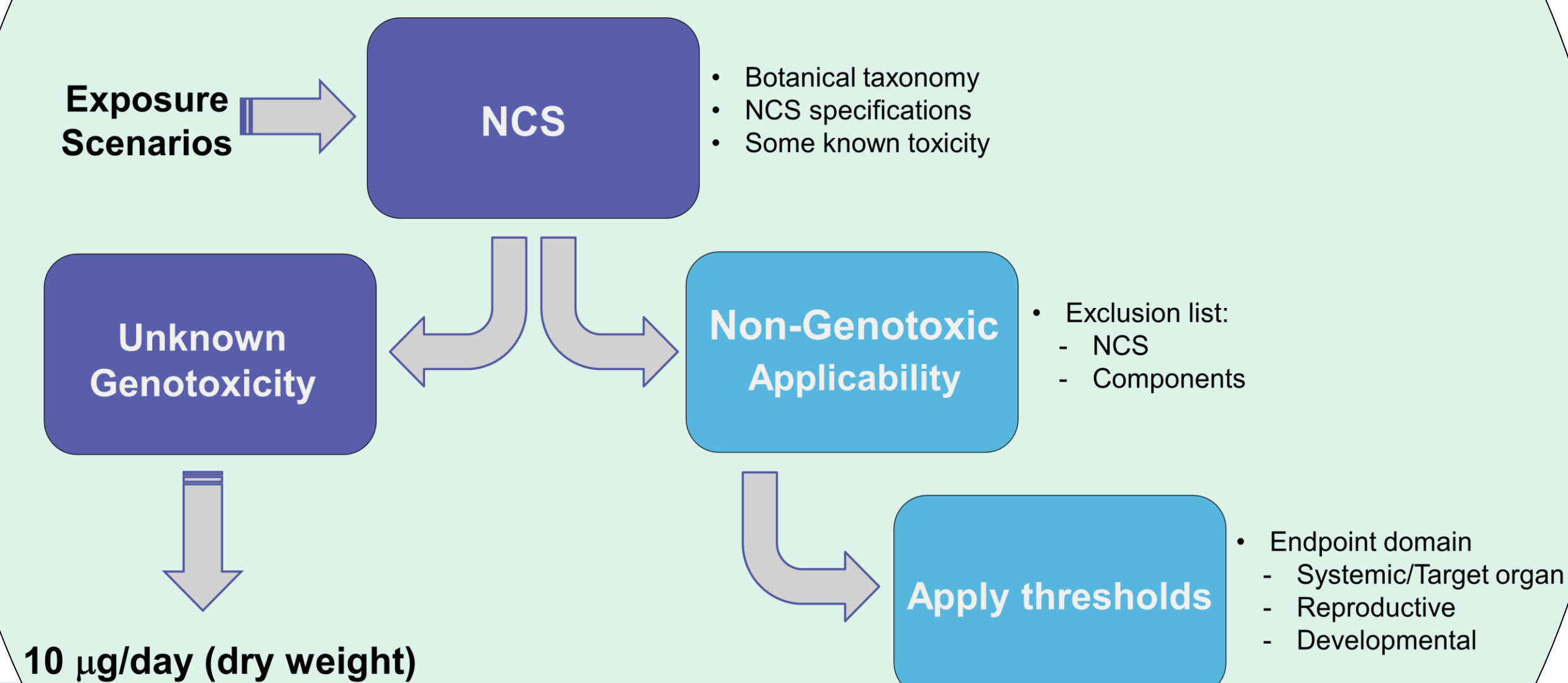
### Database Inclusion Criteria:

- Plant-based natural complex substances (NCS)
- NCS with enriched phytochemical fractions or isolates
- Substances with clear material specifications
- Acceptable toxicity studies allowing NOAEL/LOAEL derivation

Data Sources: Literature, EFSA, SCCS, EMA, ECHA, NTP, FDA, EPA, CIR

## Threshold of Toxicological Concern

A risk assessment approach used in the evaluation of low-level exposure to substances where toxicity data may be limited or unavailable. TTC provides a threshold below which the risk of adverse effects may be considered negligible without testing.



10 µg/day (dry weight)

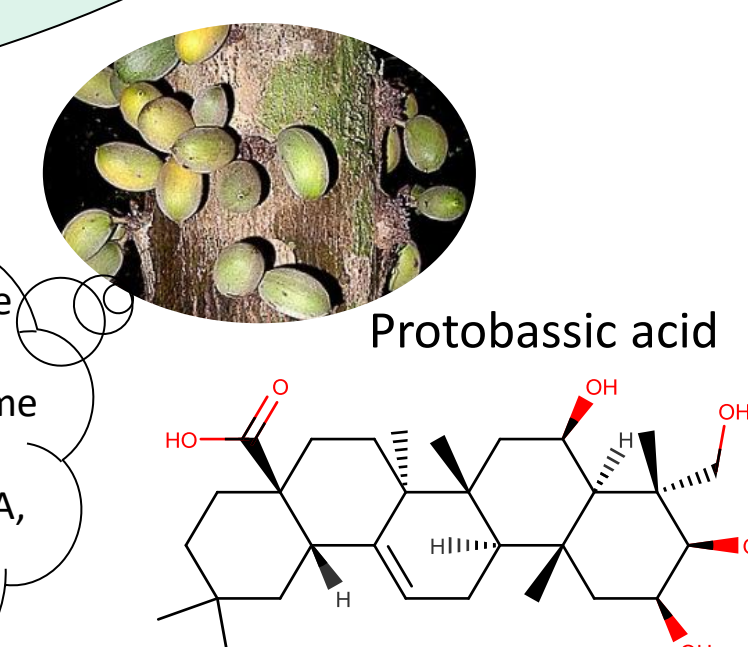
On-going 5th Percentile  
14 mg/kg-bw/day\*

\* integrated approach resulted in a 5th percentile value of the minimum POD.

### Next steps:

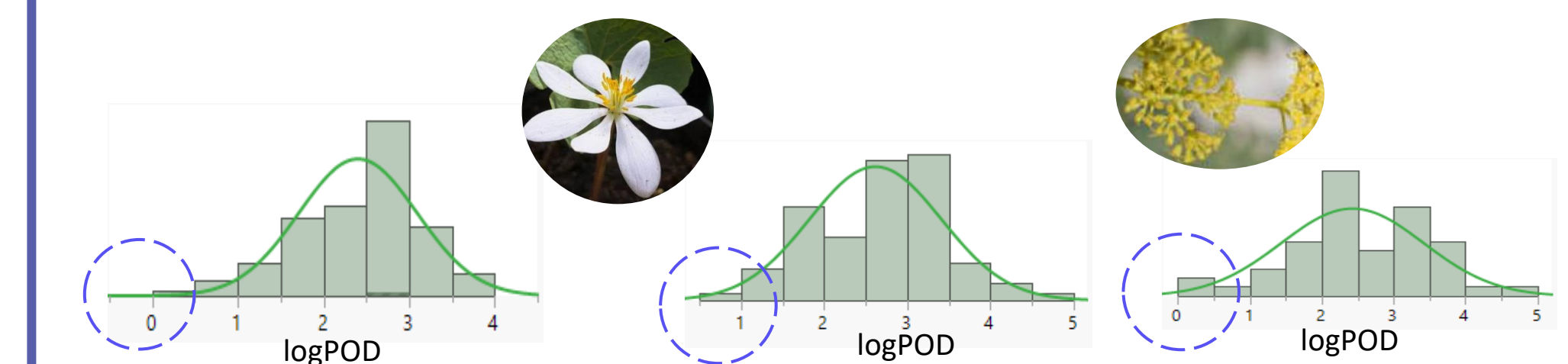
- Confirm the TTC threshold based on the final database
- Define applicability domains and exclusion criteria

I am *Pradosia huberi*, the most potent NCS in the database! You can locate me and my infamous phytochemicals in the PCA, 2-D clustering and POD heatmaps.



## POD: NCS & PHYTOCHEMICALS

Systemic/Target organ Developmental Reproductive



NCS

*A. rusticana* (+allyl isothiocyanate),  
**Sanguinaria** spp.  
*Tripterygium wilfordii*  
*Myristica fragrans* oil  
*Aristolochiae* spp.  
*Melaleuca alternifolia*

*Pradosia huberi*  
*Ginkgo biloba*  
*Lawsonia inermis*  
**Sanguinaria** spp.  
*Melaleuca alternifolia*

**Ferula hermonis**  
*Ardisia squamulosa*  
*Pueraria mirifica*  
*Tripterygium wilfordii*  
*Melaleuca alternifolia*

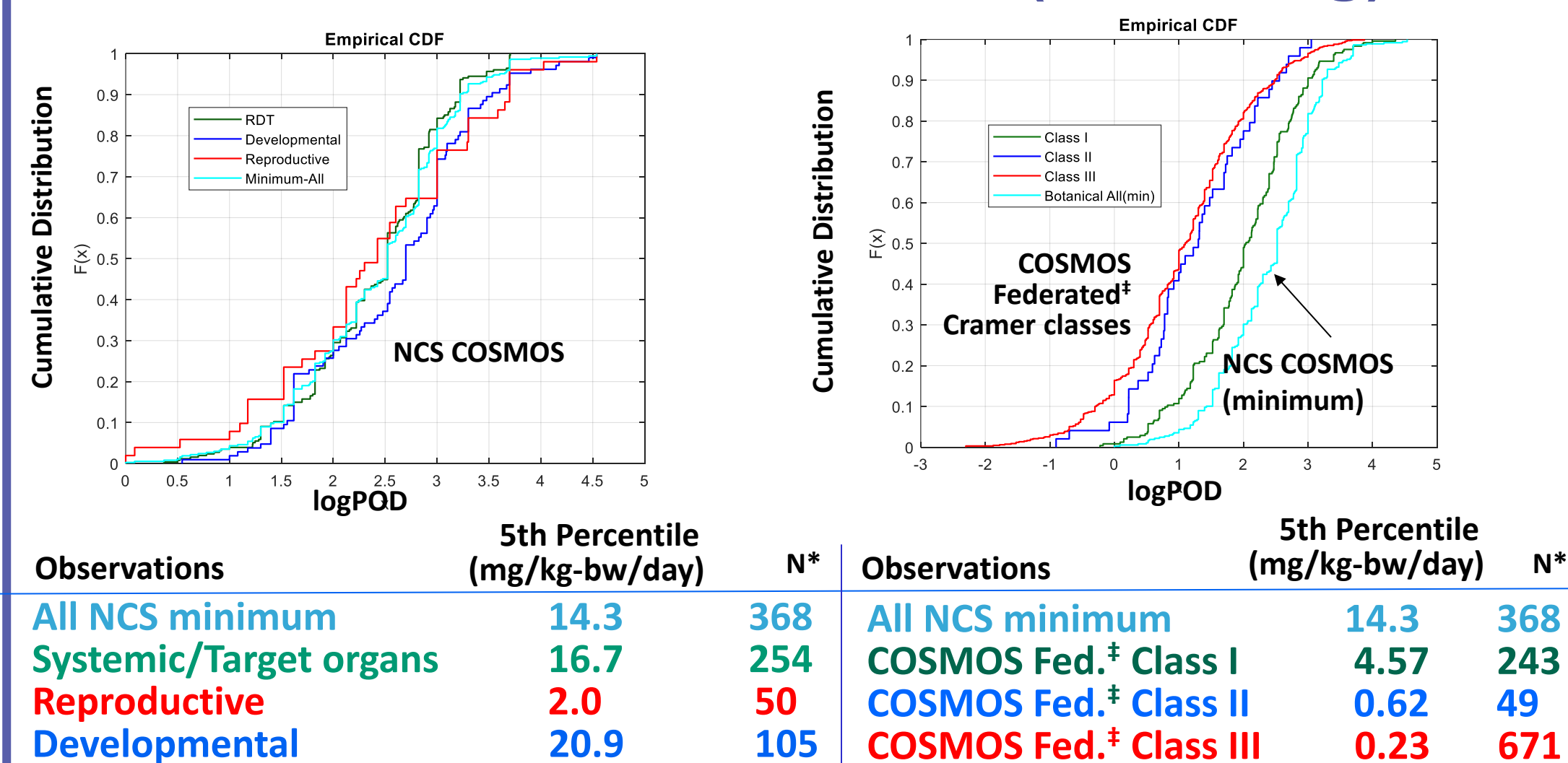
Phytochemicals

Allyl isothiocyanate  
Benzophenanthridine alkaloid  
**Sanguinaria**  
Triptolide  
Myristicin, phenylpropene (elemicin, saffron)  
Aristolochic Acid  
1,8-Cineole, terpenoids...

Pradosiosides (A-G),  
Protobassic acid  
Proanthocyanidins, tannins  
Quercetin, kaempferol, bilobalide, ginkgolide  
**Sanguinaria**  
2-Hydroxy-1,4-naphthoquinone (henna)...

**Ferutin**  
Polyphenols (embeline),  
Phytosteroid  
Phytoestrogen (miroestrol, coumestrol, genistein, daidzein)  
Triptolide  
1,8-Cineole, terpenoids...

## THRESHOLD DEVELOPMENT (On-Going)



\*Analyses are based on the database version 11-03-2025

†Thresholds based on federation of COSMOS TTC and Munro (SCCS NoG 2021)

## NCS-PHYTOCHEM-CHEMOTYPE SPACE

The genus-POD map can assist defining the Exclusion group (genus-ToxPrint combination) for TTC applicability.

