# Environmental and fate ecotoxicity models

## CATALOGIC MODEL
## 301B and 301F

Laboratory of Mathematical Chemistry, Bulgaria

# Biodegradation CATALOGIC 301C model

Experimental data: BOD at 28$^{th}$ day

$$\min_{P} RSS = \sum_{n=1}^{N} \left( BOD_n^{Obs.} - BOD_n^{Calc.} \right)^2$$

Estimates of $P_i$ ⇒ Prediction of: BOD ($ThCO_2$), $t_{1/2}$, Metabolite quantities

**Is it possible to handle experimentally observed?**

$t_{1/2}$ (primary or ultimate)
10 days window
**Kinetic curves - 301B and 301F tests**
Metabolite quantities
Molecular mass distribution of metabolites

# Biodegradation CATALOGIC 301B and F models

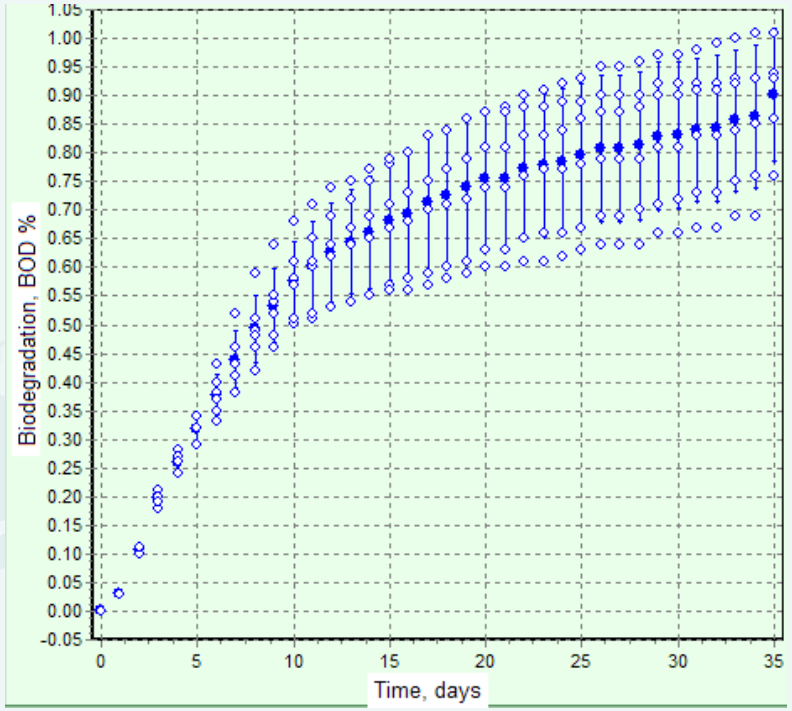
## Data

### OECD 301F test

- 633 proprietary chemicals
- 18108 kinetic BOD data
- half-lives for 359 chemicals

### OECD 301B test

- 232 proprietary chemicals
- 2574 kinetic ThCO2 data



# Mathematical formalism

## Probabilistic approach & First order kinetics

### Probabilistic approach

$$S \xrightarrow{P} M$$

$$[S] = [S]_0 (1 - P) \qquad (7)$$

$$\frac{[S]}{[S]_0} = (1 - P) \qquad (8)$$

$$[M] = [S]_0 P \qquad (9)$$

$$\frac{[M]}{[S]_0} = P \qquad (10)$$

$[S]_0$ – initial quantity of S
[S] – quantity of S at time t
[M] – quantity of M at time t
$P$ – probability of transformation

$$P = (1 - \exp(-kt))$$

$$k = -\ln(1 - P)/t$$

# Mathematical formalism

## Probabilistic approach & First order kinetics

| Probabilistic approach | First order kinetics |
|---|---|
| $S \xrightarrow{P} M$ | $S \xrightarrow{k} M$ |
| $[S] = [S]_0 (1 - P)$ (7) | $[S] = [S]_0 \exp(-kt)$ (7') |
| $\frac{[S]}{[S]_0} = (1 - P)$ (8) | $\frac{[S]}{[S]_0} = \exp(-kt)$ (8') |
| $[M] = [S]_0 P$ (9) | $[M] = [S]_0 (1 - \exp(-kt))$ (9') |
| $\frac{[M]}{[S]_0} = P$ (10) | $\frac{[M]}{[S]_0} = (1 - \exp(-kt))$ (10') |
| $[S]_0$ – initial quantity of S<br>[S] – quantity of S at time t<br>[M] – quantity of M at time t<br>$P$ – probability of transformation | $[S]_0$ – initial quantity of S<br>[S] – quantity of S at time t<br>[M] – quantity of M at time t<br>$k$ – first order kinetic constant |

$$P = (1 - \exp(-kt))$$

$$k = -\ln(1 - P)/t$$

# Mathematical formalism

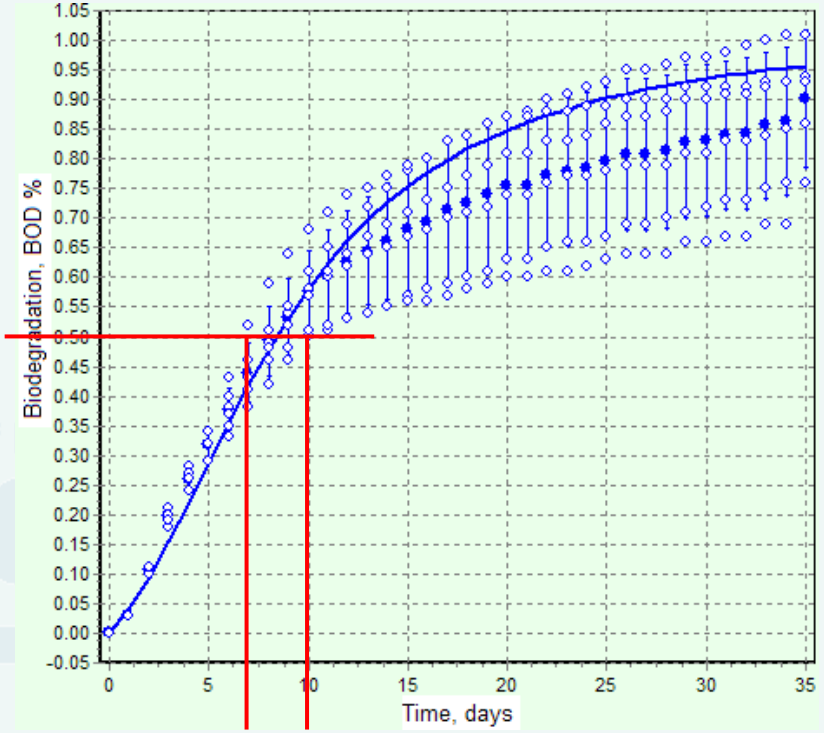
$$P = (1 - \exp(-kt))$$

$$k = -\ln(1 - P)/t$$

$$t_{1/2}^{\text{Ultimate}} = \ln(2)/k$$

$$BOD^{Calc} = f(P_i) = f[P_i(k_i, t)]$$

BOD = 50%



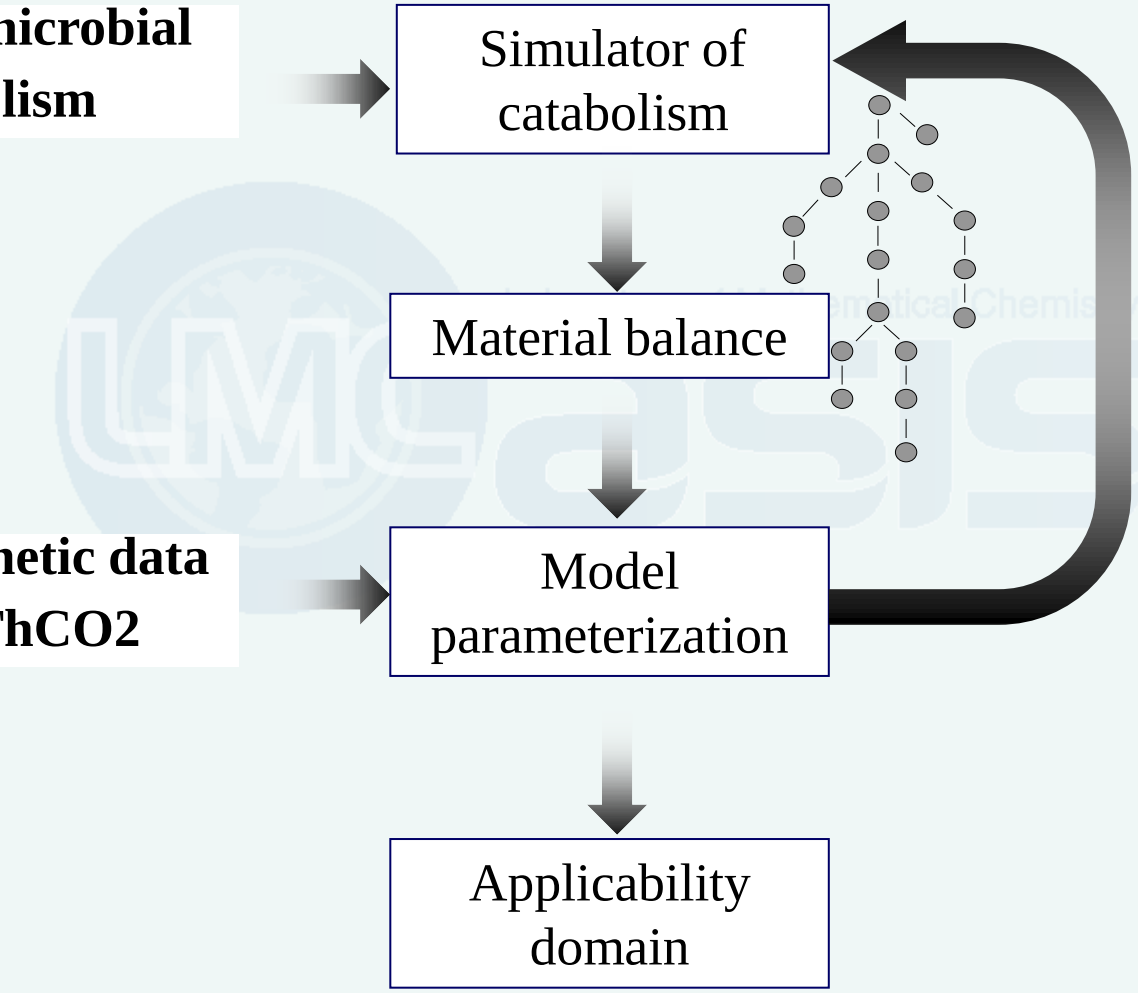

Ultimate half life

**Model parameterization**

$$\min_{\mathbf{k}} : RSS = \sum_{n=1}^{N} \left(BOD_n^{Obs.} - BOD_n^{Calc.}(\mathbf{k})\right)^2 + \sum_{n=1}^{N} \left(t_{1/2,n}^{Obs.} - t_{1/2,n}^{Calc.}(\mathbf{k})\right)^2$$

# LMC modeling approach

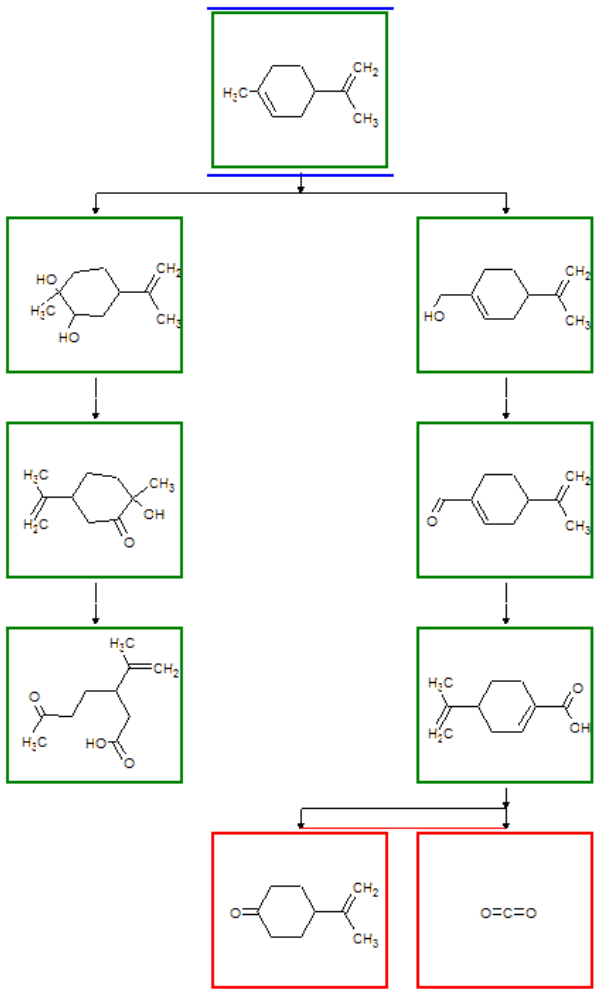
**Observed microbial catabolism**

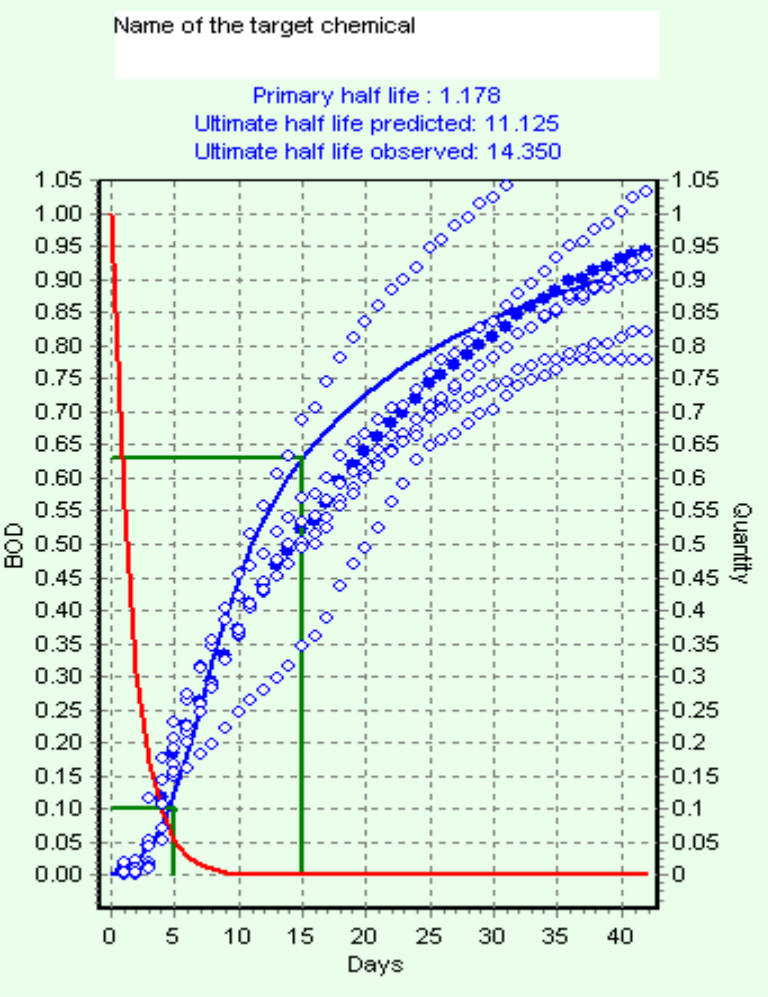



**Observed kinetic data BOD or ThCO2**

# Model predictions

## Simulated biodegradation pathways and kinetic curves

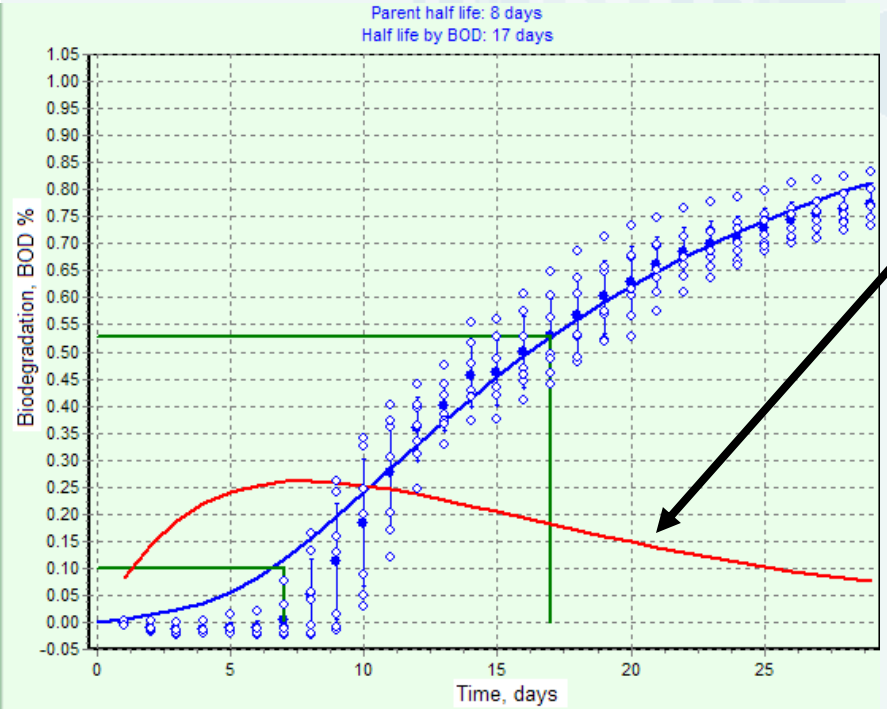




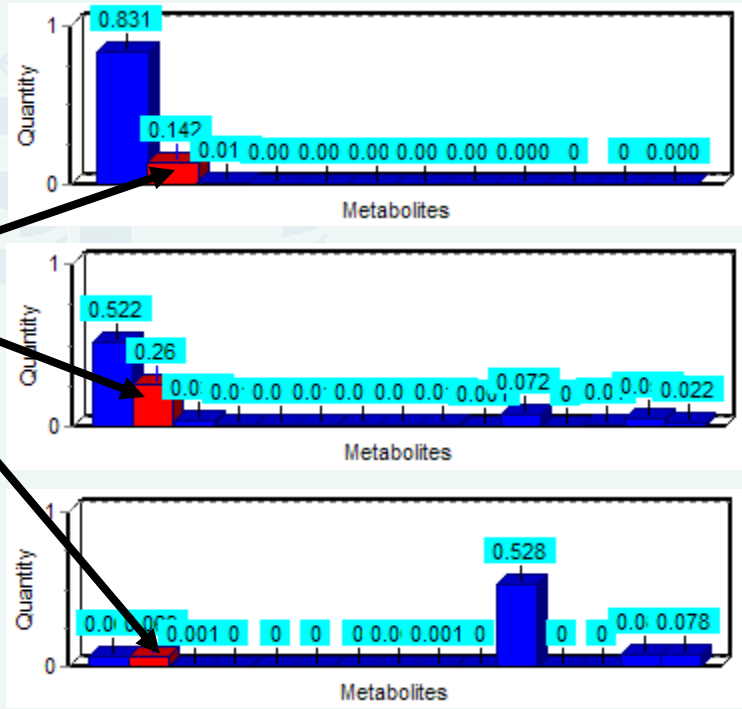
# Model predictions

**The models are able to predict within OECD 301B and F tests:**

1. Primary half-life – half-life of parent chemical
2. Ultimate half-life – half-life by BOD or ThCO2
3. Biodegradation at different days
4. Metabolites quantity at different days
5. Biodegradation within 10 days window




Metabolite



# Conclusions

**CATALOGIC 301 B and F models have**

1. Strong mechanistic background ,
2. Clear algorithm and transparent predictions,
3. Defined applicability domain,
4. Appropriate measures of goodness-of-fit, robustness and predictivity.

**Practically, these are OECD principles for use (Q)SARs for regulatory purposes**