

Screening for PBT by use of QSARs

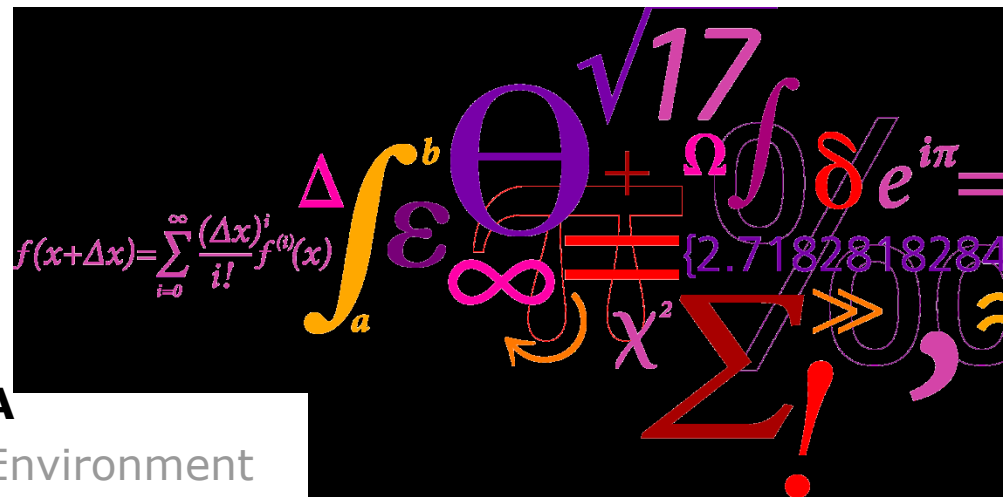
2002

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Eva B. Wedebye & J. Niemelä, DTU Food

Thomas Krig Petersen Danish Product Register

Dick Sijm, RIVM, NL



Danish QSAR prediction database

Commercial, in-house & publicly available models for

- **Physico-chemical properties**
- **Absorption, distribution, metabolism**
- **Degradation, bioconcentration, ecotoxicity** (fish, daphnia, algae, tetrahymena)
- **Human health endpoints**, e.g. acute toxicity, skin irritation, sensitization, teratogenicity, endocrine disruption, mutagenicity, cell transformation, cancer

Danish QSAR database - internet version (published 2004)

**Predictions from 60 QSAR models for around
166.000 substances
- with AD information for all DTU Food models**

- Free access: <http://qsar.food.dtu.dk>,
- Manual: <http://ecbqsar.jrc.it>

Danish QSAR database - internet version

- **Search:**
- CAS and 2D structure
- Predictions
- AD calls for Mcase predictions >(y/n)
- Combinations of predictions (and/or/not)

- **Models are made in or obtained from mainly**
- MultiCASE
- Episuite (v. 3.2)
- Equations based on literature

Screening for PB(T)s

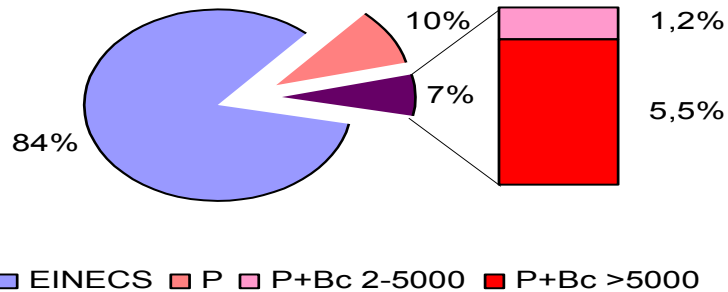
- Started in 2001: UK, Nordic, ECB and D exercise on HPVCs (> 1000 tpa/producer) mostly based on test data
- DK-EPA QSAR exercise on H- & MPVCs (>10tpa/producer)
- We proposed screening criteria based on combination of QSAR model predictions
- they are referred to in the current TGD for expert case by case use on non-tested chemicals / endpoints

DK EPA Screening for candidate PBTs by use of QSARs

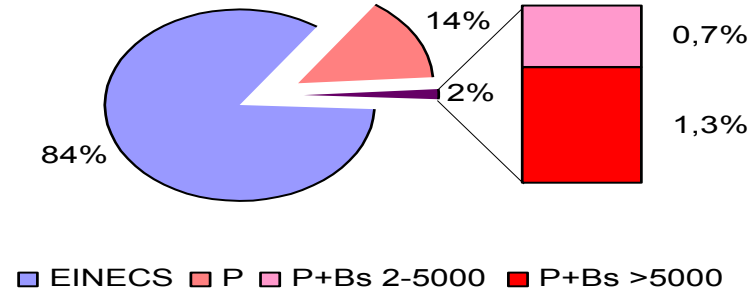
- **P**ersistency: 3 models in an algorithm predicting not
 - ready biodegradability (BIOWIN 2 & 6) and
 - long environmental half life (BIOWIN 3) \Rightarrow **P**, and then
- **2** models regarding BCF in fish:
 - BCFWIN $> 2000 \Rightarrow$ B or
 - BCFWIN < 2000 but BCF(Connell) > 2000 AND positive expert judgements (2 experts , e.g based on hindrance for uptake due to molecular dimension or the potential for metabolisation) \Rightarrow **B**; i.e.

\Rightarrow **(un-tested) PB-candidates**

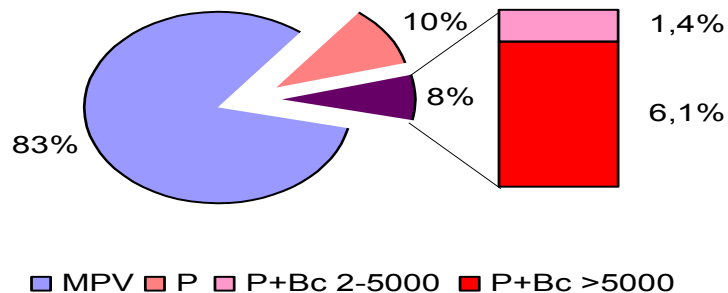
46706 EINECS



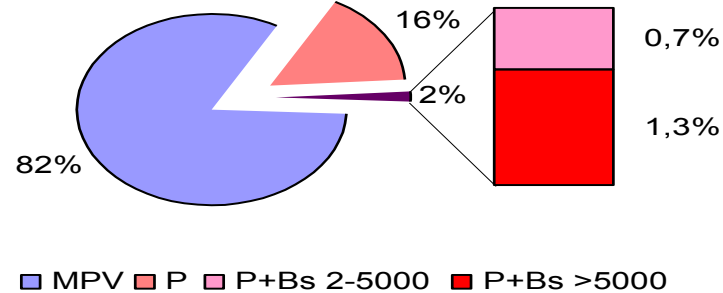
46706 EINECS



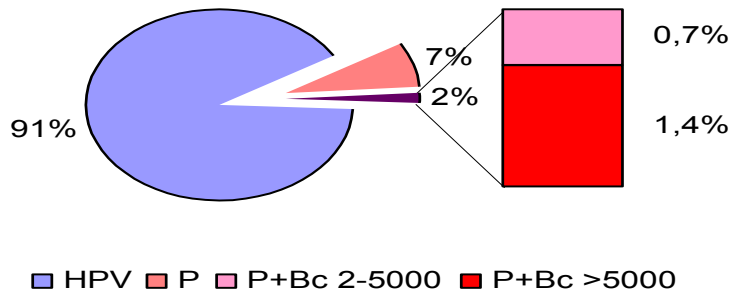
4165 MPV Substances



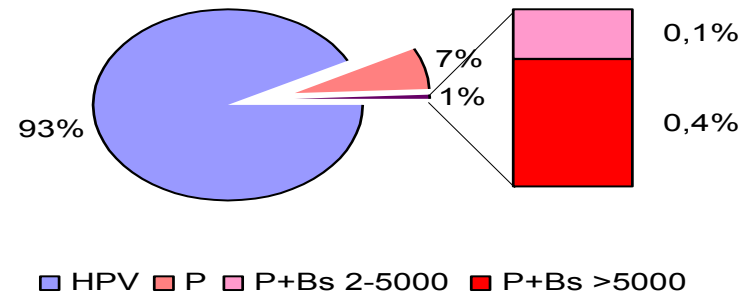
4165 MPV Substances



1351 HPV Substances



1351 HPV Substances



PB(T) screening by use of QSARs: Further evaluation: environmental release potential.

- No of substances (> 10 tpa/ EU producer) evaluated: 5716
- Total no. of PBs (potential PBTs/vPvBs) as identified by QSARs: 134
- No. of identified PBs registered in *Nordic Product Registers*: 66

- **No with potential significant environmental release due to “widespread use” in products on the market : 16-32**

(the number depends of the operational definition of “significant environmental release potential” in rel. to no & use of products)

excluded: PBT/vPvB candidates released from (industrial) processes & multi-constituent chemicals (mixtures), nevertheless:

→

no. of relevant PBT/vPVBs is relatively **small** according to this QSAR based screen (**used as an argument for the feasibility of introducing the PBT concept under REACH !**)