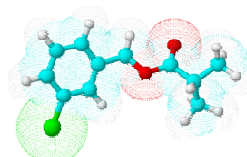


# (Q)SAR Approach for Migrants from Food Packaging Materials

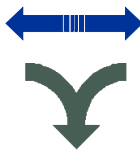
Qasim Chaudhry (Fera, York)



## (Q)SAR Modelling



Chemistry



Hazard characterisation

Physicochemical descriptors

Statistical algorithm

Mathematical equation

- Allows to assess chemical safety in the absence of test data;
- Saves time/ cost/ use of animals

NOAEL =  
...mg/kg  
bw/day



## Why consider QSAR especially for FCM ?

- Methods to estimate exposure and hazard of migrants from non-plastic FCMs is critical to any progress in legislating these FCMs
- EFSA endorses the use of thresholds of toxicological concern (TTC) to set levels of tolerable exposure for different chemical classes – with some caveats.
- ESCO reviewed status of assessments of substances in lists of Member State approvals. For many they could not find evidence of safety evaluation to modern standards (SCF/EFSA requirements fr 1991).
- The NIAS (not intentionally added substances) have to be evaluated too, which is very problematic.



3

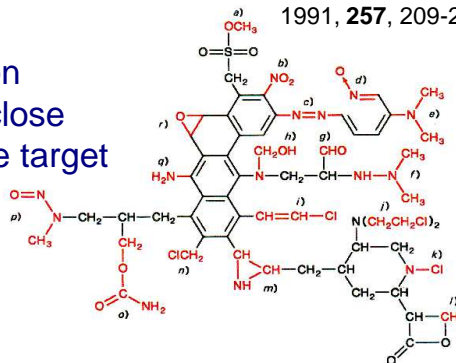
facet

## Predictive Computational Modelling

In silico models for assessment of chemical toxicity can be:

- structural alert based
- read-across based – extrapolating from data on substances that have a close structural/ similarity to the target substance
- rule-based
- SAR-based

Ashby and Tennant, Mutation Research, 1991, **257**, 209-27



facet

## QSAR Approach for Migrants from FCMs

.....

**Can predicted estimates of toxicity be derived for packaging migrants for which experimental data are not available ?**



### The study set

.....

- **Study used a set of 76 food contact substances - 47 individual substances and 29 'defined' or 'non-defined' mixtures;**
- **Single substances could be assessed as such whereas analogous substances (97) were selected to represent the mixtures**
- **Applicability of various *in silico* methods was evaluated for:**
  - Rat oral LD50
  - Carcinogenicity
  - Mutagenicity
  - Reproductive or developmental toxicity
  - Skin sensitisation.
- **Predicted values were compared with exper. data where available**



## (Q)SAR Dealing with mixtures

.....  
“ Polyester of adipic acid with 1,3-butanediol, 1,2-propanediol and 2-ethyl-1-hexanol. CAS no. 073018-26-5. The weight averaged molecular weight is 2064 and less than 8% of the substance is below 1000 Da “

- 6 individual substances were selected to represent this mixture



## The tools used

- .....
- **Where possible, *in silico* systems used were those that are either open source or publicly available software:**
    - OECD QSAR Toolbox
    - Toxicity Estimation Software Tool (TEST)
    - Structural alerts from DEREK Nexus
    - VEGA Tools Bioclipse Opentox
    - Toxtree Cramer indices
  - **A ranking scheme was developed for chemical migrants to assist in decision for further toxicological testing or not**
  - **A workflow was derived to aid end users to make reliable validated predictions from a range of freely available (Q)SAR tools**

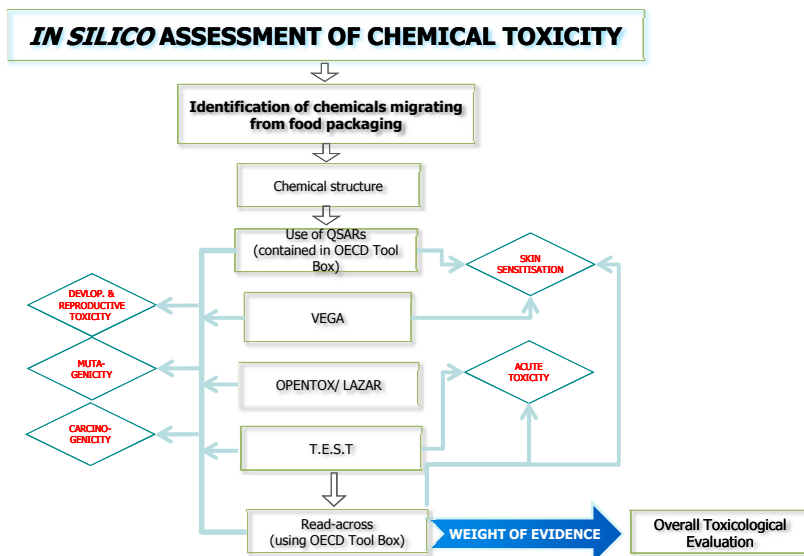


## Key Findings

- Cramer classification tends to classify most compounds towards the highest risk category;
- Excepting Cramer, *in silico* assessments showed low numbers of high-risk compounds, probably because FCM substances have already gone through some level of scrutiny for safety;
- A “weight of evidence” approach is the most promising route to *in silico* toxicity assessment of untested compounds;
- A workflow schema is proposed that uses freely available *in silico* tools, but this should be used by trained/ experienced individuals to ensure proper validation of the results obtained;
- Read across using OECD Toolbox is well suited for the purpose but cannot be reduced to a ‘black box’ system as it requires assembling structurally/ functionally similar compounds, and hence needs expert knowledge to conduct and interpret the assessment.



## Overall workflow for predicting the toxicity of new (untested) food contact substances



## Food contact materials; session outline

.....

1. Laurence Castle, FERA, UK  
**Scene setting, what was needed & how was it all put together**
2. John Dixon, Facet Industry Group, BE  
**Packaging composition and usage**
3. Roland Franz, Fraunhofer IVV, DE  
**Development of the migration model**
4. Laurence Castle  
**Use of QSAR modelling for migrants**
5. Cian O'Mahony, Crème Global, IE  
**Software description and demo**
6. All  
**General questions and discussion**

