Concawe
Environmental Science for European Refining

Challenge 2:

The Hydrocarbon Block Method for PBT Assessment of Petroleum Substances

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Challenge

How to progress PBT assessment of petroleum UVCB substances in a scientifically sound, regulatory-acceptable and timely manner, with a testing program taking into account that state-of-the-art analytical techniques cannot identify all constituents?

Preamble

According to R.11 guidance, the **recommended approach to assess the PBT properties of complex UVCBs is through the fraction or block profiling approach**, in which a "*substance can be divided into fractions/blocks, in which the constituents are structurally similar or in which the constituents are to such extent similar that their degradation, bioaccumulation and toxicity properties can be predicted to follow a regular predictable pattern*".

Concawe have adopted this approach in the form of the **hydrocarbon block method (HCBM).** To implement the HCBM, chemical composition of petroleum substances is determined by GCxGC analysis, which **separates out constituents based on volatility and polarity.** This analytical information is translated as hydrocarbon blocks defined by single carbon number and chemical class.

However, **volatility and polarity alone are not always sufficient to ensure structural similarity** for PBT purposes among near-eluting constituents, and we do not have detailed analytics providing constituent level information. Additionally, we **lack a pragmatic definition of similarity of constituents in a block**.

Specific Challenge Questions

- **Considering the complexity of the petroleum substance UVCBs, how can we bridge the analytical capabilities and the requirements of the blocking approach for Persistence/Bioaccumulation/Toxicity (PBT) assessment purposes?**

- **Specifically, what would be the criteria for homogeneity of a block* and for choosing representative constituent(s) of a block?**

* ". . .constituents are structurally similar or in which the constituents are to such extent similar that their degradation, bioaccumulation and toxicity properties can be predicted to follow a regular predictable pattern"

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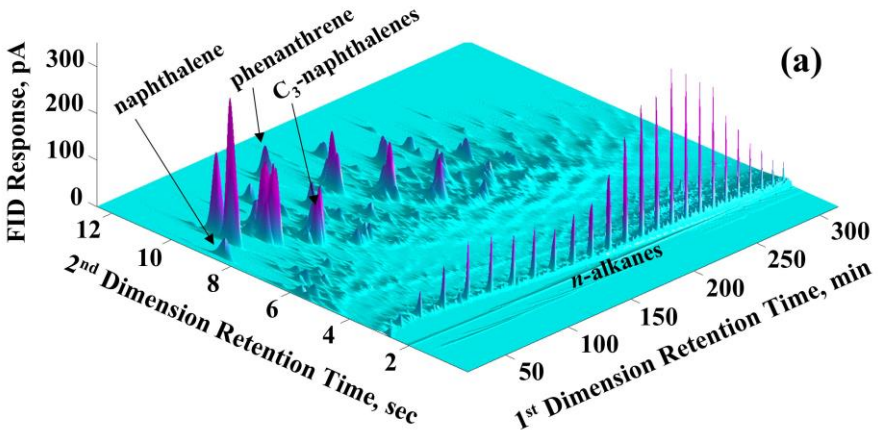
Approaches for PBT assessment of UVCBs

Petroleum substances contain hundreds to millions of constituents

Options for addressing UVCBs according to R.11 :

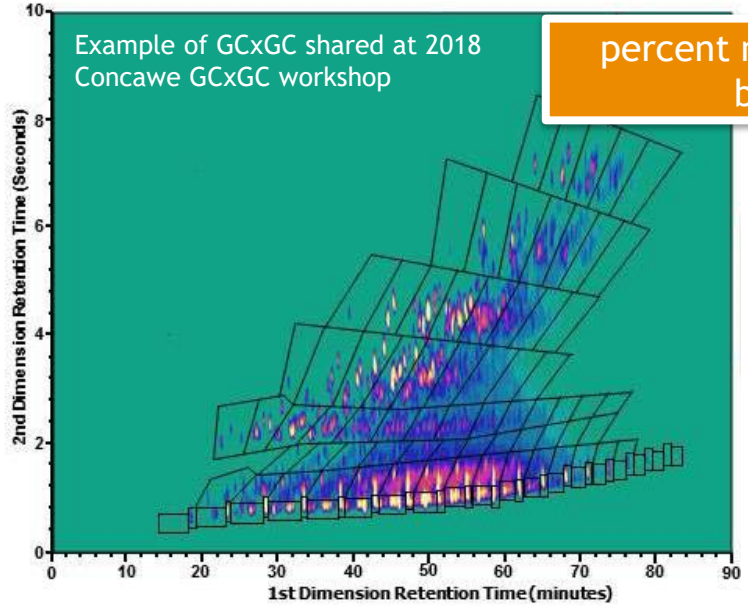
1. Whole substance testing
   - Approach for Human Health
   - *Tailored approach for P & B with constituent tracking (ongoing work)*
2. Known constituents
3. Block profiling (hydrocarbon block method)
   - Petroleum substances are different types of hydrocarbons; relatively easy to divide into blocks using analytical method
   - Like constituents are grouped to simplify the number of entities for assessment
   - Every constituent in a block is supposed to be representative of that block
   - Captures variability since biological impact of constituents in a block should be similar



Disentangling Oil Weathering Using GC×GC. 2. Mass Transfer Calculations. J. Samuel Arey, Robert K. Nelson, Desiree L. Plata, and Christopher M. Reddy. Environmental Science & Technology 2007 41 (16), 5747-5755. DOI: 10.1021/es070006p

What is Concawe's Hydrocarbon Block Method*?

- Based on a combination of polarity and volatility, yielding information on chemical class and C#
- Assumes constituents in a block will have similar fate, hazard & risk
- Most petroleum substances are resolved into selected hydrocarbon blocks with GCxGC analysis
- HCBM with test or QSAR data for each block is the basis for environmental hazard and risk assessment, with supporting whole substance experimental data



percent mass of each block

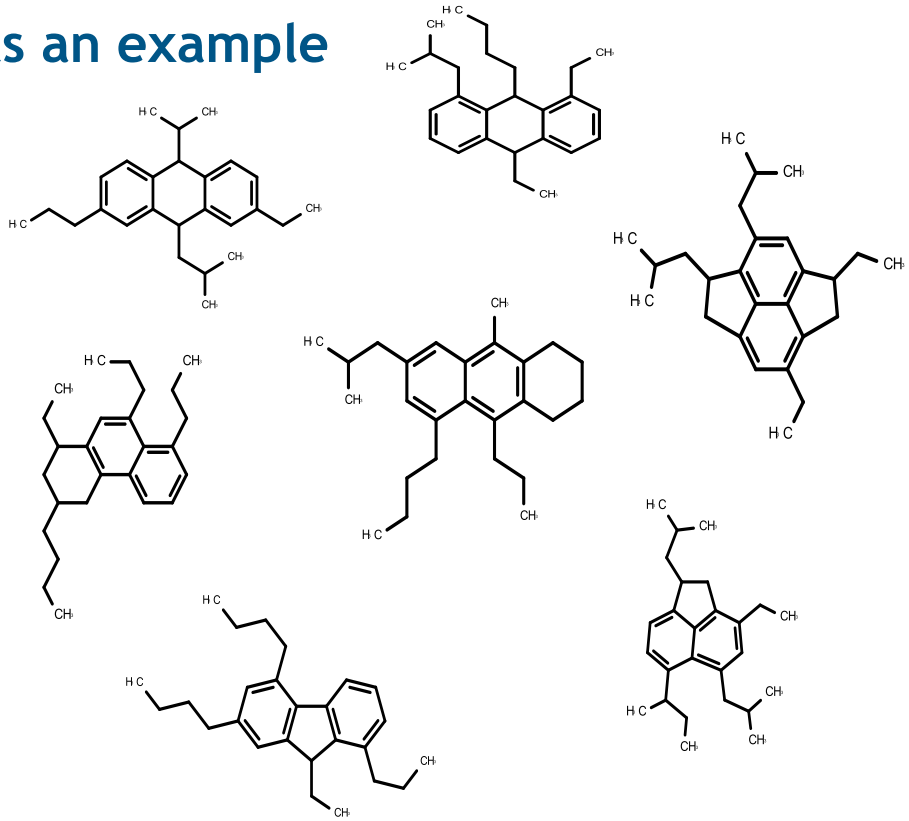
Carbon #	n-paraffins	iso-paraffins	mono-naphthenics	di-naphthenics	polynaphthenics	mono-aromatics	naphthenic mono-aromatics	di-aromatics	naphthenic di-aromatics	polyaromatics	naphthenic polyaromatics
6											
7											
8											
9											
10											
11											
...											
30											

* King DJ, Lyne RL, Girling A, Peterson DR, Stephenson R, Short D. 1996. Environmental risk assessment of petroleum substances: the hydrocarbon block method. Concawe report No. 96/52. https://www.concawe.eu/wp-content/uploads/2017/01/rpt_96-52-2004-01719-01-e.pdf

What is in a block?

C26 naphthenic diaromatics (NDA) as an example

- Range of representative constituent structures (see figures)
- Range of persistence half-life of representative constituents:
  - 20.5 - 540.8 days (BioHCWin)
  - NDA >C15 considered P/vP (based on QSAR and experimental data)
- Range of BCF of representative constituents:
  - 2.41-3.13 (based on BCFBAF Arnot-Gobas prediction)
  - NDA C12-30 concluded not B based on experimental BMF/TMF data and QSAR



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HCBM is used to assess PBT: P assessment in 2019 PBT Report

- Generated 16,000 hypothetical constituents by computational/statistical model (1 to 371 constituents/ block)[1] – these represent a small subset of possible PS constituents
- Assess the constituents in each block for P using test data & QSAR
- Majority of data is from testing, unless where a * indicates data from QSAR or read-across
- Blue indicates P/vP; tend to be harder to obtain constituents and harder to test

[1]Kutsarova, S.S. et al. 2019, Env. Toxicol. Chem.

Blocks in the petroleum substance hydrocarbon space

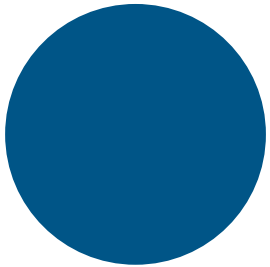
C#	n-P	i-P	MN	DN	PN	MA	NMA	DA	NDA	PA	NPA
6	Not P	Not P	Not P	-	-	Not P	-	-	-	-	-
7	Not P	Not P	Not P	Not P	-	Not P	-	-	-	-	-
8	Not P	Not P	Not P	Not P	-	Not P	-	-	-	-	-
9	Not P	Not P	Not P	Not P	-	Not P	Not P	-	-	-	-
10	Not P	Not P	Not P	Not P	-	Not P	Not P	Not P	-	-	-
11	Not P	Not P	Not P	Not P*	-	Not P	Not P	Not P	-	-	-
12	Not P	Not P	Not P	Not P	-	Not P	Not P	Not P	Not P	Not P	-
13	Not P	Not P	Not P	Not P	-	Not P*	Not P	Not P	Not P	Not P	-
14	Not P	Not P*	Not P	Not P	P/vP	Not P	Not P	Not P	Not P	Not P	-
15	Not P	Not P	Not P	P/vP	P/vP	Not P	Not P*	P/vP*	Not P	Not P	-
16	Not P	Not P	Not P	P/vP	P/vP	Not P	Not P	P/vP	P/vP	Not P	Not P
17	Not P	Not P*	Not P	P/vP*	P/vP*	Not P*	P/vP*	P/vP	P/vP*	Not P	Not P
18	Not P	Not P*	Not P	P/vP*	P/vP	Not P	P/vP	P/vP	P/vP	P/vP	P/vP
19	Not P	Not P	P/vP*	P/vP*	P/vP	P/vP*	P/vP	P/vP*	P/vP*	P/vP	P/vP
20	Not P	Not P	P/vP*	P/P*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP	P/vP*
21	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP	P/vP*
22	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP	P/vP*
23	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
24	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
25	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
26	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
27	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
28	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
29	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*
30	Not P	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*	P/vP*

HCBM is used to assess PBT: Conclusions in 2019 PBT Report

- Blue indicates P/vP
- Green indicates B/vB
- Pink indicates B & P/vP
- Based on test data, unless * indicates data from QSAR or read-across
- Blocks that screen P/vP and B are: C14-19 polynaphthenics, C19 monoaromatics, C17-18 naphthenic monoaromatics
- T assessment: screening based on test data and Target Lipid Model on all blocks screened as P + B
- No blocks screen as PBT or vPvB (subject to change with new data)

Blocks in the petroleum substance hydrocarbon space

C#	n-P	i-P	MN	DN	PN	MA	NMA	DA	NDA	PA	NPA
6	Not B*	Not B*	Not B	-	-	Not B*	-	-	-	-	-
7	Not B*	Not B*	Not B	Not B*	-	Not B*	-	-	-	-	-
8	Not B*	Not B	B	Not B*	-	Not B*	-	-	-	-	-
9	Not B	B	B	Not B	-	Not B	Not B*	-	-	-	-
10	Not B*	Not B	B	B	-	Not B	Not B	Not B	-	-	-
11	Not B*	Not B	B	B*	-	Not B	Not B*	Not B	-	-	-
12	Not B	Not B	B	B	-	Not B	B*	B	Not B	Not B	-
13	B	Not B	Not B	Not B	-	Not B	B*	B/vB	Not B	Not B	-
14	B/vB	Not B*	Not B	Not B	B*/P/vP	Not B	B	Not B	Not B	Not B	-
15	Not B	Not B	Not B*	Not B*	B*/P/vP	Not B*	B	Not B*	Not B	Not B	Not B*
16	Not B	Not B*	Not B*	Not B	B/P/vP	B	B	Not B	Not B	Not B	Not B
17	Not B*	Not B*	Not B*	Not B*	B/P/vP	B*	B*/P/vP*	Not B	Not B*	Not B	Not B
18	Not B*	Not B*	Not B*	Not B*	B/P/vP	B*	B/P/vP	Not B	Not B	Not B	Not B*
19	Not B*	Not B*	Not B*	Not B*	B/P/vP	B*/P/vP*	Not B	Not B*	Not B*	Not B	Not B*
20	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B	Not B
21	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
22	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
23	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
24	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
25	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
26	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
27	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
28	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
29	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*
30	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*	Not B*

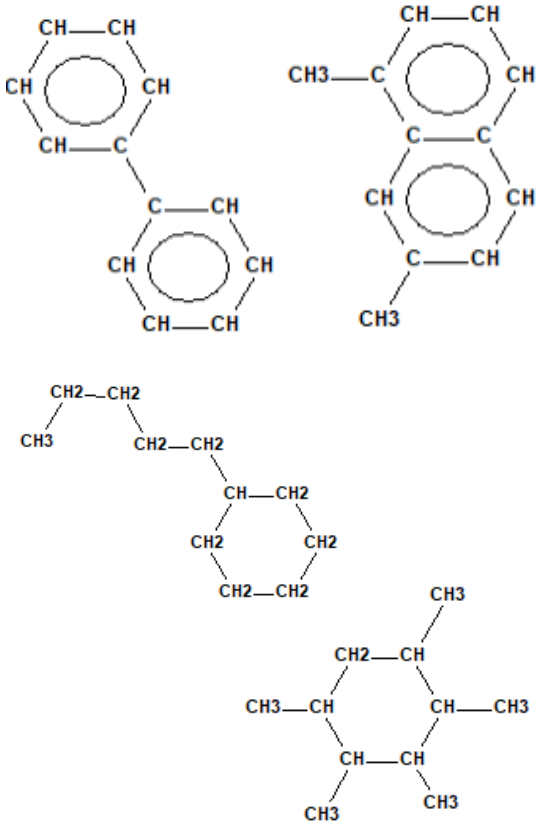


Questions on the HCBM

Hydrocarbon Block Homogeneity/ Structural Similarity (1/2)

In the current Concawe Approach:

- Substances are subdivided into blocks based on GCxGC
- Therefore, constituents in a block share polarity & volatility, but not explicitly structural similarity
  - e.g., naphthalenes and biphenyls
  - e.g., structure with 5 methyl groups would be grouped with same structure with pentyl group
- BUT every constituent in a block is supposed to be representative of that block
- SO, what variation in properties is acceptable in a block? There is no practical definition of similarity



Hydrocarbon Block Homogeneity/ Structural Similarity (2/2):

What level of similarity is needed within a block for PBT assessment?

- What metrics should be used for similarity that would be relevant for PBT assessment?
  - Phys-chem properties – current method uses polarity and volatility
  - Ecotoxicological impact – previous proposals suggested a range of persistence half-life and log Kow
  - Structure – such as similar functional group, maximum diameter, steric hindrance, etc.

- What range of variation in those metrics is acceptable?

- Is it possible to support these metrics analytically (can we distinguish the required features)?

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Choosing Representative Constituents of a Hydrocarbon Block for PBT Assessment

Current Concawe Approach:

- Representative constituents are a combination of hypothetical & identified molecules
- Many representative constituents per block

Questions to consider:

- How do you confirm that a hypothetical constituent is truly found in PS? Can whole substance work inform choice of representative constituents?
- For a homogeneous block, would one representative constituent be sufficient to represent the whole block?
- If a block is not homogeneous, what would make a good representative constituent? Most prevalent? Most conservative? Most relevant (occurs in most PS)?
- How can we bridge the analytical capabilities and the requirements of the blocking approach for PBT purposes?

GGRAPH	n-paraffins	iso-paraffins	mono-naphthenics	di-naphthenics	mono-aromatics	naphthenic mono-aromatics	di-aromatics	naphthenic di-aromatics	tri+-aromatics	naphthenic tri+-aromatics
10	1	26	11	14	4	5	1			
11	1	35	23	29	11	15	2			
12	1	46	39	42	21	32	10	1		
13	1	55	54	60	35	48	16	7	1	
14	1	64	66	60	49	54	30	24	2	
15	1	72	74	73	60	66	33	47	5	
16	1	77	80	60	68	68	54	70	14	2
17	1	82	84	71	75	79	69	83	29	10
18	1	85	86	80	79	86	79	89	50	30
19	1	88	88	85	83	89	85	92	66	56
20	1	90	90	81	85	91	89	94	78	75
21	1	92	91	86	87	93	91	95	85	86
22	1	93	91	91	88	94	92	95	89	90
23	1	93	91	93	89	94	93	95	91	94
24	1	94	91	93	89	94	93	95	93	92
25	1	94	89	93	87	94	93	95	94	94
26	1	95	87	93	84	94	93	95	94	96
27	1	95	82	92	78	94	92	95	94	95
28	1	96	75	90	68	92	90	95	95	92
29	1	96	68	86	63	89	85	94	95	95
30	1	96	48	76	48	81	71	90	95	94

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Thank you for your attention

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