Safety and toxicity assessments and methodology

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for Research & Innovation

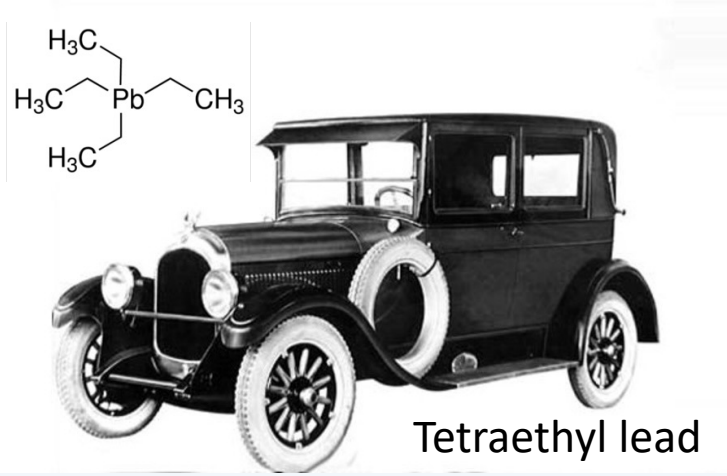
Why conduct safety testing?

Safeguard human health
Reduce environmental impact
Regulatory compliance

Maintain optimal product performance

Safety and Sustainability in PERFECOAT

How things used to be



Tetraethyl lead

Dichlorodifluoromethane
(CFC – Freon)

Thomas Midgley, Jr.
(1889-1944)
American Chemist

Develop a technology that works really well → **Find out later it is destroying the planet**

Importance of early toxicity testing

- Facilitate early go-no go decisions:
  - Prevent time loss on developing (a group of) molecules with a non-favourable toxicity profile
  - Improved overall toxicity profile from starting materials - intermediates - final materials
- Give guidance for further testing
- Facilitate compliance with regulatory requirements
- Market introduction of safe bio-based products

Safety and Sustainability in PERFECOAT

Safety testing…….how?

Chemical

?

Toxicology

Classical testing of toxicity: *in vivo* (animal) testing extrapolated to human hazard

- Time-consuming
- Non-ethical
- Technical concerns with animal testing
- Search for methods to reduce or eliminate animal testing (“3 - Rs“ – reduce, refine, replace)

SSbD of High Performance Bio-based Functional Coatings for Wood and Decorative Applications

WP6 Task 6.1 Chemical safety assessment

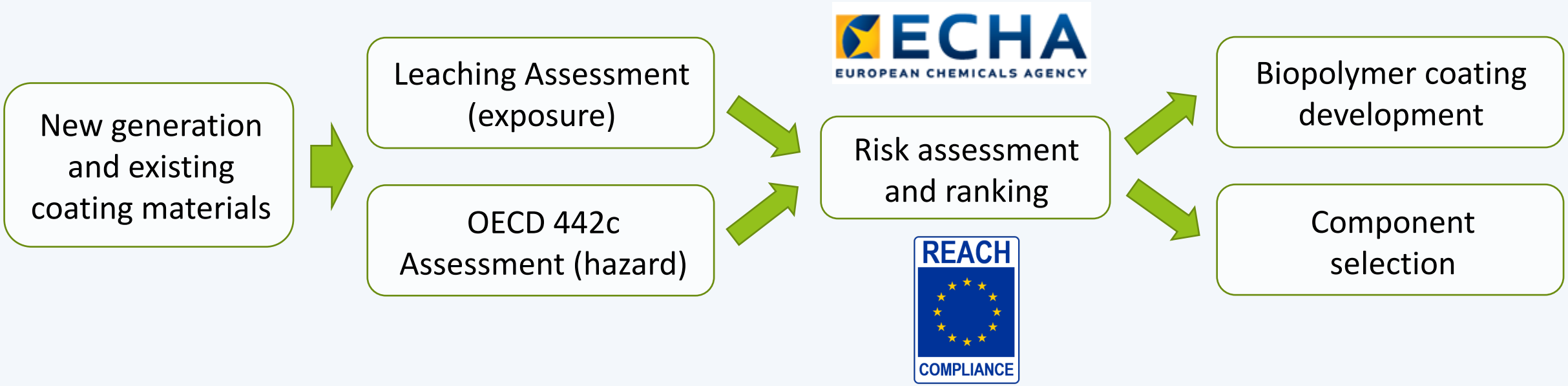
- **Objectives:**
- Feedback key chemical risk information for all candidate biopolymer coating materials (iterative 'safe by design' approach).
- Conduct leaching studies to determine components transferring from the polymer to (i) water and (ii) those that may cause skin irritation.

Task 6.1 - Chemical safety assessment

Conduct a comparison of the chemical exposure risks between the new and existing materials.

All major chemicals identified in the product leachates will be quantified and cross-referenced with the European Chemicals Association (ECHA) database and EU REACH regulation (EC 1907/2006).

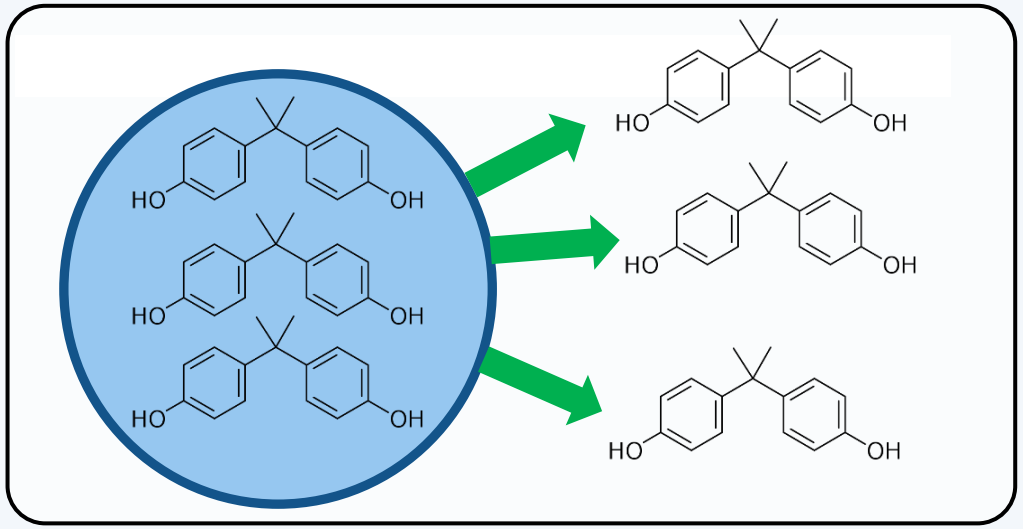
Alternative will be proposed to substitute chemicals having the highest risk.



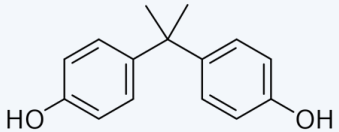
Leaching studies

Aqueous leaching

(Additives, residual chemicals, monomers)



Coating material on glass slide



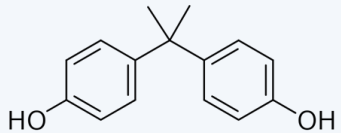
Bisphenol A

(example ingredient)

LC-MS Analysis

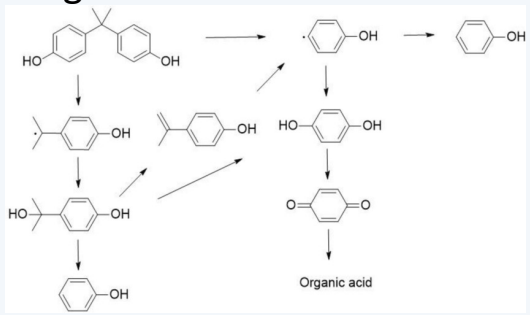
Target and non-target screening

Target

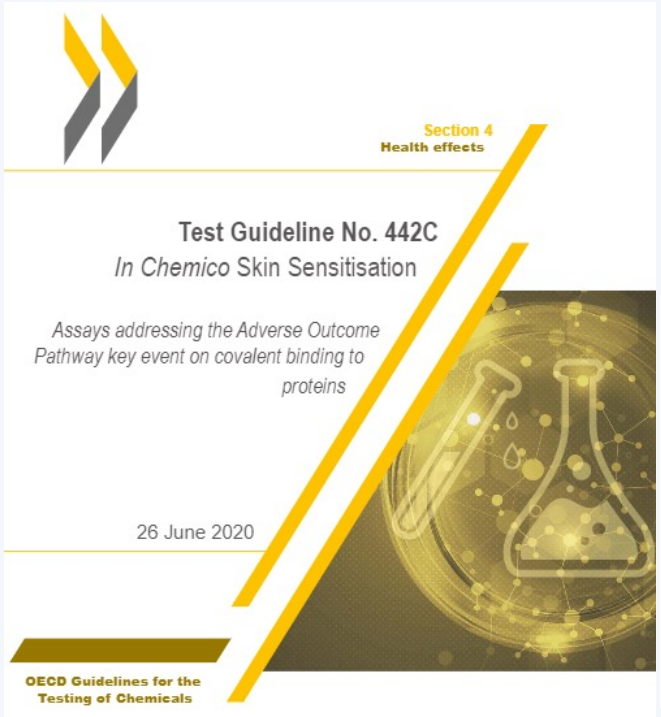


Bisphenol A

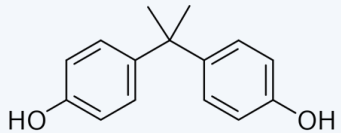
Non-target



OECD 442c – Skin Sensitisation



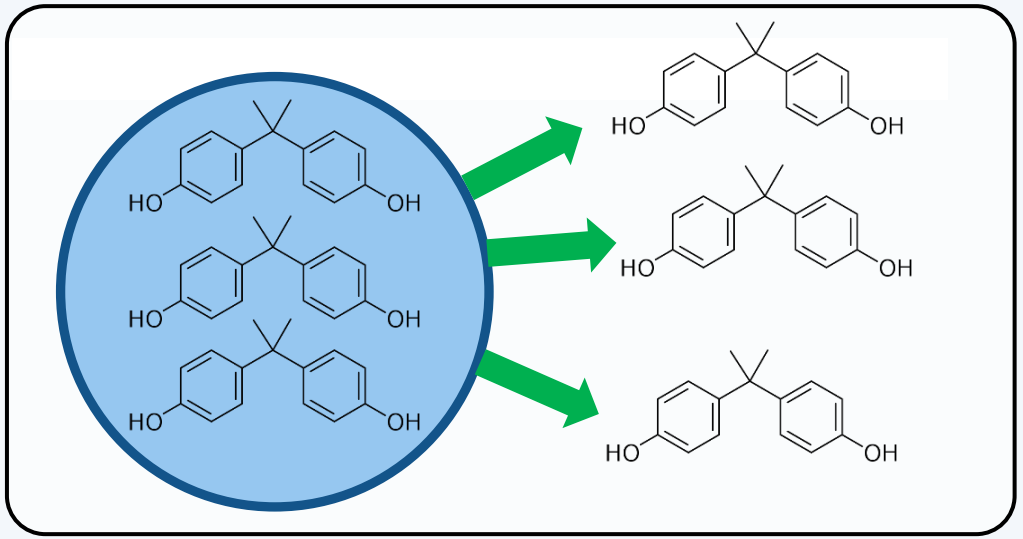
An in *chemico* procedure (Direct Peptide Reactivity Assay – DPRA) used for supporting the discrimination between skin sensitisers and non-sensitisers.



Bisphenol A (example ingredient)

Aqueous leaching

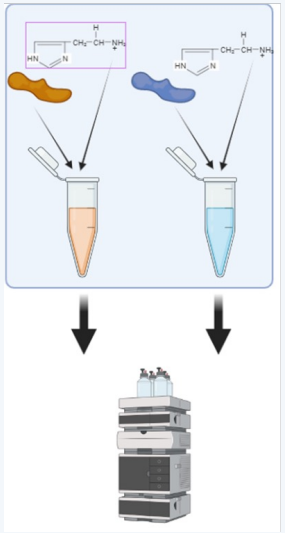
(Additives, residual chemicals, monomers)

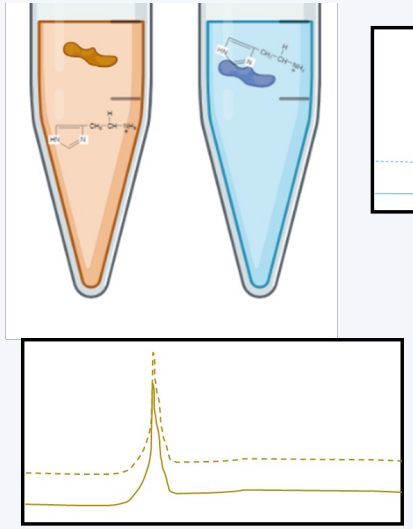


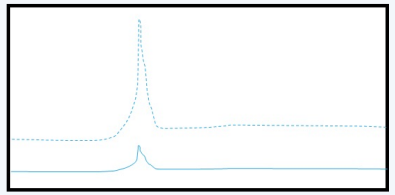
- Need to test a pure chemical with a known molecular weight or average molecular weight
- Can be done with pure chemical or as a leachate, but concentration must be known
- Cannot be used on particles – <u>only chemicals</u>

Establishment and validation

- Established skin sensitisation method based on a chemical procedure (DPRA) and using this for supporting discrimination between skin sensitisers and non-sensitisers in fossil fuel and bio-based coating ingredients.





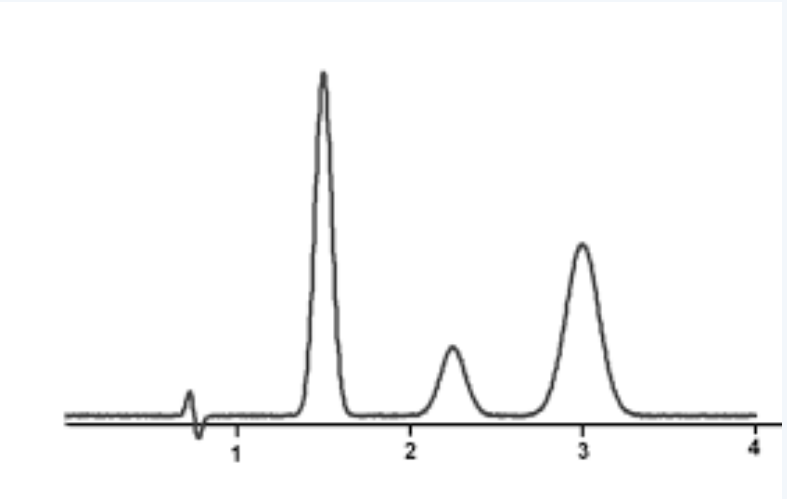


- The method tested and validated using the 4 recommended reference chemicals (see table).
- Further improvement of the accuracy and sensitivity of the method by developing an LC-MS/MS method for the quantification of peptides.
- Method is now being applied to chemicals and coatings.

	CYS	LYS	Mean depletion	Reactivity	Model
Cinnemaldehyde 1	85.63%	72.62%	79.13%	high	Cysteine/Lysine
Vanillin 1	100.00%	inconclusive	100.00%	high	Cysteine-only
Formaldehyde 1	43.19%	2.82%	23.01%	moderate	Cysteine/Lysine
Ethylene glycol 1	97.32%	4.05%	50.69%	high	Cysteine/Lysine

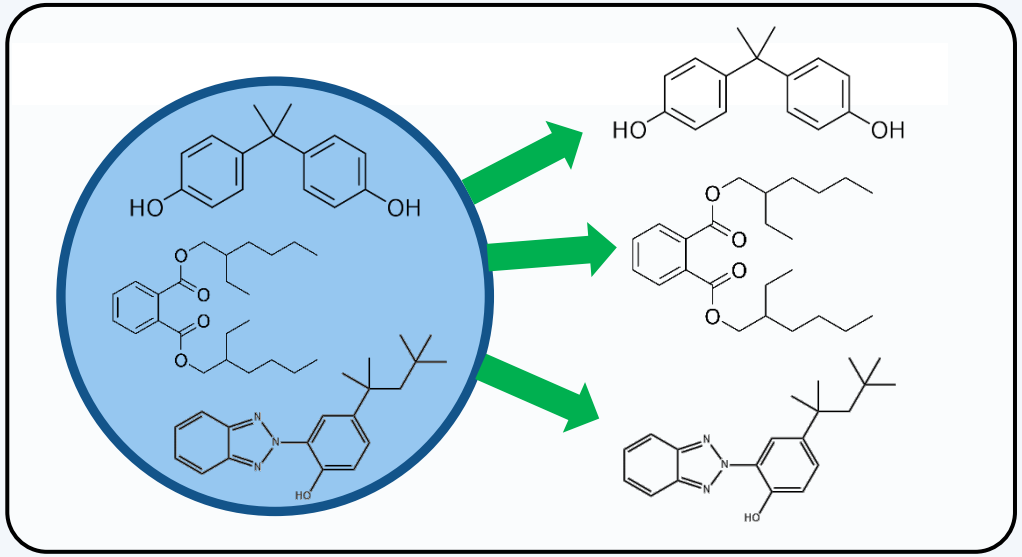
OECD 442c – Skin Sensitisation

Some ‘individual’ ingredients are actually mixtures of chemicals



Need to determine the individual or average molecular weights

Coating products produce leachates with multiple chemicals

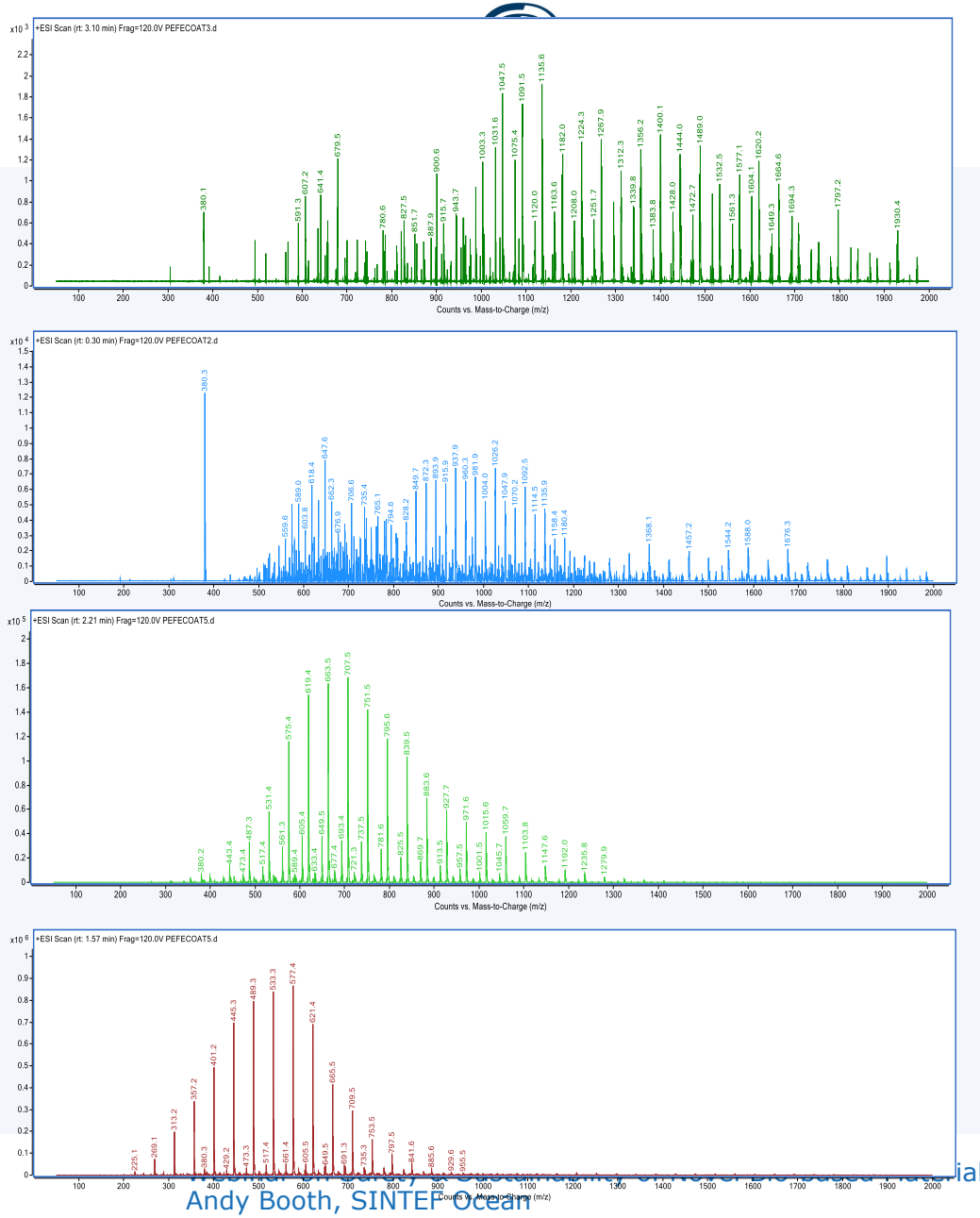


Challenge with chemical leachates mixtures: must know concs & MWs!

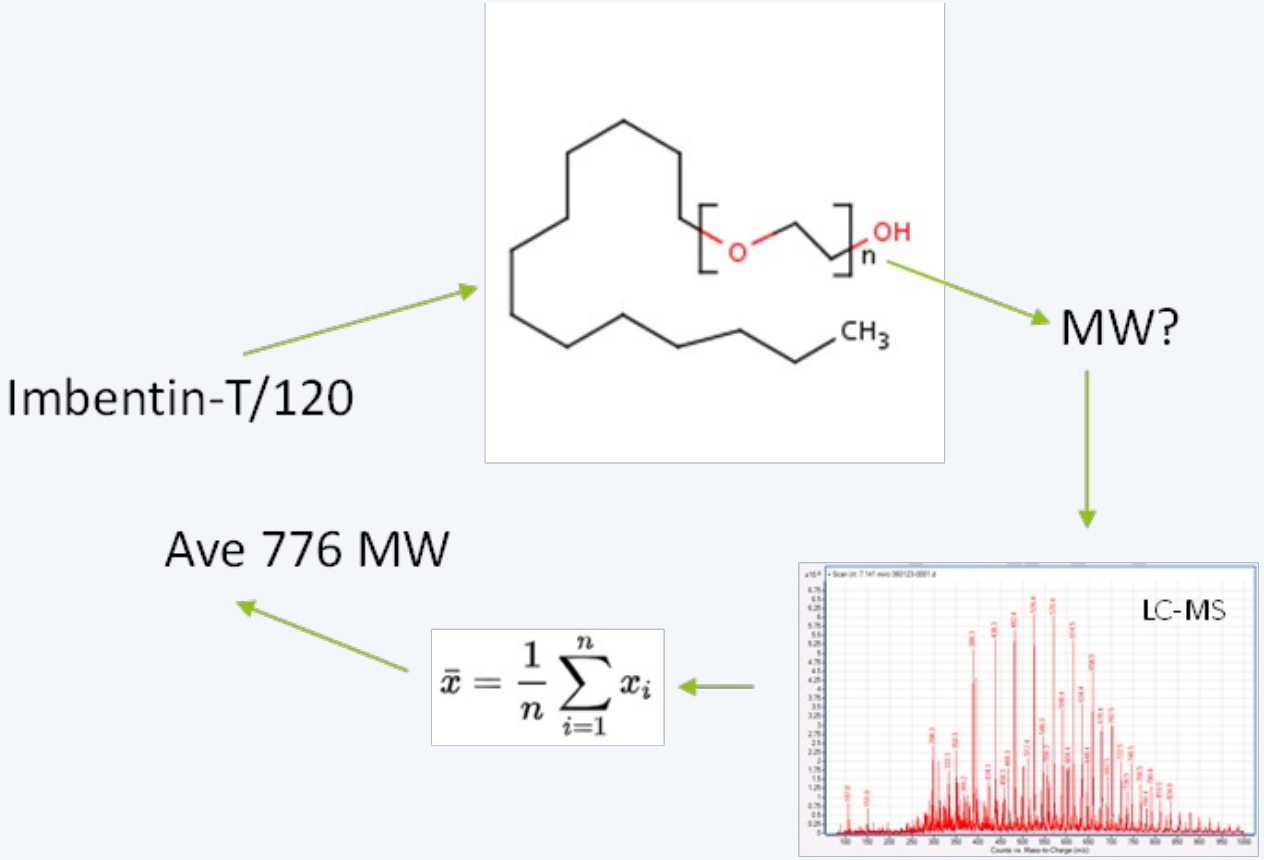
Assessment of coating components

Requires molecular weight of test chemical to be known

No.	Compound/Component	MW (g/mol)
1	Disponil SLS 101 Special	674
2	RHODAFAC RS/710-E	324
3	Emulsogen EPN 287	?
4	Polirol AL 1347	?
5	Imbentin-T/120	?
6	AEROSOL A-102 E	?
7	$CaCO_3$	100
8	TiO_2	80
9	Propylene glycol propyl ether	178
10	Irgacure 184	204
11	Trimethylolpropane ethoxylate triacrylate	av. 428
12	Polydimethylsiloxane	236
13	Epoxyacrylate	392



Average molecular weight determination



No.	Compound/Component	MW (g/mol)
1	Disponil SLS 101 Special	674
2	RHODAFAC RS/710-E	324
3	Emulsogen EPN 287	**ave.1210**
4	Polirol AL 1347	**ave. 866**
5	Imbentin-T/120	**ave. 776**
6	AEROSOL A-102 E	**ave. 713**
7	$CaCO_3$	100
8	TiO_2	80
9	Propylene glycol propyl ether	178
10	Irgacure 184	204
11	Trimethylolpropane ethoxylate triacrylate	ave. 428
12	Polydimethylsiloxane	236
13	Epoxyacrylate	392

Results for single chemicals

- Results of the DPRA testing are in line with the other classifications.
- For some chemicals this is the first sensitisation data.
- For particle ingredients skin sensitisation cannot be determined with this method
- Testing of the method and harmonisation against an internal leaching standard operating procedure (SOP) is ongoing.

Summary from the skin sensitisation testing and comparison to existing classifications

Constituent Type	Name	CAS	Classification	CLP notifications (% of all)	Effects in-vivo (REACH)	DPRA - Skin Sensitisation (PERFECOAT)
Modifier	Calcium carbonate ($CaCO_3$)	471-34-1	Skin Irritant 2	Skin Irritant 2 (10%)	N	NA
Pigment	Titanium dioxide (TiO_2)	13463-67-7		Skin Irritant 2 (<0.1%)	N	NA
Defoamer	Polydimethylsiloxane	63148-62-9		Skin Irritant 2 (1.6%)	NA	NA
Coalescent	Propylene glycol propyl ether	1569-01-3	Skin Irritant 2	Skin Irritant 2 (20%)	N	Low
Photoinitiator	Irgacure 184	947-19-3		Skin Irritant 2 (0.1%)	N	Minimal
Diluent	TMPEOTA	28961-43-5		NA	Y	High
Main resin	Epoxyacrylate	55818-57-0	Skin Irritant 2	Skin Irritant 2 (6.5%)	Y	NA
			Skin Sensitizer 1	Skin Sensitizer 1 (92%)		
Surfactant	Disponil SLS 101 Special	111072-31-2	Pre-registration			High
Surfactant	RHODAFAC RS/710-E	9046-30-5	Not in the database			Low
Surfactant	AEROSOL A-102E	68954-91-6	Skin irritant	Skin Irritant 2 (82%)	NA	High
Surfactant	Imbentin-T/120	9043-30-5	Skin irritant	Skin Irritant 2 (21%)	NA	Low
Surfactant	Emulsogen EPN 287	?	Not in the database			Minimal
Surfactant	Polirol AL 1347	?	Not in the database			Moderate

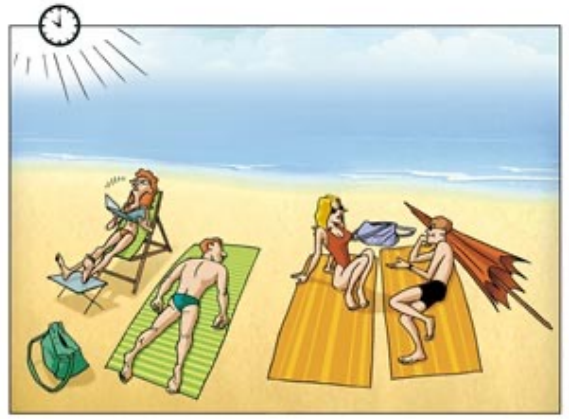
Safer by design

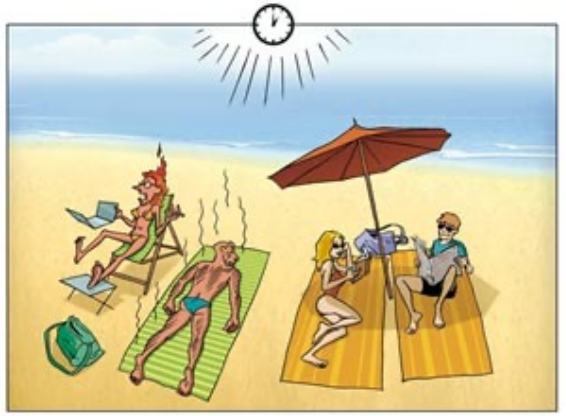
Example leaching ranking

No.	Compound/Component
1	Disponil SLS 101 Special
2	RHODAFAC RS/710-E
3	Emulsogen EPN 287
4	Polirol AL 1347
5	Imbentin-T/120
6	AEROSOL A-102 E
7	$CaCO_3$
8	TiO_2
9	Propylene glycol propyl ether
10	Irgacure 184
11	Trimethylolpropane ethoxylate triacrylate
12	Polydimethylsiloxane
13	Epoxyacrylate

Example toxicity ranking

No.	Compound/Component
1	Disponil SLS 101 Special
2	Epoxyacrylate
3	Emulsogen EPN 287
4	Trimethylolpropane ethoxylate triacrylate
5	Polydimethylsiloxane
6	Polirol AL 1347
7	$CaCO_3$
8	TiO_2
9	Propylene glycol propyl ether
10	Irgacure 184
11	AEROSOL A-102 E
12	Imbentin-T/120
13	RHODAFAC RS/710-E





Risk = Exposure x Hazard

- **Concentration**
- Prevalence
- Persistence
- Geographic location

- **Toxicity**
- Bioaccumulation
- Bioconcentration
- Species/Ecosystem levels

Safer by design

Example leaching ranking

No.	Compound/Component
1	Disponil SLS 101 Special
2	RHODAFAC RS/710-E
3	Emulsogen EPN 287
4	Polirol AL 1347
5	Imbentin-T/120
6	AEROSOL A-102 E
7	$CaCO_3$
8	TiO_2
9	Propylene glycol propyl ether
10	Irgacure 184
11	Trimethylolpropane ethoxylate triacrylate
12	Polydimethylsiloxane
13	Epoxyacrylate

Example toxicity ranking

No.	Compound/Component
1	Disponil SLS 101 Special
2	Epoxyacrylate
3	Emulsogen EPN 287
4	Trimethylolpropane ethoxylate triacrylate
5	Polydimethylsiloxane
6	Polirol AL 1347
7	$CaCO_3$
8	TiO_2
9	Propylene glycol propyl ether
10	Irgacure 184
11	AEROSOL A-102 E
12	Imbentin-T/120
13	RHODAFAC RS/710-E

High leaching + high toxicity

Med/low leaching + med/low toxicity

Low leaching + low toxicity

Example toxicity ranking

No.	Compound/Component
1	Disponil SLS 101 Special
2	Emulsogen EPN 287
3	Polirol AL 1347
4	Trimethylolpropane ethoxylate triacrylate
5	Polydimethylsiloxane
6	Epoxyacrylate
7	$CaCO_3$
8	TiO_2
9	Propylene glycol propyl ether
10	RHODAFAC RS/710-E
11	AEROSOL A-102 E
12	Imbentin-T/120
13	Irgacure 184

Summary & Reflections

- One available method for conducting safety assessment of new biobased chemicals and materials is presented
- There a many ways of conducting a safety assessment and these should be selected on a case by case basis
- Important to note that no single test allows a full safety assessment
- Standard methods increase the comparability of different data sets and increase robustness
- The approaches outlined here are cost effective and high throughput methods – potential for widespread use
- The method uses only analytical chemistry, no animals, cells or biological material

Thanks for your attention!

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