Research and Development

Modern Food Packaging Safety

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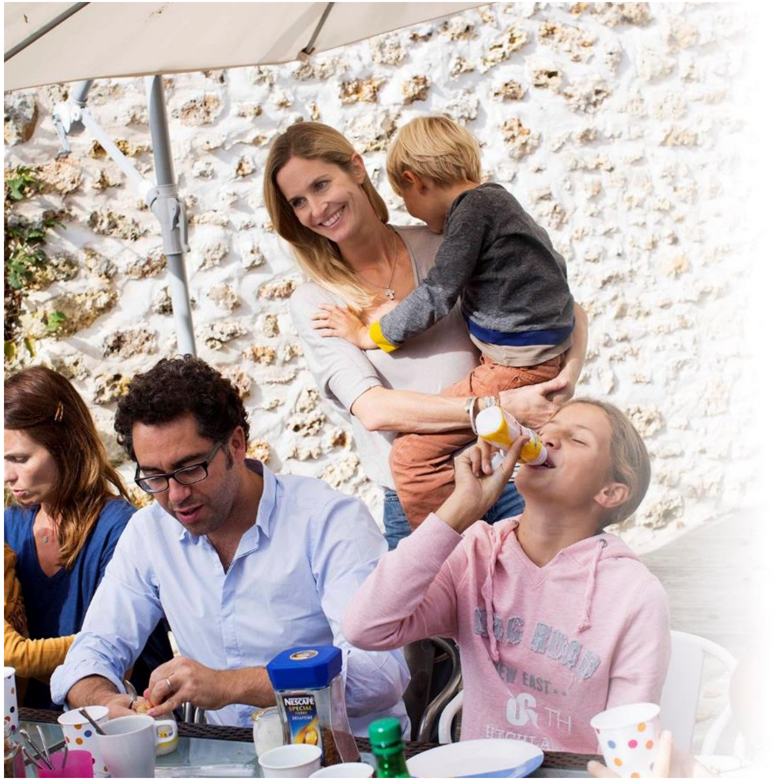
Nestlé at a Glance



- $95 billion in sales in 2017
- 323,000 employees in over 150 countries
- 413 factories in 85 countries
- > 1 billion Nestlé products sold every day in 189 countries
- Over 2,000 brands

Strong Global and Local Brands

Wide & Diverse Packaging Portfolio

$8 billion	Annual expenditure on packaging materials
4000	Packaging suppliers
66 000	Packaging materials specifications
170 000	Packaging items

Nestlé does not produce any packaging but:

- All Nestlé products are packed with printed packaging
- Nestlé is responsible for the **safety & compliance** of its products
- Packaging is a potential **source of food contamination**

Trust a fragile concept

It takes years to build trust and fidelity in brands & products

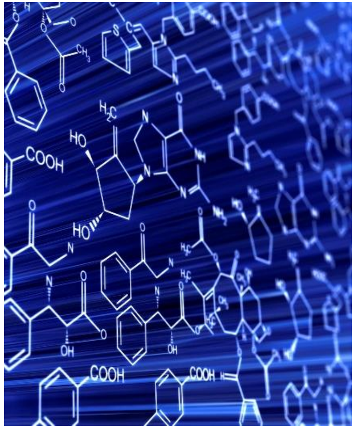
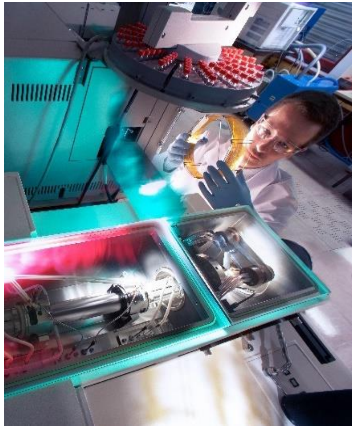
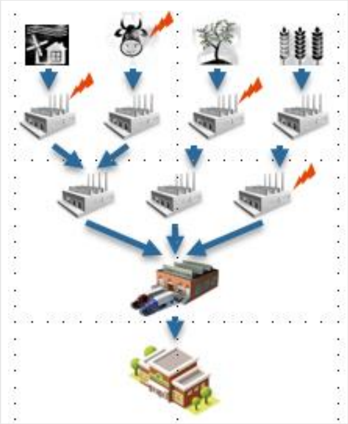
It takes seconds to destroy that trust

Packaging: a Potential Source of Food Contamination

- Mineral oils in jute sacs (1991) 
- BADGE from metal coating (1996) 
- Mineral oils from printing paperboard (1997-) 
- SEM, ESBO from metal closures (2003) 
- **ITX from UV-printing (2005)** 
- Bisphenol A from polycarbonate and epoxy lacquers (2008-) 
- Benzophenone from printing inks (2009) 
- Mineral oils from printed/recycled paper (2010-) 

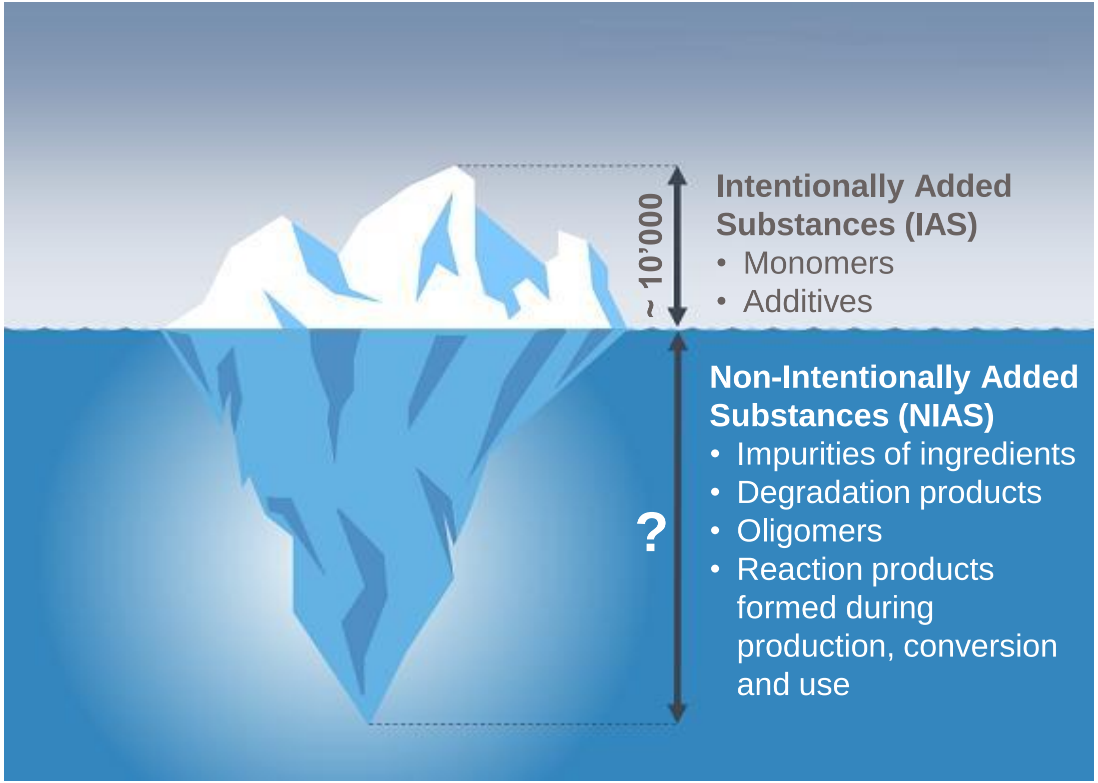
- Odor issues – (many) 

The Challenges in Packaging Safety

Many chemicals (>10’000) used in food packaging	Packaging materials are diverse and often complex	Testing of packaging or food is costly and challenging	Lack of supra-national and harmonized regulation	Complex, often fragile supply chains
				

Packaging Materials contain a Wide Range of Substances

Phthalates, mineral oils, heavy metals, EDCs, PAAs, PFCs, photoinitiators, BPA…

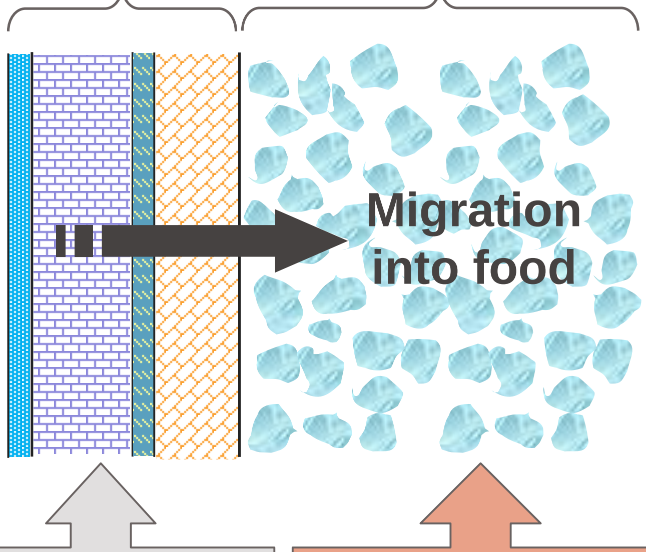


Testing of packaging and food is very challenging

Analytical investigations (sensitive & performant) are costly and complicated

Packaging

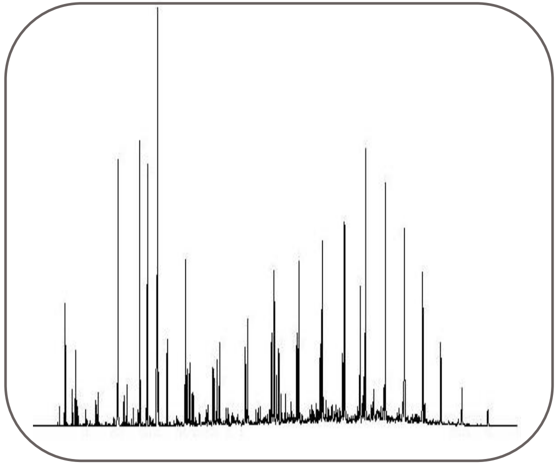
Food or Food Simulant



Check what is present in Packaging

Check what actually migrates from Packaging

GC-MS analysis of FCM after migration in food simulant



Many chemicals have the potential to migrate

How Nestlé tackles these challenges

Many chemicals (>10’000) used in food packaging	Packaging materials are diverse and often complex	Testing of packaging or food is costly and challenging	Lack of supra-national and harmonized regulation	Complex, often fragile supply chains





Multidisciplinary approach

- *In vitro* bioassays
- Chemical analysis
- *In silico* toxicology

Nestlé requirements

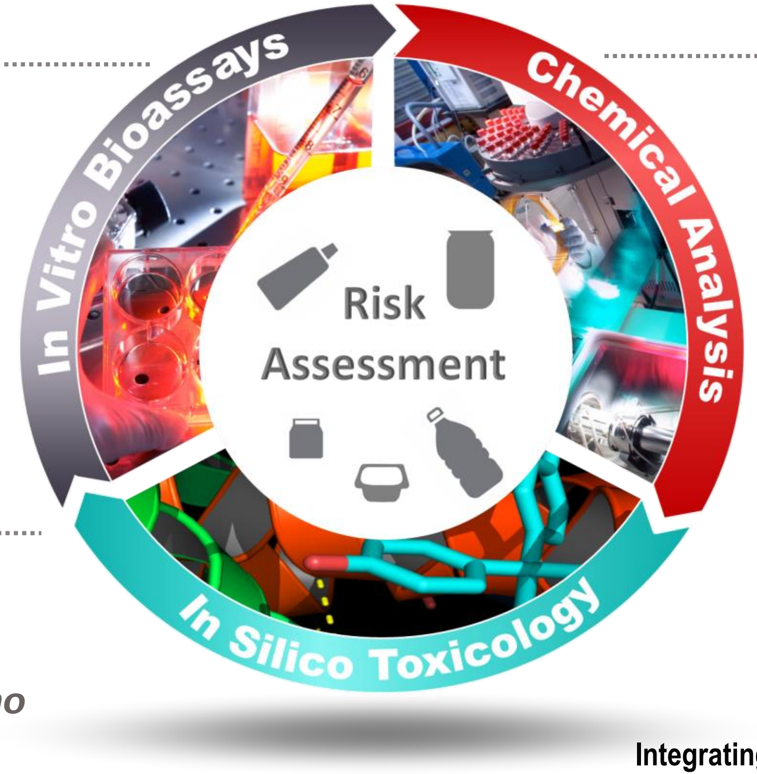
Nestlé Guidance Note on Packaging Inks, Nestlé Standards

Certificate of Compliance

Collaboration with suppliers

Nestlé R&D multidisciplinary approach to packaging safety assessment

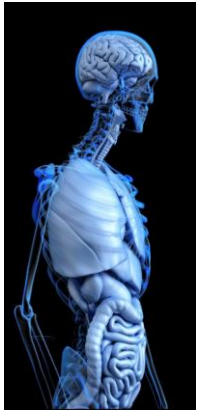
Make possible the risk assessment of packaging, even if ***presence of unidentified migrants***



Detect and characterize chemicals of concern migrating from packaging (e.g. NIAS and IAS)

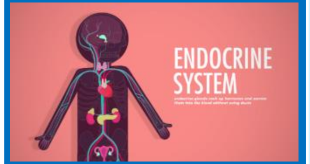
Make possible the risk assessment of packaging, even if ***presence of identified migrants with no toxicological data***

Digestion & Xenobiotic Metabolism



Integrating bioassays and analytical chemistry as an improved approach to support safety assessment of FCM
Food Additives & Contaminants, Part A (2017), 34(10), 1807-1816

In vitro Battery of Tests for Packaging Safety

Target	Method	Endpoints	Principle of test	Effectors
Nuclear receptors 	**CALUX & RealTime Glo**	Estrogen Androgen Nrf2 Arylhydrocarbon	Transcription activation, Luminescence	ER activator/inhibitor/ metabolism AR activator/inhibitor/ metabolism Electrophiles, oxidative stress PAHs
DNA damage  Image from MIT News	**BlueScreenHC**	Gadd45α & Cell count	Transcription activation, Luminescence	Any substances → damage DNA (mutagens, clastogens, aneugens)
	Histone-Phosphorylation	γH2AX & Cell count	Nuclear Foci formation	

WITH OR WITHOUT METABOLIC ACTIVATION (S9 fraction)

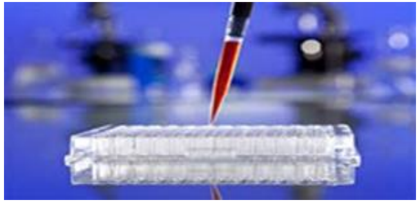
Sample Preparation for Analytics & Bioassays

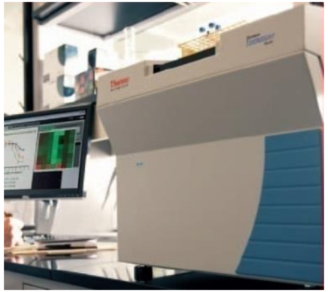
FCM samples

Migration test
in food simulant

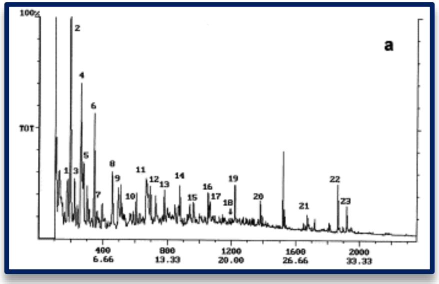
DMSO

Bioassays battery



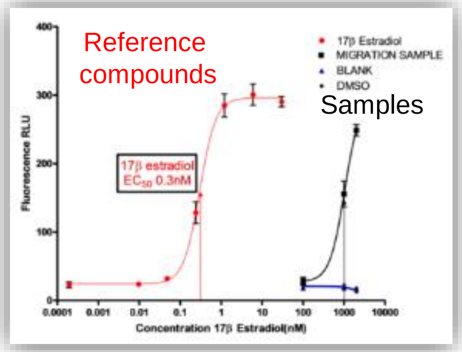


Analytical tools

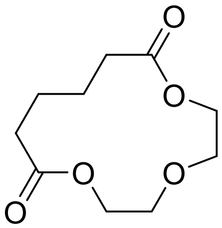


GC-MS & LC-MS

Dose
response
curve



Case study: 1,4,7-Trioxacyclotridecane-8,13-dione



1,4,7-Trioxacyclotridecane-8,13-dione (CAS: 6607-34-7)
Synonyms: Adipic acid, diethyleneglycol cyclic ester
AADEG cyclic ester

- Cyclic oligomer from polyurethane-based adhesives
- **NIAS found in packaging screenings at Nestlé**
- median level of 0.0046 mg/dm^2 (≈ 30 ppb)
- no health-based guidance value

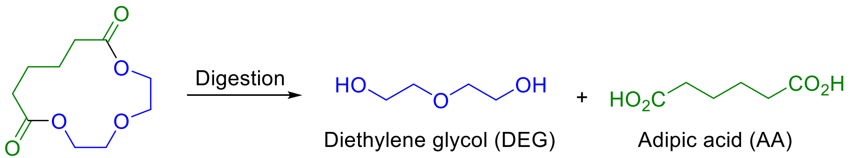
When NIAS > 10 ppb ➔ need for a Risk Assessment

What is the fate of AADEG cyclic ester during digestion?

Nestlé

Complexity for RA

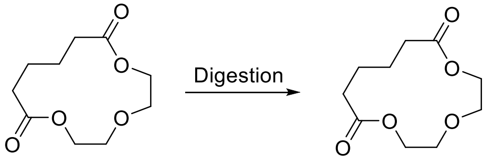
Scenario 1
Hydrolysed into monomers



AADEG cyclic ester

Monomers

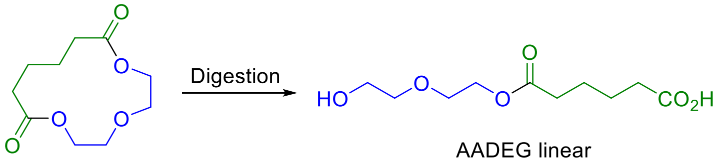
Scenario 2
No hydrolysis



AADEG cyclic ester

AADEG cyclic ester

Scenario 3
Partially hydrolysed



AADEG cyclic ester

AADEG linear
Intermediate

After *in vitro* digestion
- No formation of monomers
- 60-80% of AADEG cyclic left
- 20-40% of AADEG linear

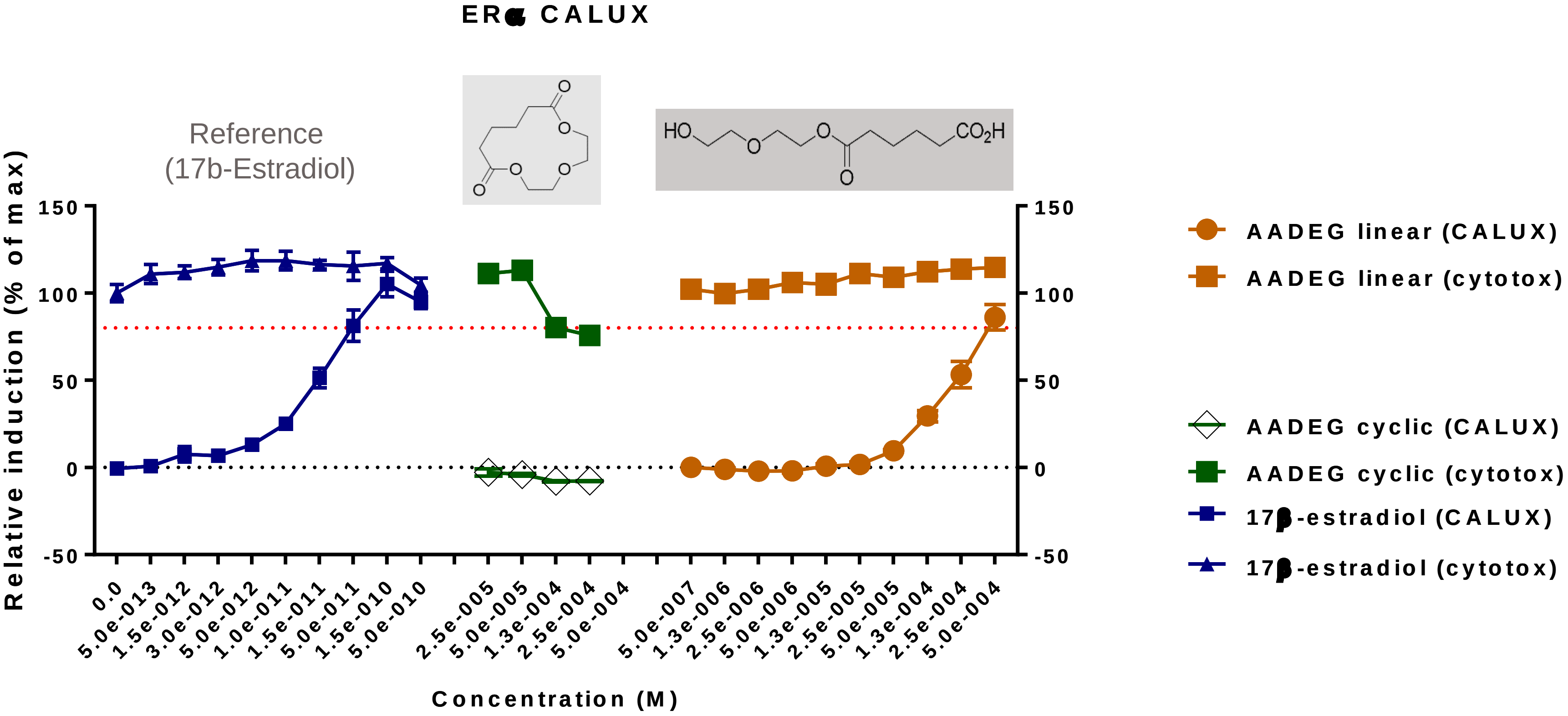
Both AADEG cyclic and AADEG linear have to be taken into account for the Risk Assessment

In vitro digestion conditions from EFSA:
- gastric: HCl 0.07M, 2h, 37°C
- intestinal: Pancreatin, 4h, 37°C

efsa
European Food Safety Authority

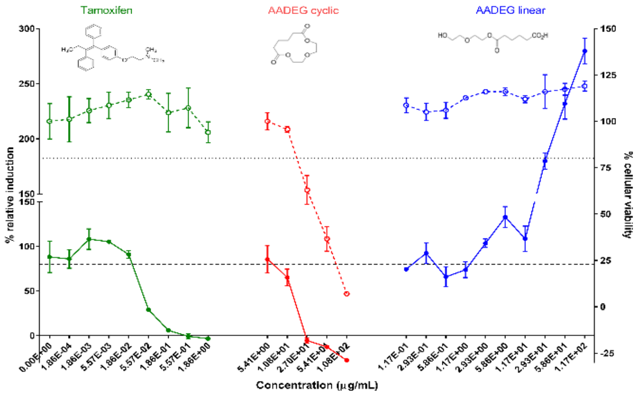
Lipolytech®

Dose-Response CALUX Assay

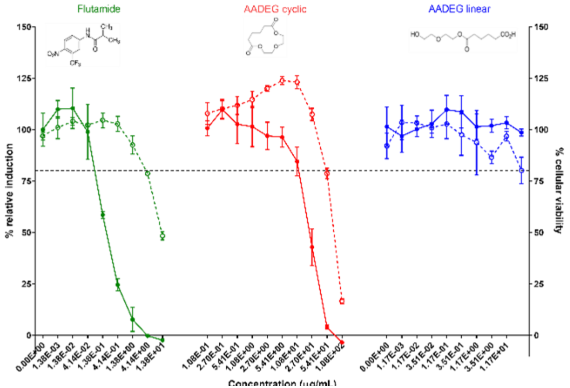


Dose-Response CALUX Assay

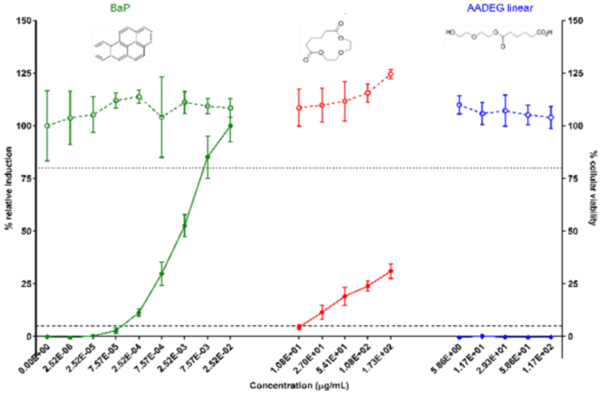
Anti-ERα



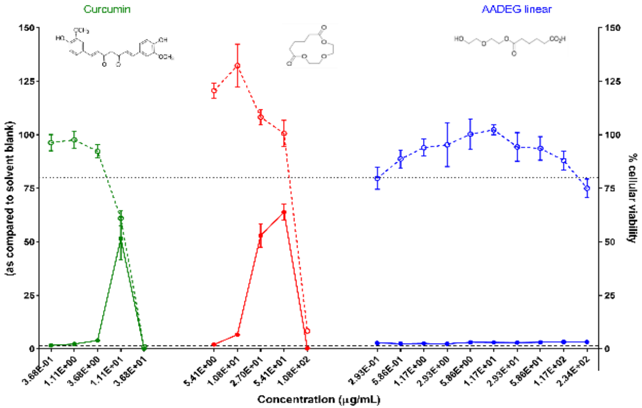
Anti-AR



AhR

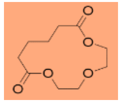


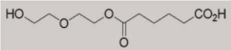
Nrf2

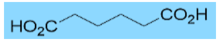


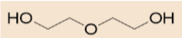
Summary bioscreening

**NA: No activity detected*





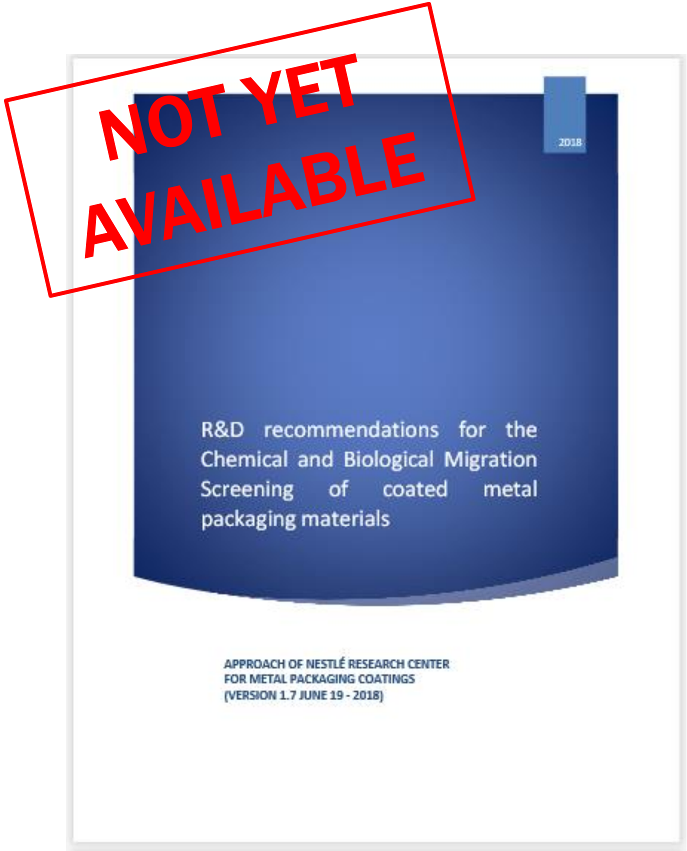




	Endpoint	AADEG cyclic	AADEG linear	Adipic acid	Diethylene glycol
Nuclear Receptor	ERα	NA	**ACTIVITY**	NA	NA
	Anti-ERα	NA	NA	NA	NA
	AR	NA	NA	NA	NA
	Anti-AR	**EQUIVOCAL**	NA	NA	NA
	AhR	**ACTIVITY**	NA	NA	NA
	Nrf2	**ACTIVITY**	NA	NA	NA
DNA-DAMAGE	GADD45α +/- METABOLIC ACTIVATION	NA	NA	NA	NA
	H2AX	NA	NA	NA	NA
	MICRONUCLEUS	NA	NA	NA	NA

Final risk assessment on-going

R&D recommendations for the Chemical and Biological Migration Screening of Coated Metal Packaging Materials



Describe the process established at Nestlé to perform chemical and biological characterization of R&D food contact materials (FCM) for safety prioritization purposes

Validation on-going through an **interlaboratory study**

Interlaboratory study for the validation of the Nestlé R&D recommendations (on-going)

R&D recommendations for the Chemical and Biological Migration Screening of Coated Metal Packaging Materials

→

Evaluate variability of sample preparation, chemical and bioassays analysis

→

Common scientific publication

Conclusion

Ensuring safety of food packaging is very complex and challenging due to

- Number of substances that could potentially migrate (> 10 000)
- Difficulty to identify and quantify all of them with analytical tools
- No tox data available for most of them
- Difficulty to predict their fate in the body (digestion, metabolism)

→ Need to develop new tools on both chemical analysis and *in vitro* bioassays

Packaging Food Safety Group

Early warning Group

Chemical Food Safety Group