Methods for identifying chemicals that migrate into food and how their concentrations vary with time and temperature

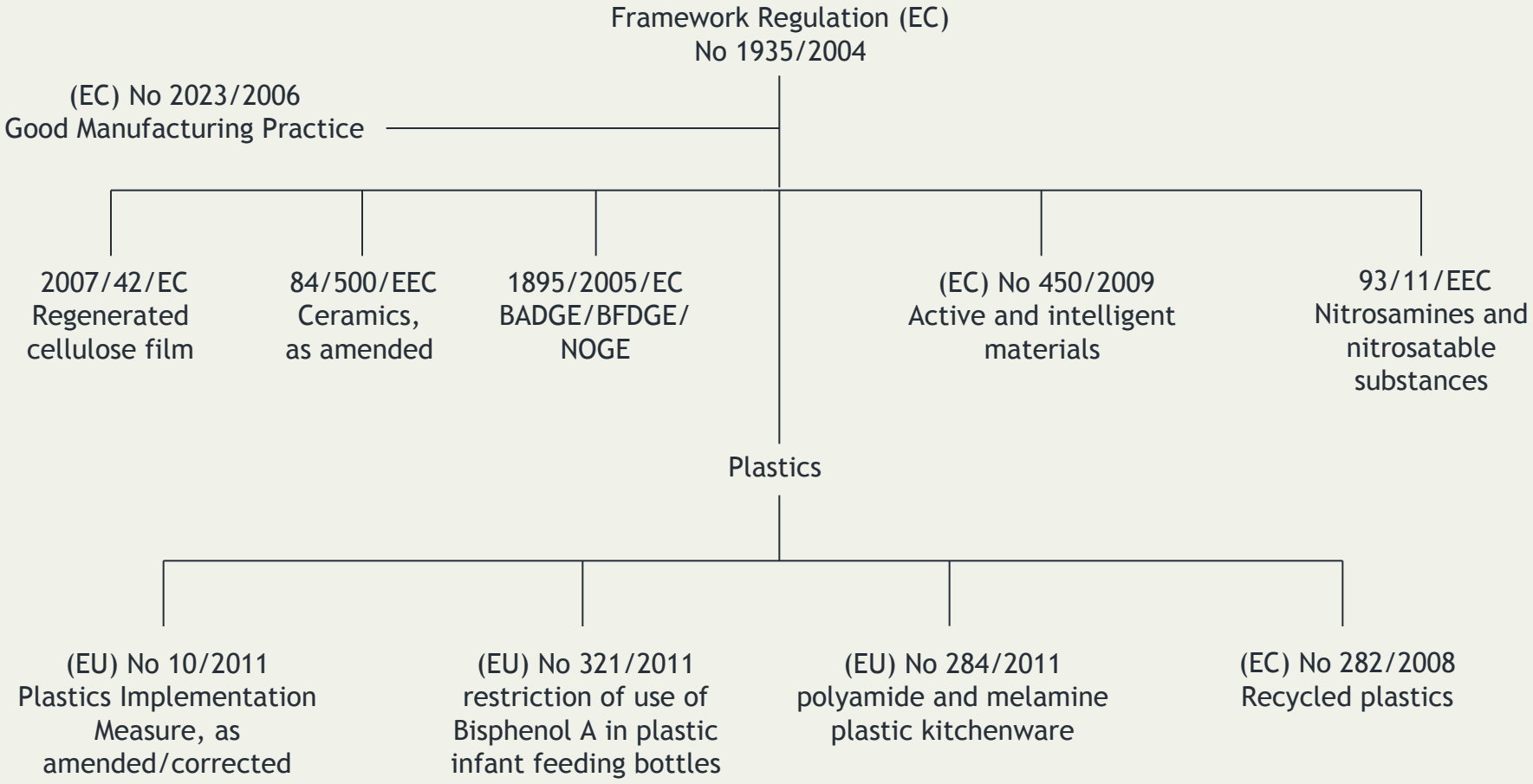
Emma Bradley
Fera Science Ltd.
emma.bradley@fera.co.uk

Migration from food contact materials

- Packaging is beneficial
  - Protects foodstuff from spoilage

- However the transfer of chemicals from packaging to food may have a negative impact on the quality and safety of the food
  - No food contact material is completely inert
  - Need to ensure the safety of these materials

EU legislation



Migration testing

- Rules defined to test for compliance of migration from food contact materials and articles in legislation (for plastics)

Extraction > Migration modelling > Food simulants > Foodstuffs

- Special cases
  - Some substances are ubiquitous and their presence does not necessarily mean migration from the material or article
  - Some migrants react with food components

What can migrate?

- Known ingredients such as monomers, catalysts, solvents, suspension media, additives etc.

IAS

- Known or unknown isomers, oligomers (arguable if NIAS or not), impurities, reaction products and breakdown products of these ingredients
- Possible contaminants from the manufacturing process such as recycled materials, irradiated products etc
- Contamination from indirect sources such as printing inks, external coatings, adhesives, secondary packaging

NIAS

Targeted vs. non-targeted analysis

Specific extraction
Clean-up
Specific analysis

Generic
extraction
Minimal clean-up
Generic analysis

Targeted

Non-targeted

IAS - Know
exactly
what to
measure

Predictable
NIAS – oligomers,
impurities,
literature
references

NIAS -
Complete
unknowns

Can coating IAS

- Ingredients may include:
  - Resins
  - Cross linking agents
  - Catalysts
  - Lubricants
  - Wetting agents
  - Solvents
- Methods developed and validat
  of interest
  - Migration limits for plastics
  - Conversion of TDI
  - EFSA thresholds based on toxicolog

NIAS using non-targeted analysis

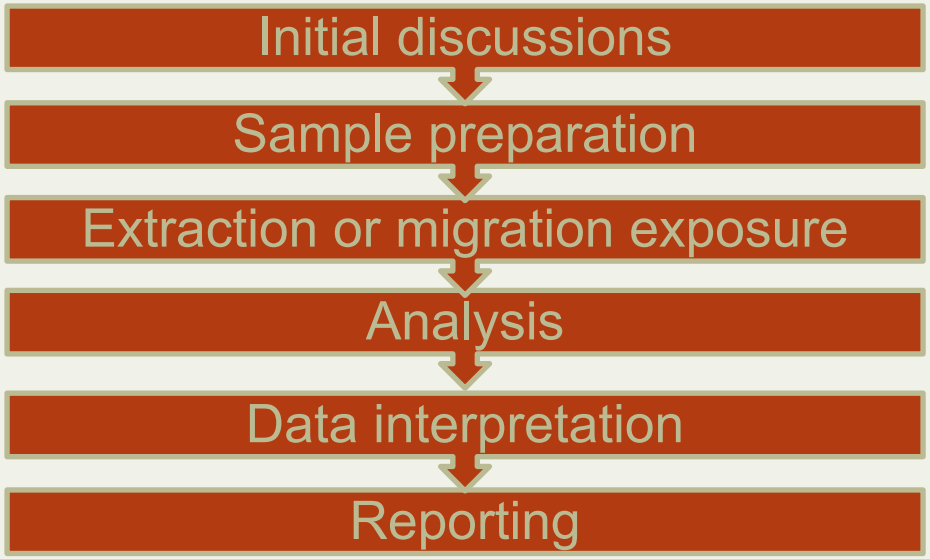






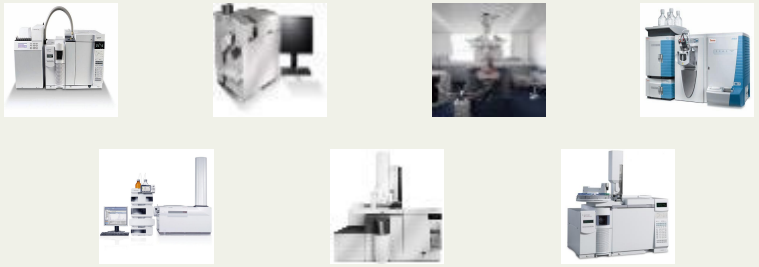

Protocols to follow……

- Presently no legally prescriptive guidelines on how to assess the safety of NIAS
  - ILSI Monograph - Guidance on best practices on the risk assessment of NIAS in Food Contact Materials and Articles (July 2015)
- What approach should be taken?

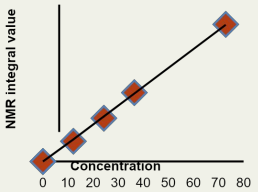


Analysis and data interpretation

- Initial discussions
- Sample preparation
- Extraction or migration exposure
- Analysis
- Data interpretation
- Reporting



- Identification
- Detection
- Quantification

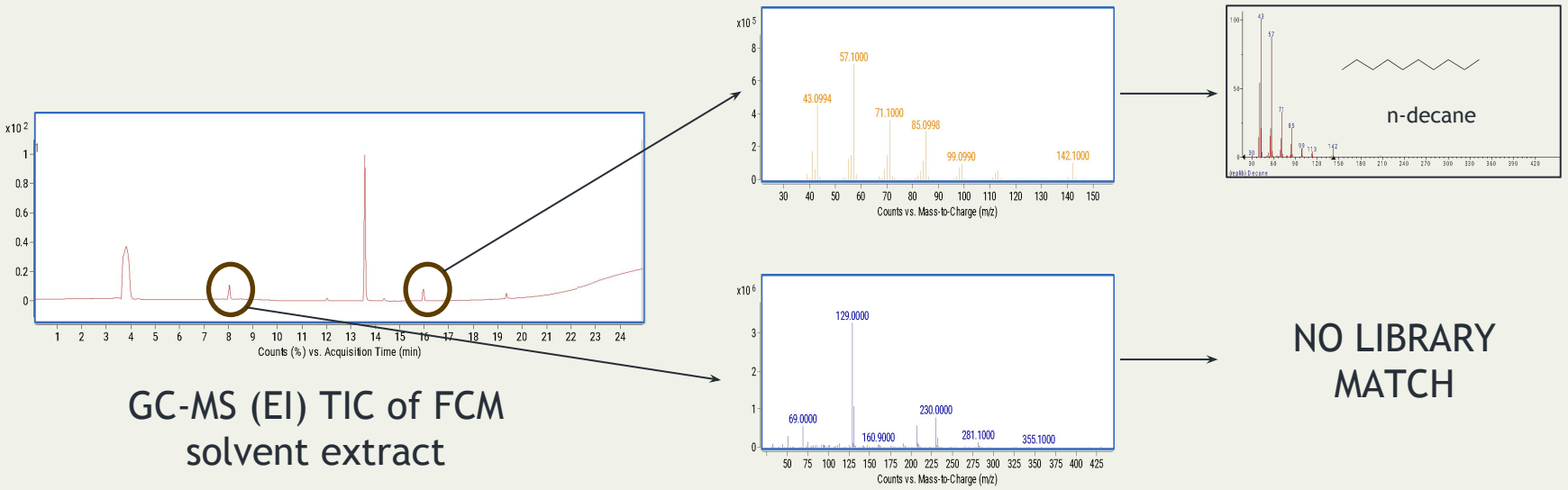


TIC vs. EIC?

vs.

Identification of NIAS – GC-MS

- Volatile and semi-volatile NIAS - GC-MS
- Identification can be carried out by comparison to electron impact (EI) MS libraries
  - Libraries contain many 10,000's of substances but often still unknown NIAS with no library match



GC-MS (EI) TIC of FCM solvent extract

Identification of NIAS – HR-MS

- Volatile NIAS detected by GC-MS
- Non-volatile and polar NIAS detected by LC-MS

- HR-MS
  - Accurate mass, isotope information (spacing and intensity), fragmentation (in-source or MS/MS)
  - Positive and negative ionisation modes possible

Database searching

- Comparison of list of accurate masses to theoretical database
  - Can include retention time, structures, MS/MS fragment data
- Theoretical oligomers and reaction products associated with starting materials (and impurities if known) below 1000 Da
  - Should consider simulant-oligomer interactions
- Can contain tens of thousands of compounds….
- Not confirmed unless compared to authentic standard

		AA	TMA	PA	CHDM	BD	EG	DEG	PG	HD	HMP	TMP	NPG	H2O	MW
PA+EG	linear			1			1							1	210.0528
EG+PA+EG	linear			1			2							2	254.0790
PA+EG+PA+EG	linear			2			2							3	402.0951
PA+EG+PA+EG	cyclic			2			2							4	384.0845
PA+EG+PA+EG+PA	linear			3			2							4	550.1111
PA+EG+PA+EG+PA+NPG	linear			3			2						1	5	636.1843
PA+EG+PA+NPG+PA+EG	linear			3			2						1	5	636.1843
PA+PG+PA+PG+PA+PG	linear			3					3					5	636.1843
PA+PG+PA+PG+PA+PG	cyclic			3					3					6	618.1737

Quantification

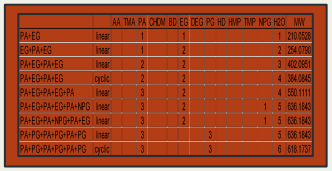
- How can we quantify if we don't know what we are looking for?
- Internal standards
  - ^{2}H, ^{13}C analogues – not naturally occurring
  - Range of compounds to cover the mass range of interest?
  - IS that responds in positive and negative ionisation (for LC-MS)
- External standards
  - Chemically similar to substances of interest

    e.g. BADGE or BADGE hydrolysis products for epoxy-related

    e.g. Polyester diol urethane substance for polyester-related
- Synthesis of authentic standards to confirm identity
  - Retention time, accurate mass, fragmentation comparison
  - Expensive and time consuming

Quantification by LC-TOF-MS and NMR

Oligomer determination



		AA	TMA	PA	CHDM	BD	EG	DEG	PG	HD	HMP	TMP	NPG	H2O	MW
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EG+PA+EG	linear		1				2							2	254.0790
PA+EG+PA+EG	linear		2				2							3	402.0951
PA+EG+PA+EG	cyclic		2				2							4	384.0845
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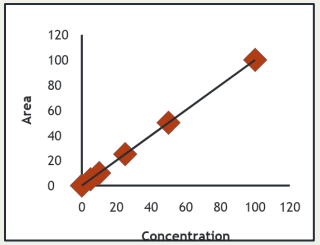
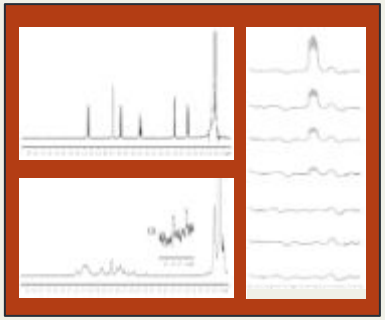
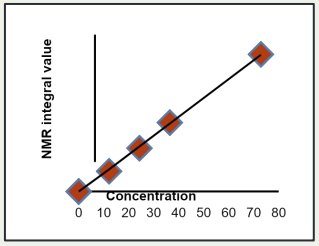


0.04 mg/6 dm^2

Extraction of a FCM with solvent

Monomer functional group quantification





0.03 mg/6 dm^2

Extraction

- Approaches described thus far cover extraction
- Assumption – 100% transfer
- Concentration in food – “EU cube”
- Worst case concentration “in food” data

Extraction > Migration modelling > Food simulants > Foodstuffs

Migration modelling

- Models developed for some plastics
- Accepted approach for demonstrating compliance
- Developed to at least equal (but typically overestimate) migration – consumer protection

Migration into simulants (plastics)

- Migration into food simulants (simple media intended to mimic foodstuffs) is permitted for use to demonstrate the suitability for contact with a range of foods. In Europe the simulants are:

Simulant	Abbreviation
Ethanol 10% (v/v)	Simulant A
Acetic acid 3% (w/v)	Simulant B
Ethanol 20% (v/v)	Simulant C
Ethanol 50% (v/v)	Simulant D1
Vegetable Oil	Simulant D2
Modified polyphenylene oxides, particle size 60-80 mesh, pore size 200 nm	Simulant E for dry foods

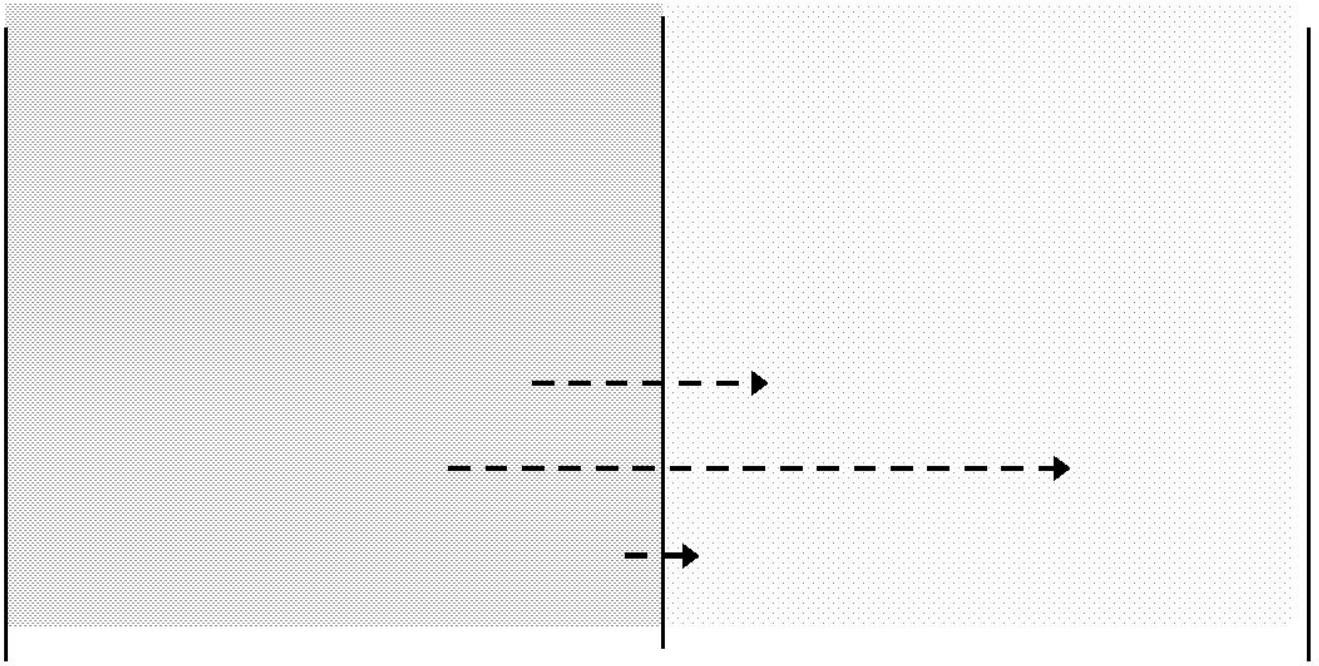
Extraction > Migration modelling > Food simulants > Foodstuffs

Factors affecting migration

- Migration is a diffusion and partitioning process that is dependent on:
  - The nature of the food contact material
  - The nature and concentration of the migrating substance
  - The nature, the extent and the type of contact between the food contact material/article and the foodstuff
  - The nature of the foodstuff

The nature of the food contact material

Depiction of chemical migration from a **permeable material**

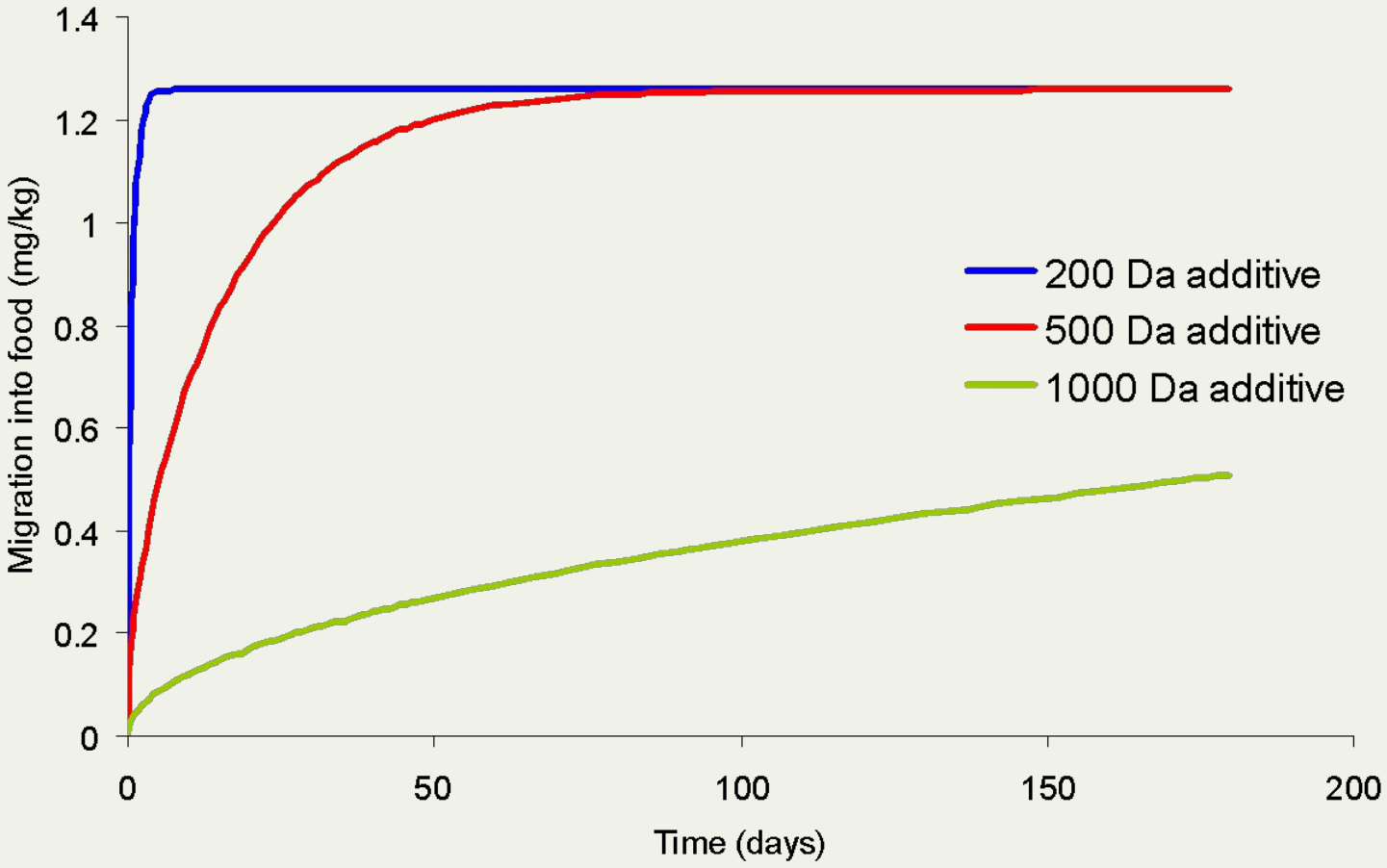


The nature of the substance

- Ingredients needed to make can coatings
  - Monomers and starting substances
  - Catalysts
  - Solvents and suspension media
  - Additives
    - Antioxidants, antistatics, antifogging, slip additives, plasticisers, heat stabilisers, nucleating agents, dyes and pigments

- Different chemistries and so different rates of migration expected

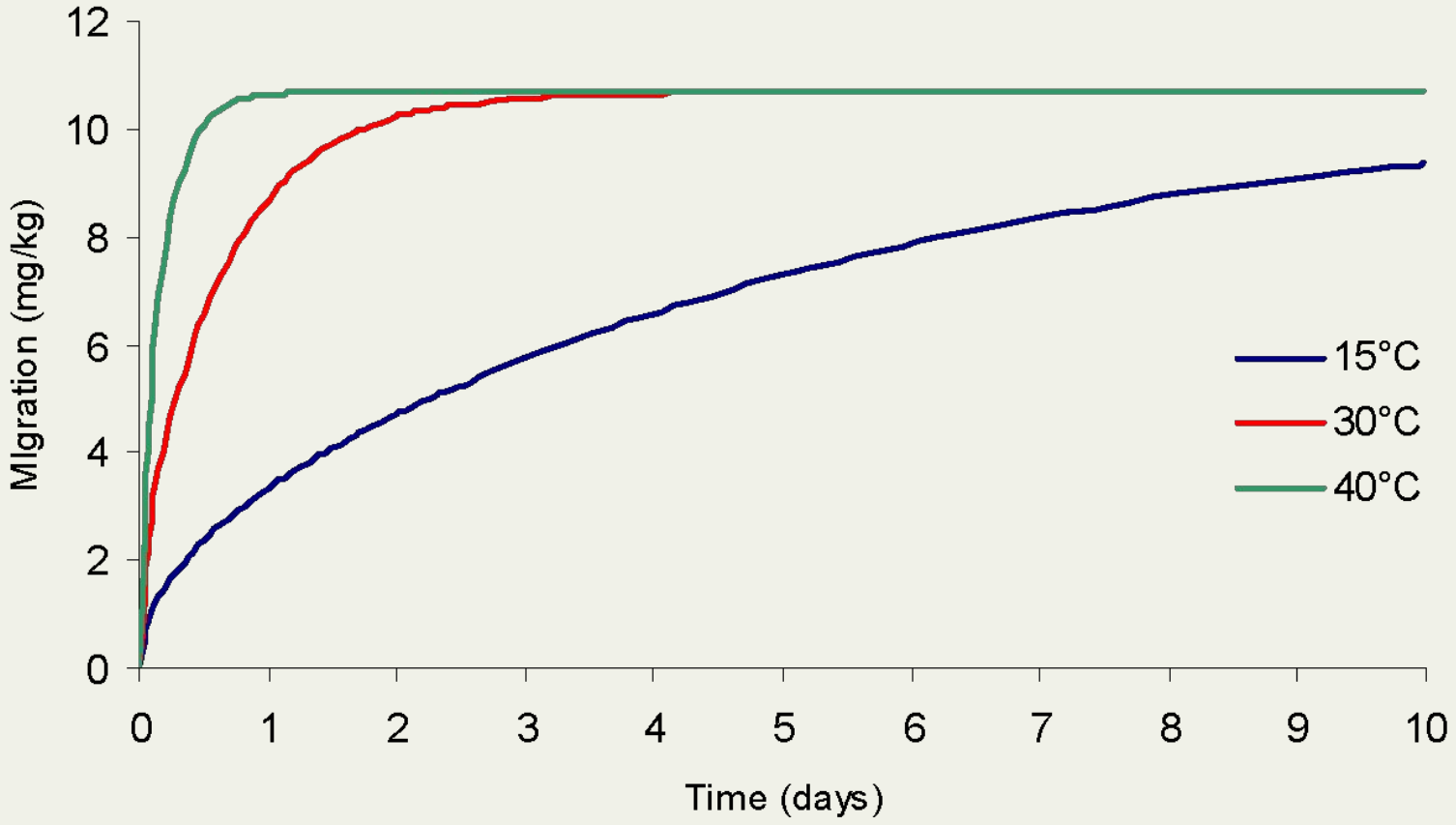
The nature of the substance



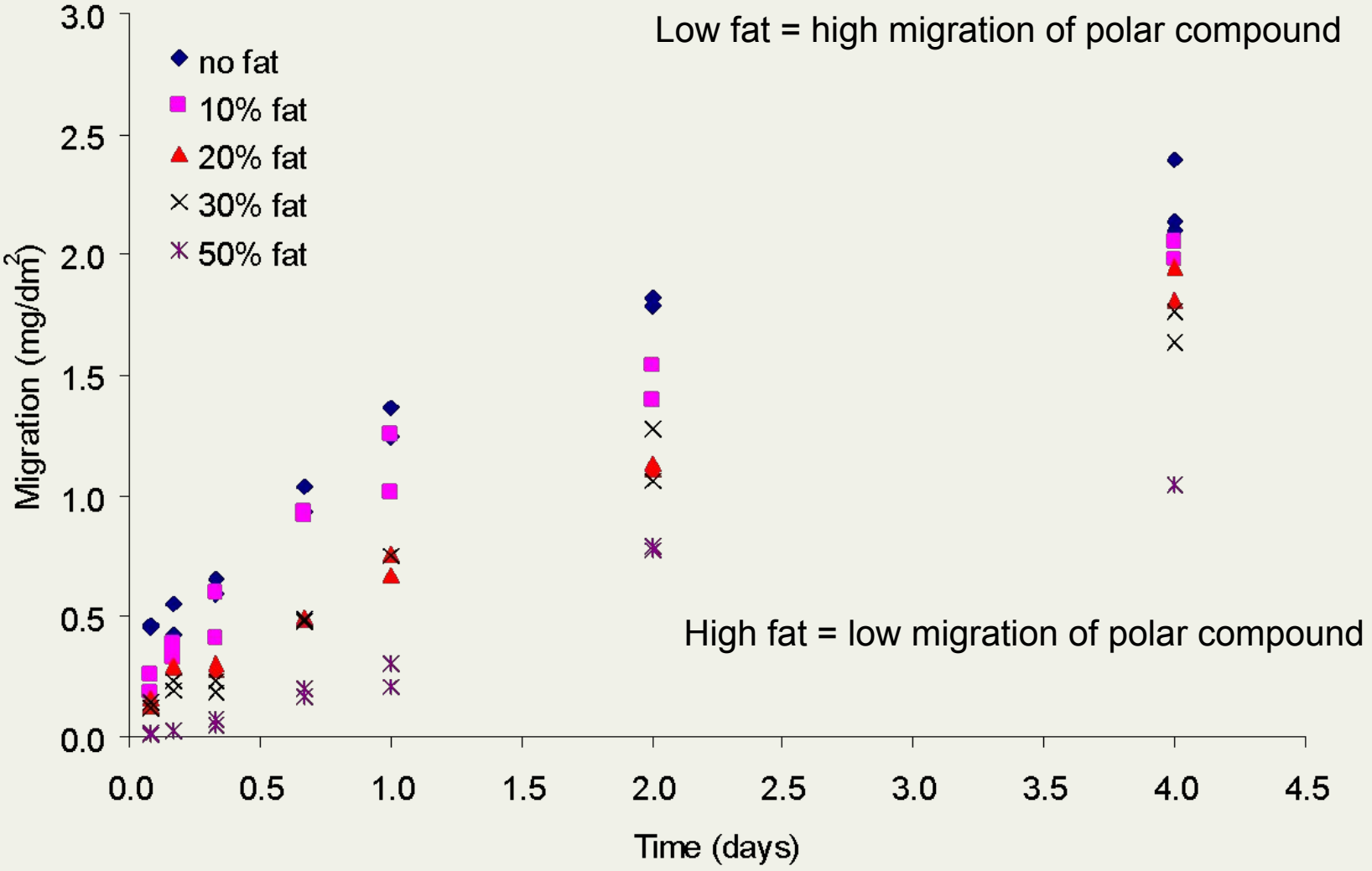
The nature of the contact

- Interaction between food and packaging
- *Direct versus indirect contact*
- *Point or continuous contact*

The nature of the contact – time and temperature



The nature of the foodstuff



Migration into foods

- When to test with foods
  - Where the foodstuff is water
  - Where the representativeness of the food simulant is in doubt
  - When a migration test into a food simulant fails, e.g. unacceptable QA
  - When testing with a food simulant is more analytically challenging than testing with the foodstuff itself
  - Where the material/article is intended to come into contact with a single and well defined foodstuff or a given food type for which a representative worst case foodstuff can be selected

Migration into foods

- Test foods in contact with the FCM under worst foreseeable conditions of use
  - Homogenise the foodstuff and analyse for the substance of interest
  - Test a portion of the food that has not been exposed to the material or article to confirm any substances present occur due to migration from the tested material or article

- Test packed foods at end of shelf life
  - Remove non-edible parts
  - Homogenise remainder and analyse for the substance of interest
  - For solid foods compare concentrations at the food contact surface with concentrations in the bulk of the food to confirm derived from the packaging rather than

Summary

- Ever-advancing analytical instrumentation provides very powerful tools for determination of IAS and NIAS
- As instruments become more readily available and sensitivity increases there is the potential for more and more NIAS to be detected
- Identification and quantification are still providing challenges
- Extraction methods used to detect NIAS overestimate migration
- Use of migration modelling, migration into simulants and better still migration into foods can refine the data for exposure estimations

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emma.bradley@fera.co.uk

Tel: +44 (0) 1904 462604
Mob: +44 (0) 7866 799012