NEW COMPUTATIONAL METHODOLOGIES AS ENABLERS OF SAFER FOOD CONTACT ARTICLES

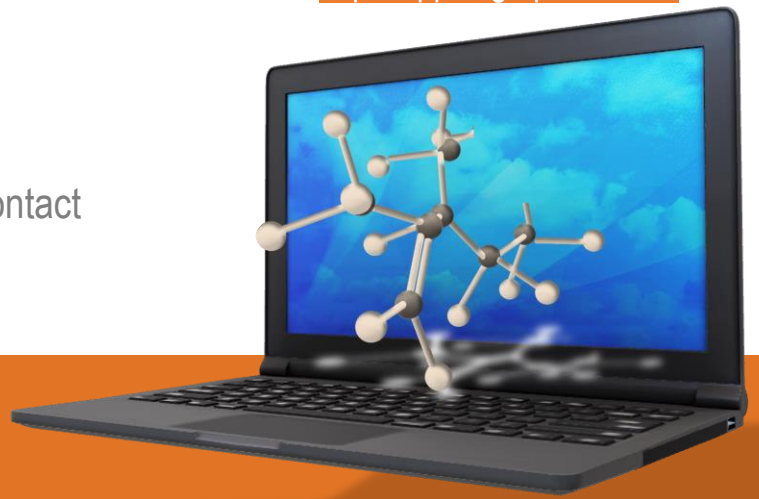
UMT SAFEMAT
MATÉRIAUX AU CONTACT DES ALIMENTS

Olivier Vitrac, PhD, olivier.vitrac@agroparistech.fr

Yan Zhu, PhD student
Phuong-Mai Nguyen, PhD
Xiaoyi Fang, PhD
Guillaume Gillet, PhD
Manuel Durand, PhD
Jérôme Lézervant, PhD

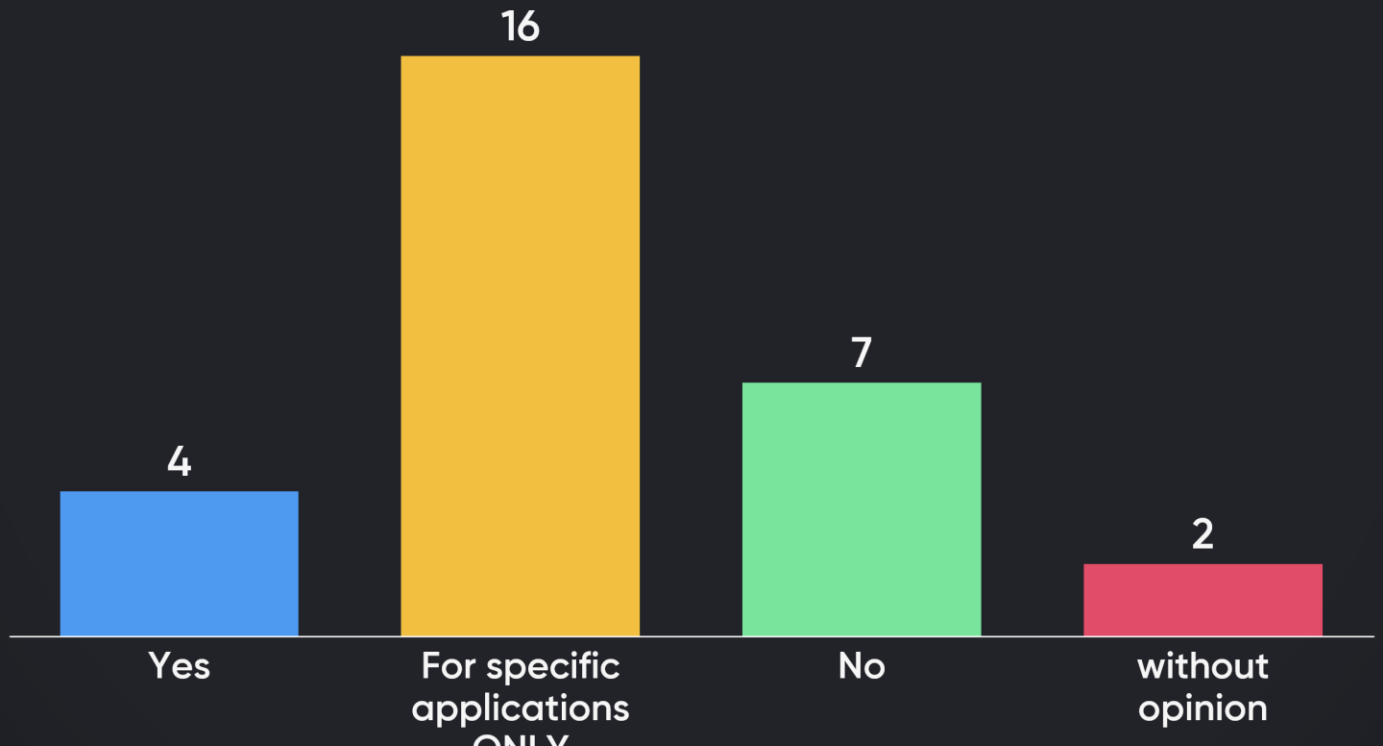
UMR 1145 Food Processing and Engineering
Group Interactions between Materials and Media in Contact
UMT SafeMat "Safe Materials"
AgroParisTech site de Massy, France

http://sfpp3.agroparistech.fr



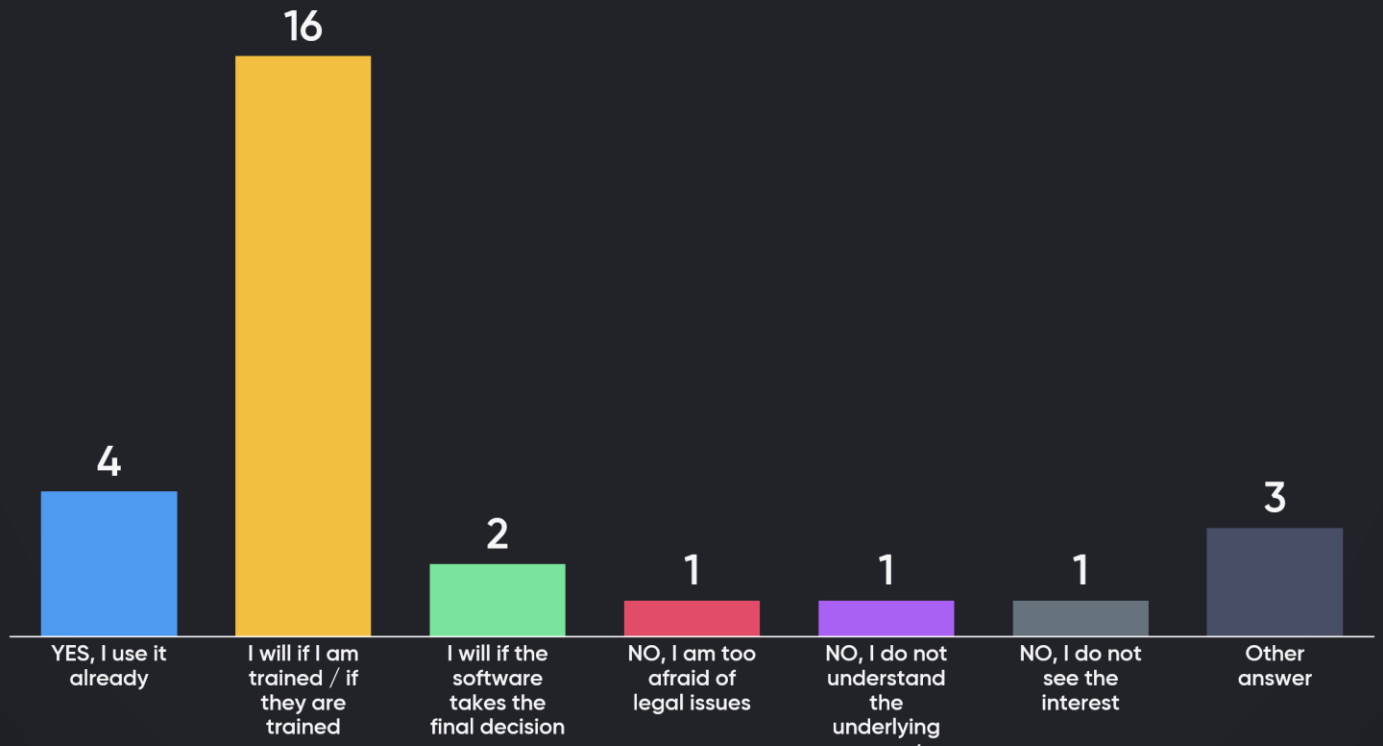
Do you think that calculations are as safe as experiments?

Mentimeter

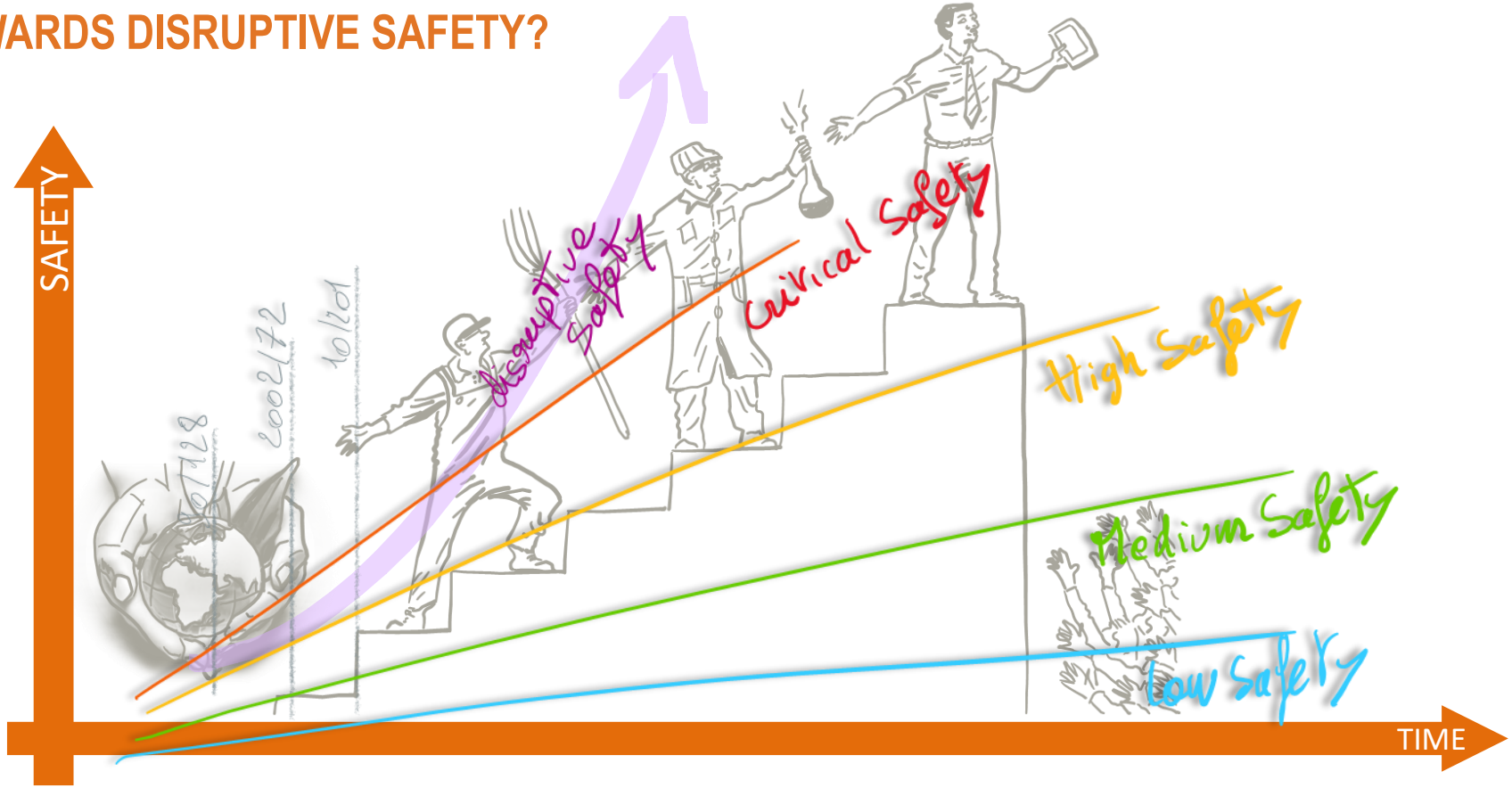


Would you use or recommend migration modeling?

Mentimeter



TOWARDS DISRUPTIVE SAFETY?



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Disruptive innovation = an innovation that creates a newmarket by providing a different set of values, which ultimately (and unexpectedly) overtakes an existing market (e.g., the lower-priced, affordable Ford Model T, which displaced horse-drawn carriages)

IS IT SAFE TO USE A COMPUTER INSTEAD OF DOING EXPERIMENTS?

- **In the law (EU, US) and in the practices for plastics materials and their applications including recyclability**
- **Very few requirements and limitations**
  - No more requirement on “generally recognized diffusion model”
  - Scientific-sound
  - No distinction between a virtual experiment reproducing a lab one (food simulant) or a real food
  - Conservative assumptions = maximizing the amount released in food
- **Known issues**
  - **Insufficient guidance and training, it requires interdisciplinary education (polymer science, mass transfer, packaging technology, food science and engineering)**
  - **No “universal” software (*open-source available*)**
  - **Dependent on research results**

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Compliance of FCM tested extensively by calculations in EU (≥50%)

HOW MODELING WAS INTRODUCED IN THE LAW

89/109/EEC

Directive
90/128/EEC

2002/72/EC

1935/**2004**/EC

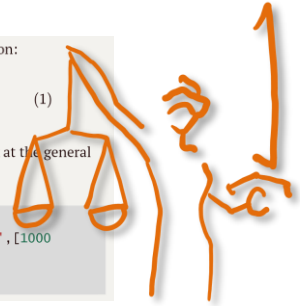
10/**2011**/EC

The contamination of food by packaging materials has been put in equation:

$$C_F^{(Fo)} = \left(\frac{1}{K} + \frac{1}{L}\right) \cdot \overline{v^*}_{(Fo,K,L)} \cdot C_P^0 \qquad (1)$$

Do you want to learn how to solve this equation in the general case? Look at the general code written in Matlab®/GNU-Octave.

```
S0 = permpatankar('init');
R=permpatankar('k',1,'D',1e-16,'l',300e-6,'C0',0,'CF0',[1000
0],S0);
figure, plot(R.t,R.CF1)
```



5 (14) For certain types of plastics the availability of generally recognised diffusion models based on experimental data allows the estimation of the migration level of a substance under certain conditions, therefore avoiding

18 As migration testing is complex, costly and time consuming it should be admissible that compliance can be demonstrated also by calculations, including modelling, other analysis, and scientific evidence or reasoning if these render results which are at least as severe as the migration

At each stage of manufacture, supporting documentation, substantiating the declaration of compliance, should be kept available for the enforcement authorities. Such dem onstration of compliance may be based on migration test ing. As migration testing is complex, costly and time consuming it should be admissible that compliance can be demonstrated also by calculations, including modelling, other analysis, and scientific evidence or reasoning if these render results which are at least as severe as the migration testing. Test results should be regarded as valid as long as formulations and processing conditions remain constant as part of a quality assurance system.

"…including modelling, other and analysis, and scientific evidence or reasoning if these render results which are at least as severe as the migration testing."

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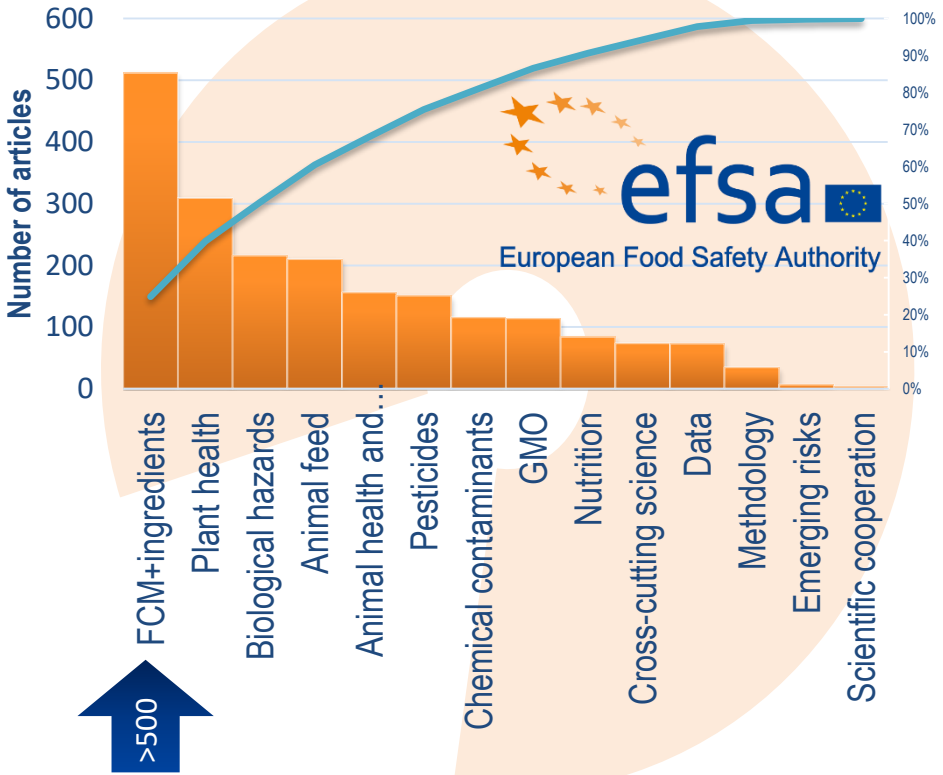
3,529 results for "modelling" in EFSA J.



retrieved on Sep 30th, 2018

IS MODELING A TRUSTED SCIENCE ?

FDA U.S. FOOD & DRUG ADMINISTRATION

"We have reviewed the proposed recycling process as well as the information you obtained from surrogate testing and migration modeling, which were submitted to demonstrate the capability of the proposed recycling process to remove potential contaminants from PCR-PET.

Based on our review of these data, we have determined that the proposed recycling process, as described in the subject submission, …."

https://www.fda.gov/Food/IngredientsPackagingLabeling/PackagingFCS/RecycledPlastics/default.htm

INRA SCIENCE & IMPACT

BANER, A. L., FRANZ, F., and PIRINGER, O., 1994, **Alternative methods for determination and evaluation of migration potential from polymeric food-contact materials**. *Deutsche Lebensmittel-Rundschau,* 90(5), 137-143 and 90(6), 181-185.

FOOD ADDITIVES AND CONTAMINANTS, 1996, VOL. 13, NO. 8, 949–967

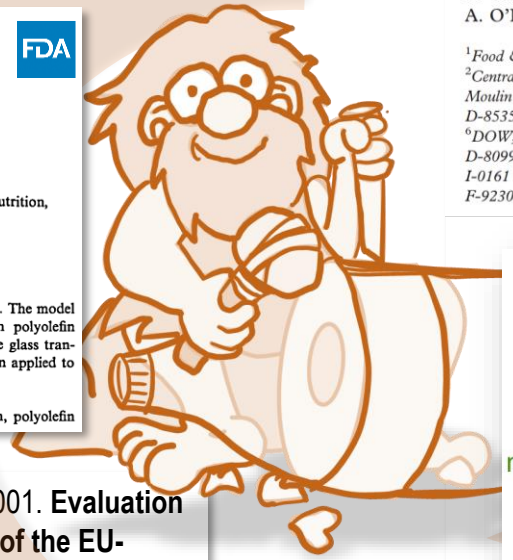
Modelling of additive diffusion in polyolefins

WILLIAM LIMM and HENRY C. HOLLIFIELD
US Food and Drug Administration, Center for Food Safety and Applied Nutrition, 200 C Street, SW, Washington, DC 20204, USA

(Received 31 October 1995; accepted 13 November 1995)

A semi-empirical model has been developed for additive diffusion in polymers. The model estimates apparent diffusion coefficients of an additive migrating through polyolefin polymers into a fatty food simulant for a range of temperatures between the glass transition and melting temperatures of the polymer. This diffusion model has been applied to several additive/polyolefin systems to determine its validity and limitations.

Keywords: antioxidant, diffusion coefficient, food additive petition, migration, polyolefin

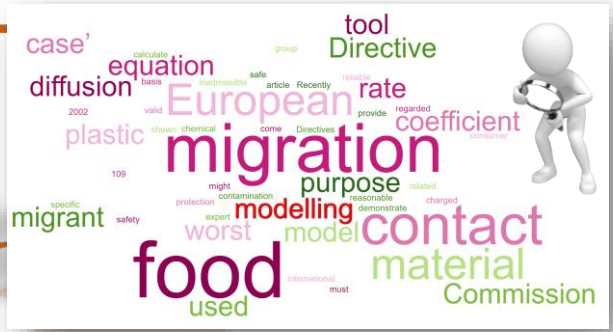


Food Additives and Contaminants, January 2005; 22(1): 73–90

Evaluation of migration models that might be used in support of regulations for food-contact plastics

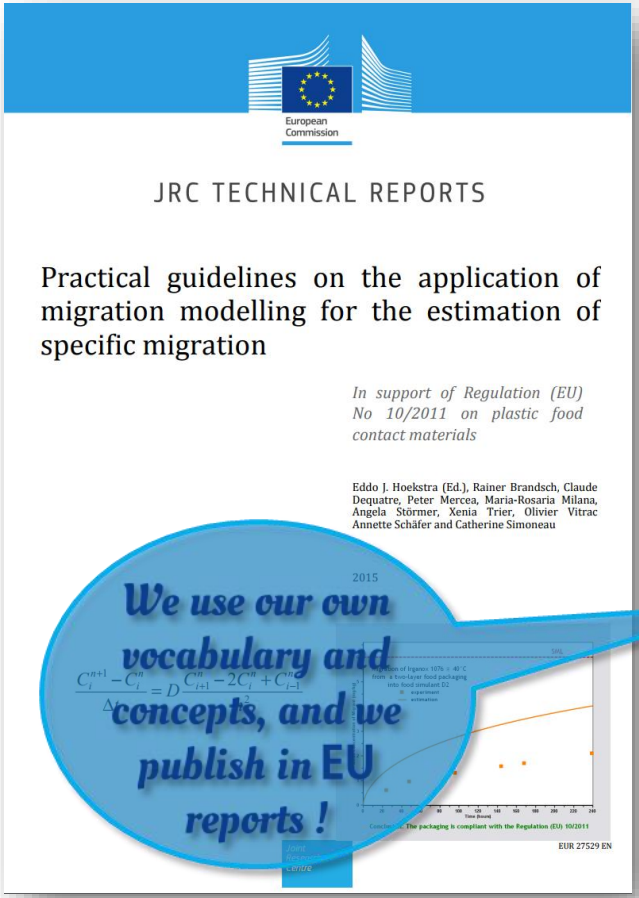
T. BEGLEY[1], L. CASTLE[2], A. FEIGENBAUM[3], R. FRANZ[4], K. HINRICHS[5], T. LICKLY[6], P. MERCEA[7], M. MILANA[8], A. O'BRIEN[9], S. REBRE[10], R. RIJK[11], & O. PIRINGER[7]

[1]*Food & Drug Administration, 5100 Paint Branch Parkway, College Park, MD 20740, USA,* [2]*Central Science Laboratory, Sand Hutton, York Y041 1LZ, UK,* [3]*INRA — CPCB, Moulin de la Housse, F-51697 Reims Cedex 2, France,* [4]*Fraunhofer-Institut IVV, Giggenhauser Straße 35, D-85354 Freising, Germany,* [5]*Cognis GmbH, Henkelstraße 67, D-40551 Dusseldorf, Germany,* [6]*DOW, 1803 Building, Midland, MI 48674, USA,* [7]*Fabes GmbH, Schragenhofstraße 35, D-80992 Munich, Germany,* [8]*Istituto Superiore de Sanita, Viale Regina Elena, 299, I-0161 Rome, Italy,* [9]*PIRA International, Leatherhead KT22 7RU, UK,* [10]*Atofina, Rue Danton 95, F-92300 Levallois-Perret, France, and* [11]*TNO, Utrechtseweg 48, NL-3700 AJ Zeist, the Netherlands*

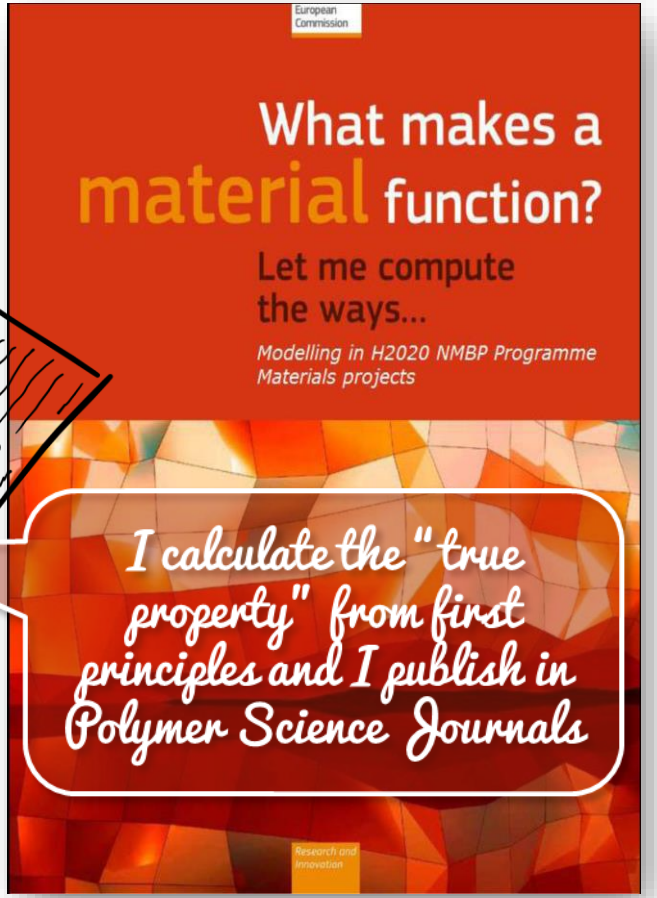


HINRICHS, K., PIRINGER, O. G., 2001. **Evaluation of Migration Models. Final Report of the EU-project contract SMT-CT98-7513**, Brussels

$$\frac{\partial C}{\partial t} = \frac{\partial}{\partial x}\left(D \frac{\partial}{\partial x} C\right) \qquad \ln D = A_p - 0.1351\, M^{2/3} + 0.003M - \frac{T + 10454}{RT}$$



http://publications.jrc.ec.europa.eu/repository/handle/JRC98028



https://publications.europa.eu/en/publication-detail/-/publication/e0845ae1-1b60-11e7-aeb3-01aa75ed71a1

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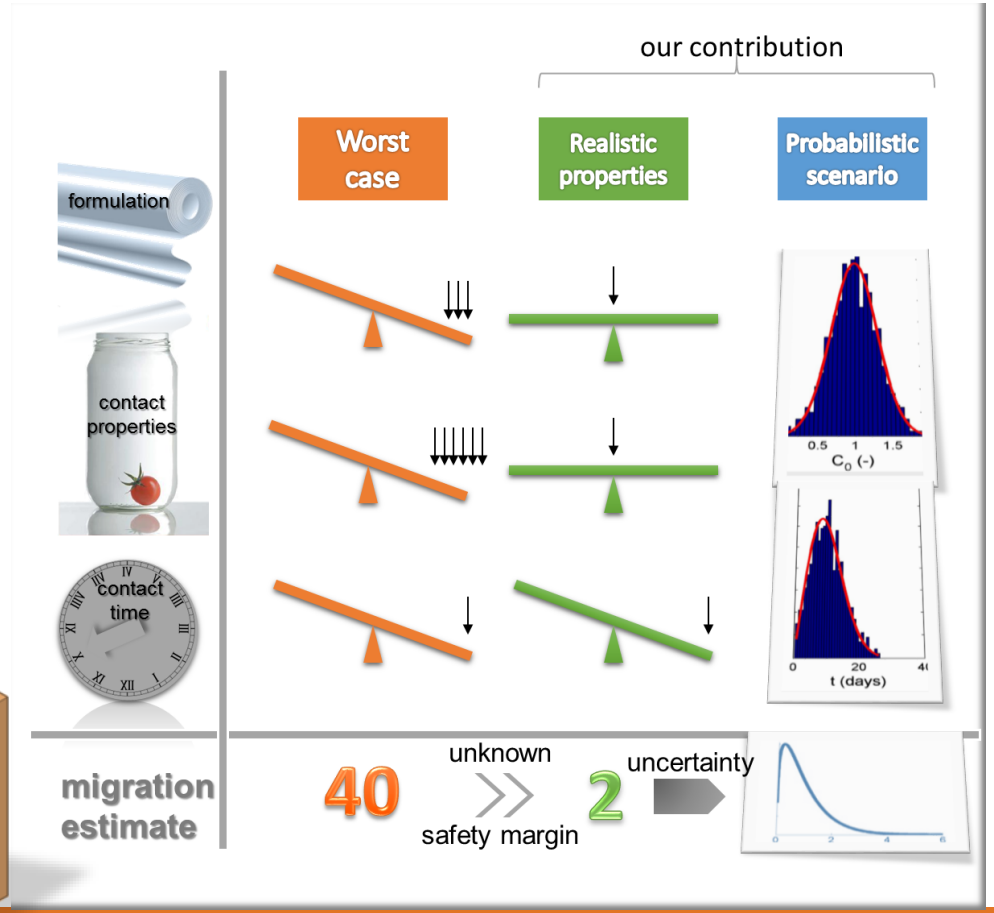
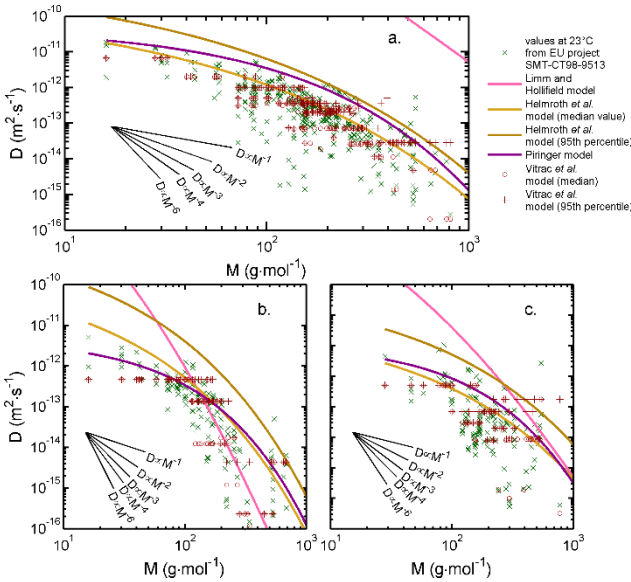
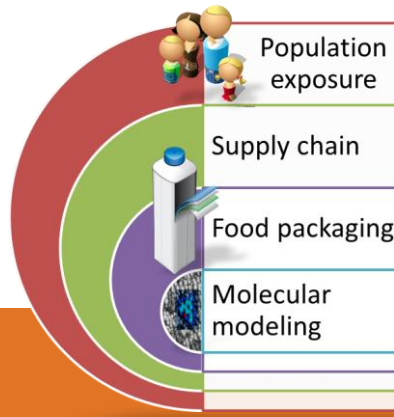
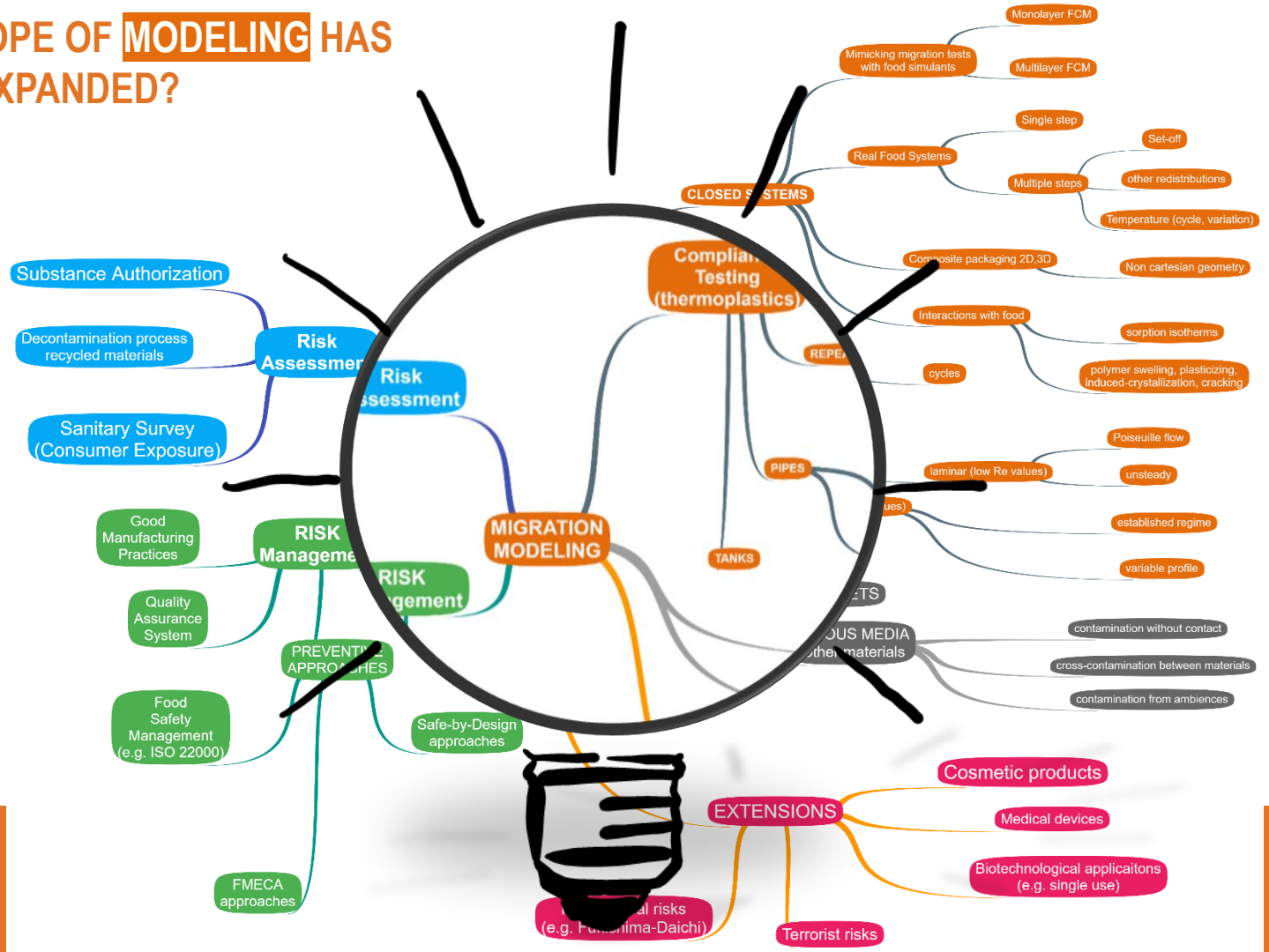
Dispute, controversy, misunderstanding or complementarity ?


our contribution
Worst case
Realistic properties
Probabilistic scenario
formulation
contact properties
contact time
migration estimate
40
unknown
safety margin
2
uncertainty
C_0 (-)
t (days)


a.
b.
c.
D (m²·s⁻¹)
M (g·mol⁻¹)
values at 23°C from EU project SMT-CT98-9513
Limm and Hollifield model
Helmroth et al. model (median value)
Helmroth et al. model (95th percentile)
Piringer model
Vitrac et al. model (median)
Vitrac et al. model (95th percentile)


Population exposure
Supply chain
Food packaging
Molecular modeling

WITH TIME THE SCOPE OF MODELING HAS BEEN STRONGLY EXPANDED?



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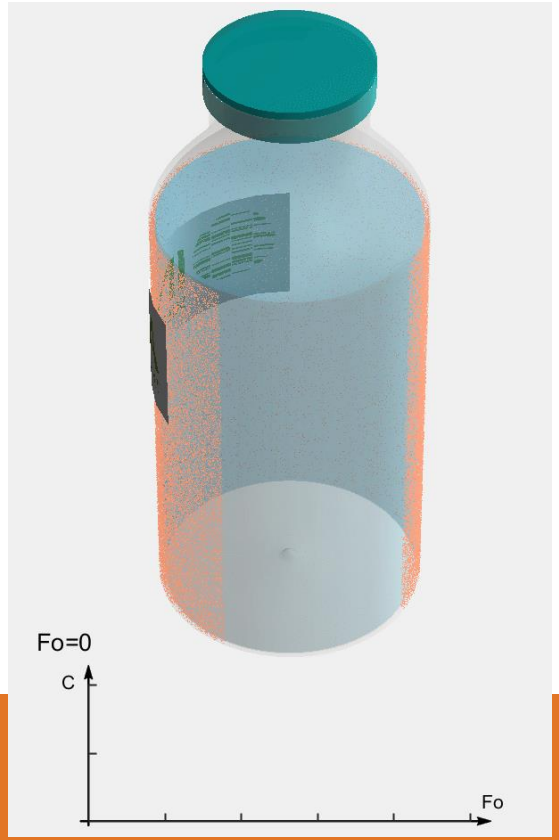
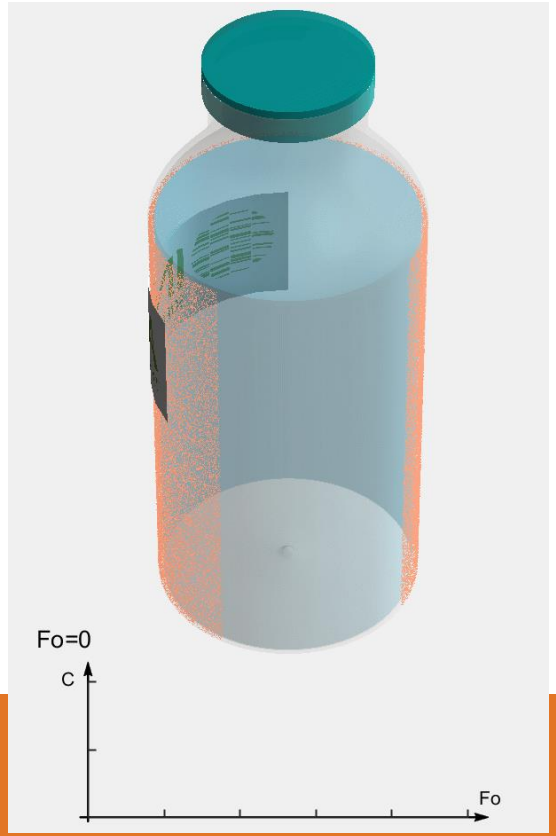
MIGRATION: SOME TYPICAL CASES, $Fo = \frac{D_P t}{l_P^2}$=dimensionless time

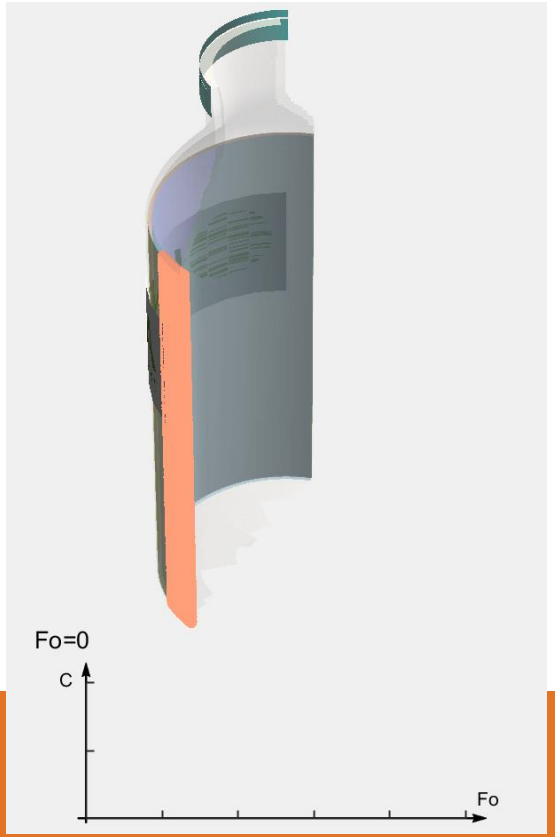
monolayer



with barrier to diffusion

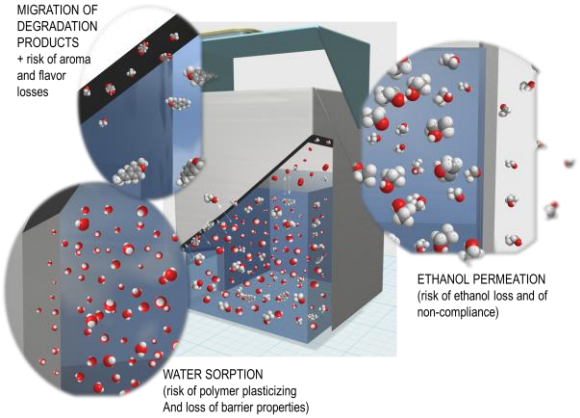


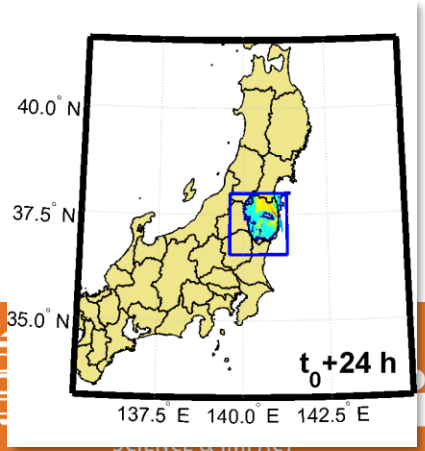
multilayer

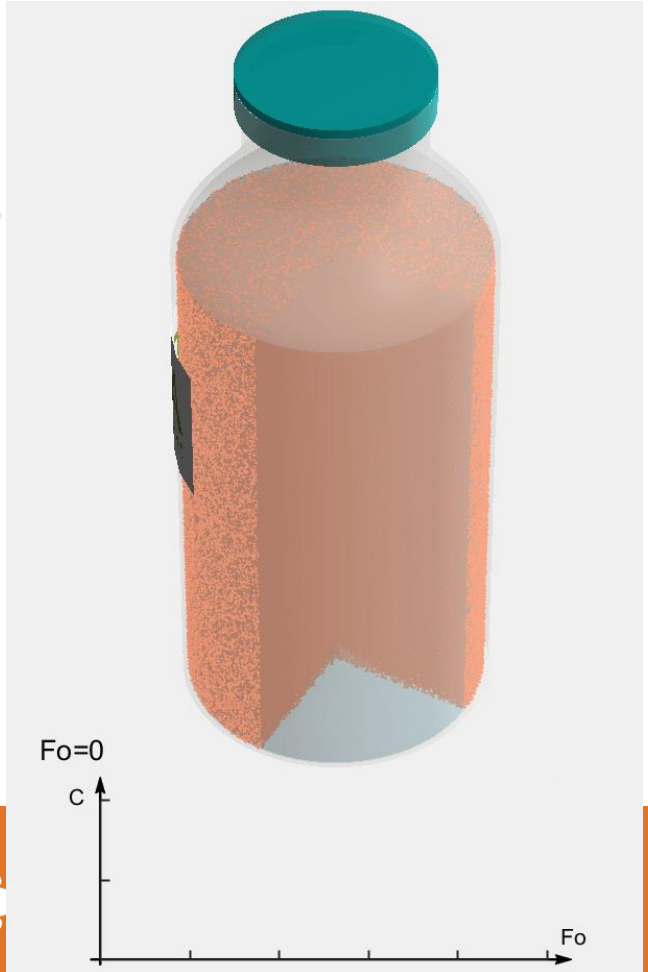


Interactions with food

radionuclides





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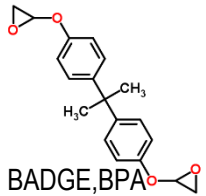
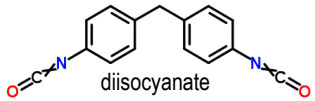
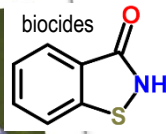
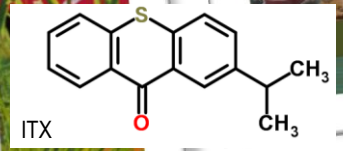
SAFEMAT
MATÉRIAUX AU CONTACT
DES ALIMENTS

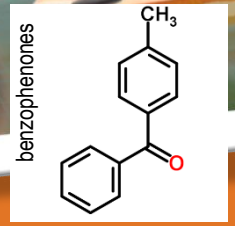

Is it safe?
How to assess it?
How to grant it?
MILK
MILK
AgroParisTech
TUNA
INRA
SCIENCE & IMPACT

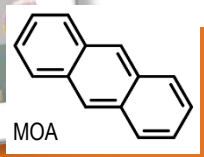

BADGE,BPA


diisocyanate

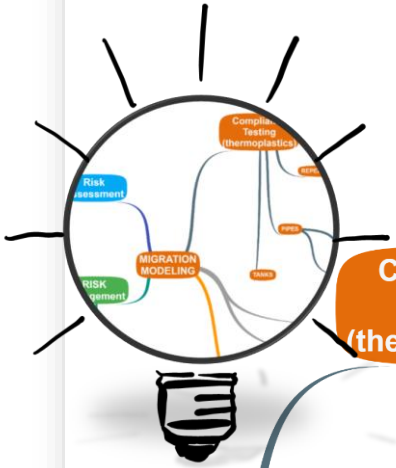

biocides


ITX

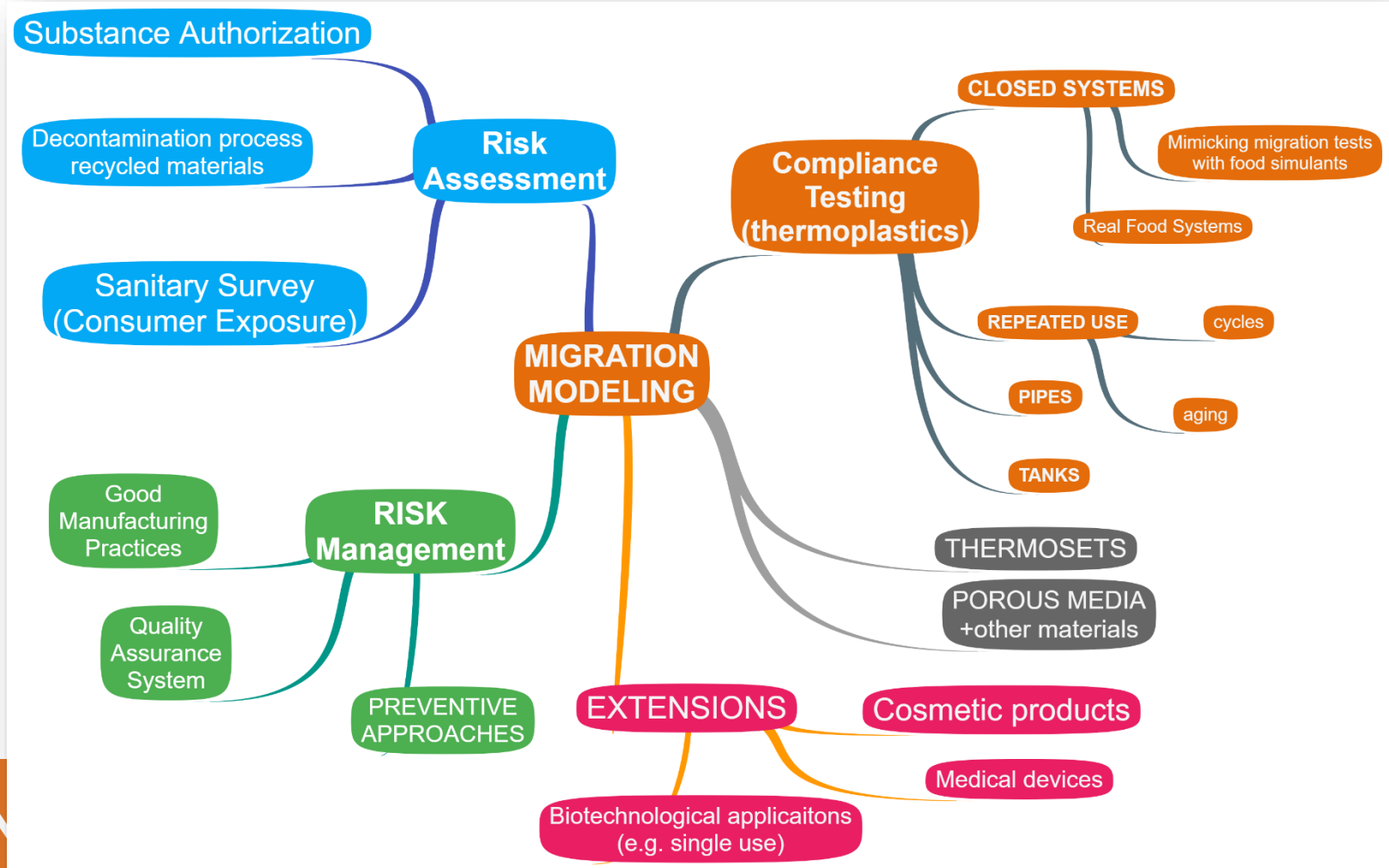

benzophenones

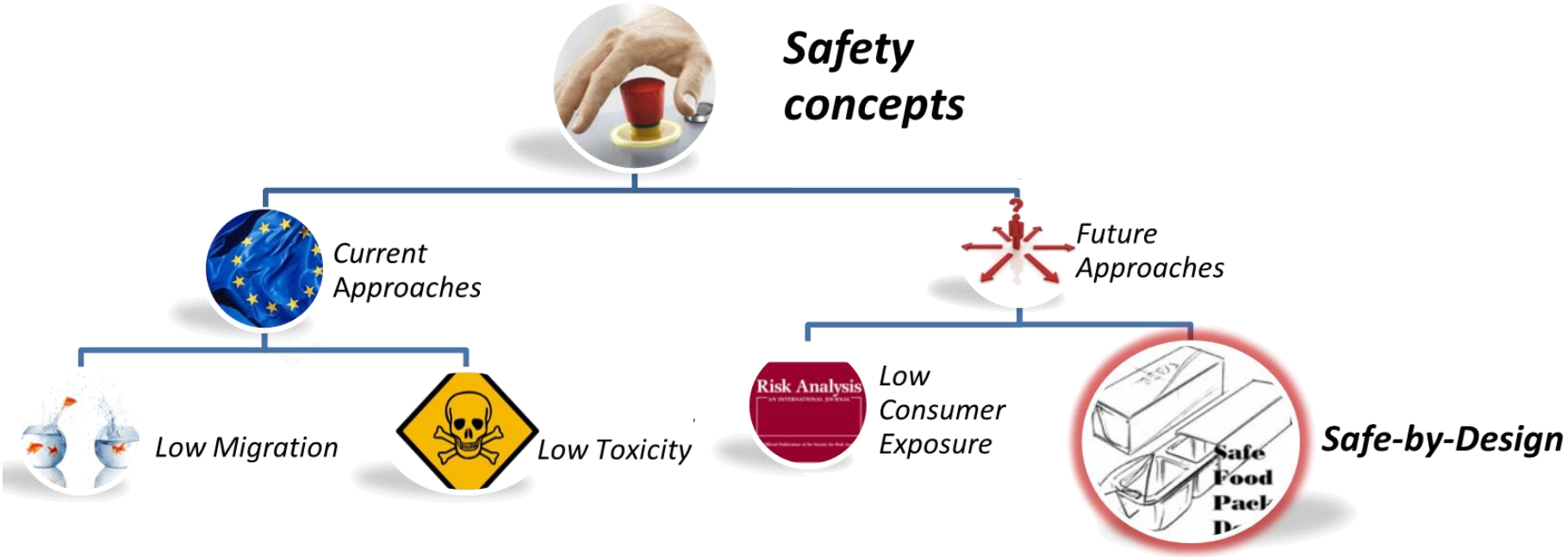

MOA

WITH TIME THE SCOPE OF MODELING HAS BEEN STRONGLY EXPANDED?



- Compliance Testing (thermoplastics)
  - CLOSED SYSTEMS
    - Mimicking migration tests with food simulants
      - Monolayer FCM
      - Multilayer FCM
    - Real Food Systems
      - Single step
      - Multiple steps
        - Set-off
        - other redistributions
        - Temperature (cycle, variation)
    - Composite packaging 2D,3D
      - Non cartesian geometry
    - Interactions with food
      - sorption isotherms
      - polymer swelling, plasticizing, induced-crystallization, cracking
  - REPEATED USE
    - cycles
    - aging
  - PIPES
    - laminar (low Re values)
      - Poiseuille flow
      - unsteady
    - turbulent (high Re values)
      - established regime
      - variable profile
  - TANKS
- MIGRATION MODELING

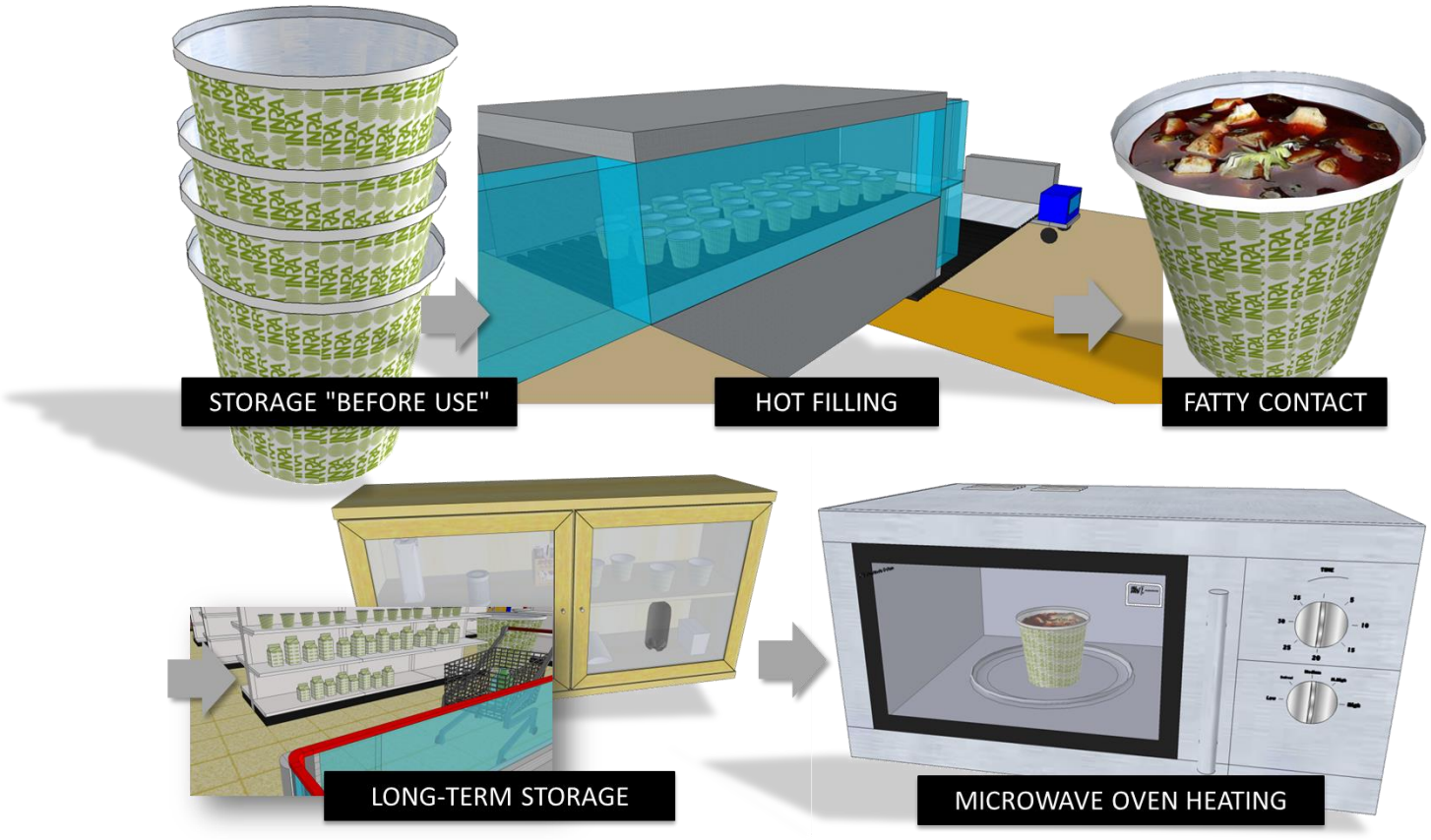

Substance Authorization
Decontamination process recycled materials
Risk Assessment
Sanitary Survey (Consumer Exposure)
CLOSED SYSTEMS
Mimicking migration tests with food simulants
Compliance Testing (thermoplastics)
Real Food Systems
REPEATED USE
cycles
MIGRATION MODELING
PIPES
aging
TANKS
Good Manufacturing Practices
RISK Management
THERMOSETS
POROUS MEDIA +other materials
Quality Assurance System
PREVENTIVE APPROACHES
EXTENSIONS
Cosmetic products
Medical devices
Biotechnological applicaitons (e.g. single use)

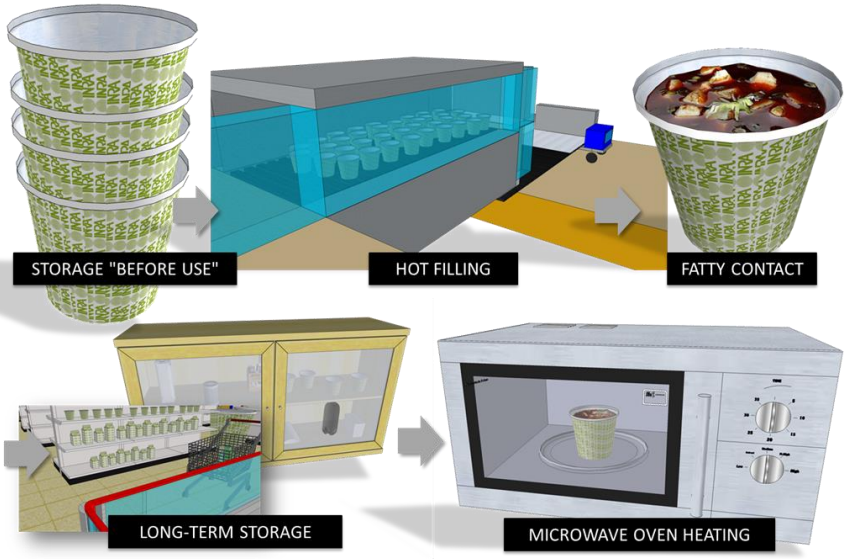


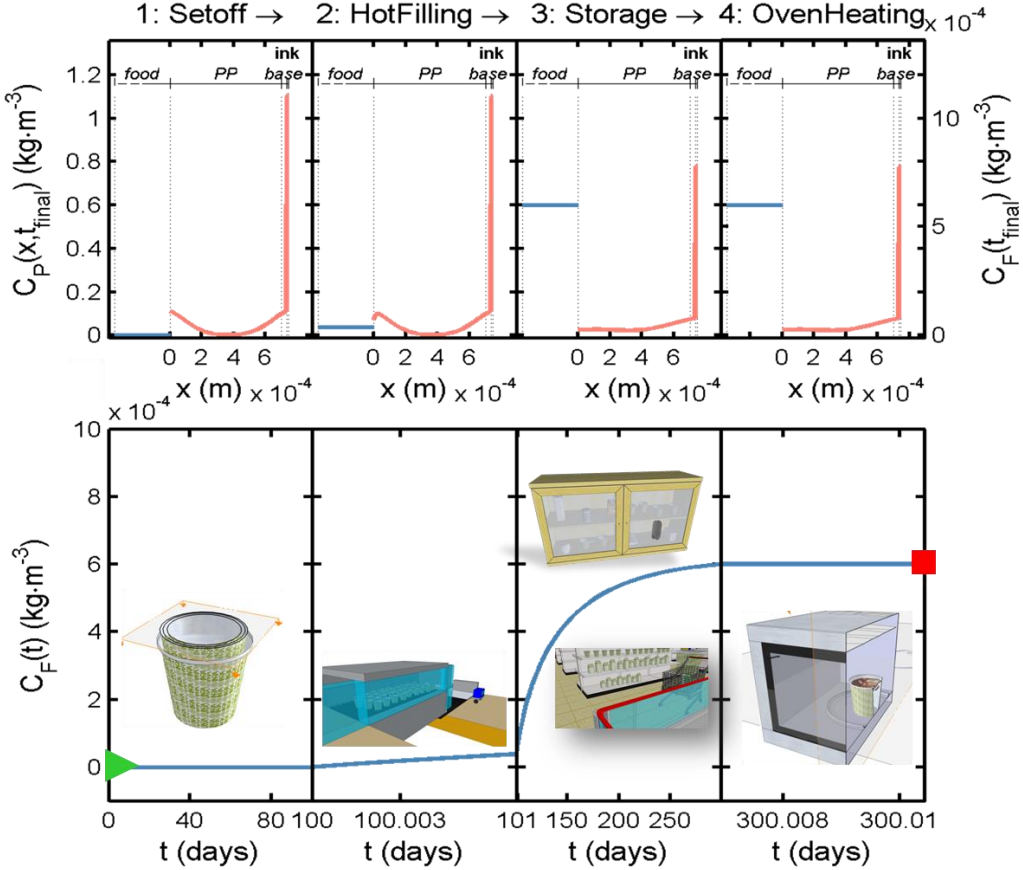
+VOLUNTARY APPROACHES & LOCAL ORDINANCES

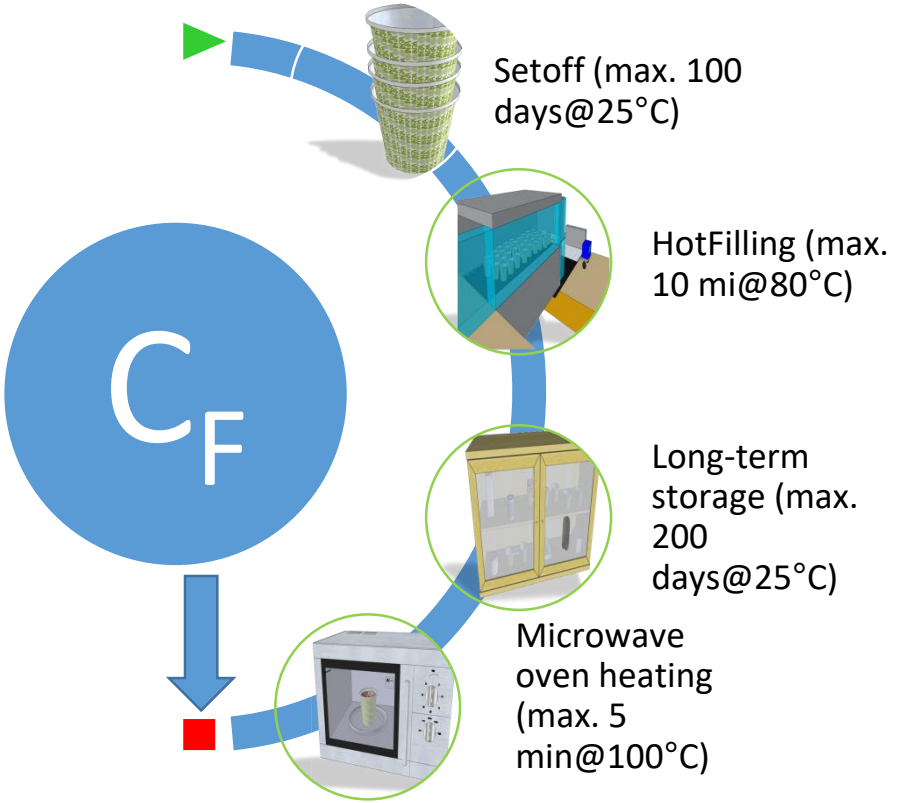
Regulation EC 2023/2006 - Good Manufacturing Practice for materials and articles intended to come in contact with food

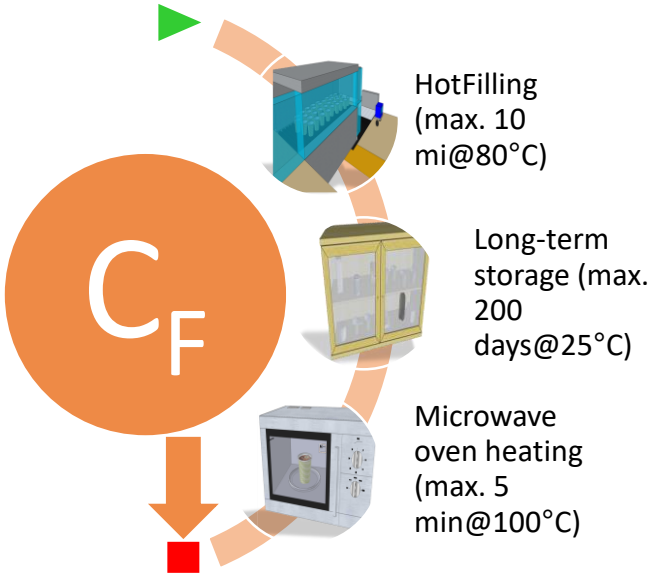
Risk of contamination by a photo-initiator in UV-curing printing ink



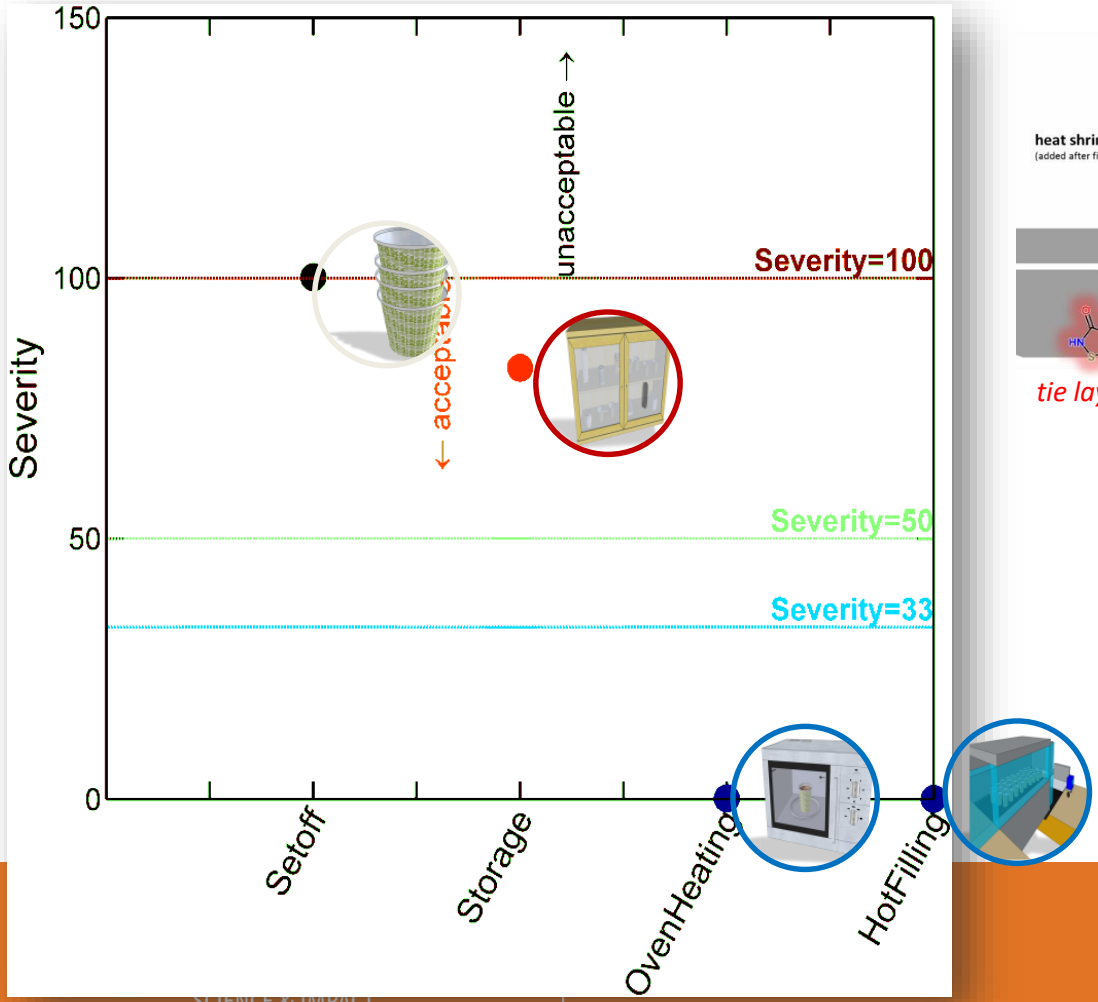

STORAGE "BEFORE USE"
HOT FILLING
FATTY CONTACT
LONG-TERM STORAGE
MICROWAVE OVEN HEATING

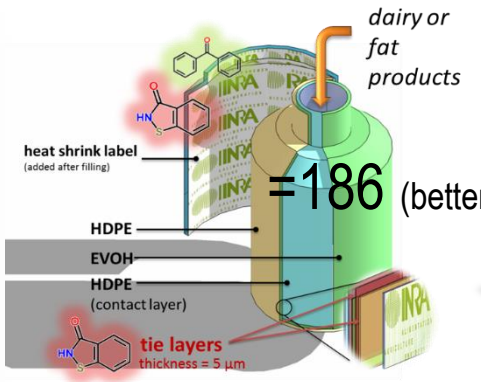

1: Setoff →
2: HotFilling →
3: Storage →
4: OvenHeating
ink
food
PP
base
$C_P(x,t_{final})$ (kg·m^{-3})
$C_F(t_{final})$ (kg·m^{-3})
x (m) x 10^{-4}
$C_F(t)$ (kg·m^{-3})
t (days)





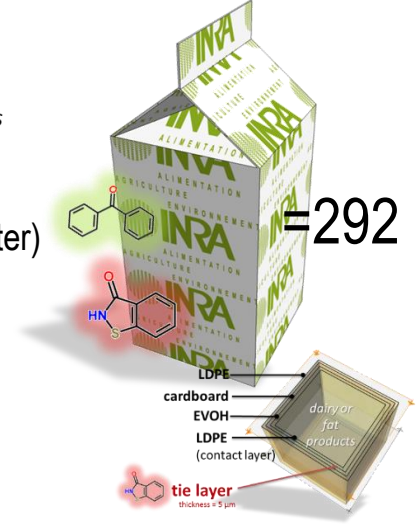
AIChE J. 2013, **59**(4), 1183-1212



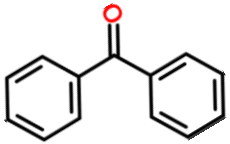


=186 (better)

tie layer = EVA



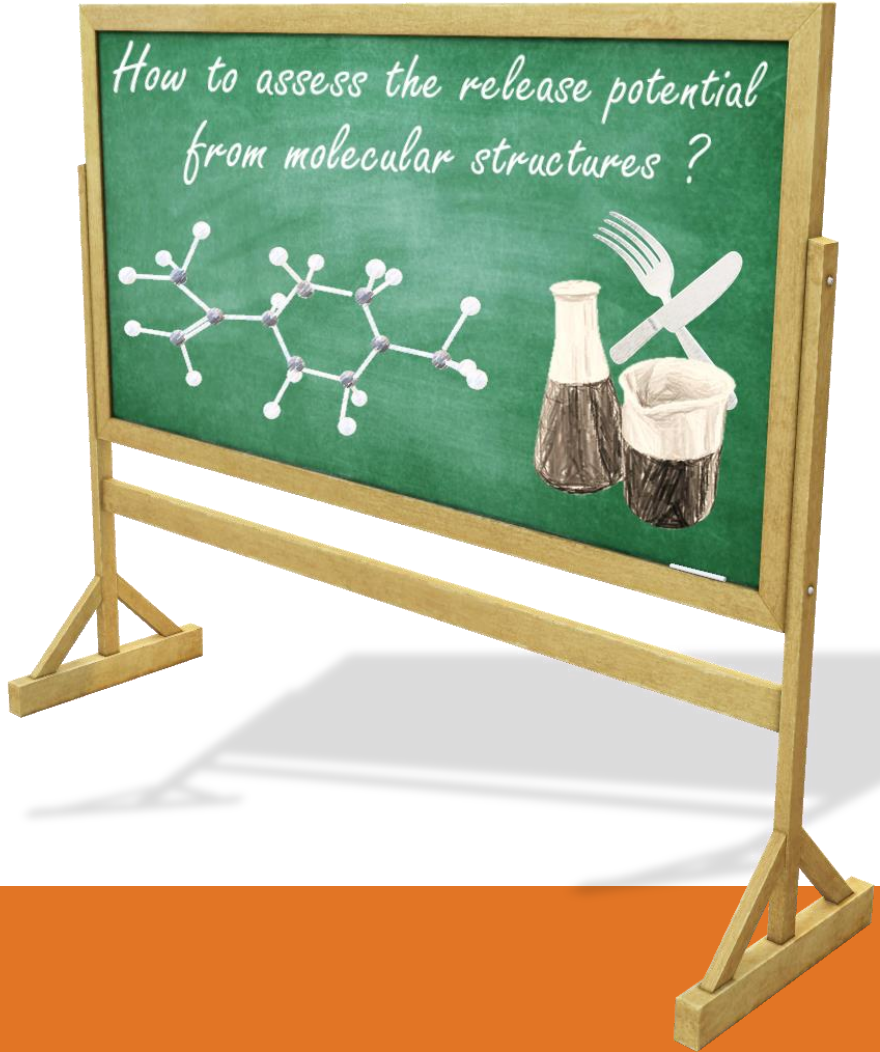
=292



=115

(almost acceptable)

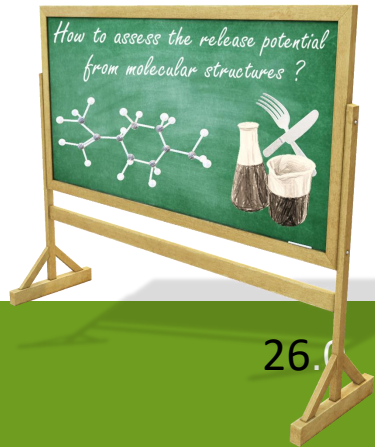
=124



MOLECULAR MODELING CAN BE APPLIED TO ANY SUBSTANCE:

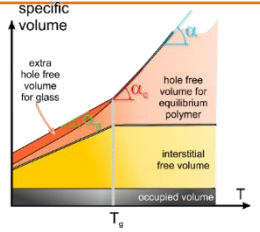
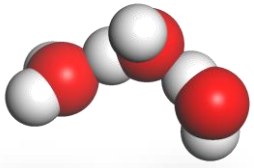
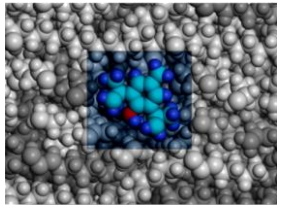
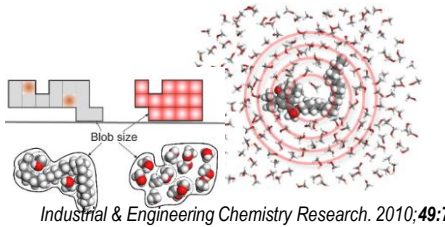
- INTENTIONALLY-ADDED
- NON-INTENTIONALLY-ADDED
- WELL CHARACTERIZED OR NOT

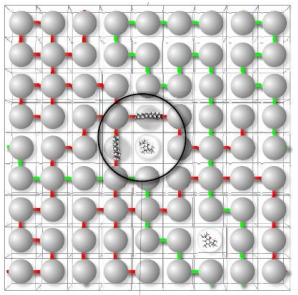
IS THE RECYCLED MATERIAL AS SAFE AS THE ORIGINAL ONE ?

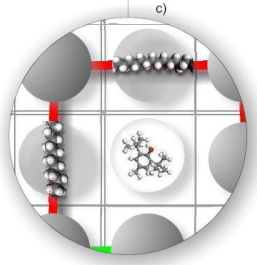


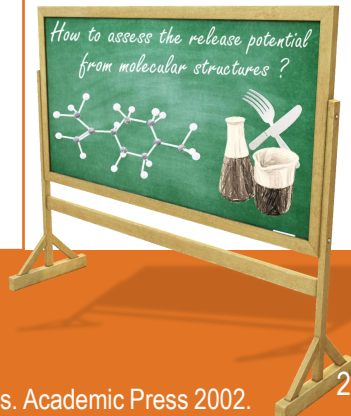
coarse

detailed

	TRANSPORT diffusion coefficients D and their activation E_a	THERMODYNAMICS chemical affinity (Flory-type isotherms)
Worst-case approaches (arbitrary)	For compliance testing (Piringer's equation) *Food Additives and Contaminants. 2005;**22:73-90.***	$K_{F/P} = 1 \; or \; 10^{-3}$ JRC Scientific and Technical Reports EUR 27529 EN. Ispra (Italy): European Commission; 2015.
Group contribution methods (fitting)	Decision tree *Journal of Applied Polymer Science. 2006;**101:2167-86.***	UNIQUAC, UNIFAC, Flory—Huggins Prausnitz, Lichtenthaler & de Azevedo. Molecular Thermodynamics of Fluid-Phase Equilibria: Pearson Education; 1998.
Theory from first principles (statistical physics)	Free-volume theory (Vrentas-Duda)  *European Polymer Journal. 1998;**34:797-803.***	Self-association theory  Kontogeorgis & Folas. Thermodynamic Models for Industrial Applications: From Classical and Advanced Mixing Rules to Association Theories: Wiley; 2009.
Full atomistic simulation or coarse-grained (no assumptions)	for $D \geq 10^{-14} m^2 \cdot s^{-1}$  *Journal of Chemical Physics. 2010;**132:194902.***	 *Industrial & Engineering Chemistry Research. 2010;**49:7263-80.***



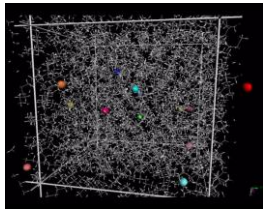


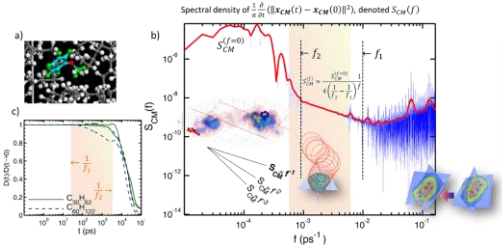


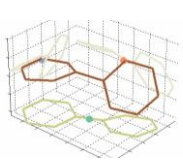
INRA SCIENCE & IMPACT

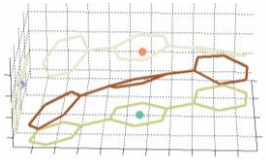
Suggestion of reading
Frenkel & Smit. Understanding Molecular Simulation: From Algorithms to Applications. Academic Press 2002.

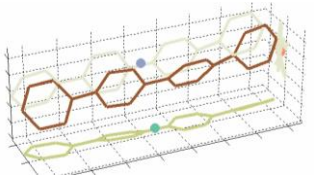
TIME SCALES ACCESSIBLE TO BRUTE FORCE MOLECULAR MODELING

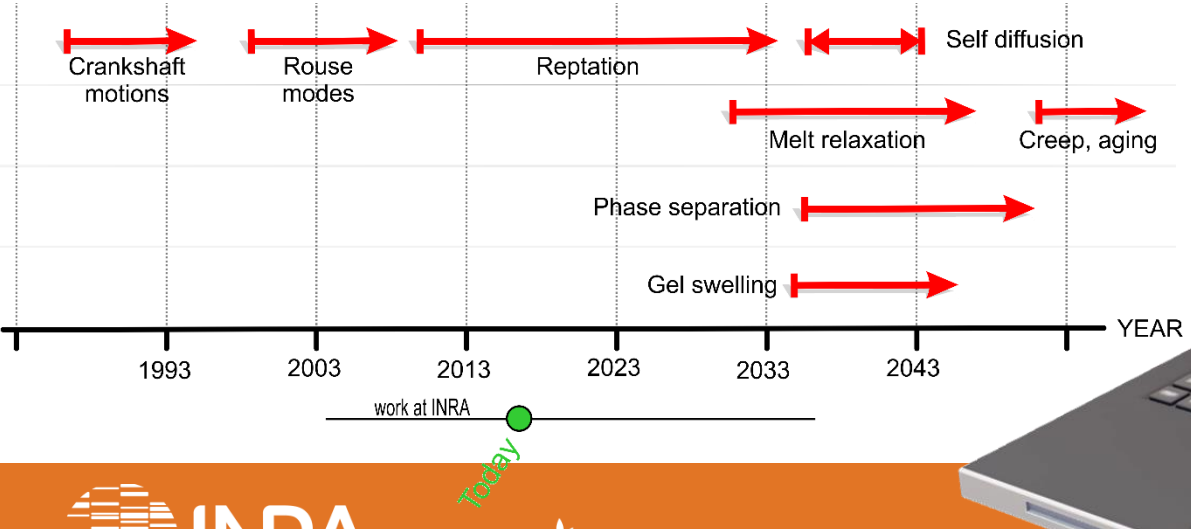


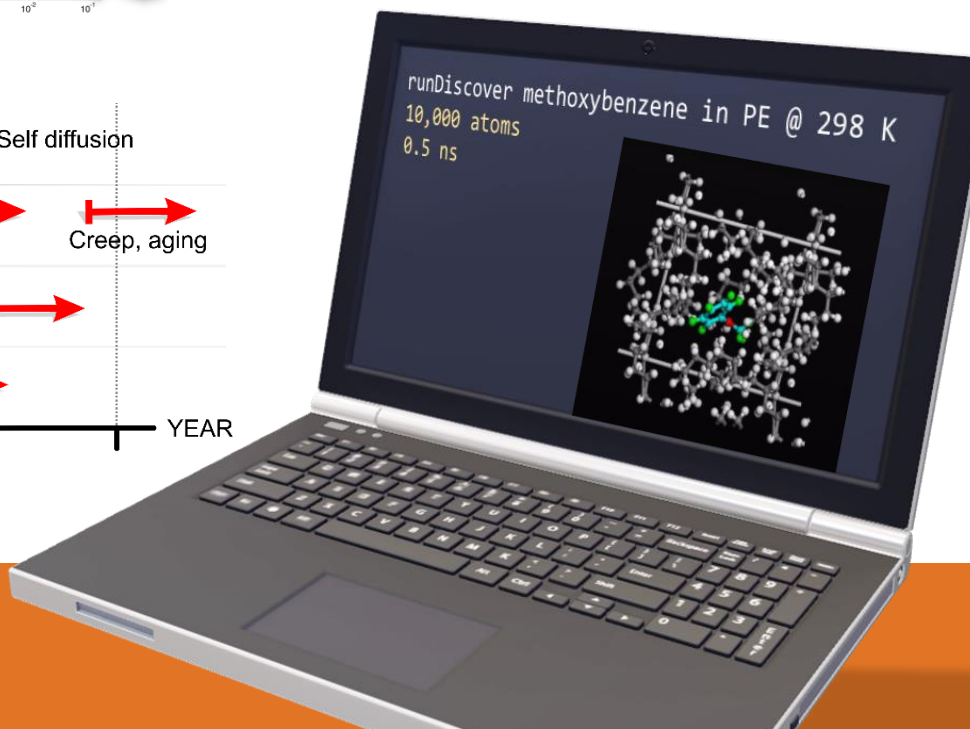






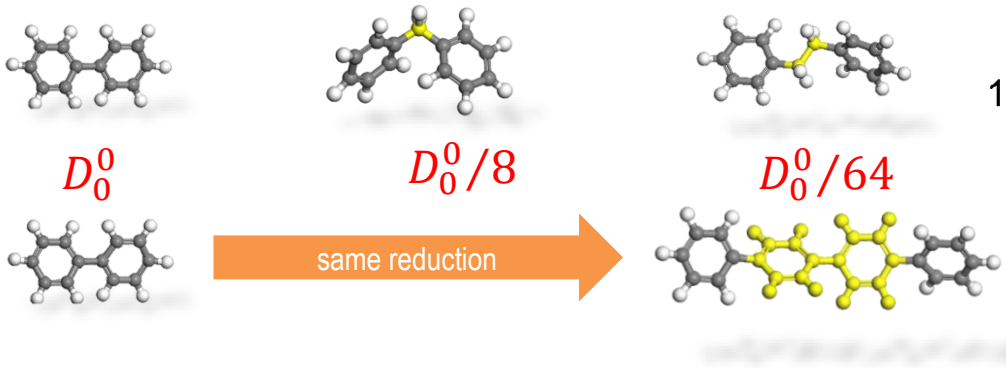


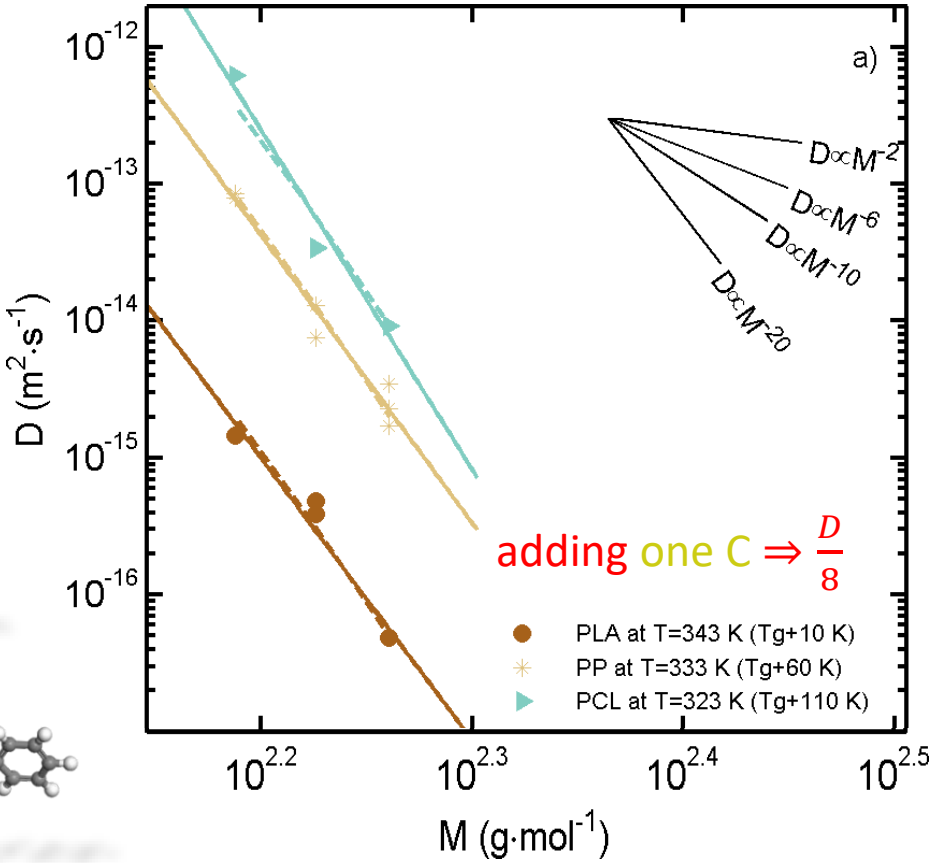




INRA
SCIENCE & IMPACT

$$D(M,T,T_g) = D_0 \exp\left(-\frac{E_a^{\,blob}}{RT}\right) \times \exp\left(-\frac{E^{*(M)} - E^*_{blob}}{RT}\right)\left(\frac{M}{M_{blob}}\right)^{-\alpha(T,T_g)}$$

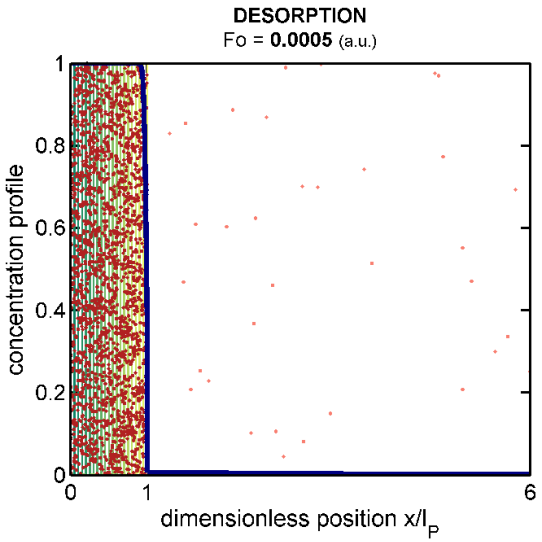


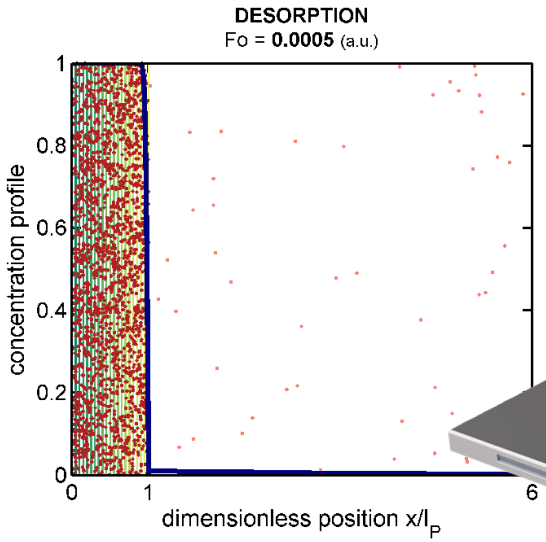


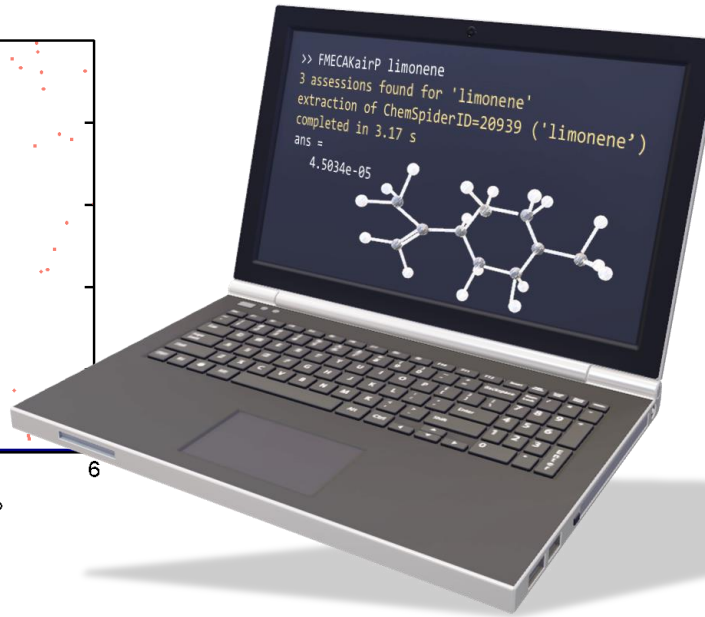
INRA SCIENCE & IMPACT

50 × more chemical affinity for P | 50 × more chemical affinity for F

$K_{i,F/P}$ = 1/50 | 50







$$K_{i,F/P} = \frac{C_{i,F}^{eq}}{C_{i,P}^{eq}} = \frac{1}{1 - crystallinity} \frac{\gamma_{i,P_{amorphous}}^{v}}{\gamma_{i,F}^{v}}$$

P = POLYMER
F = FLUID, FOOD

Italian police seize contaminated Nestle baby milk

22 Nov 2005 16:45:09 GMT

Source: Reuters

PREVIOUS | NEXT

Forest Ranger officials check a package of baby milk made by Swiss food group Nestle in a supermarket in Italy November 22, 2005. Italian police seized around 30 million litres of baby milk produced by Nestle on Tuesday after tests showed traces of ink, and the company said it was recalling the infant food in four European countries.
REUTERS/HO

(Adds Tetra Pak comment in paragraph 11)

By Massimiliano Di Giorgio and Isabel Strassheim

ROME/ZURICH, Nov 22 (Reuters) - Italian police seized around 30 million litres of baby milk produced by Swiss food giant Nestle <NESN.VX> on Tuesday after tests showed it was contaminated with traces of ink used in the packaging.

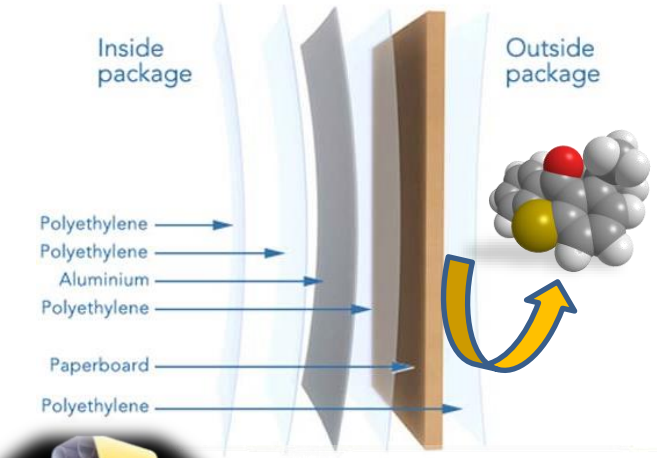
Nestle said the chemical substance was not harmful, but announced it was recalling the infant food in four European countries, including Italy, because of the problem, which related to Tetra Pak cartons.

Italian Agriculture Minister Gianni Alemanno demanded tests to see if babies given the contaminated milk over a prolonged period faced health risks.

"It is incredible that such defenceless beings as babies should face such serious risks in a product as widely used as milk," Alemanno said in a statement.

Italian officials said they had already seized about 2 million litres of Nestle baby milk earlier this month after finding traces of isopropylthioxanthone (ITX), an ink

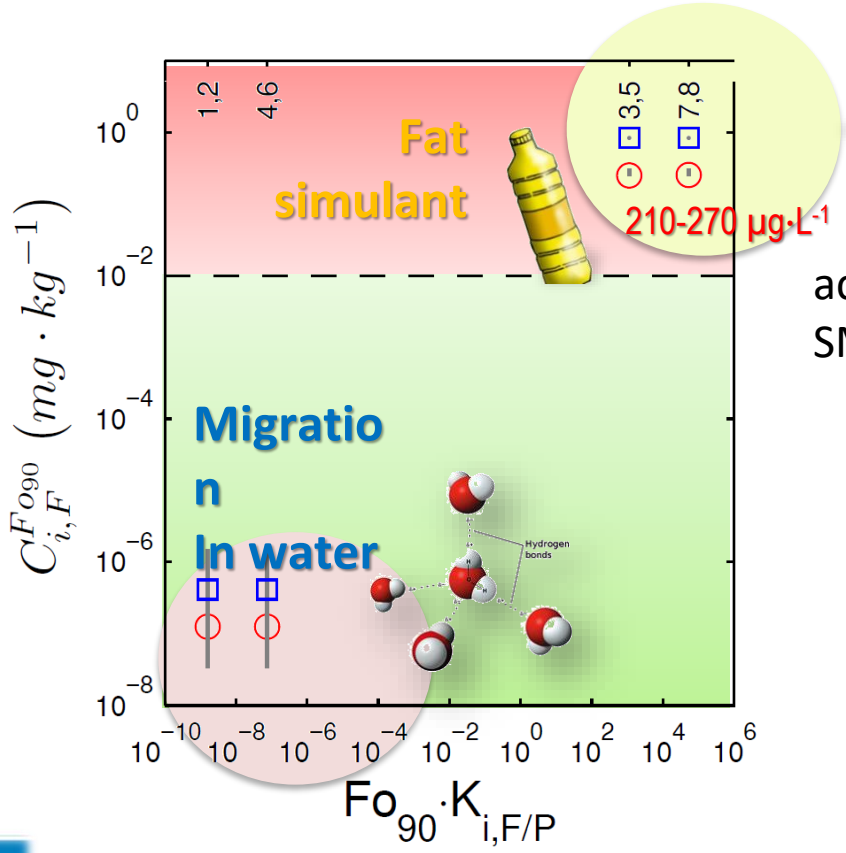
"It is incredible that such defenseless beings as babies should face such serious risks in a product as widely used as milk"



REUTERS AlertNet FOUNDATION

	Migrant	2-ITX
	Homologous migrant†	not available
	Polymer	LDPE††
PARAMETER	notation (unit)	
Thickness	l_P (μm)	50
Volume dilution ratio	$L_{F/P}$ (-)	360
Biot mass number	Bi (-)	10^3
Contact Time	t (days)	90
Temperature	(°C)	4
Likely initial concentration[a]	$\overline{C}^0_{i,P}$ [a] (mg·kg^{-1})	100 ± 10
Conservative initial concentration[b]	$\left(C^0_{i,P}\right)^+$ [b] (mg·kg^{-1})	300
Likely diffusion coefficient[c]	$\overline{D}_{i,P}$ [c] (m^2.s^{-1})	$8.4\cdot10^{-16}$ [$7.6\cdot10^{-16}$ $9.2\cdot10^{-16}$]
Conservative diffusion coefficient[d]	$D^+_{i,P}$ [d] (m^2.s^{-1})	$3.9\cdot10^{-14}$
Likely partition coefficient[e]	$\overline{K}_{i,F/P}$ (-)	$1.4\cdot10^{-9}$ [$3.7\cdot10^{-10}$ $5.1\cdot10^{-9}$]
Conservative partition coefficient	$K^+_{i,F/P}$ (-)	10^3

Food Additives and Contaminants, 2009, 26(12), 1556-1573.

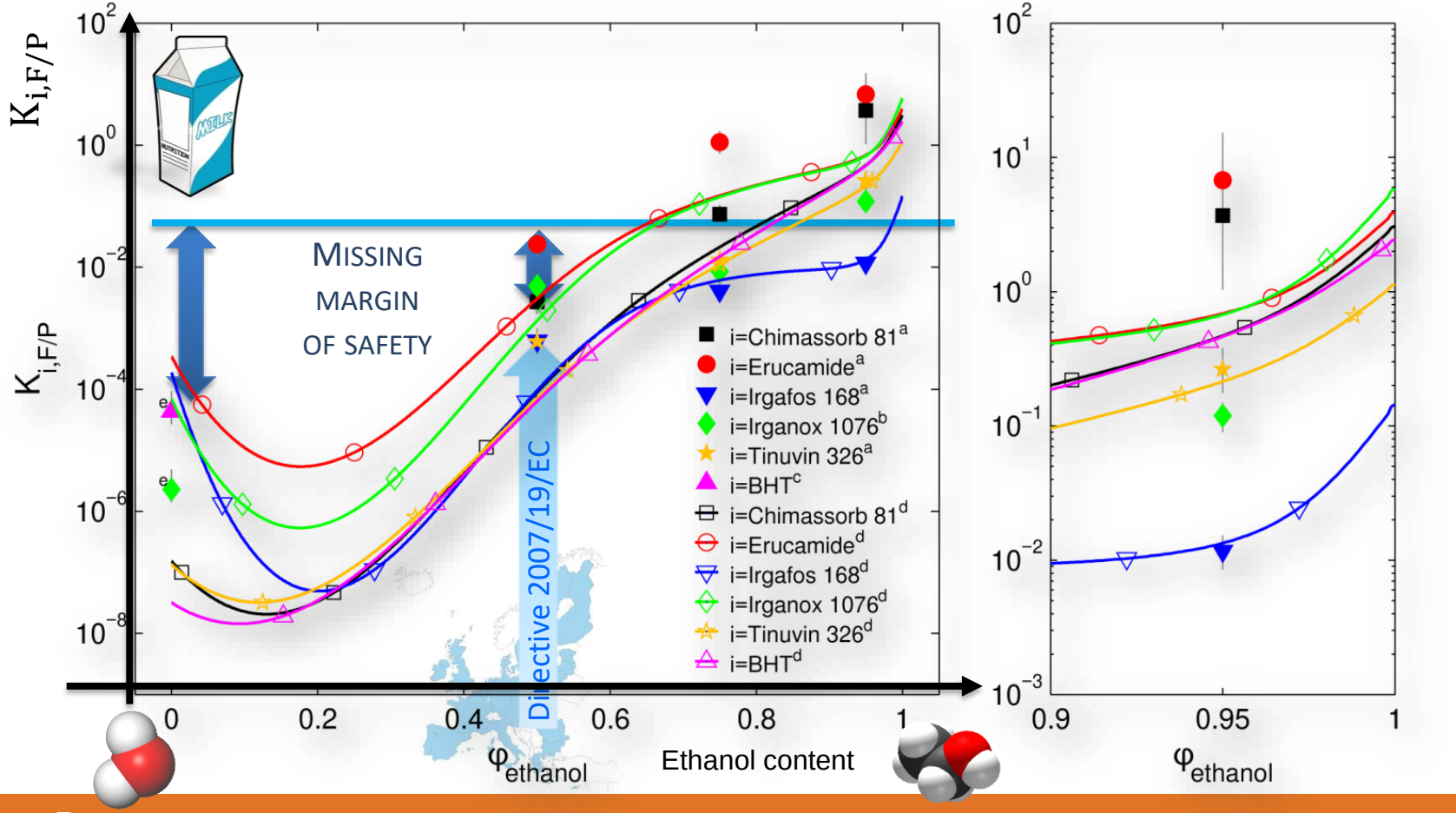


M=241 g·mol^{-1}

acceptable SML

	Date of case	Last change	Reference	Country	
6.	08/09/2005		2005.631	ITALY	food contact materials
					migration of isopropyl thioxanthone (250 µg/l) from packaging of milk for babies from Spain

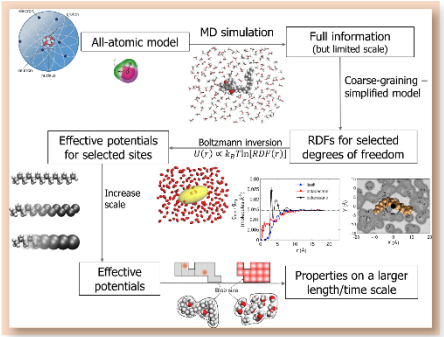
RASFF Portal

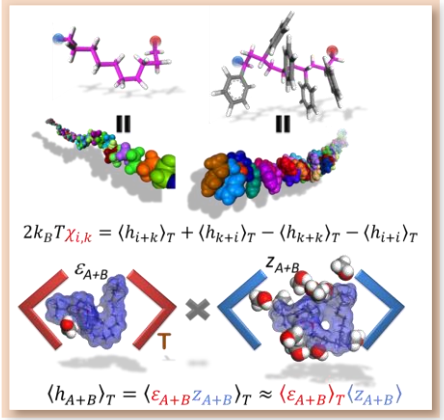


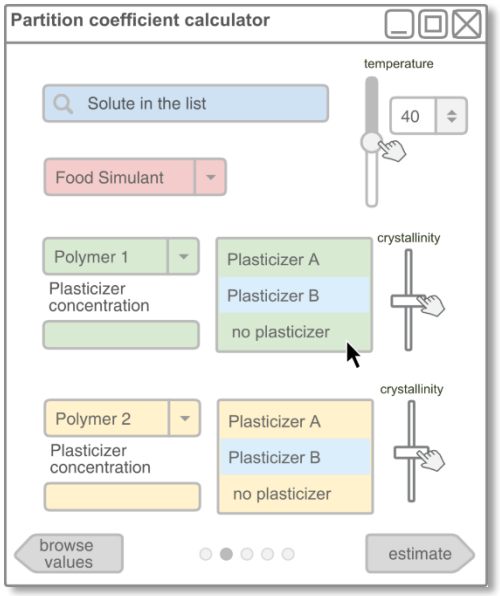
Industrial & Engineering Chemistry Research 2010, 49, 7263-7280.

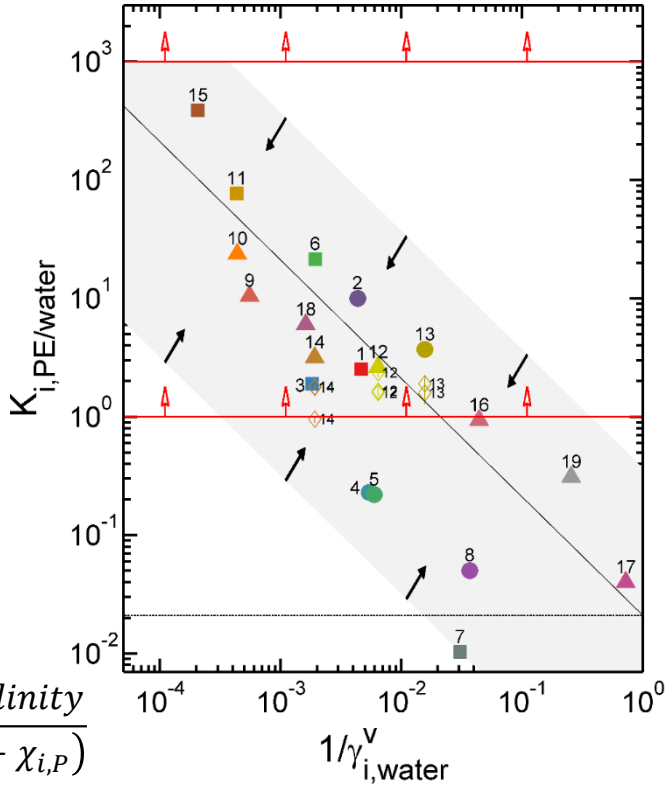
APPROACHES DEVELOPED FOR THE INDUSTRY

OVERVIEW









$$K^{semi-crystalline}_{i,P/F} \approx \frac{1 - crystallinity}{\phi^{sat}_{i,F}\exp(1+\chi_{i,P})}$$

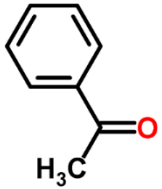
$$\left\{\mu^{excess}_{i,k}\right\}_{k=P,F} = \ln\gamma^{v}_{i,k} = \left(1 - \frac{1}{r_k}\right)\phi_k + \chi_{i,k}\phi_k^2$$

$$2k_BT\chi_{i,k} = \langle h_{i+k}\rangle_T + \langle h_{k+i}\rangle_T - \langle h_{k+k}\rangle_T - \langle h_{i+i}\rangle_T$$

INRA SCIENCE & IMPACT

PARTITION COEFFICIENTS WITH AIR

OVERVIEW

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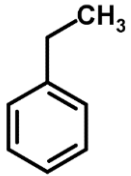


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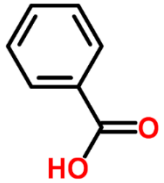


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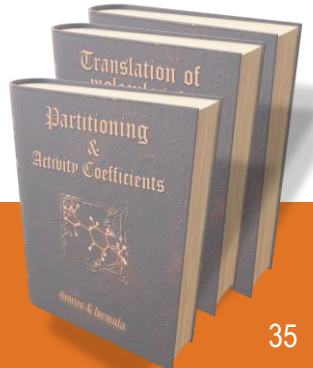
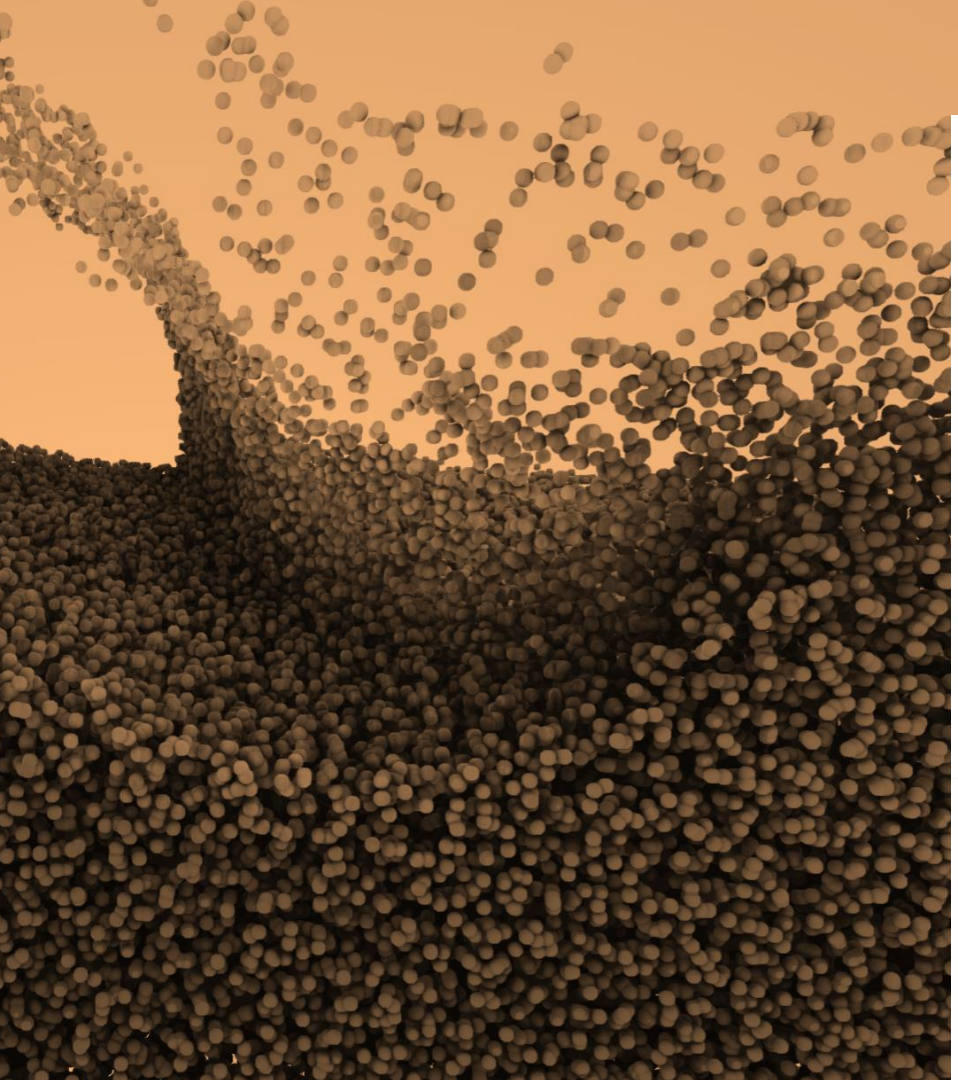
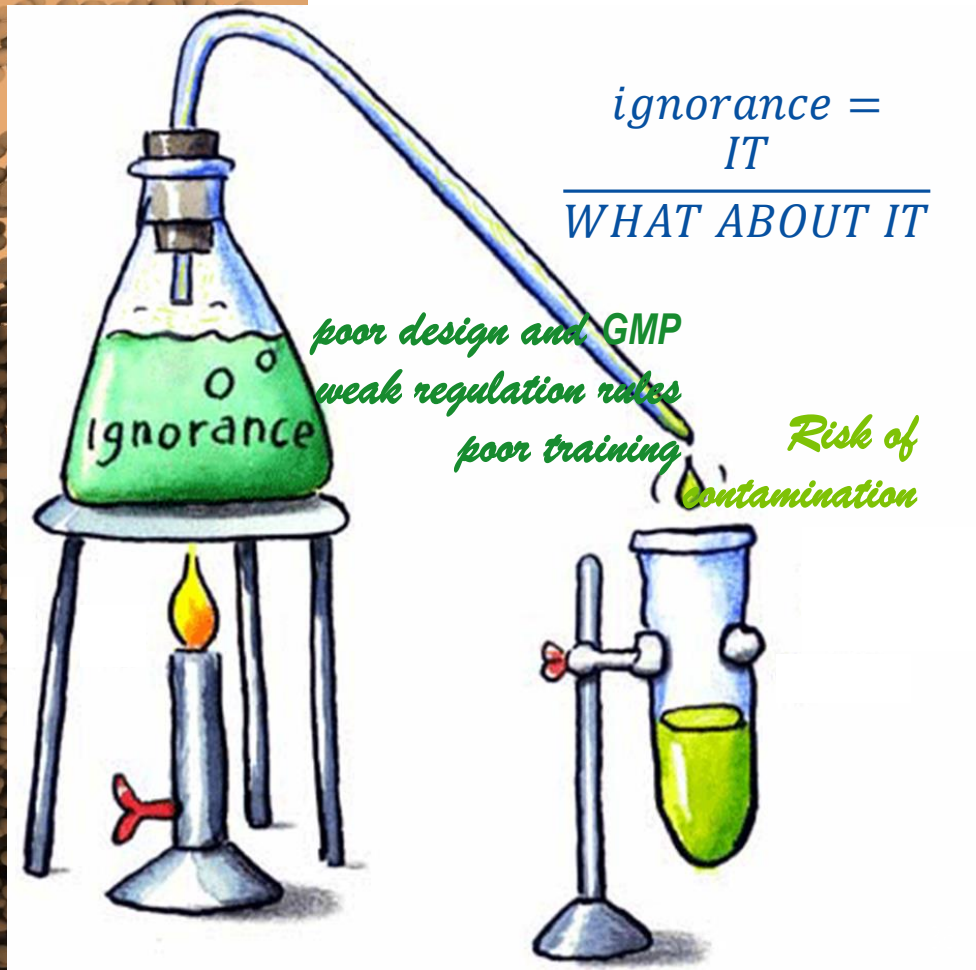


CONCLUSIONS

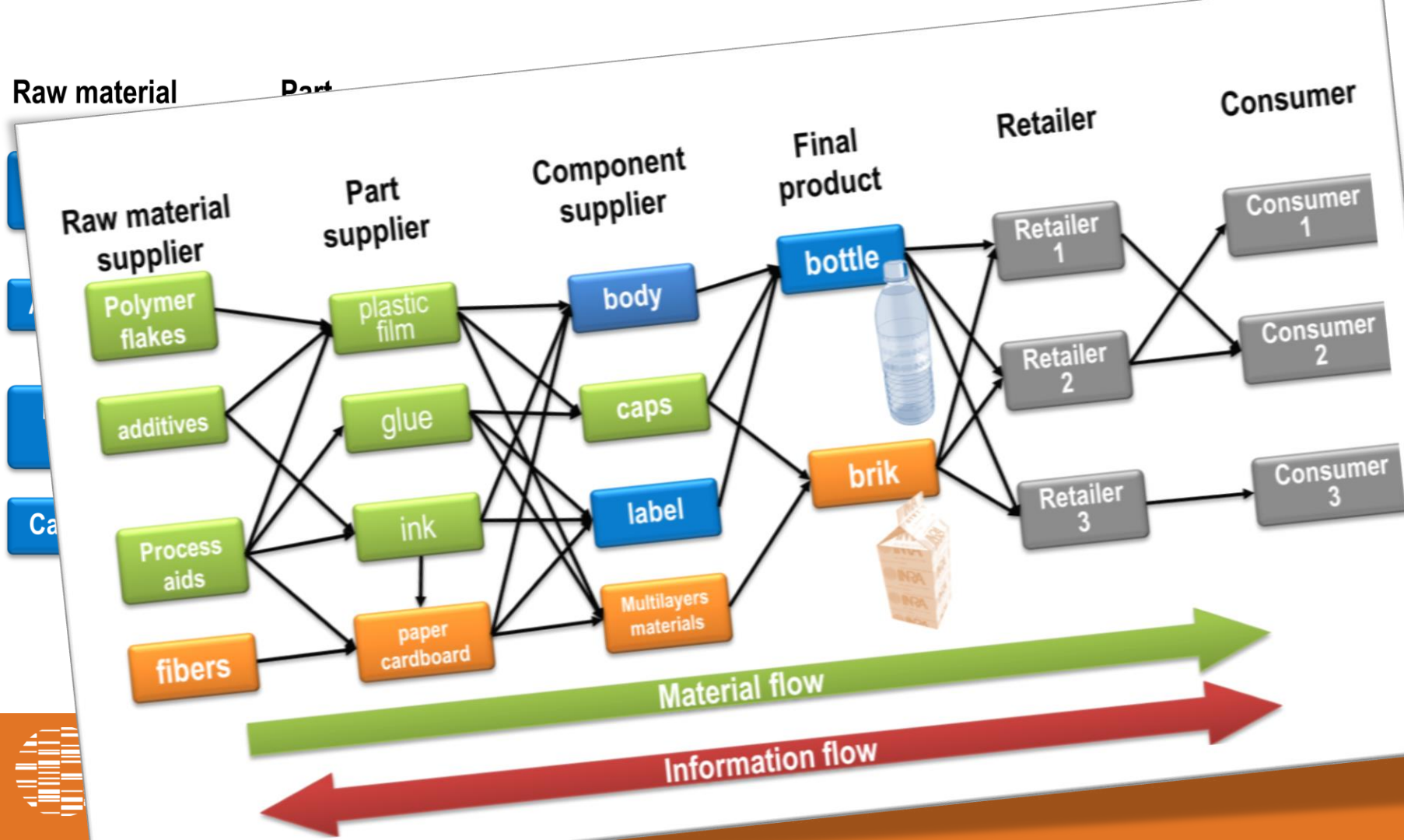


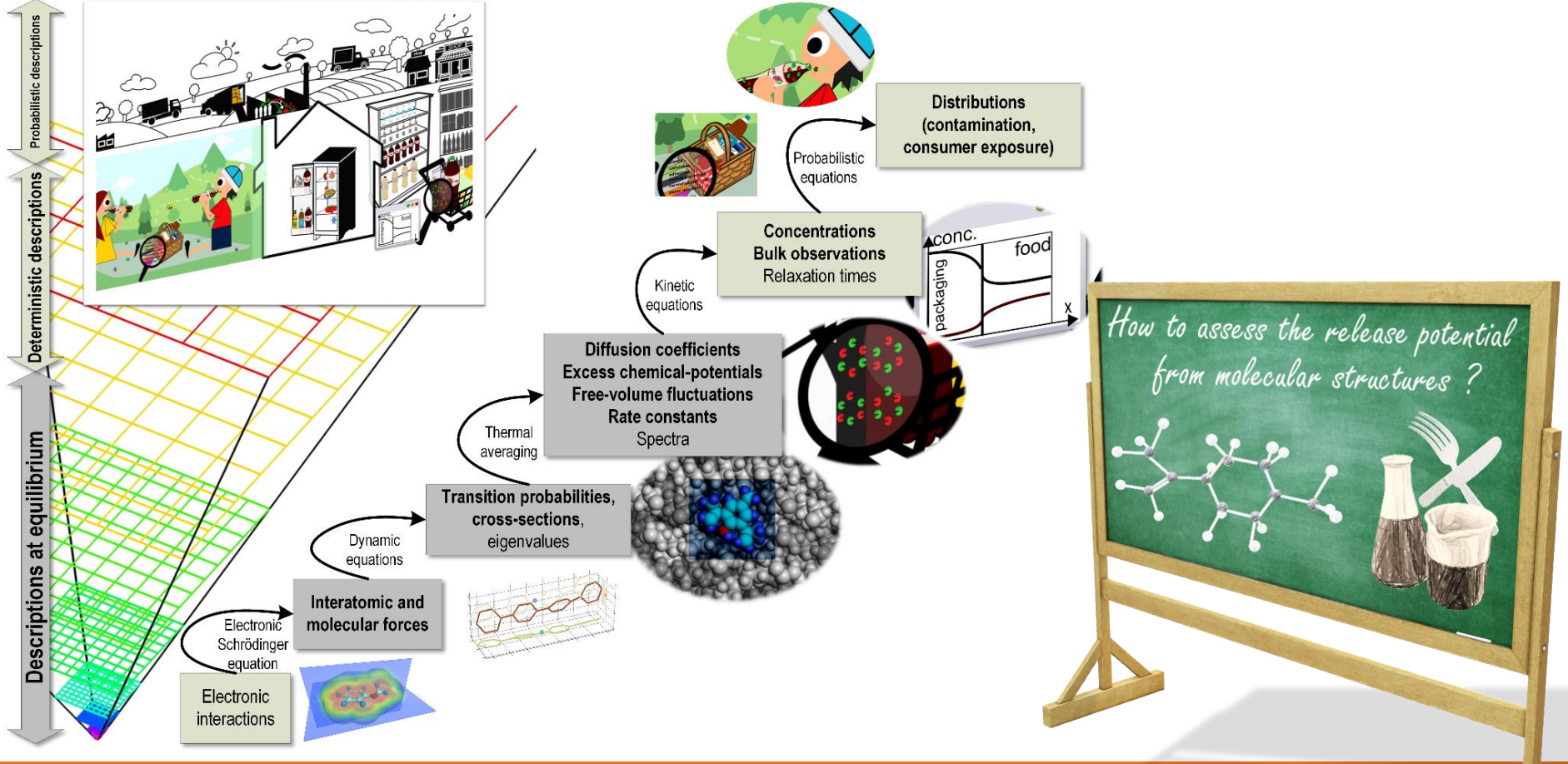


$$ignorance = \frac{IT}{WHAT\ ABOUT\ IT}$$

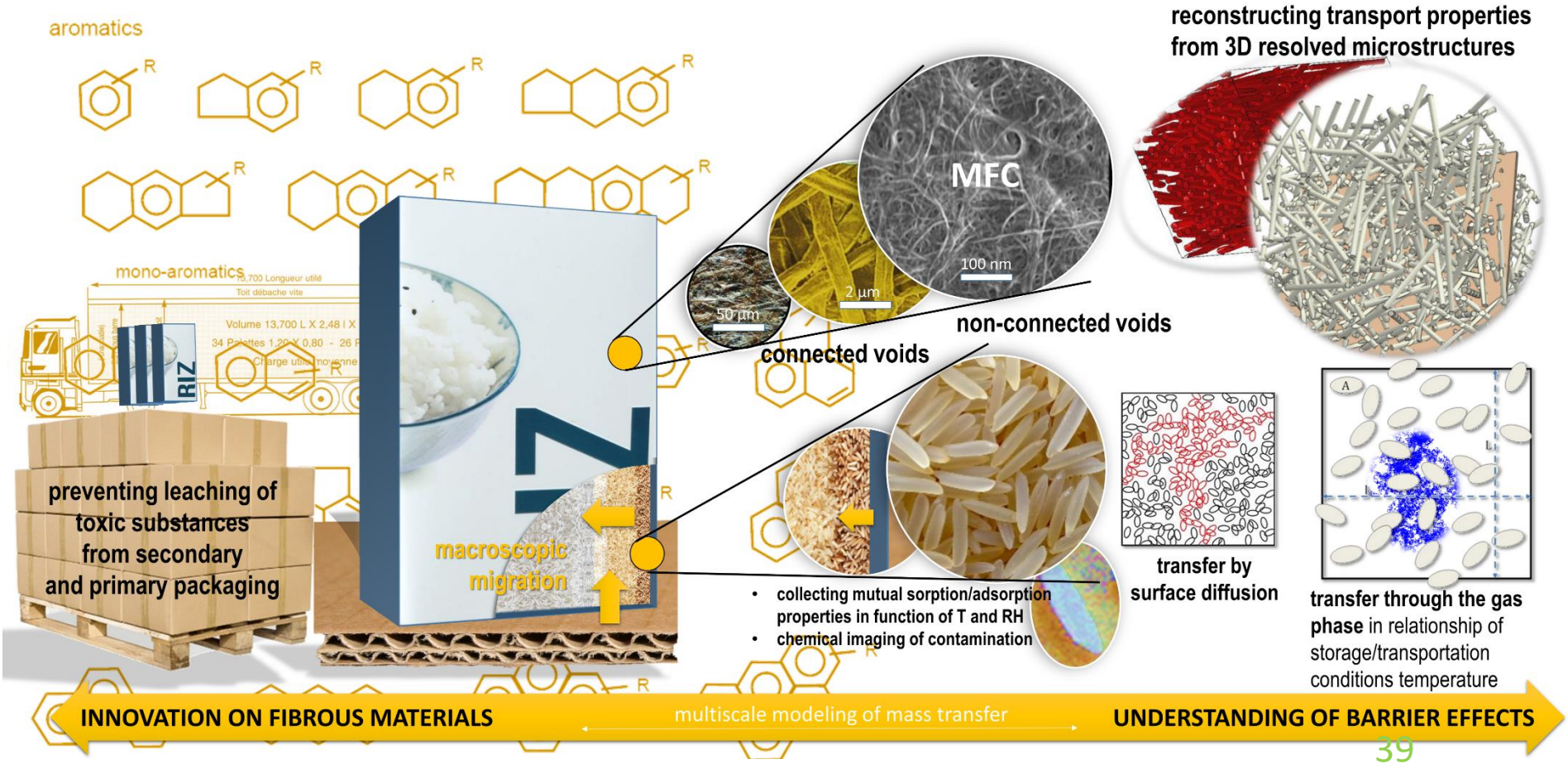
poor design and GMP
weak regulation rules
poor training

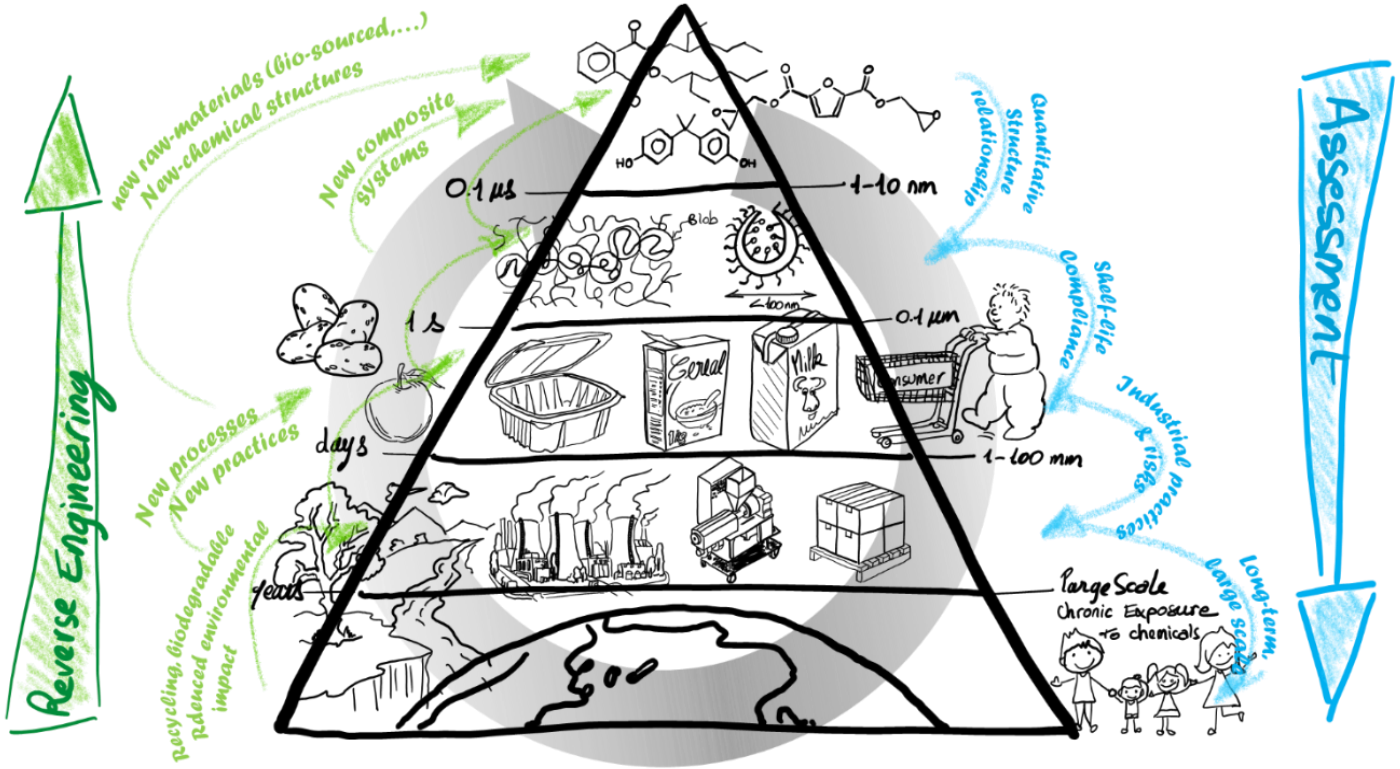
Risk of contamination

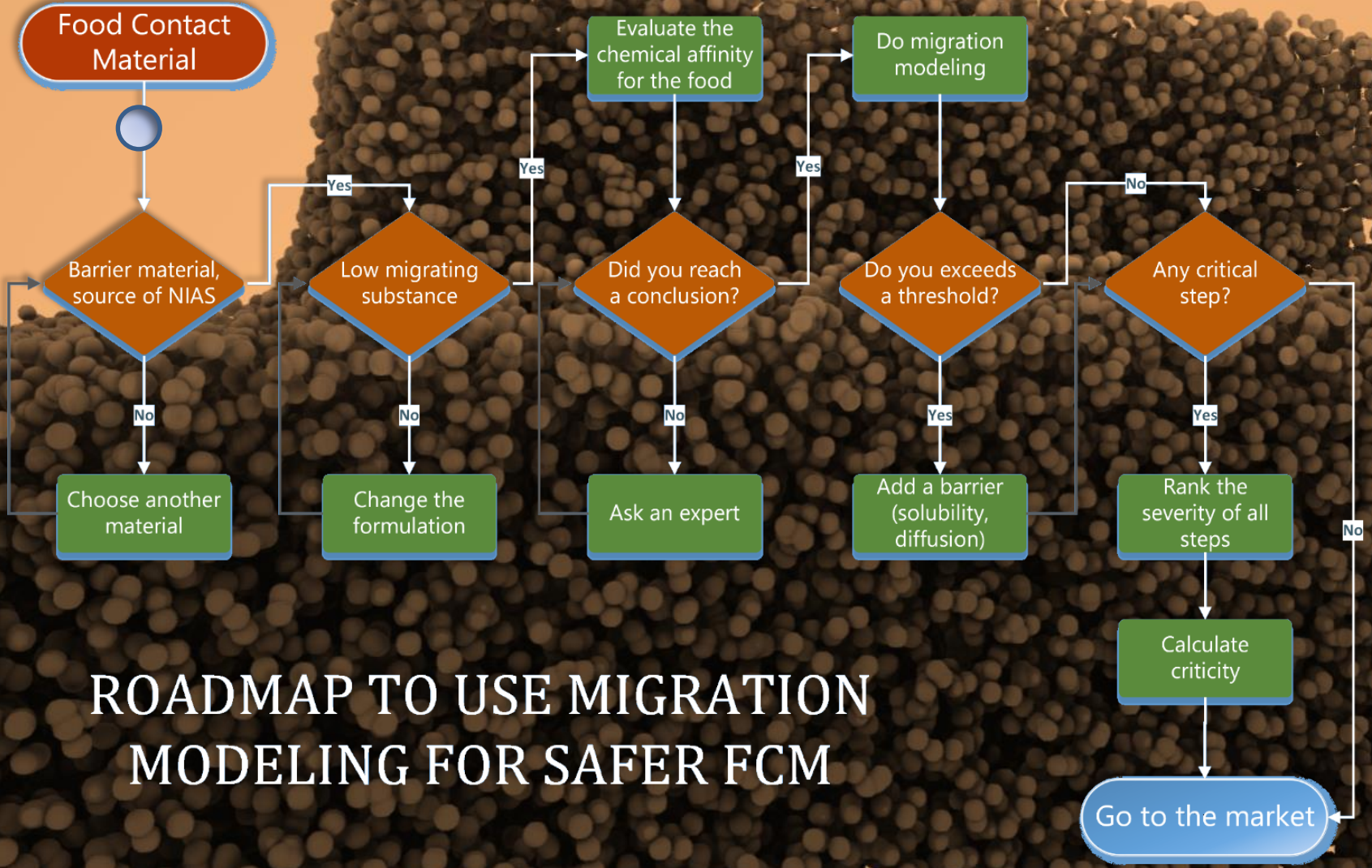

Raw material
Raw material supplier
Part supplier
Component supplier
Final product
Retailer
Consumer
Polymer flakes
additives
Process aids
fibers
plastic film
glue
ink
paper cardboard
body
caps
label
Multilayers materials
bottle
brik
Retailer 1
Retailer 2
Retailer 3
Consumer 1
Consumer 2
Consumer 3
Material flow
Information flow


Probabilistic descriptions
Deterministic descriptions
Descriptions at equilibrium
Distributions (contamination, consumer exposure)
Probabilistic equations
Concentrations
Bulk observations
Relaxation times
Kinetic equations
conc.
food
packaging
x
Diffusion coefficients
Excess chemical-potentials
Free-volume fluctuations
Rate constants
Spectra
Thermal averaging
Transition probabilities, cross-sections, eigenvalues
Dynamic equations
Interatomic and molecular forces
Electronic Schrödinger equation
Electronic interactions
How to assess the release potential from molecular structures ?

Evaluating and preventing the migration from mineral oil



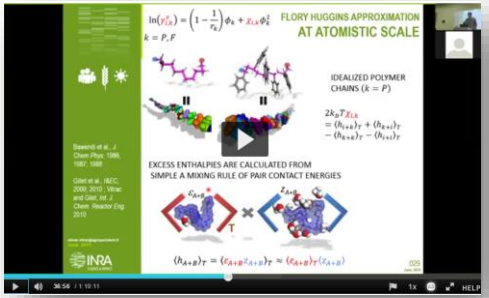

Reverse Engineering
new raw-materials (bio-sourced,...)
New-chemical structures
New composite systems
New processes
New practices
Recycling, Biodegradable
Rdanced environmental impact
0.1 µs
1-10 nm
1 s
0.1 µm
days
1-100 mm
years
Large Scale
Chronic Exposure
to chemicals
Assessment
Quantitative Structure relationships
Shelf-life compliance
Industrial practices
Long-term large scale
Cereal
Milk
Consumer



ROADMAP TO USE MIGRATION MODELING FOR SAFER FCM

AgroParisTech

THE SCHOOL OF PACKAGING MICHIGAN STATE UNIVERSITY



ONLINE TOOLS

http://modmol.agroparistech.fr/

MY LECTURES AT MSU (MI,USA):
http://www.fshn.msu.edu/events/event/Vitrac

DIFFUSION
https://mediaspace.msu.edu/media/dr.+olivier+vitrac+presentsa+diffusion+coefficients+of+organic+solutes+in+polymersa/1_zz20dgt9

PARTITIONING
https://mediaspace.msu.edu/media/Dr.+Olivier+Vitrac+presentsA+An+atomistic+Flory-Huggins+formulation+for+the+tailored+prediction+of+activity+and+partition+coefficients/1_uzi6h91k

SAFETY MANAGEMENT
https://mediaspace.msu.edu/media/WorkshopA+Prediction+of+the+migrationA+beyond+conventional+estimates*/1_won1m7aw

RISK ASSESSMENT (EFSA)
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