A Computer-Aided Methodology to Design Safe Food Packaging and Related Systems

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A specific "Failure Mode, Effects, and Criticality Analysis" (FMECA) methodology has been developed to detect substances, materials, and steps that are critical for the safety of packaging systems used in food contact and related applications. Contamination levels in the finished product beyond acceptable thresholds are screened via a systematic analysis of crossed mass transfer between components and a serialization of mass-transfer instances during product lifetime. The whole framework, including physical modeling and expert systems, has been integrated within the open-source simulation software FMECAengine. The whole approach is illustrated on three case studies representative of applications along the food packaging supply chain: (1) identification of critical routes of the contamination by printing ink constituents, (2) concurrent engineering of multipurpose packaging, and (3) application to surveys or control plans. The implementation of this framework within industrial commitments such as compliance with EU regulations and ISO 22000 type food safety management systems is discussed. © 2013 American Institute of Chemical Engineers *AIChE J*, 59: 1183–1212, 2013

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Introduction

Almost all food, cosmetic, and pharmaceutical products are in contact with materials during production, distribution, shelf-life, and final use. The risk of contamination of the product by substances originating from the polymer materials is ubiquitous as soon as the involved substances (additives, residues, etc.) are noncovalently bounded to the polymer.[1] The intricate relationship between industrial practices and exposure to chemicals in the environment, food and related products is managed by public policies with strong variations according to the considered market (e.g., US, EU, China, Japan, etc.), product (e.g., food and cosmetic), materials (e.g., plastics and nonplastics), and final usage (e.g., material with direct or not direct contact with the product or heating in packaging). Most of the current regulations managing chronic exposure hazard—including the recent EU REACH regulation[2] and Joint FAO/WHO recommendations on Food Standards Issues[3]—rely on a functional separation of risk assessment and risk policy decision, as theorized early by the US National Research Council.[4] According to this ideal framework, each regulatory option must be considered with respect to the benefit of a significant reduction of the exposure intensity or of the number of persons exposed. In practice, the expectation of an altered exposure can be inferred only in obvious situations where the links between affected products, material, substances, engineering, and technical knowledge are well established. For example, such advanced methods integrating consumer practices have been carried out by one of us for the styrene originating from yogurt

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pots[5] but cannot be routinely used for any packaging. Besides, the outcome of each policy may appear all the more ambiguous than the reference "No-Further-Action Level," to which the estimated exposure value must be compared, relies also on scarce toxicological data[6,7] and uncertain mathematical models.[8,9] When no reliable toxicological data exist, several "default" thresholds of "no action" have been proposed based either on the classification of carcinogenic substances[10,11] or for each class of noncarcinogenic substances in Cramer's class decision tree.[12]

The institutional set-up provides a robust framework for prioritizing future regulation and identifying hard scientific data gaps.[13,14] As they are mainly directed at chemical substances envisioned only as stressors, the overall approach remains, however, too coarse to provide guidance on engineering and industrial practices. In particular, important safety margins and many worst-case assumptions incorporated in assessment do not enable subsequent ranking between alternatives according to costs, risks, and benefits.[15,16] For food contact materials involving several components (multimaterials, multilayers, etc.), the substances are not directly incorporated in the food in contact, and the conclusions are significantly affected by the occurrence of the substance within each material, the leaching extent by each material and the contamination pathways (e.g., the substance must permeate through one or several layers). Most of the past and recent crises have thus involved materials, which were considered either "safe" or "inert" before a proof of leaching and a contamination of the product in contact has been demonstrated. Without being exhaustive, it includes contamination of aquaculture systems by di-*n*-octylphthalate,[17] contamination of noodles by mineral oil from paperboard,[18,19] contamination of milk by bisphenol A from polycarbonate baby bottles,[20–22] contamination of butter by polybrominated diphenyl esters from wrapping paper,[23] contamination by melamine from tableware[24] or can coating,[25] contamination of dairy products and dry food by photoinitiators of printing ink,[26–28] contamination of fatty or aqueous-alcoholic food by phthalate plasticizers[29,30] or adipate plasticizers,[31] contamination of food by primary aromatic amines,[32,33] and so forth.

The recent multiplication of crises heightened the public concern of consumers.[34] Substances, such as bisphenol A and its derivatives such as bisphenol A diglycedyl ether, start to be enforced by national parliaments regardless the recommendations of official food safety authorities.[35,36] Popular and scientific publications contribute to fuel the scientific controversy and to spread rumors on the real safety of food contact materials respectively with headings such as "How dangerous is Plastic"[37] or editorials such as "… drinking bottled water that has been left in a warm car can cause breast cancer."[38] The response organized and promoted by the upstream industry relies on two approaches: realistic consumer exposure to chemicals[39,40] and threshold of toxicological concern (TTC).[41,42] Regardless their real efficiency, such tolerance concepts on negative effects on human health appear however unlikely to restore durably consumer confidence in the safety of processed foods, whereas it is shown to be declining in recent years.[43]

The scientific controversy growing both in EU and in US must not be misunderstood. It occurs in countries where the chemical hazards are the most regulated. For food contact materials, the article 3 of the general EU regulation 1935/2004/EC[44] requires, thus, that "… any material or article intended to come into contact directly or indirectly with food must be sufficiently inert to preclude substances from being transferred to food in quantities large enough to endanger human health…" The weakness associated with the whole regulatory system appears in its application. As surveyed in Ref. 45 similar transport phenomena are known to occur across different materials; nevertheless, the EU approach remains mostly material-oriented, with different rules according to the considered material. Among the 17 groups of materials listed in Annex 1 of Ref. 44, only the plastic ones have received a specific attention with detailed procedures (1) for authorizing substances based on migration and toxicological data and (2) for compliance testing on finished products (i.e., food and its packaging). Compliance testing aims at checking that used monomers and additives are all positively listed and that their migration levels in prescribed worst-case contact conditions are within acceptable limits, so-called overall and specific migration limits, denoted OML and SML, respectively. SML verifications for plastic materials can be carried out either using migration experiments and sophisticated analytical techniques, as detailed in the technical guide[46] or using mathematical modeling. Modeling of the diffusion and desorption of uniformly distributed substances within a plastic layer has been accepted since almost two decades by FDA[47,48] and was first introduced in EU regulation in article 14 of Directive 2002/72/EC[49] and recently consolidated by article 32 of the general EU Regulation (EU) 10/2011 of plastic materials.[50] Mathematical models to be used specifically with a legal purpose have been reviewed in Refs. 51 and 52 and address usually simple contamination problems (one substance and one material) as discussed in Ref. 53. Although the mathematical approach accelerates considerably the verification process for the upstream chemical industry, it tends to lose its intent when it is used downstream by compounders, transformers and packaging fillers, public authorities, and so forth. The main limitations arise from its lack of generality: (1) it targets only some components (plastics) and once the finished food-packaging system is ready to be on the market, (2) it tends to propose an upper bound of the real migration (i.e., conservative estimates) without a robust estimation of the safety margin as required to set alternatives under uncertainty,[1,54] (3) it handles mainly simple physics (e.g., one single step or set of conditions, one-by-one material and substance, transfer by direct contact), and (4) it is strongly limited by the availability of composition and physicochemical data.[55]

The presented study extends dramatically the existing predictive and modeling approaches to real packaging systems by integrating multicomponent and flowchart considerations within a single and expandable quantitative FMECA (Failure Mode, Effects, and Criticality Analysis) methodology. The final goal is to reach a preventive approach "safe-by-design" *in lieu* of *a posteriori* one "safe-as-tested." As reviewed by Refs. 56 and 57, FMECA approaches have been used by a wide range of industries including aerospace,[58] ship,[59] automotive,[60,61] nuclear,[62] electronic,[63] medical,[64] analytical chemistry,[65,66] and so forth, but, to our knowledge, without application for the food packaging or related sectors. Adapting the cause–effects concepts to the physics and physicochemistry of mass transfer between a multicomponent packaging and the medium in contact represents the main challenge. Although our primary target was food packaging, the same approach could be applied without additional

modifications to cosmetic, pharmaceutical, or biotechnological products and water utility sectors. The framework presented in this study is currently under development within the collaborative research project "SAFEFOODPACK DESIGN,"[67] which set out in January 2011 to engineer the safety or inertia of food contact materials. The project assumes reasonably that a single packaging design cannot fit safety needs for all purposes (food type, food shelf-life, food preparation, etc.) and requirements (e.g., recycling). In addition, it argues that the multidimensional safe design problem can be solved or at least optimized systematically as soon as critical substances, critical materials and critical steps during processing, storage, and use conditions are identified. In this perspective, the safety defined as the absence of leaching substances into food is a standard end-use property that can fall into the industrial "molecular Processes-Product-Process Engineering" (3PE) challenge[68] and whose improvements could be signaled on retail markets via proper labeling initiatives.[69] "3PE" approaches combine many bottom-up modeling and simulation strategies and computer-aided tools.[70] Diffusion–dissolution molecular mechanisms of bulky solutes (additives, oligomers, etc.) in polymers and their activation by temperature start, for instance, to be efficiently calculated by molecular simulation at atomistic and coarse-grained scales.[71–73] Such tailored transport and thermodynamic properties can be subsequently used in one-dimensional (1-D) or two-dimensional (2-D) mass-transfer models to suggest a selection of substances, concentration ranges and association of materials to lower the risk of contamination.[54]

The article is organized into five sections. Section two details the theoretical principles of our proposed FMECA methodology for functional (e.g., process effect) and piece-part (e.g., packaging component) analyses. Two important features have been incorporated: (1) Markov chained and Bayesian simulations for multicomponent packaging systems and (2) a rule-based expert system enabling forward and backward chaining via combinatorics techniques to solve composition problems and to derive realistic/conservative thermodynamical/transport properties from databases. The considered scenarios are detailed in "Materials and Methods" section with results presented in "Results and Discussion" section. They were designed to represent three real-life problems and contexts: (1) identification of critical steps in the product life cycle, (2) concurrent food-packaging engineering design, and (3) screening materials and final uses when subjected to information asymmetries. The two first case studies were motivated by the multiplication of crises involving printing inks[74] or equivalently adhesives,[75] whereas such components are not specifically regulated neither in European Union nor in the United States. The last study is mainly a proof of the concept of our inference rules implemented in the open-source software FMECAengine,[76] by showing that an automatic expert system can generate conclusions acceptable by a human expert. Our pretension must not, however, be mistaken; our intent is to assist the end-user in feeding numerical tools, which require many inputs and knowledge, by providing emulated expert skills rather than fully substituting the human reasoning. Finally, "Conclusions" section draws future directions of research and sketch recommendations for the proposed FMECA concepts for the different involved stakeholders: chemical industry, compounding and processing industry, food and retailing industry, enforcement and technical laboratories.

Theories

Food safety management principles and systems

Risk analysis is well established for chemical hazards, and FAO and WHO are now extending the experience and expertise developed from risk analysis of chemical hazards to that of microbiologic hazards,[77] OECD[78,79] recommends, for emerging risks included, holistic methods that are not only based on a systematic procedure of hazard assessment applied globally to the supply chain but on sound prevention practices all along that chain, from production to final use. In food industries, prevention and safety are managed via two complementary "zero-defect" paradigms: Total Quality Management System (TQM) and Failure Mode and Effects Analysis (FMEA). TQM, fostered early by W. E. Deming in Japan, was rapidly adopted by food industry to maximize high-quality standards while reducing costs.[80] FMEA methods developed by construction and aeronautic industry[81] have been imposed to food industry suppliers contributing to US space race. Its implementation for food industry better known as Hazard Analysis and Control Critical Point (HACCP) has been recommended for spread use in 1971 in the United States[82,83] and mandatory in European Union since 1993.[84] Although first guidelines focused on foodborne illness, the Codex Alimentarius Commission[85] adopted it worldwide in 1997 as a general principle for ensuring food hygiene,[86] with a broad definition of "hazard" defined as any "biological, chemical, or physical agent in, or condition of, food with the potential to cause an adverse health effect."[87] Among the large number of quality and safety systems and business-to-business standards, ISO 22000[88] provides a harmonized framework for the implementation of HACCP[89] while accounting for prerequisite good manufacturing practices, compliance testing, and training program.[90,91]

A survey in the United States and in Europe[92] has recently concluded that product recalls are growing in both the United States and Europe. Contrary to expectations due to the methodological investment and involvement of the food industry, the authors found that operational hazards were the most common cause, with a majority of recalls detected by regulators rather than by the supply chain. In this perspective, some approaches mixing FMEA and HACCP systems have been suggested[93–95] to circumvent inherent limitations of existing HACCP systems: (1) HACCP targets control and corrective actions at production or distribution stage but does not integrate early product or process design; (2) HACCP is mainly qualitative whereas FMEA method can quantify the risk; and (3) HACCP principles are applied independently to each part and finally jointed together to form the whole figure,[96] but relations between parties are not considered. Because modern applications of FMEA or FMECA approaches can integrate uncertainty[97] and the consequences of linked causes via a consistent Bayesian approach[98] or related weighting,[99] they appear superior to integrate the risk of contamination along a real flowchart with bifurcations, many materials, and components as well as many substances. In addition, it is argued that helping stakeholders to encode the information according to a FMECA framework could trigger information sharing upstream and downstream the value chain without breaching confidentiality. Indeed, only information critical for the final safety needs to be exchanged during all the packaging life cycle.

Although the roots are different, it is important to recognize that the proposed framework exhibits some formal

analogies with early works mixing HACCP principles and predictive microbiology.[100–103] In particular, they addressed the hazard of foodborne disease from primary production (where microbiologic contamination prevalence can be described by the dynamics of infectious diseases in populations of animals or plants) to food transformation, handling, and consumption. Process stages along the farm-to-fork pathway are captured through input–output relationships centered and recoded according to few elemental operations for the considered micro-organism: growth, inactivation, partitioning, mixing, removal, and cross contamination. With this respect, chemical contaminants can also propagate (i.e., they diffuse from material to another one), be diluted, and their transport is activated/inactivated by temperature.

Common model assumptions

This study assumes that all transfer between all packaging components, and food can be described by 1-D transport equations in Cartesian coordinates. This approximation is acceptable as soon as the thickness, of each material is small comparatively to the typical food thickness and the gyration radius of the food packaging system is large (i.e., when internal and external surface areas of the material remain close). In other words, we assume for modeling purposes that the packaging material, which surrounds the food product, can be unwrapped and covered by a quantity of food with an equivalent surface area of contact (to verify the conservation of mass fluxes) and an equivalent volume of food (to verify the same dilution effect). As a result, the conversion of 3-D into 1-D depends on the part of the packaging that will be considered, for example, it differs for the bottle and the label stuck on the bottle. The resistance to mass transfer in the food volume (i.e., food texture and composition effects, quality of contact between the food, and the packaging) is governed by a mass-transfer resistance located at the interface between the food and the packaging layer in contact of food. Far from the interface, the concentration in food is assumed to be homogeneous. This simplification avoids describing explicitly the distribution of the contaminants in the food product, while predicting in a satisfactory manner the amount transferred. In addition, food is considered not to transfer its constituents to the packaging (possible plasticization effects due to absorption of water, terpenic aroma, etc. are, therefore, neglected).

Contaminants/migrants are initially uniformly distributed in the considered materials according to industrial formulation practices. Migrants such as surfactants are not considered in this study. The initial concentration in food is assumed to be zero. Temperature is constant during considered step (temperature can vary between steps). Transport properties (diffusion coefficients) and thermodynamic properties (activity coefficients) are constant with time during a same step (note that different conditions can be applied between steps). Possible reactions (in the food or in the material) as well as possible interaction between diffusing substances are neglected. Under the assumption that all sorption/desorption isotherms in each material are reversible and obey to Henry's law, all transport equations governing the solubilization-diffusion[104] of one substance within n materials are linear with respect to concentration. The proposed linear approximation of sorption/desorption isotherms is well verified for plastic additives (such as antioxidants, UV-stabilizers, chock agents, etc.), polymer residues, catalysts, etc. used at low concentration (below few wt %) well dispersed in the initial material (i.e., no blooming effect, no phase separation). For substances used at high concentration (ca. 50 wt %), such as plasticizers, the previous approximation is acceptable, when the modification of the content in the layer does not cause a significant modification of the glass transition of the polymer.

It follows that the contamination originating from different materials is the sum of independent transport problems, obeying possibly to different 1-D approximations.[54] According to such superposition principles, the contamination by a substance present, for instance, in the bottle body and in the cap can be, therefore, inferred from the cumulated solution of two distinct problems: migration from the bottle in contact with food and migration from the cap in contact with the same food but with a different contact surface area. The proposed description of mass transfer is assumed to account for most of the practical cases when the materials are in direct contact with food (e.g., during long-term storage), when they are not yet in contact with food (e.g., storage of packaging material before filling them), or when a gas layer exists between food and the considered material. It is important to note that the proposed FMECA approach is not limited by the simulation assumptions presented in this section. For technological problems more complicated than those presented in this article, the underlying physics can be either refined (nonisothermal treatments, nonlinear isotherms, coupling with reactions with known mechanisms, polymer swelling by food constituents, etc.) or subdivided into more successive steps with variable conditions.

Mass balance, transport equations, and boundary conditions

The physical assumptions and notations are those used in several articles.[1,54,105] This part summarizes the transport equations used to describe diffusion-solubilization through a composite structure comprising n parallel layers of different materials. Layers are indexed from 1 to n, where 1 is the layer in contact with food, as shown in Figure 1. Although food is preferably indexed F in the remainder part of the work, the food layer appears as indexed 0 in the following series expansions. The thickness of each layer is noted l_j where $\sum_{j=1}^{n} l_j = l_P$ is total thickness of the considered component (e.g., film).

The conservation of mass between an initial state, denoted t_0, and the final thermodynamical equilibrium, denoted t_{eq}, is given by

$$\sum_{j=1}^{n} \left(\rho_j l_j C_j|_{t \to t_{\text{eq}}} \right) + \rho_0 l_0 C_0|_{t_{\text{eq}}} = \sum_{j=0}^{n} \left(\rho_j l_j C_j|_{t=t_0} \right) \qquad (1)$$

where C_j and ρ_j are the mass concentration (as used in the industry) and the material density, respectively. By introducing the following Henry's law definition, $p_j = k_j C_j$ and by noticing that all partial pressure, p_j, are equal at equilibrium, the concentration in food at equilibrium becomes

$$C_0|_{t \to t_{\text{eq}}} = \sum_{j=0}^{n} \left(\frac{\rho_j}{\rho_0} \frac{l_j}{l_0} C_j|_{t=t_0} \right) \Big/ \left(1 + \sum_{j=1}^{n} \left(\frac{k_0}{k_j} \frac{\rho_j}{\rho_0} \frac{l_j}{l_0} \right) \right) \qquad (2)$$

Equation 2 highlights that the contamination of food (at thermodynamical equilibrium) is controlled by important

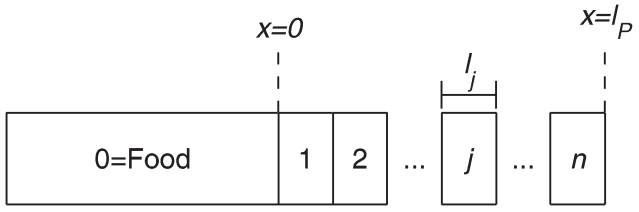

Figure 1. Indexing rule of a material including *n* layers (total thickness l_P) in contact with a food product (appearing as a layer indexed 0).

dimensionless quantities, such as the partition coefficient between each layer and the food $k_0\rho_j/k_j\rho_0$ and the dimensionless thickness of each layer l_j/l_0. l_0 is the equivalent food thickness defined as the ratio between the volume of food, V_F, and the considered surface area in contact, A.

When the system is out of equilibrium, the local mass flux within layer j ($1 \le j \le n$) obeys to first Fick law. As the diffusion coefficient D_j is assumed to be constant along the thickness l_j, the local transport equation becomes

$$\frac{\partial}{\partial t}C_j|_{t,x}=D_j\rho_j\frac{\partial^2}{\partial x^2}C_j|_{t,x} \tag{3}$$

Mass-balance conservation and local thermodynamical equilibrium on both sides of the interface between layer j and $j+1$ enforces the following conditions

$$\text{for } 1 \le j \le n-1$$
$$\begin{cases} D_j\rho_j\dfrac{\partial C_j}{\partial x}\Big|_{t,x=\sum_{i=1..j} l_i}=D_{j+1}\rho_{j+1}\dfrac{\partial C_{j+1}}{\partial x}\Big|_{t,x=\sum_{i=1..j} l_i} \\ k_jC_j\Big|_{t,x=\sum_{i=1..j} l_i}=k_{j+1}C_{j+1}\Big|_{t,x=\sum_{i=1..j} l_i} \end{cases} \tag{4}$$

Between the layers 1 and 0 (when the food is present), a mixed Robin boundary condition is assumed, as discussed in Ref. 105

$$J_0|_t=D_1\rho_1\frac{\partial C_1}{\partial x}|_{t,x=0}=h\rho_0\left(\frac{k_1}{k_0}C_1|_{t,x=0}-C_0|_t\right);$$
$$\text{with } C_0|_t=C_0|_{t=t_0}+\frac{1}{\rho_0 l_0}\int_0^t J_0|_\tau d\tau \tag{5}$$

Equation 5 accounts for the accumulation of the substance and a mass-transfer resistance on the food side. The latter is controlled by a mass-transfer coefficient h (SI units in m s^{-1}). As h values are poorly tabulated in the literature, a dimensionless mass Biot number is preferred: $Bi=hl_{j_{\min}}/D_{j_{\min}}$ where $j_{\min}$ is the layer index, which minimizes the effective permeability $D_j\rho_j/k_jl_j$.

On the boundary opposite to food (layer n), a periodic boundary condition is applied when the packaging is stored before use as roll films, stacked (e.g., containers), or wrapped together

$$D_n\rho_n\frac{\partial C_n}{\partial x}|_{t,x=l_P}=D_1\rho_1\frac{\partial C_1}{\partial x}|_{t,x=0}; k_nC_n|_{t,x=l_P}=k_1C_1|_{t,x=0} \tag{6}$$

When the food is present, a conservative impervious boundary condition is applied: $\partial C_n/\partial x|_{t,x=l_P}=0$.

Numerical resolution strategy

Analytical solutions to Eqs. 3–6 including finite volume effects and external mass-transfer resistance have been published only for $n=1$ by Sagiv[106,107] and by Vitrac and Hayert.[105] For n larger than 1, only numerical solutions are available. Numerical difficulties arise from Rankine-Hugoniot jumps (discontinuities in $C_j(x)$ and its derivative at each interface between different materials) caused by contact conditions (4) when large jumps in diffusion and Henry coefficients exist. They have been specifically investigated in Ref. 108 by computing the numerical errors associated with a finite element (FE) technique and by comparing it with a highly accurate spectral element technique (i.e., high-order FE technique using orthogonal polynomials instead of Lagrange ones). Despite the decomposition onto domains matching the positions of each material, errors were found to be much higher with the FE technique and maximal at interfaces with values up to percent. Using a FE method, Roduit et al.[109] has reported similar numerical errors, up to 5%, with a systematic overestimation of the amount leeched in food by a multilayer material. Finite difference (FD) techniques[110,111] have been also used to solve small-scale problems obeying to similar physics but without reporting errors, stability criteria, or any computational cost.

As our proposed FMECA framework required highly accurate and consistent solutions for an arbitrary number of layers and successive steps (i.e., the calculated solution becomes the initial condition from a next step), it was decided to prefer to previous techniques a finite volume (FV) technique, which enforces—by construction— a verification of the mass balance at the full numerical accuracy. We used essentially the standard formulation originally proposed by Patankar[108] while including some redesigned features to ensure (1) that the proposed set of discretized equations is mathematically exact at steady state (without any approximation) and (2) that the relative error is uniform along the multilayer structure whatever the initial condition at $t=t_0$. The proposed spatial discretization scheme is presented in Figure 2 with concentrations discretized at control nodes and denoted $C(i)$, where $i = 1\ldots N$ is the index of the control volume. It leads to weak mathematical solutions that have two important features. On one hand, it accepts an arbitrary number of layers and property discontinuities with layers as small as few nanometers (e.g., plasma deposit) mixed with millimeter thick layers. For this, the formulation accepts that discontinuities can occur at the interface of each control volume. On the other hand, all Rankine-Hugoniot jump conditions (see Figure 2a) are exactly verified by enforcing the following constraints

$$\frac{k(i-1)}{\rho(i-1)}C_{i-1}^e=\frac{k(i)}{\rho(i)}C_i^w \quad \text{for all } 2 \le i \le N \tag{7}$$

In practice, interface concentrations are not calculated explicitly but are included in the equivalent conductances $\mathrm{hw}(i)=\mathrm{he}(i-1)$ derived at steady state. As a result, the mass conservation enforced by finite volume formulation and the constraints of Eq. 7 enable the numerical solution to

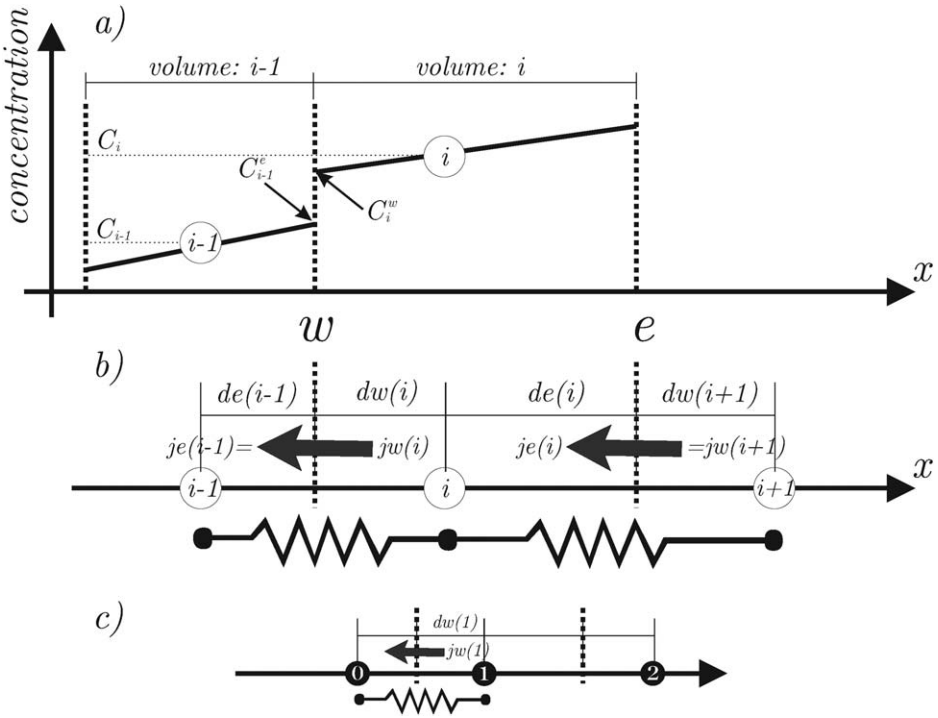

Figure 2. Finite volume discretization scheme: (a) typical control volumes; (b) distances associated with the interfaces "e" (east) and "w" (west) and equivalent mass-transfer resistances at the interface between two control volumes; and (c) special case of the food layer interface.

converge exactly to Eq. 2. This last property is required to get reliable estimates of severity, when several processing steps are involved (see section Severity and Criticality Calculations).

Consecutive node points are optimally located on both sides of the interface, so that the mass-transfer resistances from each node to the interface are equal. By noting $de(i)$ and $dw(i+1)$, the distance of the interface to nodes i and $i+1$, respectively, one gets

$$\frac{dw(i+1)}{de(i)} = \frac{D(i+1)}{D(i)} \frac{k(i)}{k(i+1)} \frac{\rho(i+1)}{\rho(i)} \tag{8}$$

The equivalent conductance between node i and node $i-1$ (west direction), $hw(i)$, is given by Eq. 9. Similarly, the equivalent conductance between node $i+1$ and node i (east direction) is given by: $he(i)=hw(i+1)$ (see Figure 2b).

$$\frac{1}{hw(i)} = \left(\frac{de(i-1)}{D(i-1)} \frac{k(i-1)}{k(i)} \frac{\rho(i)}{\rho(i-1)} + \frac{dw(i)}{D(i)} \right) \tag{9}$$

The corresponding normal mass fluxes between node i and node $i-1$, denoted $jw(i)$, and between node $i+1$ and node i, denoted $je(i)$, are given by Eq. 10 and $je(i)=jw(i+1)$, respectively.

$$jw(i) = hw(i) \left(\frac{k(i-1)}{k(i)} \frac{\rho(i)}{\rho(i-1)} C(i-1) - C(i) \right) \tag{10}$$

The local mass balance applied to volume i yields finally

$$\frac{dC(i)}{dt} = \frac{jw(i) - je(i)}{dw(i) + de(i)} = \frac{1}{dw(i)+de(i)} \begin{bmatrix} hw(i) \frac{k(i-1)}{k(i)} \frac{\rho(i)}{\rho(i-1)} \\ -hw(i) - he(i) \frac{k(i)}{k(i-1)} \frac{\rho(i-1)}{\rho(i)} \\ he(i) \end{bmatrix}^T \begin{bmatrix} C(i-1) \\ C(i) \\ C(i+1) \end{bmatrix} \tag{11}$$

On the food side, the Robin boundary condition (5) is implemented by adding a theoretical control volume indexed 0 as shown in Figure 2c.

$$\frac{dC(0)}{dt} = -\frac{jw(1)}{l_0} = \frac{1}{l_0} \begin{bmatrix} -hw(1) \frac{k(0)}{k(1)} \frac{\rho(1)}{\rho(0)} \\ hw(1) \end{bmatrix}^T \begin{bmatrix} C(0) \\ C(1) \end{bmatrix} \quad \text{with} \quad \frac{1}{hw(1)} = \frac{1}{h} \frac{k(0)}{k(1)} \frac{\rho(1)}{\rho(0)} + \frac{dw(1)}{D(1)} \tag{12}$$

The impervious boundary is implemented by applying Eq. 11 to $i=N$ and by taking $he(N)=0$. The periodic boundary condition is applied by replacing $i-1$ by N and $i+1$ by 1 in Eq. 11, respectively, for nodes $i=1$ and $i=N$.

The mass-transfer problem is assembled as a linear system of $N+1$ (N if the food is not present) ordinary differential equations written as $d\mathbf{C}/dt=\mathbf{M}C$, where $\mathbf{C}$ is the $N \times 1$ vector of concentration at each node and $\mathbf{M}$ is a $(N+1) \times (N+1)$ tridiagonal constant matrix whose rows are given by Eqs. 11 and 12. The system is finally integrated in time using a variable order backward differences (maximum order

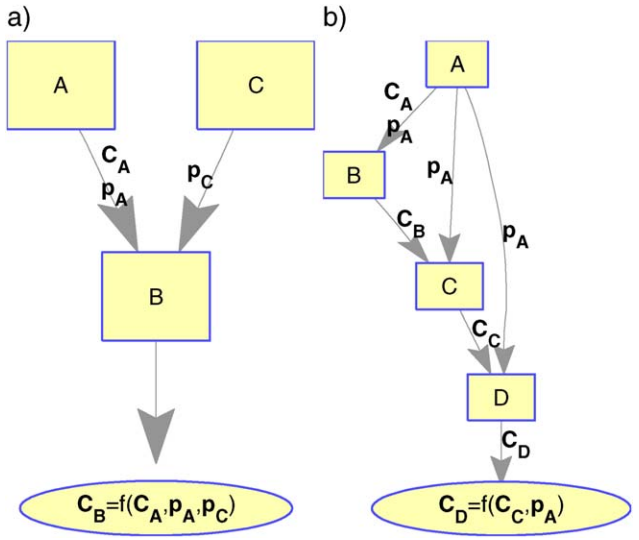

Figure 3. Illustrations of general topologies used in our FMECA approach.

(a) Two step flowchart illustrating the functional dependence (A is the parent of B, that is "B is occurring after A") and the statistical dependence (B inherits some parameters from steps A and C without step C being logically related neither to B nor to A) between steps. (b) Block diagrams involving four steps functional cascading and global inheritance of some parameters of A for steps B–D. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

does not exceed 2 for stability reasons) for a starting solution $\mathbf{C}_0$, which can be either a solution set by the end-user or a solution originating from a previous simulation.

Simulation chaining

Simulation chaining is implemented within a flexible simulation pattern derived from object-oriented programming concepts. Chaining is consequently understood into two complementary ways: (1) using a previously calculated output (from a parent simulation) as an input for a new simulation with different parameters, (2) using a previous set of parameters as the foundation for an independent simulation (some parameters are inherited with some alterations to study some modality effects). Figure 3 illustrates the principles on simple functional block-diagrams. In Figure 3a, A is the parent of step B and B inherits from the properties used in simulation C. The interest of such abstraction is more obvious in Figure 3b where a packaging is subjected to four process steps or conditions of use: A → B → C → D. Some parameter values from simulation A can be propagated to all following steps such as the packaging geometry.

By noting modalities with an index k and steps with an index i, chaining and inheritance are resolved through a step-wise approach

1. read the first guess of $\tilde{\mathbf{p}}_{\mathbf{i},k}$ in the (mainly sparse as most of the properties are inherited);
2. read on the flowchart the parent step, $i-1$, and the parent modality, k_{parent};
3. derive the Boolean modificator vector $\delta\mathbf{p}_{\mathbf{i},k}^{\mathbf{i}-1,k_{\text{parent}}}$ coding inheritance relationships from parent, with the following convention for each element. 1 when the parameter is inherited and 0 otherwise;
4. read the additional step and modality to inherit additional parameter/attribute values, denoted i_{inherit}, k_{inherit} (e.g., special process or storage conditions independent of geometry);
5. derive the Boolean modificator vector $\delta\mathbf{p}_{\mathbf{i},k}^{i_{\text{inherit}},k_{\text{inherit}}}$ coding for additional inheritance;
6. apply inheritance rules (with lower precedence for $\delta\mathbf{p}_{\mathbf{i},k}^{i_{\text{inherit}},k_{\text{inherit}}}$):
$$\mathbf{p}_{\mathbf{i},k}=\tilde{\mathbf{p}}_{\mathbf{i},k}+\delta\mathbf{p}_{\mathbf{i},k}^{\mathbf{i}-1,k_{\text{parent}}}\circ\mathbf{p}_{\mathbf{i}-1,\mathbf{k}_{\text{parent}}}+\delta\mathbf{p}_{\mathbf{i},k}^{i_{\text{inherit}},k_{\text{inherit}}}\circ\times\left(1-\delta\mathbf{p}_{\mathbf{i},k}^{\mathbf{i}-1,k_{\text{parent}}}\right)\circ\mathbf{p}_{\mathbf{i}_{\text{inherit}},\mathbf{k}_{\text{inherit}}}$$
7. perform the simulation $\mathbf{C}_{i,k}=f_i\left(\mathbf{C}_{i-1,k_{\text{parent}}},\mathbf{p}_{i,k},C_{F_{i-1,k_{\text{parent}}}}\right)$ where f in the numerical solver of step i
8. update the concentration in food from mass balance:

$$C_{F_{i,k}}=C_{F_{i-1,k_{\text{parent}}}}+\frac{A}{V_F}\sum_{j=1}^{n-1}\int_{l_j}^{l_{j+1}}\left(C_j|_{t_k,x}-C_j|_{t_{0,k},x}\right)dx \qquad (13)$$

where $\mathbf{C}_{i,k}$ is the concentration field for the ith step and the kth modality, calculated according to the numerical scheme defined in "Numerical resolution strategy" section and lumped here as a function f_i. It depends on the concentration field at previous step $\mathbf{C}_{i-1,k}$, on the concentration in food at previous step, $C_{F_{i,k}}$, and on the vector of parameters $\mathbf{p}_{i,k}$(e.g., including initial and final simulation times $t_{0,k}$ and t_k, respectively, $\{D_j\}_{j=1\ldots n}$, $\{k_j\}_{j=1\ldots n}$, $\{\mathrm{p}_j\}_{j=1\ldots n}$, etc.) used for the simulation. For $i>1$ or $k>1$, the user needs only to supply a sparse input parameter $\tilde{\mathbf{p}}_{\mathbf{i},k}$ and all missing inputs are obtained by inheritance from parent or from a related step i_{inherit} and/or modality k_{inherit}. The inheritance process is depicted in step 6 of Eq. 13, as a succession of Boolean operations involving Hadamard products (also known as entry-wise products and denoted $\circ$). They enforce that only one parameter can be inherited at a time and that the inheritance from the parent step has a higher precedence than from a "relative" step. For most complex situations, step 6 can be extended to inheritance from multiple related steps while keeping the same precedence rules. To improve reusability, the framework accepts virtual/template steps not directly involved in the flowchart (with no calculation associated) but that are used to derive special instances of previously defined industrial or household operations, with the same philosophy as in used in object-oriented programming.
In practice, Eq. 13 can be applied to study an arbitrary collection of effects with or without propagation of modalities to children while keeping easy coding and simple abstraction. Both cases are illustrated in Figure 4 for a flowchart A → B → C → D, where B is split into three levels/modalities. When the levels correspond to three temperatures, the subsequent levels are only impacted by the causality between B and C: concentration distribution between all layers (including the food) has been modified but the following process/use conditions remain unchanged (Figure 4a). On the opposite, if step B is associated with a packaging filling step with three different liquid foodstuffs (e.g., aqueous, dairy, and fatty products), all subsequent steps are affected, and the modifications introduced at step B are propagated to all following steps (cascading) as shown in Figure 4b.

Severity scale

In FMEA and FMECA methods, the concept of severity is central, as it is used for risk prioritization. It is obvious that the severity should be related to the extent of substance transferred to the food or equivalently to the estimated concentration in the food $\hat{C}_F$ when the food mass is kept constant. However, in case of multiple contaminants originating from

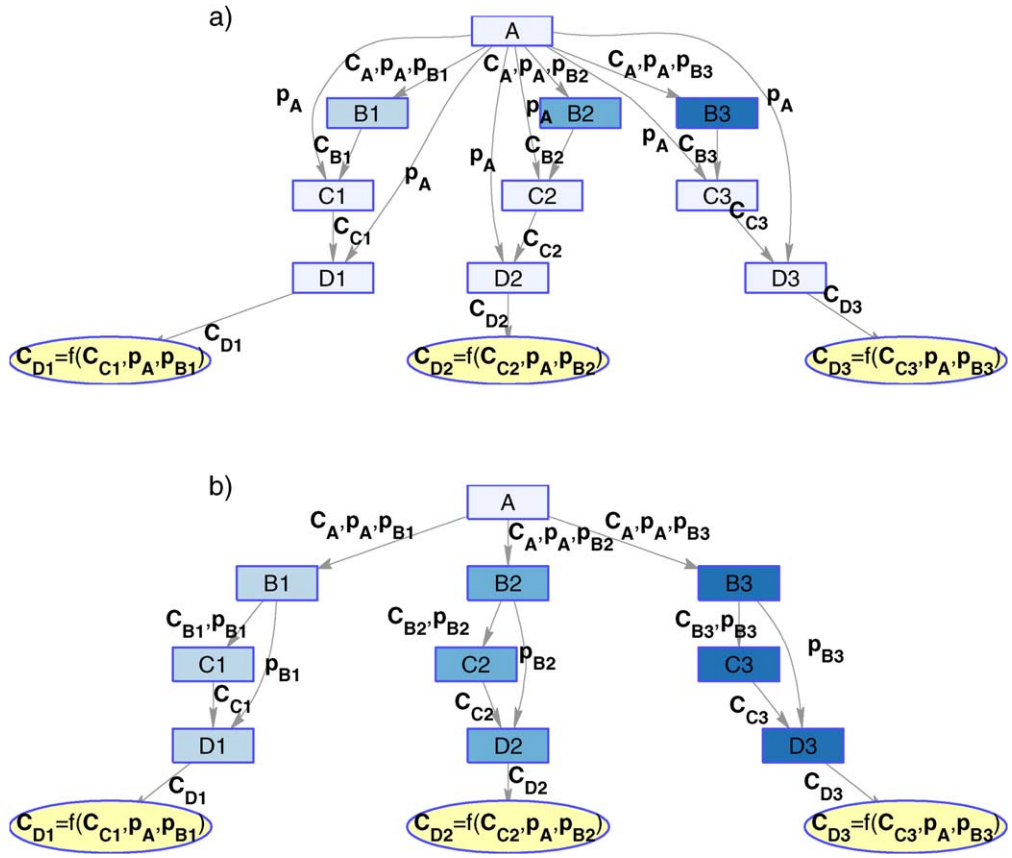

Figure 4. Generalized dependence rules when step B in Figure 3b is split into three possibilities (levels or modalities), denoted $\{\mathrm{Bi}\}_{i=1,2,3}$.

(a) First case, levels B1–B3 are not statistically related to subsequent steps (only functional dependence exits, e.g., three temperatures of packaging filling at step B). (b) Second case, a statistical dependence exists between B1–B3 and the following steps (e.g., three different foods are put in contact with the packaging at step B). Colors illustrate the span of the statistical dependence. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

one or several packaging components, the different amounts associated with different substances must be compared on a same scale. An intuitive approach would consist in normalizing $\hat{C}_F$ by a threshold of concern based on toxicological and consumer exposure assumptions. For plastics, the reference value could be the legal limit, so-called SML, defined in the European regulation of plastics.[50] By assuming that a human of 60 kg eats 1 kg of food on daily basis,[112] SML values (expressed in mg kg^{-1} food) are usually set proportional to tolerable daily intake (denoted TDI and expressed in mg kg^{-1} body weight daily), so that: SML = 60·TDI. Not all substances positively listed in the European Regulation (EU) 10/2011 of plastic materials have a SML value but an upper bound can always be derived by assuming that the migration must not exceed the OML set to 60 mg kg^{-1} of food.

The main disadvantage of a severity defined as $\hat{C}_F/\mathrm{SML}$ is that it increases linearly with $\hat{C}_F$ without a clear identification of magnitude orders that are assessed by the risk manager as "catastrophic" from those that are assessed only "critical" due, for instance, to an overestimation of $\hat{C}_F$ in the presence of too conservative assumptions. An alternative has been chosen by relating the "catastrophic domain" to the safety margin introduced by toxicologists when no observable adverse effect levels (NOAEL) measured on animals are transposed to TDI values for humans. The transposition integrates conventionally two 10-fold safety factors: one for the differences between rodents and humans and another one for variations among the human population.[113] From heuristic considerations, it was proposed to scale severity with Eq. 14, so that values lower than 100 were acceptable (i.e., compliant with SML values). Proportionality to $\hat{C}_F$ was almost kept until $\hat{C}_F \leq 10\mathrm{SML}$ (first 10-fold safety margin) and diverged rapidly beyond with $\mathrm{Severity}\left(\hat{C}_F\right) \to \infty$ when $\hat{C}_F/\mathrm{SML} \to \mathrm{NOAEL}/\mathrm{TDI}$.

$$\mathrm{Severity}\left(\hat{C}_F\right) = 100\left(1-\frac{\mathrm{TDI}}{\mathrm{NOAEL}}\right)\frac{1}{\max\left(\frac{\mathrm{SML}}{\hat{C}_F}-\frac{\mathrm{TDI}}{\mathrm{NOAEL}},0\right)} \quad (14)$$

Severity and criticality calculations

The main goals of the proposed FMECA methodology are to analyze the effect of every mode of migration ("failure") upon the final food contamination and to rank them comparatively to a threshold of concern. The method can be implemented using either a component (substance, material, etc.) or a functional approach (e.g., contribution of microwave heating comparatively to aseptic hot filling).

When the component approach is used, the severity is obtained by applying Eq. 14 to the concentration in food assessed at the last step of the block diagram, here with an

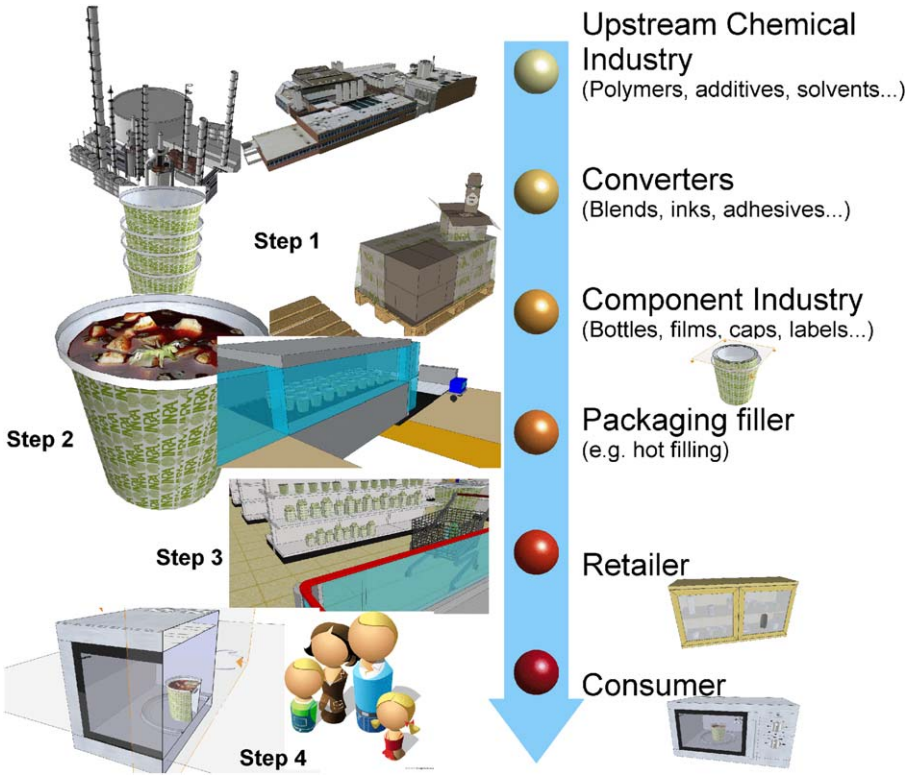

Figure 5. Food packaging supply chain for a typical ready-to-eat soup, commercialized in this example in a pot with the external surface printed with the research institute logo (INRA).

Captions highlight main critical steps for the migration of printing ink constituents (1) step 1: during long-term storage of pots in stacks within a secondary card-box packaging possibly made from recycled fibers; (2) step 2: during aseptic filling of printed pots with hot soup; (3) step 3: during long-term storage at retailers or consumers; and (4) step 4: during final preparation with microwave heating with steam convection. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

index M, and when the only the component j is considered as a source of contaminants.

$$\hat{C}_F(\text{component } j) = C_{F_M}\big|_{1\to 2\to\cdots\to M}^{C_l|_{l=0,x}=0 \text{ for all } l=1..n \text{ with } l\neq j} - C_{F_0} \quad (15)$$

where C_{F_0} is the concentration of the substance in food that could be present before the incorporation of component j (e.g., prior contamination, substance also used as a food ingredient). The Mth step is usually the household preparation step (e.g., after microwave heating) as reproduced in Figure 5.

When the functional approach is applied, the concentration scale to be used along with Eq. 14 must be relative to the contribution of the considered step i itself, as

$$\hat{C}_F(\text{step } i) = \max\left(C_{F_M}|_{1\to 2\to\cdots\to M} - C_{F_M}|_{1\to 2\to\cdots\to M/i}, C_{F_i}|_i\right) \quad (16)$$

where $C_{F_M}|_{1\to 2\to\cdots\to M}$ is the concentration at the end of a causal path of length M and $C_{F_M}|_{1\to 2\to\cdots\to M/i}$ is the same concentration when step i is removed. $C_{F_i}|_i$ is the concentration obtained when only step i is considered.

When several "causal/modal" paths include component j or step i (e.g., three paths include step A in Figure 4), the previous approaches must be applied along to all paths. A unique final severity value can be finally derived (if needed), by weighting severities with the joint probability of each individual path. When it is cumulated over all substances s, $s = 1\ldots N_S$, the value gives the criticality of either a component j or of a step i

$$\text{Criticality}\left(\hat{C}_F(\text{step } i \text{ or component } j)\right) = \sum_{s=1}^{N_S}\sum_{p=1}^{N_P} pr(p\text{th path including } i \text{ or } j) \times \text{Severity}\left(\hat{C}_F(\text{step } i \text{or component } j)\right)$$

As variability and uncertainty can be represented as block diagrams fulfilling Eq. 13, specific branches (i.e., belief network or subnetworks) can be added to assess the consequences of different assumptions, such as intuitive rules: "unknown value/class," "flawed value," "justified value," and "intuited value/class." The final severity (or criticality) ranking will subsequently help to determine whether the level of knowledge or accuracy affects or not the final outcome. When probabilities are *a priori* known, Eqs. 14–17 will enable to calculate either the distribution of the outcome or important moments of this distribution.

Materials and Methods

Databases and models

The proposed quantitative FMECA approach requires a significant amount of numeric data. They are gathered within

relational databases sketched in Figure 6. First-order predicate logic is used in particular to feed a same final table, so-called "sim," that gathers all numeric data required for the simulation. One practical consequence is that complex problems can be addressed in more comprehensible terms, based on the name of a substance, a material, application type, and so forth. The table "sim" contains two important fields "parent" (to set which output is used as input) and "inherit" (to set which set of parameters will be used as reference) that enable a straightforward construction of block diagrams obeying to Eq. 13.

The proposed approach is mainly limited by the availability of data: list of likely substances, occurrence of these substances in each category of materials, process conditions, toxicological data, packaging design, physicochemical properties (e.g., density, partition coefficients), transport properties (diffusion coefficients and activation by temperature), and so forth. Our expandable databases relied mainly on data available in the open literature or accessible from public bodies (specific task forces, regulatory documents, guidance documents, and collections of data from collaborative European Projects) or from professional associations, and so forth. Databases were consolidated (codifications, list of synonyms, etc.) and completed with data originating from collaborative ChemSpider databases[120] (Royal Chemical Society, UK). Substances were uniquely identified with their InChiKey.[123] Transport properties, principally partition coefficients, and diffusion coefficients were collected from Refs. 71,73,114, and 124, respectively. When no diffusion coefficient or partition coefficient was available, "worst-case" values derived from Piringer equation (Eq. 18)[53] and from Ref. 115 were used respectively.

$$D(T,M)=\exp\left[A'_P-0.135M^{2/3}+0.003M-\frac{\tau+10454}{T}\right] \quad \text{in m}^2\text{s}^{-1} \tag{18}$$

where M is the molecular mass of the diffusants in g mol^{-1}, T is absolute temperature in K; A'_P is a polymer specific "diffusion conductance" parameter, and τ (K) is a polymer-specific "activation energy" parameter. Equation 18 scales D with M ($D{\cdot}M^{-\alpha}$) with an effective exponent, α, less or equal than 1, for intermediate molecular masses ranging between 200 and 600 g mol^{-1}, that underestimates significantly the real dependence in thermoplastics.[72] As a result, robust overestimates of D tend to be derived as soon as parameters A'_P and τ are fitted on the behavior of small solutes at high temperature (i.e., when measurement conditions are easier).

Inference rules and knowledge model

According to conventions used in FMECAengine,[76] all inputs required for simulation and sensitivity analysis are collected within a single table/database called "sim" in Figure 6. This table can be filled either directly by numeric data or indirectly by building requests between databases and expected entries in "sim." An example of front-end interface/form using only natural or seminaïve expressions is depicted in Figure 7a and is used in case study 3 "risk-oriented screening" (see section "Case study 3: Risk-oriented screening" in the "Materials and Methods" section). In practice, numerical and inference rules can be mixed in the table "sim." At run-time a special inference engine (so-called key2key() included in FMECAengine[76]) is used to look up matches between requests and numerical values available within databases. Cascading of elementary rules is implemented as a generic entity-relationship model including one-to-one, one-to-many, and many-to-many relationships without depth limitations. For convenience, expert rules can be coded as separated text files or within spreadsheets via a symbolic syntax specifically designed for its compactness and its ability to mix functional evaluations (multivalued), regular expressions, and SQL-type requests. Without limitation of size and branching, the basic syntax obeys to chained IF…THEN sequences (identified by a "→") between columns/fields within a same table/database or different tables/databases

$$\begin{aligned} \textit{request}\text{:}\mathbf{databaseA}\text{::}\ \text{fieldA}_1 &\rightarrow \text{fieldA}_2\text{:}\mathbf{databaseB}\text{::}\ \text{fieldB}_1 \\ &\rightarrow \text{fieldB}_2\text{:}\mathbf{databaseC}\text{::}\ \text{fieldC}_1 \\ &\rightarrow \ldots \end{aligned} \tag{19}$$

where *request* is any imaginable query combining logical operators, regular expressions, scalar, or lists of values; database$X$ (X = A, B, C…) is any of tables depicted in Figure 6, with fields (columns) denoted fieldX_1, fieldX_2, and so forth. It is worth to notice that contrary to standards databases, the value corresponding to a field can be not only a scalar, a list but also another entity–relationship (subrule) used as shorthand. The final consistency of a complex query is ensured by a flattening procedure of the query tree that guarantees that any output is a unique collection of nonduplicated items, so that the real distribution of the considered quantities matches the one available in our databases. Several data reductions can be combined to sample modalities.

Advanced rules were used typically in case study 3. The typical syntaxes to generate automatically scenarios from qualitative information about the name of polymer and the conditions of storage (see Figure 7a) are listed in Table 1. Composite requests generate many-to-many hierarchical trees. For validation purposes, they could be expanded automatically as spanning trees (with a special function key2keygraph() included within the project FMECAengine[76]). An example of such multivalued and composite requests is shown graphically in Figure 7b to extract typical percentile values of worst-case diffusion coefficients, D_1, based on: (1) the relationship between the polymer name and the classes of migrants/contaminants, (2) the relationships between the classes of migrants, their names, and their molecular masses, and (3) the relationship between the storage method and typical temperatures reported in table "storage." A simpler example to extract partition coefficients from the name of food simulants is also sketched in Figure 7c. Scenarios involving vectors as parameters were spanned automatically as subscenarios by following the conventions of Figure 4: a row vector applied modalities only to the considered simulation step (see Figure 4a) whereas a column vector affected the modalities of all children/dependent steps (see Figure 4b).

Simulation and inference engines

All methods described in this article have been implemented within an open-source software so-called FMECAengine[76] coded primarily in the Matlab Language (version 7.6 above, MathWorks). It does not offer any input interface for the user but uses natively OpenOffice files (version 3.0 and above, Apache Software Foundation) instead to build

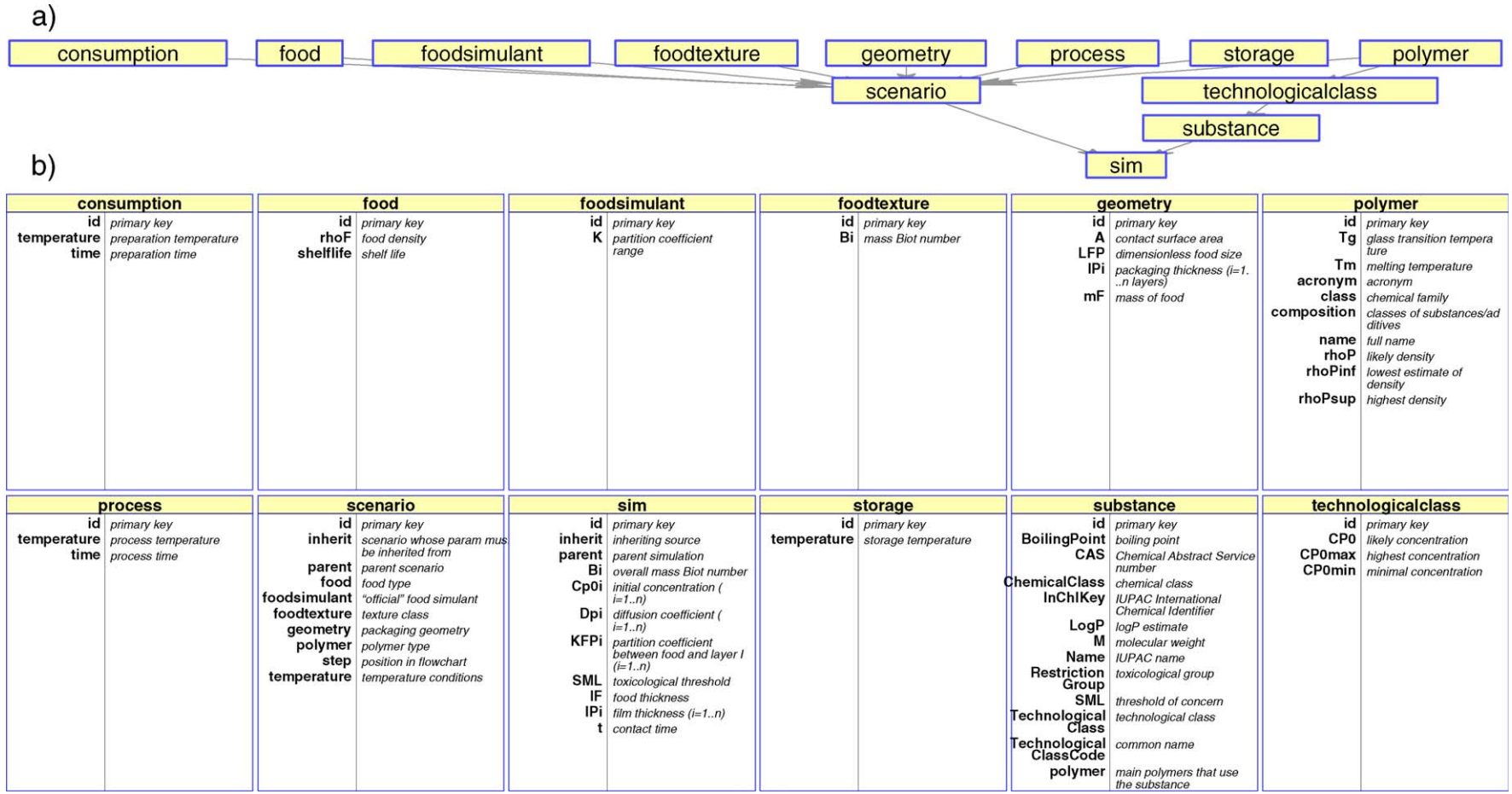

Figure 6. Databases (user and internal tables) and their relationships used in the case study 3 "Risk-oriented screening": (a) overview and (b) detailed description of main fields (tables are listed in alphabetic order).

The final user uses the table "scenario" to set in a natural language the problems to analyze as shown in Figure 7a. The inference rules to translate "concepts" into numerical data are coded in table "sim" with the syntax (19) as illustrated in Figures 7b,c. The internal tables "consumption," "food," "process," and "storage" gather commercial and industrial data on the product shelf-life, process, and storage conditions as well as final preparation. The internal tables "foodsimulant" and "foodtexture" list basic physicochemical properties of food (expert's dire and regulatory data, partition coefficients are collected from Refs. 71,73,116, and 118) to set boundary conditions between food and the first layer in contact. Packaging related data are broken into characteristics measured on real food-products (table "geometry"), data extracted from literature such as physicochemical polymer properties and occurrences of substances[116–119] (table "polymer"). The table "substance" lists substance identifiers and their characteristics,[120] and related regulatory data.[50] Typical concentration ranges[115,121,122] are tabulated in the internal table "technologicalclass" according to the class of the considered substance recorded in the table "substance." [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

a)

id	parent	geometry	polymer	food	foodsimulant	foodtexture	step	temperature	comment
LDPEYogurtBottle		smallbottle	LDPE	yogurt	ethanol50	liquid	storage	chilled	*pot of yogurt*
HDPEOilCap		cap	HDPE	oil	fatty	liquid	storage	ambient	*oil bottle cap*
PPDrinkGoblet		gobletPP	PP	hotdrink	ethanol50;fatty	liquid	consumption	hot	*coffee goblet*
PPButterContainer		container	PP	butter	fatty	semisolid	storage	chilled	*butter container*
PPCreamPot		container	PP	cream	fatty	semisolid	storage	chilled	*pot of cream*
PPDrinkStraw		straw	PP	yogurt	ethanol50	liquid	consumption	ambient	*straw*
PSYogurtPot		pot	PS	yogurt	ethanol50	semisolid	storage	chilled	*pot of yogurt*
PSDrinkGoblet		gobletPS	PS	hotdrink	ethanol50;fatty	liquid	consumption	hot	*coffee goblet*
PVCSauceLid		gasket	pPVC	sauce	fatty	liquid	process	sterilization	*cover gasket*
PVCSauceLid2	PVCSauceLid		pPVC	sauce	fatty	liquid	storage	ambient	

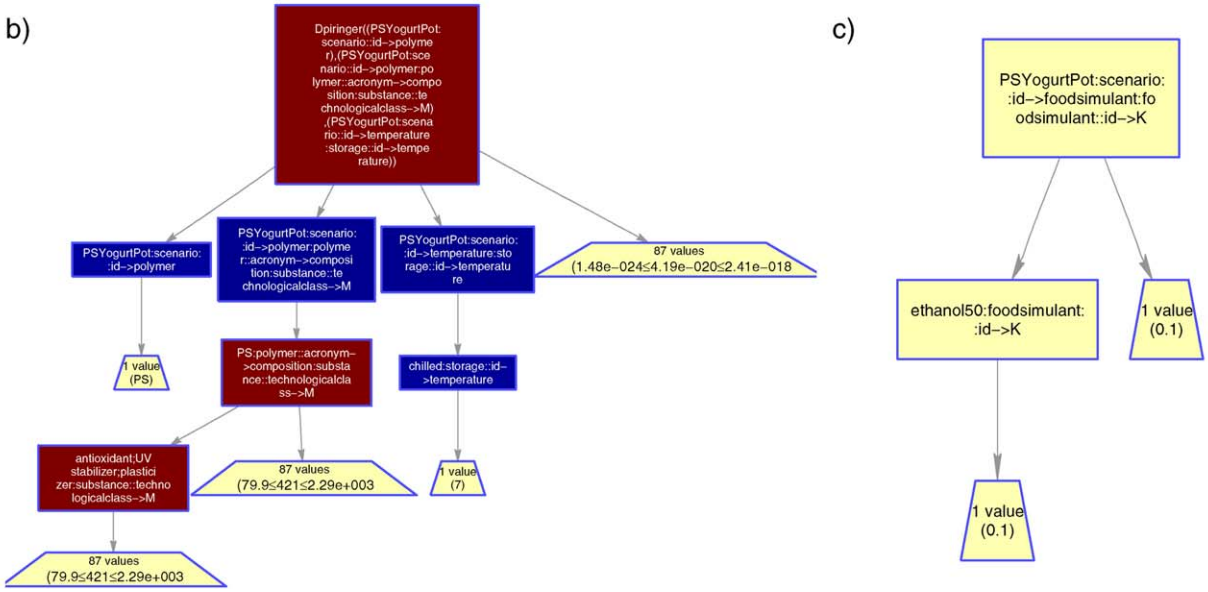

Figure 7. Migration scenarios used in the case study 3 "Risk-oriented screening" for nine real products purchased on the local French market.

(a) Details of the table "scenario" (see Figure 6). Two inference rules obeying to syntax (19) are illustrated to extract: (b) the distribution of overestimated diffusion coefficients based on Eq. 18 and (c) the partition coefficient between PS and simulant "Ethanol 50%." Complex requests are translated into composite or successive subrequests (rectangular boxes). Cardinality and range of outputs are plotted within trapezoidal boxes. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

databases and workflows. Outputs are available to the end-user as interactive HTML documents linking to figures, graphs, FMECA analysis either in PNG format or PDF. For advanced Matlab users, a set of oriented-object functions enable to perform complex analyses and specialized plotting including block diagrams and graphical visualization of composite queries.

FMECAengine addresses automatically all steps involved in the presented approach: (1) translating queries into values, (2) building dynamically simulation trees accounting for simulation chaining and inheritance of parameters, (3) updating dynamically simulation trees by adding or removing branches in particular to solve Eq. 16, (4) performing simulations, (5) maintaining a database of all intermediate results and deriving corresponding severity and criticality values.

Case *studies*

Case Study 1: Functional Analysis. The functional approach is applied to the identification of the critical steps depicted in Figure 5 and involving the migration of an ink photoinitiator (benzophenone, denoted X) in a ready-to-eat soup. The main characteristics of the packaging design (denoted A) and of the migrating substance are summarized in Tables 2 and 3, respectively. The proposed case study presents several analogies with previous food alerts in Europe.[28,132,133] As the conditions of long-term storage and final preparation can be highly variable, a combination of two storages conditions along two oven heating were compared according to conditions tabulated in Table 4.

Case Study 2: Risk-Ruled Concurrent Engineering. The risk of contamination by two ubiquitous substances coming from printing ink alone (substance X) and both from printing inks and adhesives (one biocide substance denoted Y: 1,2-benzoisothiazolin-3-one, see Table 3) were compared for two designs: a multilayer brik (denoted B) and a multilayer bottle (denoted C), used to store dairy or aqueous liquid foodstuffs. All assumptions for each design are summarized in Table 5. The flowchart and the food contact conditions are listed in Table 6.

Case Study 3: Risk-Oriented Screening. The case study was designed to demonstrate that even the nonsupervised application of the proposed FMECA approach could help the screening of nine real cases with intermediate complexity (monolayer materials, a maximum of two steps in the flowchart). The assumed available information was mainly qualitative and comprised information on the packaging geometry, type of polymer, and food and conditions of storage as shown in Figure 7. The geometries summarized in Table 7 were chosen to match real products. Numerical parameters required in the simulation were retrieved from inference rules as shown in Figures 7b and c. According to

Table 1. Prototypes of Automatic Requests Used in the Case Study 3 "Risk-Oriented Screening" to Translate Inputs in Natural Language, as Depicted in Figure 7a, into Numerical Values (Either Scalar or Vectors) to be Used in Table "Sim" Presented in Figure 6

	Parameter: Description	Examples of Request for Monolayer Materials Subjected to a Step Called "Storage"	Output
Simple requests	*Bi*: mass Biot number determined according to food texture	`$S:scenario::id->foodtexture:foodtexture::id->Bi`	Scalar
	K_{FP1}: partition coefficient between food and layer 1	`$S:scenario::id->foodsimulant:foodsimulant::id->K`	Numerical vector of the same size of the input (e.g., "ethanol50;fatty" leads to two values)
Composite requests	D_1: typical overestimates of diffusion coefficients in layer 1 according to the likely migrants from the polymer and storage temperature	`Dpiringer(($S:scenario::id->polymer),($S:scenario::id->polymer:polymer::acronym->composition:substance::technologicalclass->M),($S:scenario::id->temperature:storage::id->temperature))`	Vector of three values based on 5th, 50th, and 95th percentile values
	t: contact time of scenario $S according to considered step (with conversion in SI unit)	`($S:scenario::id->food:food::id->shelife)*($S:scenario::id->food:food::id->shelifeunit:units::unit->SI)`	Scalar
	l_F: equivalent food thickness (with conversion in SI unit)	`($S:scenario::id->geometry:geometry::id->mF)*($S:scenario::id->geometry:geometry::id->mFunit:units::unit->SI)/(($S:scenario::id->food:food::id->rhoF)*($S:scenario::id->geometry:geometry::id->A)*($S:scenario::id->geometry:geometry::id->Aunit:units::unit->SI))`	Scalar
	l_1: thickness of layer 1 (with conversion in SI units)	`($S:scenario::id->geometry:geometry::id->lP1)*($S:scenario::id->geometry:geometry::id->lPunit:units::unit->SI)`	Scalar
	SML: 25th percentile of the collection of the specific migration limit severity calculation (with conversion in SI units)	`prctile(($S:scenario::id->polymer:polymer::acronym->composition:substance::technologicalclass->SML)*($S:scenario::id->food:food::id->rhoF)*($S:scenario::id->polymer:polymer::acronym->composition:substance::technologicalclass->SMLunit:units::unit->SI),25)`	Scalar
	$C_1\|_{t_0}$: maximum initial migrant concentration in layer 1 for the considered polymer and related class of migrants (with conversion in SI units)	`max($S:scenario::id->polymer:polymer::acronym->composition:technologicalclass::id->CP0)*($S:scenario::id->polymer:polymer::acronym->rhoP)*($S:scenario::id->polymer:polymer::acronym->composition:technologicalclass::id->Cunit:units::unit->SI)`	Scalar

$S is a placeholder for a scenario code/identifier as reported in the column "id" of Figure 7a (e.g., "LDPEYogurtBottle," "PPCreamPot," "PSYogurtPot," etc.). The tables and related keys are described in Figure 6. It is worth to notice that the table "units" is not depicted in Figure 6, as it is a generic table relating user-friendly units to SI units as used in FMECAengine.[76] Mathematical operators and functions use a Matlab (Mathworks) like syntax, whereas the SQL syntax obeys to Eq. 19 and is implemented via the function key2key() in FMECAengine.

Table 2. Detailed Description, Including Geometry, Composition, Formulation, of the Food Packaging Design (Design A) Used in the Case Study 1 "Functional Analysis" (see Figure 5)

		Layer $j = 0$		Layer $j = 1$	Layer $j = 2$	Layer $j = 3$
Design A	Food	Soup (fatty)	Function	Barrier layer	Corona modified surface	Ink
	Geometry	Truncated cone				
	Dimensions$\times 10^2$ (m)	$\varnothing_1 = 7$, $\varnothing_2 = 9$, $H = 10$	Material	Polypropylene	Polypropylene	
			$l \times 10^6$(m)	700	35	10
	$V_F \times 10^6$ (m^3)	200	ρ (kg m^{-3})	910[116]	910	1000
	$A \times 10^4$ (m^2)	220	$C_{X,j}\|_{t_0}$(mg·kg^{-1})	0	0	4000[125]
			$K_{X,F/j}$	2.5×10^{-2} [114]	2.5×10^{-2}	2.5×10^{-2}
			D (m^2 s^{-1}) at 23°C	7.6×10^{-16} [126]	7.6×10^{-16}	7.6×10^{-16}

$K_{X,F/j}$: partition coefficient of migrant X between food product (F) and each layer j which corresponds to the ratio of k_j/k_F with $k_F = 1$.

supplied composition databases of involved polymers, the automatic tool screens possible contaminants from three technological classes of substances: antioxidants, UV-stabilizers, and plasticizers. Automatically retrieved values were used to derive three typical scenarios based on the 5th, 50th, and 95th percentile values of the distributions of molecular masses found for each polymer. Overestimates of diffusion coefficients were derived from Eq. 18.

Results and Discussion

As the proposed FMECA and computational frameworks cover more conditions and situations than it can be experimentally tested (it is the original intent), a direct validation by comparison with known or newly collected results is not directly tractable. An inductive approach is preferred instead: if we accept its premises what is the kind of conclusions we can reach? Are they consistent with already known crises? With existing human expertise? With the physics of mass transfer? Three representative application cases are illustrated hereafter and discussed in an attempt of validating or invalidating the correctness of the conclusions generated in a semisupervised way.

Case study 1: identification of the critical steps in a process-storage diagram

The functional application of our proposed FMECA methodology is first detailed on a technological problem of general interest for the food packaging industry: the contamination of food by printing ink constituents. Main causes are known now but failed to be identified by human expertise before major crises started. This case study is used to infer three generic and counter-intuitive properties that can be considered as lemma for the identification of a set of critical steps along industrial, retailing, and household practices. Formally, Lemma 1 presents the conditions of commutativity of steps and is used to derive a second lemma for evaluating in a robust fashion the severity of a step or a combination of steps in a sequence. The last lemma enables finally Bayesian estimators of severity in sequences subjected to uncertainty or variability.

As only external parts of the packaging are printed, it has been thought during many years that ink constituents required permeating through all layers to contaminate the food content. The risk of contamination was therefore envisioned to occur only when the packaging was in contact with food and to be delayed by the successive barrier to diffusion met before the contaminant reaches the opposite face. It was in particular commonly estimated that the risk vanishes when a metallic layer (aluminum foil) was present between the printing ink and the layer intended to be in contact with food. On the contrary, recent crises involving low molecular weight photoinitiators in UV-curable printing-inks (141 entries in the European Rapid Alert System for Food and Feed[138]) showed that the contamination tended to be ubiquitous regardless the packaging structure and food shelf-life. Evidence of a second route was subsequently confirmed experimentally on rolled films[139]: putting in contact printed regions with the internal surface layer intended to be in contact with food would bring the contaminant closer to the food (setoff phenomenon), even when the food is not initially present. It is worth to notice that because such phenomena can be easily captured through mass-transfer modeling, numeric simulation offers a very efficient way to assess the effect of each combination of practices.

Lemma 1. The final contamination of food is not significantly affected by the order of steps in a sequence

Figure 8 plots the concentration profiles of a typical migrant of inks, benzophenone, and the corresponding food contamination kinetics for a technological problem, chosen to be anonymous but presenting several analogies with previously reported crises and known as "setoff effect." In the considered case, rolled flexible films are replaced by rigid containers such as pots and cups stored in stack for a typical period of 6 months in ambient conditions before as sketched in Figure 5

Table 3. Properties of the Migrants (So-Called X and Y) in the Case Studies 1 "Functional Analysis" and 2 "Risk-Ruled Concurrent Engineering"

	Migrant X	Migrant Y
Name	Benzophenone	1,2-Benzoisothiazolin-3-one
CAS number	119-61-9	2634-33-5
PM/REF number	38240	37520
Technological functions	Photoinitiator, UV-stabilizer[45]	Biocide[127]
M (g mol^{-1})[120]	182.073	151.009
TDI (mg kg^{-1} body weight)	0.01[128]; 0.03[129]	0.02[128]
SML (mg kg^{-1} food)	0.6[50]	1.2[130]
log P[120]	3.18	1.77
Breakdown products	Diphenyl-2-methanol (91-01-0)[131]	–

Table 4. Flowchart Associated with the Food Packaging A Used in the Case Study 1 "Functional Analysis" (see Figure 5)

Step	Designation	Condition	Modality		Food in Contact
1	Storage before use (setoff)	100 days at 25°C	–		–
2	Hot filling	10 min at 80°C	–		Fatty product
3	Storage	200 days at 25°C	Storage t (reference)		
		400 days at 25°C	Storage t^+		
4	Oven heating	5 min at 100°C	Oven heating tD (reference)	Oven heating t^+D	
		5 min at 135°C	Oven Heating tD^+	Oven heating t^+D^+	

Reference conditions used in Figures 8–10 are denoted "reference."

and detailed in Table 4. The four main steps involved in the flowchart of a "ready-to-eat soup type" product were considered: "1:Setoff" (no food contact), "2:HotFilling" (contacting phase at a high temperature), "3:Storage" (long-term contact at ambient temperature assuming that food is pasteurized/sterilized), and "4:OvenHeating" for final preparation. "2:HotFilling" and "4:OvenHeating" steps were idealized as isothermal processes at high temperatures (Table 4). Intermediate nonsteady stages of heating and cooling were indeed consistently neglected with respect to the overall duration of mass transfer. Simulation proceeds as follows. During "1:Setoff", periodic boundary condition (6) enables mass transfer to both sides (internal and external) of the cup material (polypropylene layer indexed $j=1$ in Table 2). Such redistribution triggers a contamination of food without delay during "2:HotFilling." Long-term "3:Storage" completes the redirection of the overall mass transfer from ink layer to food. Additional contact time at high temperature during "4:OvenHeating" does not change the final figure.

The aforementioned analysis based on a rapid reading of mass-transfer equations and simulated results tends to impose logically long-term "3:Storage" as the main contributor to the final food contamination. Without additional analysis, it would reinforce the common expert idea that the choice of the cup material (polymer, thickness), and the conditions of storage (time and temperature) are the principal causes when the final contamination is found to exceed a prescribed threshold of detection or of concern. In addition, the literature does not report clear evidence that the practices of material suppliers (here stacking pots/cups), before putting them in contact with food, could affect the final food contamination. Further comprehension is, however, provided by plotting the contamination levels reached at the end of each step when the steps involving a contact with food are permuted. It is shown in Figure 9 that the contribution of a step (variation of the contamination after this step) depends on its position in the flowchart but does not affect the final contamination after the last step. Such counter-intuitive results were verified exactly with the prescribed numerical accuracy (absolute tolerance of 10^{-8}) and even verified by enforcing an absolute accuracy up to 14 digits.

At first sight, these new results breach the common sense of causality, because the same cause (the step) does not lead always to the same effect according to its position in the sequence. The contribution of "3:Storage" varies thus in a range of 20% according to it is the last step or the second step (after "Setoff"). "4:HotFilling" changes by 100% when it is displaced from position 2 to position 4. A nonparadoxical assessment of the contribution of a single step was reached by replacing the analysis on isolated steps in a sequence by the study of the whole sequence.

The mathematical justification and validity of the exchangeability property found in most of met situations are briefly discussed for a process starting at $t=0$ and involving two steps of duration t_1 and $T-t_1$, respectively. Matrix $\mathbf{M}$ given by Eqs. 11 and 12 is defined in a piece-wise constant manner

$$\begin{cases} \mathbf{M}=\mathbf{M_1} & 0 \le t \le t_1 \\ \mathbf{M}=\mathbf{M_2} & t_1 < t \le T \end{cases} \tag{20}$$

The general solution at $t=T$ of $d\mathbf{C}/dt=\mathbf{M}C$ that satisfies an initial condition $\mathbf{C_0}$ is given by the product of matrix exponentials that accepts the following expansion series

$$\begin{aligned} \mathbf{C}(T) &= \exp\left((T-t_1)\mathbf{M_2}\right)\exp\left(t_1\mathbf{M_1}\right)\mathbf{C_0} \\ &= \left(\mathbf{I}+(T-t_1)\mathbf{M_2}+\frac{(T-t_1)^2}{2}\mathbf{M}_2^2+\cdots\right)\left(\mathbf{I}+t_1\mathbf{M}_1+\frac{t_1^2}{2}\mathbf{M}_1^2+\cdots\right)\mathbf{C_0} \\ &\approx \left(I+(T-t_1)\mathbf{M_2}+t_1\mathbf{M}_1+\frac{1}{2}\left((T-t_1)^2\mathbf{M}_2^2+2(T-t_1)t_1\mathbf{M_2}\mathbf{M}_1+\frac{t_1^2}{2}\mathbf{M}_1^2\right)+\cdots\right)\mathbf{C_0} \end{aligned} \tag{21}$$

One sufficient condition to reach a same solution at time T when steps 1 and 2 are permuted is to have tridiagonal matrices $\mathbf{M}_1$ and $\mathbf{M}_2$ to commute. By appending a " ' " to coefficients of $\mathbf{M}_2$ and by noticing that $he(i)=hw(i+1)$ and $he'(i)=hw'(i+1)$, it is straightforward to demonstrate $\mathbf{M}_1\mathbf{M}_2=\mathbf{M}_2\mathbf{M}_1$ as soon as all partition coefficients are kept constants between steps 1 and 2

$$\frac{k(i-1)}{k(i)}\frac{\rho(i)}{\rho(i-1)}=\frac{k'(i-1)}{k'(i)}\frac{\rho'(i)}{\rho'(i-1)} \quad 1\le i\le N \tag{22}$$

When the decomposition in steps corresponds to stages at different temperatures (as it occurs for "HotFilling," "Storage," and "OvenHeating"), the equality (22) is reasonable as the isosteric heat of sorption in the different materials is usually

Table 5. Detailed Description of the Food Packaging Systems (Designs B and C), Including Geometry, Formulation, Composition, Used in the Case Study 2 "Risk-Ruled Concurrent Engineering"

		Layer 0		Layer $j = 1$	Layer $j = 2$	Layer $j = 3$	Layer $j = 4$	Layer $j = 5$	Layer $j = 6$	Layer $j = 7$
Design B	Food F_1	Soup (fatty)	Function	Layer in contact	Adhesive	Gas barrier layer	Barrier layer	Label	LDPE corona	NaN
	F_2	Dairy product	Material	LDPE	VAE	EVOH	Cardboard	LDPE	LDPE	
			$l \times 10^6$ (m)	10	5^{134}	15^{135}	200	7	3	
	Geometry	Parallelepiped	ρ (kg m^{-3})	917^{117}	1200	1165^{135}	700	917	917	
			Migrant $i = X$							
	Dimensions$\times 10^2$ (m)	$W = 6$, $D = 6$, $H = 8$	$C_{X,j}\|_{t_0}$(mg·kg^{-1})	0	0	0	0	0	4000^{125}	
	$V_F \times 10^6$ (m^3)	250	$K_{X,F_1/j}$	1	1	5	10	1	0.1	
	$A \times 10^4$ (m^2)	260	$K_{X,F_2/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	
			Migrant $i = Y$							
			$C_{Y,j}\|_{t_0}$(mg kg^{-1})	0	1000^{136}	0	0	0	400^{137}	
			$K_{Y,F_1/j}$	1	0.1	5	10	1	0.1	
			$K_{Y,F_2/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	
Design C	Food F_1	Soup (fatty)	Function	Layer in contact	Adhesive	Gas barrier layer	Adhesive		Label	LDPE corona
	F_2	Dairy product	Material	HDPE	VAE	EVOH	VAE	HDPE	LDPE	LDPE
			$l \times 10^6$ (m)	50	5	15	5	50	7	3
	Geometry	Cylinder	ρ (kg m^{-3})	950^{117}	1200	1165	1200	950	917	910
			Migrant $i = X$							
	Dimensions$\times 10^2$ (m)	$Ø = 5.5$, $H = 11.5$	$C_{X,j}\|_{t_0}$(mg kg^{-1})	0	0	0	0	0	0	4000
	$V_F \times 10^6$ (m^3)	250	$K_{X,F_1/j}$	2	1	5	1	2	1	0.1
	$A \times 10^4$ (m^2)	220	$K_{X,F_2/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$ j	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$	$0.1 \times K_{X,F_1/j}$
			Migrant $i = Y$							
			$C_{Y,j}\|_{t_0}$(mg kg^{-1})	0	1000	0	5000	0	0	400
			$K_{Y,F_1/j}$	2	0.1	5	0.1	2	1	0.1
			$K_{Y,F_2/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$	$0.1 \times K_{Y,F_1/j}$

EVOH: ethylene vinyl alcohol; HDPE: high-density polyethylene; LDPE: low-density polyethylene; VAE: vinyl acetate ethylene. $K_{X,F_1/j}$: partition coefficient of migrant X between fatty food product (F_1) and each layer j, which is associated with ratio of k_j/k_{F_1} with $k_{F_1} = 1$.

Table 6. Main Steps Involved in the Food Packaging System Lifetime of Designs B and C Used in the Case Study 2 "Risk-Ruled Concurrent Engineering"

Step	Designation	Condition	Modality		Food in Contact
1	Storage before use	6 months at 25°C	–		–
2	Hot filling	5 min at 80°C	Hot filling + fatty	Hot Filling + dairy	Fatty and dairy products
3	Storage	1 month at 4°C	Short shelf-life + fatty (a)	Short shelf-life + dairy (c)	
		6 months at 25°C	Long shelf-life + fatty (b)	Long shelf-life + dairy (d)	

similar. In details, the apparent activation energy of partition coefficients is equal to the difference in sorption energy (see Refs. 71 and 73), it is assumed to be significantly different of zero for polar solutes exchanged between a polar medium (exothermic mixing process) and an apolar one (endothermic mixing process). Additional deviations could occur when the constituents are initially solid or crystallized and need to melt before migrating. Finally, the condition of exchangeability will be lost when the substance is blocked behind a barrier material (e.g., aluminum foil) or when the food is not present (e.g., "Setoff"). It is worth to notice that activation of diffusion must not require being homogeneous among the compartments to reach the condition of exchangeability.

Lemma 2. *The* severity of a single step (or set of steps) in a sequence is obtained by difference in the final contamination when it is removed from the sequence or by considering the step (or set of steps) alone in the sequence. For many applications, it cannot be asserted that the same step order will be applied. For instance, the order of temperature variations when materials or food products are transported in trucks, trains, or boats is not known *a priori* and can be significantly affected by intermediate storage, diurnal, or seasonal variations. A robust estimate of the contribution of a single step (or a combination of steps), which is almost order invariant can be inferred by applying Eq. 16 to the difference of the final contamination values between the complete sequence and the sequence without the sequence of interest, as justified by Lemma 1. However, it is worth to notice that the proposed difference method does not hold for long sequences when the concentration in food reaches its maximum value enabled by thermodynamic and mass balance considerations (equilibrium value) before the end of the sequence. In this case, some differences can vanish as one single step may have the same contribution as several steps on the final contamination. To solve efficiently the issue, the contribution of one step was defined as the maximum value between the difference of the two sequences (with and without the considered step) and the value obtained when the step is considered alone in the sequence. The latter estimate can be interpreted intuitively as the difference between the singleton sequence (one single step) and the null sequence (no step). A more formal derivation can be obtained by replacing the generic two-step sequence $1 \rightarrow 2$ of total duration T—governed by Eq. 20—by a sequence $0' \rightarrow 1 \rightarrow 2$, where the concentration profile after step $0'$ of duration t'_0, $\mathbf{C'_0}$, approaches enough the equilibrium value, so that the subsequent steps of duration $t_1 - t'_0/2$ and $T - t_1 + t'_0/2$, respectively, would lead to: $\mathbf{M_1 C'_0} \approx \mathbf{M_2 C'_0} \approx \mathbf{0}$. As $(\mathbf{M_1} - \mathbf{M_2})\mathbf{C'_0} \approx \mathbf{0}$, any contribution of 1 and 2 assessed by difference and the approximation (21) vanishes also. Finally, as the final contamination is governed by the mass balance and thermodynamical equilibrium conditions (2) coded as mathematical constraints in $\mathbf{M_1}$ and $\mathbf{M_2}$. As a result, $\mathbf{M_1}$ and $\mathbf{M_2}$ can be used indifferently to assess the contribution of step $0'$, which is also the contribution of steps 1 and 2 alone. To summarize former principles, it is worth to notice that the contribution of a set of steps is not the sum of the contributions of parts. A corollary result is that acting on a single step does not guarantee necessarily a significant reduction in the final contamination of the packaged food product.

Abstract concepts of Lemmas 1 and 2 were applied again to the printing ink mass-transfer problem. Figure 10a presents all oriented paths corresponding to Figure 8 when one, two, or three steps are removed. In practice, it suffices to calculate all branches ending by "4:OvenHeating" (coded from a to h) and starting from one of the four possible steps. The contribution of "4:OvenHeating" for any path of length 1–4 is read from the different branches by stopping at the step before the last. The cumulative concentrations along all eight paths are plotted in Figure 10b. The severity of step "1:Setoff" is for instance found proportional to the concentration difference between paths a and e. As the distance between a and e is the largest, it confirms unambiguously the major role of this first step on the final food contamination. Corresponding severities calculated by means of Eq. 14 and using SML value in Table 3 are depicted as a Pareto chart in Figure 10c. "1:Setoff" appears with a severity ~20% higher than "Storage" and approaching the unacceptable domain. In other words, although "1:Setoff" does not contaminate directly food (food is not present), it affects the subsequent steps so that the legal limit (SML) could be overpassed regardless the overestimations introduced in the

Table 7. Detailed Description of Nine Food Packaging Systems Purchased on the French Local Market and Used in the Case Study 3 "Risk-Oriented Screening"

		Bottle	Cap	Goblet		Container	Pot	Straw	Cover Gasket
Polymer		LDPE	HDPE	PP	PS	PP	PS	PP	pPVC
Geometry	Contact surface $\times 10^4$ (m^2)	200	20	170	170	250	120	30	13
	Mass of food $\times 10^3$ (kg)	250	330	200	200	400	125	200	450
	Thickness $\times 10^6$ (m)	300	1100	160	100	500	300	160	50
Food		Liquid yogurt	Oil	Hot drinks		Butter, cream	Yogurt	Liquid yogurt	Sauce
Steps studied		Storage	Storage	Consumption		Storage	Storage	Consumption	Process, storage
Food in contact		Dairy	Fatty	Fatty, dairy		Fatty	Dairy	Dairy	Fatty

HDPE: high-density polyethylene; LDPE: low-density polyethylene; PP: polypropylene; PS: polystyrene; pPVC: plasticized polyvinyl chloride (plasticization rate: 30 wt %).

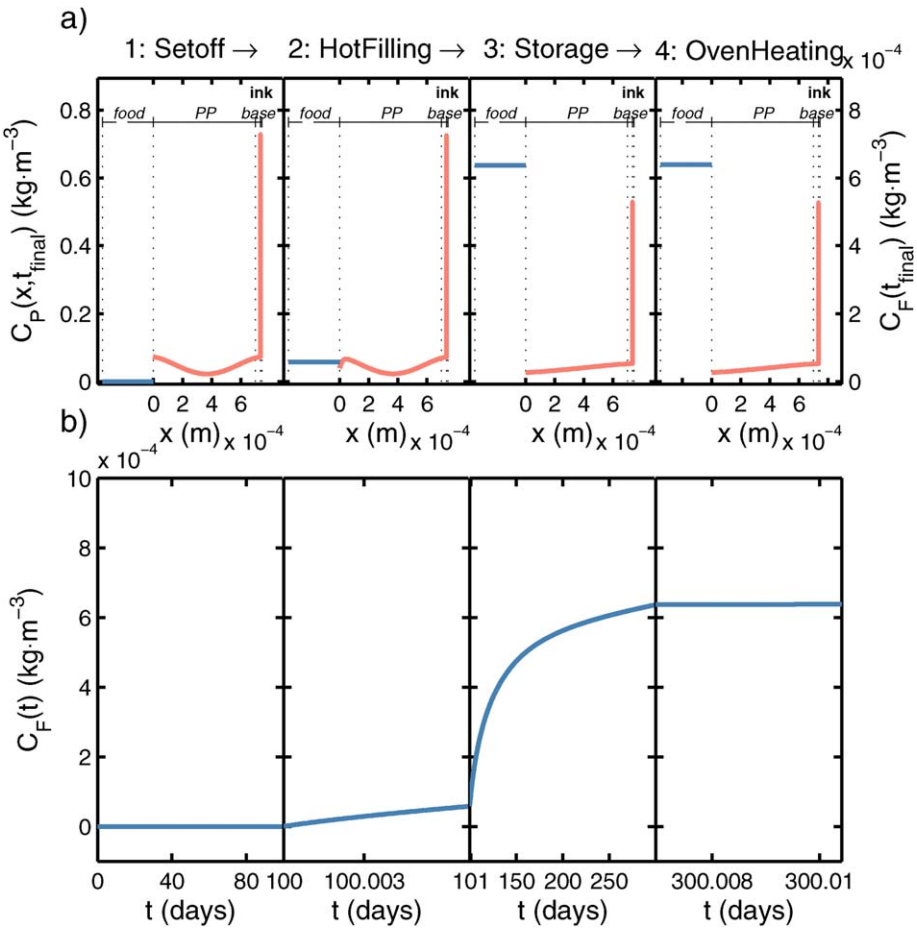

Figure 8. (a) Concentration profiles and (b) food contamination kinetics associated with the migration of a photoinitiator (substance X in Table 3) during a four steps flowchart as described in the case study 1 "Functional analysis" (see Figure 5, Tables 2 and 4 with reference conditions).

The ink layer is depicted in contact with a layer so-called "base" corresponding to the corona-modified surface with the same properties as the PP. Only part of the food layer is represented at position $x \leq 0$. Periodic boundary condition (6) and mixed Robin boundary condition (5) are applied at $x = 0$ for step 1 and steps 2–4, respectively. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

simulation. Indeed, all steps are simulated with similar overestimations. Similarly, Lemma 2 clears steps "2:HotFilling" and "4:OvenHeating" from significant responsibility in the final food contamination.

Lemma 3. Severity values of a single step in the sequence depends on the context of its parent and child steps

It can be thought that conclusions depicted in Figure 10c can be affected by variability and uncertainty, so that an absolute value of severity may not have enough ground to enable decision making. In particular, it is not intuitive how conservative estimates of severities could be affected in an uncertain context. At this stage of sophistication, it is important to notice that the food industry is quite familiar with such large extent risk assessment studies under uncertainty. The interested reader will find in Ref. 140 an example of such a large-scale study carried out to minimize the presence of genetically modified organisms in chocolate-filled products at the scale of a whole pilot plant.

The hierarchy of steps is challenged in Figure 11 when the steps of "3:Storage" and "4:OvenHeating" are broken into two different levels: previous level used as a reference and an additional worst-case scenario corresponding to a longer storage time (suffixed t^+) or higher heating temperature (suffixed D^+) as reported in Table 4. As depicted in Figure 11, the causal tree decomposition shows that "3:Storage" and "4:OvenHeating" have to be assessed for two conditions (denoted "Storage t" and "Storage t^+") and four conditions (denoted "OvenHeating tD," "OvenHeating tD^+," "OvenHeating t^+D," and "OvenHeating t^+D^+"), respectively. The practical consequence was that "1:Setoff" and "2:HotFilling" needed to be compared to four different scenarios/paths leading to four values of severity. It is highlighted that "1:Setoff" remained the most critical step whatever the following conditions of use, with a severity remaining close to 100. The intrinsic contribution of "3:Storage" was less intuitive to capture, as it depends not only on storage conditions ("Storage t" and "Storage t^+") but also on the "4:OvenHeating" conditions. In details, the contribution of the first one was found much lower than the last one. Indeed, the severity of the long-term storage step decreased consistently by a half when it was followed by an exaggerated final oven heating. Such results make practical sense: reducing storage time (or equivalently product shelf-life) would impact final contamination if and only if it is not

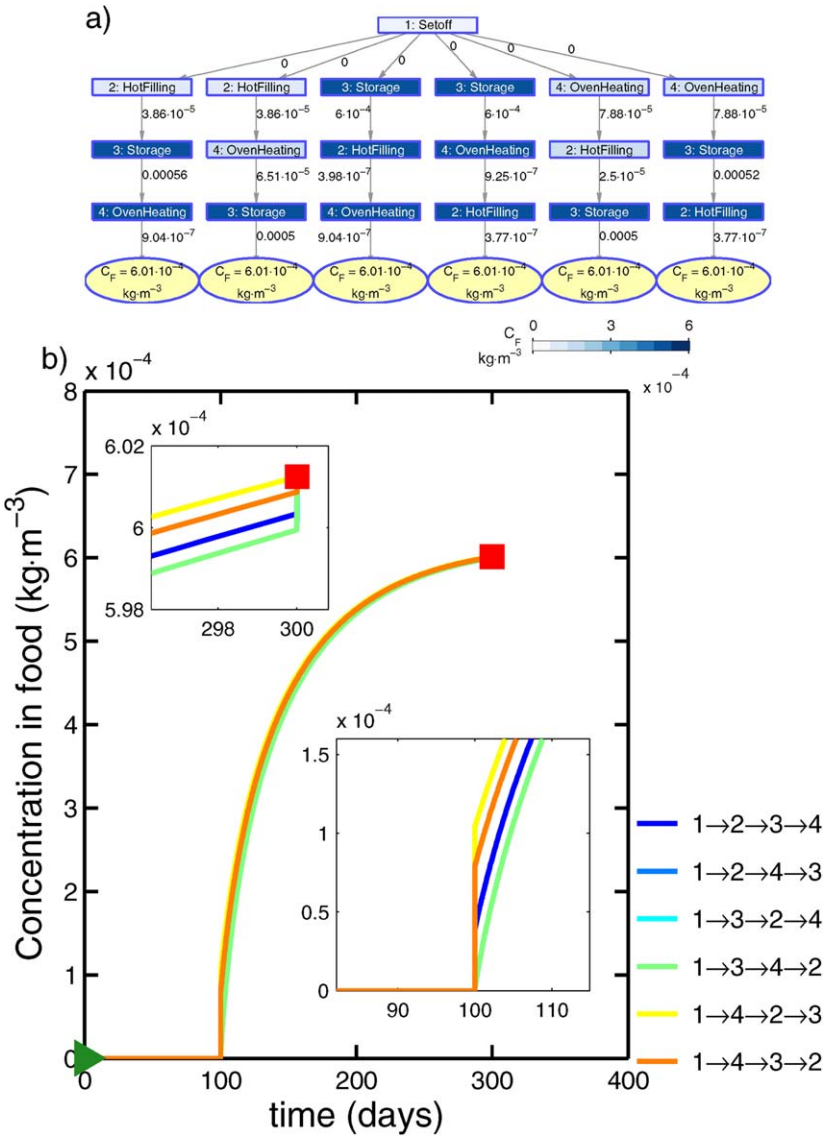

Figure 9. Effect of the permutation of the three last steps (2–4) depicted in Figure 8 on the final food contamination (C_F).

(a) Functional dependence tree, where the color scale maps the cumulated concentration in food. The contribution of each individual step appears along each arrow following the considered step (with concentration unit in kg m^{-3}). (b) Kinetics of food contamination of the six permutations. Insets present zoom on the beginning and the end of the kinetics. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

followed by a step that would partly compensate the missing contact time. The presented case study exemplifies how compensation between sequential steps could be detected in complex situations involving arbitrary combinations of steps. According to the expected intent of the analysis, previous 16 (4 steps × 4 paths) severity values can be lumped into criticality values either by considering only the maximum values for each step or by averaging them according to the probability of each path (see Eq. 17).

For the decision maker, only the corresponding criticality profiles describing the "averaged" criticality value at each step is really enlightening. Figure 11c plots the corresponding criticality profile when all conditional probabilities at each bifurcation of the tree depicted in Figure 11a are equal; the values along the flowchart are: 1:100 → 2:0.03 → 3:62.8 → 4:0.4. Steps, whose criticality does not depend on the context, generate similar values whatever conditions assigned to parent and child steps. The previous analysis, which can be executed in few minutes, confirm thus the universal role of "1:Setoff" as the main source of contamination regardless the final storage and use of the food packaging as previously discussed by us in Refs. 55 and 73. In the next case study, "risk-ruled concurrent engineering" (see the section "Case Study 2: Risk-Ruled Concurrent Engineering"), the contribution of "Setoff" effect is challenged with other criteria such as the number of layers containing initially possible migrants/contaminants. The industry must be aware that the risk known as "Setoff" occurs not only when a printed surface is put in contact with a surface intended to be in contact with food during a significant period (storage as stacks as depicted in Figure 5 or as rolls) but more generally when there is any physical route, which reduce the mass-transfer

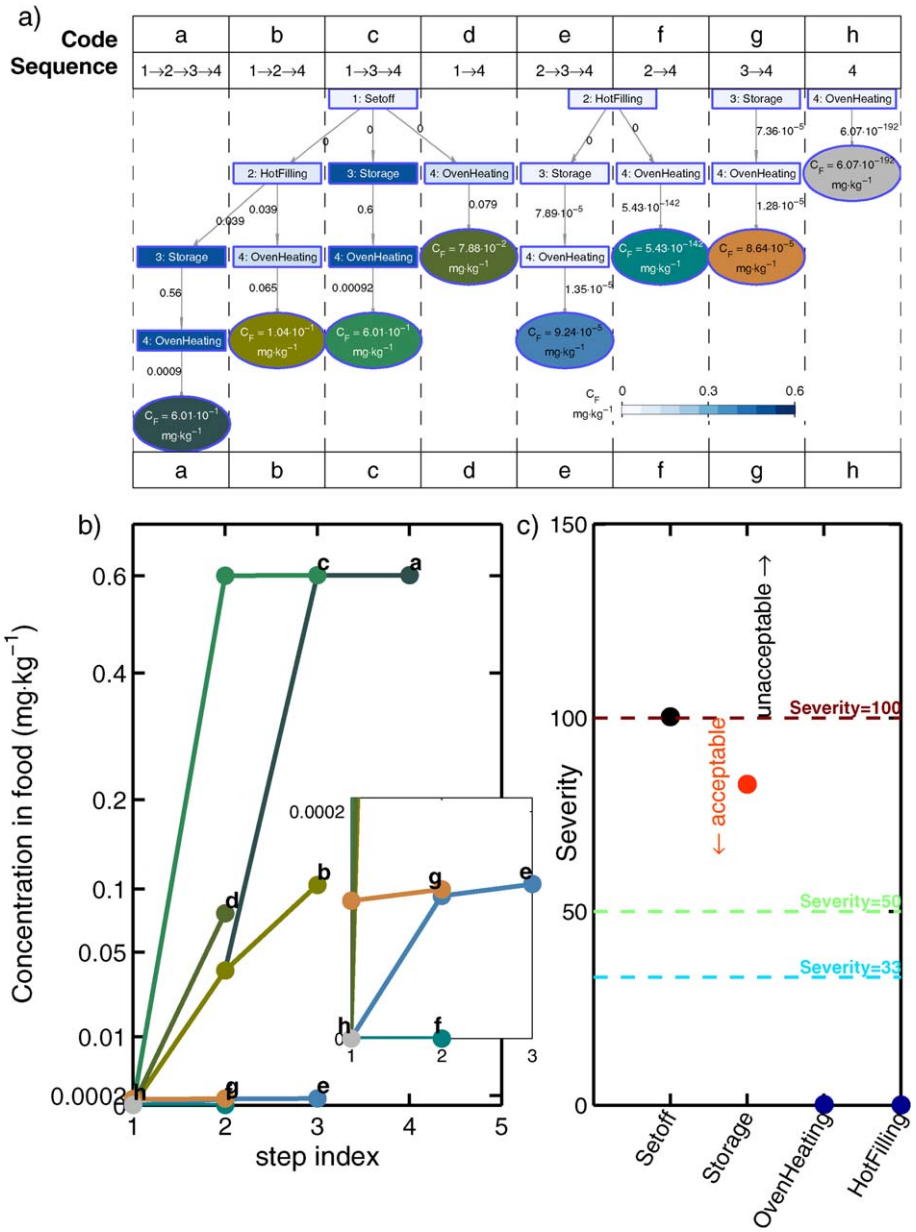

Figure 10. Effect of the deletion of one or several steps in the sequence 1 → 2 → 3 → 4 depicted in Figure 9: (a) corresponding functional dependence tree (with the same conventions used in Figure 9a); (b) evolution of the concentration in food along each of eight branches (denoted from a to h); (c) Pareto chart associated with the severity of a single step as calculated from Eq. 16.

[Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

resistance (i.e., diffusion path length or diffusion time). Without being exhaustive, it includes alone or in combination:

- Contaminants behind a barrier material or a "functional barrier,"[141] which can be transferred in the opposite direction due to the periodic organization of layers during industrial storage (rolls or stacks);
- Volatile contaminants, which can be exchanged between packaging components (from primary or secondary packaging), during common storage at industrial scale in a room with insufficient air renewal. Such contaminants may include polymerization or processing aids, preservative substances (e.g., biocide substances, cleaning or decontamination solvents, etc.), solvent residues of nonproperly dried/cured adhesive or printed layer, residues from recycled (paper, cardboard, plastics, etc.) or aged materials, and so forth

Case study 2: risk-ruled concurrent engineering

Ongoing food consumption is oriented toward minimally processed food, with fewer food preservatives, higher nutritive value, and fresh sensory attributes. To comply with shelf-life requirements and with higher risks of microbiological food poisoning, specific process-conditioning-packaging-distribution flowcharts are used, such as flash pasteurization immediately followed by aseptic conditioning and combined with chilled short-term storage.[142] Complex and multilayer packaging materials are conventionally preferred to minimize

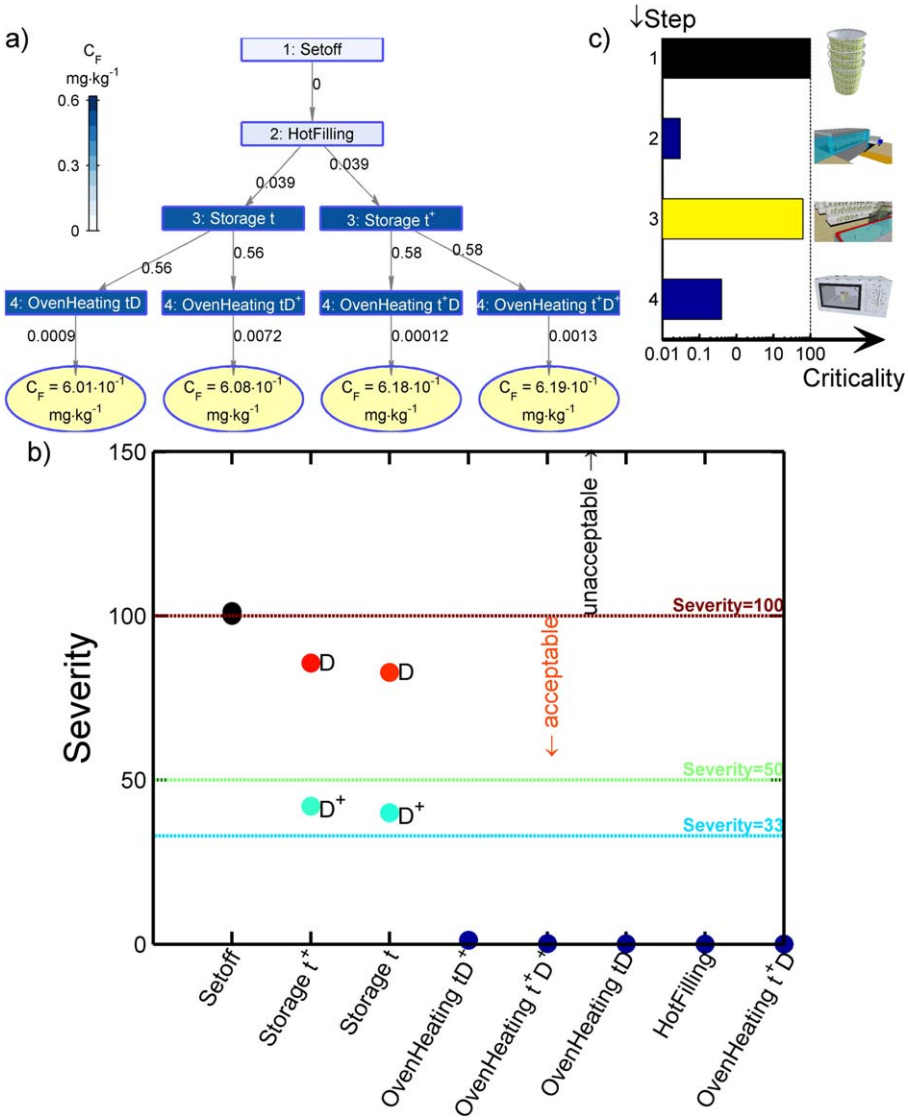

Figure 11. Effects of the duplication of levels 3 and 4 in the sequence 1 → 2 → 3 → 4 depicted in Figure 9 (see details in Table 6): (a) corresponding functional dependence tree and (b) severities.

Four severity values are associated with "Setoff" and "HotFilling," but they appear overlapped. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

oxygen permeation and consumer convenience (reusable packaging with easy opening and closure, packaging transparency, etc.). To reach low unit costs, such sophisticated packaging systems have to be easily adaptable to several food-type products and duration of storage. We argue that safety requirements can be addressed in the early stages of packaging development, in particular, through a concurrent engineering methodology. The main idea is to anticipate the discovery of defects, lacks of optimization or misconceptions when the packaging concepts are still abstract or flexible and open to redesign.

Concurrent engineering principles were applied to two designs used for typical minimally processed liquid or semi-liquid food such as dairy products and vegetable soups. Chosen designs are detailed in Table 5. They were either aseptic tetrahedron packages including a printed cardboard layer and internal gas barrier layers (denoted design B) or aseptic multilayer plastic bottle including an external corona-treated polyethylene shrink sleeve for decoration and marketing purposes (denoted design C). As most packaging designers are not conversant with the composition of each material (four and five different materials for the sole packaging body of designs B and C, respectively), we illustrate the risk of contamination for two ubiquitous migrants: benzophenone (denoted substance X) used as photoinitiator in printing inks and 1,2-benzoisothiazolin-3-one (denoted substance Y) used as a common biocide in adhesive and ink formulation as reported in Table 3. All assumptions are summarized in Tables 5 and 6. We assumed a first step of 6-month storage of packaging systems before use in rolls or stacks (i.e., with "setoff" risk) for design B and in bulk for design C. Both packaging systems were filled at 80°C with dairy or fatty type products. Finally, packaged food products were either chilled at 4°C for 1 month or stored at room temperature for 6 months.

The contamination levels associated with the 2^4 combinations of factors (design × substance × food product × storage conditions) are tabulated in Figure 12a, and their

corresponding severities are plotted on a dual severity scale in Figure 12b. The region, where all substance severities were lower than 100, was defined as "Acceptable." Only design B with chilled storage fell within this region. On the opposite side, design C including with long-term storage exceeded thresholds for both substances. Other conditions led to mitigated severity with one severity exceeding thresholds defined in Table 3. Specifically, design C including two tie layers (i.e., two sources of substance Y) and not subjected to a "setoff" risk (sleeve added only during the conditioning step) maximized the risk of contamination by any substance entering ubiquitously in the formulation of adhesives. On the opposite, design B maximized the "setoff" risk. A more synthetic view was gained by calculating the marginal criticalities associated with each design, each substance, each food type, and each storage condition according to Eq. 17 and the contamination trees depicted in Figure 12a. The corresponding values are listed in Table 8. As an example, the marginal criticality of design B is the sum of the criticalities associated with substances X and Y, when they are averaged over all possible paths {a,b,c,d}: the same design is assumed to be used for many different conditions of contact and shelf-life. The marginal criticality of one single substance was assessed as the criticality of the considered substance when averaged over all possible designs (B and C) and paths {a,b,c,d}. The marginal criticality associated with food type was calculated a similar way by averaging over all possible substances (X and Y), designs (B and C), and storage conditions (paths {a,b} or paths {c,d}). The aforementioned analysis is summarized in Table 8iii and refined in Table 8i,ii for short-term and long-term contact applications respectively.

Cumulating the criticalities of substances X and Y gave a marginal criticality of 186 and 293 for designs B and C, respectively. By considering, that both packaging designs have, hence, an equal market share, criticality values of 115 and 124 were obtained for substances X and Y, respectively. Criticality figures suggested that design C "bottle design," repeating many materials with likely contaminants (two tie layers and one printing ink) yielded a higher risk of contamination. Although it is subjected to a high risk of Setoff (see "Lemma 2" of the case study 1), design B "brik design" looked by contrast more acceptable. In details, criticality of substances X and Y were found close, with values over 100 that might deserve special surveillance. It is worth to notice that restricting the usage of proposed designs to chilled applications (short-term contact and low temperature) would reduce their critical figures by 30 and 37%, for B and C, respectively. In this case, almost all individual (joint) criticalities (by product-type, by substance, and by packaging) were lower than 100. Only the criticality of substance Y in design C exceeded 100 with a value of 148. To reach an "acceptability" for design C similar as the one for B (with all values lower than 100), the initial concentration in substance Y (biocide) should be lowered at least divided by two (i.e., 148/100). This corrective action was logically suggested by the linear relationship between severity and concentration (see Eq. 14), while the contamination does not exceed 10 times the threshold of contamination.

The design of a safer packaging is a difficult task. Via the presented case study, we justify a global approach mitigating all contamination risks rather the simplistic approach consisting in avoiding only the "risks" spread via media. As an illustration, a rapid analysis via Google Trends[143] will show a maximum search hits for "bisphenol A" or "BPA" in April 2008—at the maximum intensity of the public debate about the safety of "bisphenol A"—and also a strong correlation with the search "bisphenol A free" or "BPA free bottles." We thought that the safety of the alternative packaging designs should also be challenged with a global index (overall criticality), which integrates the criticality of all known significant migrants. According to the progress in the understanding of negative effects of some chemicals on human body, the value of the criticality of some substances can be increased by lowering the threshold-of-concern used in the calculations (see Eq. 14). Possible corrective actions may include: reducing initial residues, changing condition of uses, changing geometry, adding a barrier layer, and so forth.

In an attempt to provide rationale for the anticipation of potential crises or safety concerns rather than simple material substitutions, Table 9i summarizes the distribution by materials of scientific and regular articles dealing with the migration of packaging constituents into food. An attempt of correlation between scientific studies and "sanitary crises" is suggested by listing the number of notifications/alerts recorded at EU level and the number of entries in Google News. The most illustrative example is the migration of photoinitiators from printing UV curing inks (mainly thioxanthone and benzophenone families). Such a risk led to 43% of all "food contact material" alerts in EU since 2005 and 19% of related entries in Google News. These crises involving paper and cardboard as printed surfaces raised substantially the number of scientific publications on this topic (about 10% today). For comparison, the migrants of adhesives, not currently involved in any crisis, represent only 3–4% of all scientific studies. The distribution of scientific studies by plastic materials is more representative of their market share (polyolefins: 17%, Polyethylene Terephthalate (PET): 17%, PVC: 10%, and PS: 9% according to Ref. 118) than their real class of risks. The category "paper and cardboard" is by contrast very illustrative of new trends for nonspecifically regulated materials with contaminants originating from surface modifications (printing, chemical grafting, etc.) and nonintentionally added substances due to the use of recycled materials.

Case study 3: risk-oriented screening

At the end of the food-packaging chain, a retro-engineering of the safety of food contact materials is complicated by the availability of the expertise and data as discussed in Ref. 55. One possibility for retailing industry, enforcement laboratories, and consumer associations is to use a knowledge-based technology or some support decision system that enables to share automatically some levels of expertise. The feasibility and opportunity of such an approach to evaluate or audit suppliers, technological choices (e.g., materials, systematic use of recycled materials, nanobased systems, etc.) is discussed on a case study aiming at assessing a "global" safety index of nine typical food-packaging systems sampled on the French local market in 2011 (Table 7). A similar study targeting some ubiquitous substances was already performed by us.[147] The presented case study was, however, coarser as no specific substance was *a priori* assumed. The possible end-user of our approach was indeed expected to know only: the packaging geometry and type, the type of food in contact and its shelf-life. All numeric quantities required to initiate the proposed FMECA approach were automatically extracted from incremental and generic databases (Figure 6) and inference rules as illustrated in Figures 7b,c. The names of polymers were

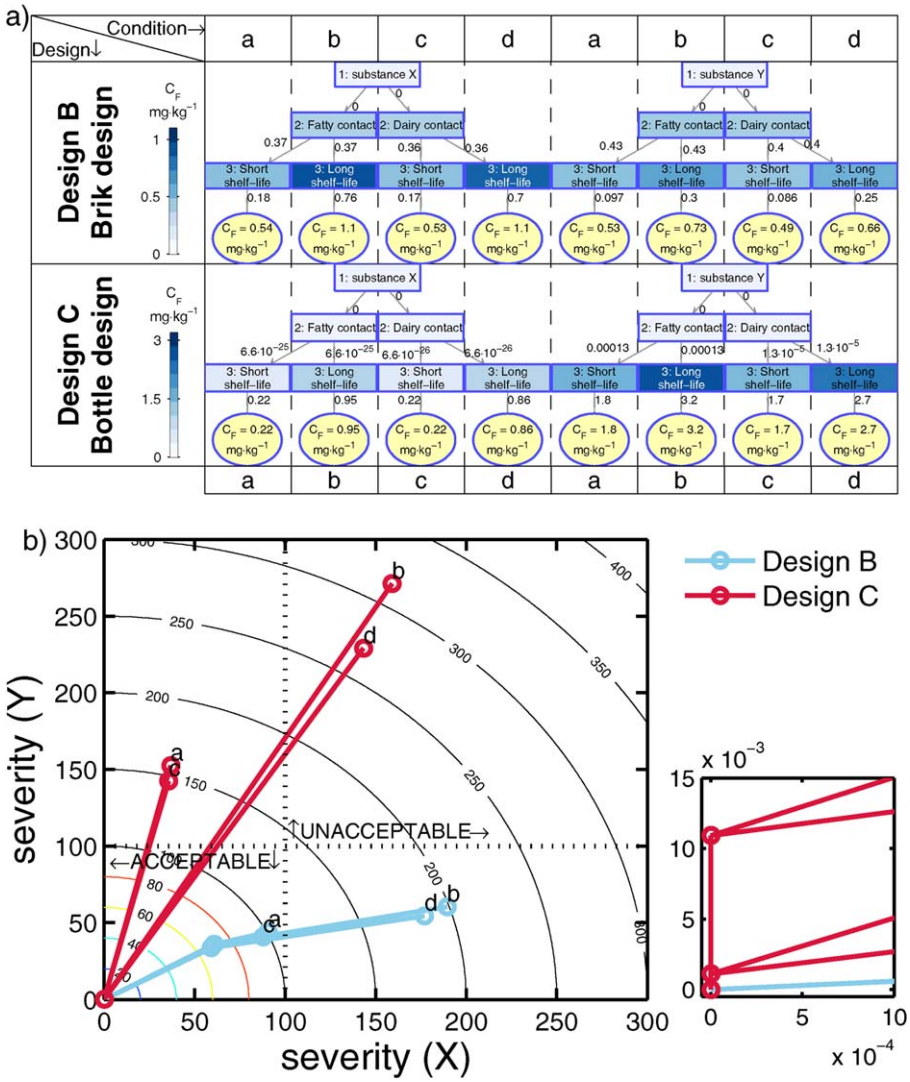

Figure 12. Results of the case study 2 "Risk-ruled concurrent engineering" (comparison of designs B and C defined in Tables 5 and 6).

(a) Functional dependence associated with the two considered designs (B and C) and substances (X and Y). Each flowchart includes three steps: (1) storage before use; (2) hot filling, and (3) short-term refrigerated storage or long-term storage at ambient temperature. (b) Severity of photoinitiator (migrant X) vs. severity of biocide substance (migrant Y) for all steps depicted in (a). The inset shows the details of the plot for low severity values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

consistently converted into a list of possible migrant families (mainly antioxidants, UV-stabilizers, and plasticizers) and hence substances. According to our physicochemical, transport, and thermodynamic properties available in our databases or according to robust overestimates (e.g., Eq. 18), typical scenarios were automatically generated. To keep calculations tractable within few seconds up to few minutes, a reduction of possibilities was operated with importance sampling. In our case study, we focused on the substances matching the 5th, 50th, and 95th percentiles of the distribution diffusion coefficients (corresponding results are suffixed "D5," "D50," and "D95," respectively) combined when necessary with conditions of fatty and dairy contacts (Table 6 and Figure 7a). A "robust" threshold of concern was set equal to the 25th percentile of SML values listed in European regulation of food contact materials in plastics.[50] Initial concentration in each material was set to the 95th percentile of values recommended by industry for this family of substance.

Previous rules led finally to 39 scenarios combining nine packaging systems and three levels for diffusion coefficients. Additional 12 arose from the combination of steps and food contact as described in Figure 7a. Results are summarized as a single Pareto chart in Figure 13a and as a generic abacus depicting a severity scale according to the type of materials, the typical molecular masses of additives in this material, and the type of food contact. Although several combinations of overestimations were combined together, only 13/39 of scenarios led to a severity beyond 100. In other words, the proposed method attracted attention only on one-third of cases. Figures 13b,c elucidate the risks by showing that the risk of a significant contamination, respectively, to a threshold of precaution might occur for low-molecular weight substances (e.g., volatile) used in rubber materials (e.g., polyolefins). By contrast, glassy materials (e.g., polystyrene) present the lowest risks of contamination. In our case study, the effect of contact

Table 8. Marginal (Global) and Joint (Individual) Criticality Values of the Case Study 2 "Risk-Ruled Concurrent Engineering" Corresponding to Severity Trees Depicted in Figure 12

	Substances		Food Types[a]		Marginal Criticality
Designs	X (1)	Y (2)	Dairy	Fatty	(1) + (2)[b]
Short-term storage at 4°C					
B	89	42	64	67	131
	(B × X × {a,c})	(B × Y × {a,c})	(B × {X,Y} × c)	(B × {X,Y} × a)	
C	36	148	89	95	184
	(C × X × {a,c})	(C × Y × {a,c})	(C × {X,Y} × c)	(C × {X,Y} × a)	
Marginal criticality	63	95	77	81	
	({B,C} × X × {a,c})	({B,C} × Y × {a,c})	({B,C} × {X,Y} × c)	({B,C} × {X,Y} × a)	
Long-term storage at 25°C					
B	183	58	116	125	241
	(B × X × {b,d})	(B × Y × {b,d})	(B × {X,Y} × d)	(B × {X,Y} × b)	
C	151	250	186	215	401
	(C × X × {b,d})	(C × Y × {b,d})	(C × {X,Y} × d)	(C × {X,Y} × b)	
Marginal criticality	167	154	151	170	
	({B,C} × X × {b,d})	({B,C} × Y × {b,d})	({B,C} × {X,Y} × d)	({B,C} × {X,Y} × b)	
All modes of storage					
B	136	50	90	96	186
	(B × X × {a,b,c,d})	(B × Y × {a,b,c,d})	(B × {X,Y} × {c,d})	(B × {X,Y} × {a,b})	
C	94	199	138	155	293
	(C × X × {a,b,c,d})	(C × Y × {a,b,c,d})	(C × {X,Y} × {c,d})	(C × {X,Y} × {a,b})	
Marginal criticality	115	124	114	125	
	({B,C} × X × {a,b,c,d})	({B,C} × Y × {a,b,c,d})	({B,C} × {X,Y} × {c,d})	({B,C} × {X,Y} × {a,b})	

The sets of paths and conditions used to average severities (assuming all paths equiprobable) are indicated between brackets. X: benzophenone; Y: 1,2-benzoisothiazolin-3-one; B: brik design; and C: bottle design.
[a]Food types detailed in the case study 2 "Risk-ruled concurrent engineering" (Tables 5 and 6).
[b]Criticality calculated with Eq. 17.

type was less significant, as all packaging systems had relatively large internal volumes ranged between 0.125 and 0.5 L.

Conclusions presented in this case study may look quite obvious to some human experts in this area. Indeed, most of the reported alerts or notifications on "food contact materials"

Table 9. Literature and Database Survey (Since 2000) of the Contamination of Food by Substances Originating from Packaging Materials

Category	Food Additives and Contaminants[144]	ISI Web[145]	RASFF[133]	Google News[146]
By material				
Thermoplastics	52% (94)	49% (178)	39% (129)[n]	19% (3)
Polyolefins	17% (31)[a]	17% (61)[a]	nd	0[v]
PET	17% (30)[b]	12% (45)[b]	nd	0[w]
PVC	9% (17)[c]	12% (43)[c]	nd	19% (3)[x]
Polystyrene	9% (16)[d]	8% (29)[d]	nd	0[y]
Paper and cardboard	22% (39)[e]	24% (88)[e]	7% (22)[o]	38% (6)[z]
Varnishes and coatings	13% (23)[f]	13% (46)[f]	11% (36)[p]	12% (2)[aa]
Printing inks	10% (19)[g]	10% (35)[g]	43% (141)[q]	19% (3)[ab]
Adhesives	3% (6)[h]	4% (14)[h]	nd	12% (2)[ac]
Total	100% (181)	100% (360)	100% (328)	100% (16)
By food type				
Fatty food	39% (32)[i]	48% (87)[i]	52% (102)[r]	nd
Dairy food	28% (23)[j]	18% (33)[c]	22% (44)[s]	nd
Dry food	25% (21)[k]	27% (49)[k]	5% (9)[t]	nd
Juices	8% (7)[l]	7% (13)[l]	21% (42)[u]	nd
Total	100% (83)	100% (182)	100% (197)	
By temperature of contact[m]				
Ambient (20–40°C)	47% (24)	48% (48)	nd	nd
High (>60°C)	43% (22)	32% (32)	nd	nd
Low (<10°C)	10% (5)	20% (20)	nd	nd
Total	100% (51)	100% (100)		

The figures of the two first columns represent the number of scientific articles published in food additives and contaminants and reported in ISI databases. The column RASFF lists the number of notifications (information, alert, and border rejection) from European enforcement laboratories and reported by the European Rapid Alert System for Food and Feed in the "product-category" as "food contact materials." The column "Google News" collects the number of general "news" (on-line articles) as aggregated by Google. List of search keywords (only the logical operator OR is explicitly mentioned): [a]"polyolefin" or "PP" or "LDPE" or "HDPE" in excluding all references concerning permeability studies, innovative packaging; [b]"PET"; [c]"PVC" or "vinyl chloride"; [d]"styrene"; [e]"paper" or "cardboard" or "carton"; [f]"coating" or "varnish"; [g]"print" or "benzophenone" or "thioxanthone"; [h]"adhesive"; [i]"fatty"; [j]dairy" or "milk"; [k]"dry" or "cereal" or "rice" or "powder"; [l]"juice"; [m]"temperature"; [n]"plastic"; [o]"paper" or "cardboard" or "carton"; [p]"coating" or "varnish"; [q]"benzophenone" or "thioxanthone"; [r]"Fatty products" are related with "sauce" and "lid of jars" and "meat"; [s]"dairy" or "milk"; [t]"rice" or "cereal" or "powder"; [u]"juice"; [v]("polyethylene" or "polypropylene") "food packaging" contaminant; [w]"polyethylene terephthalate" "food packaging" contaminant, [x]PVC "food packaging" contaminant; [y]styrene "food packaging" contaminant; [z]paper "food packaging" contaminant; [aa]("coating" or "varnish") "food packaging" contaminant; [ab]printing ink" "food packaging" contaminant; [ac]adhesive "food packaging" contaminant.

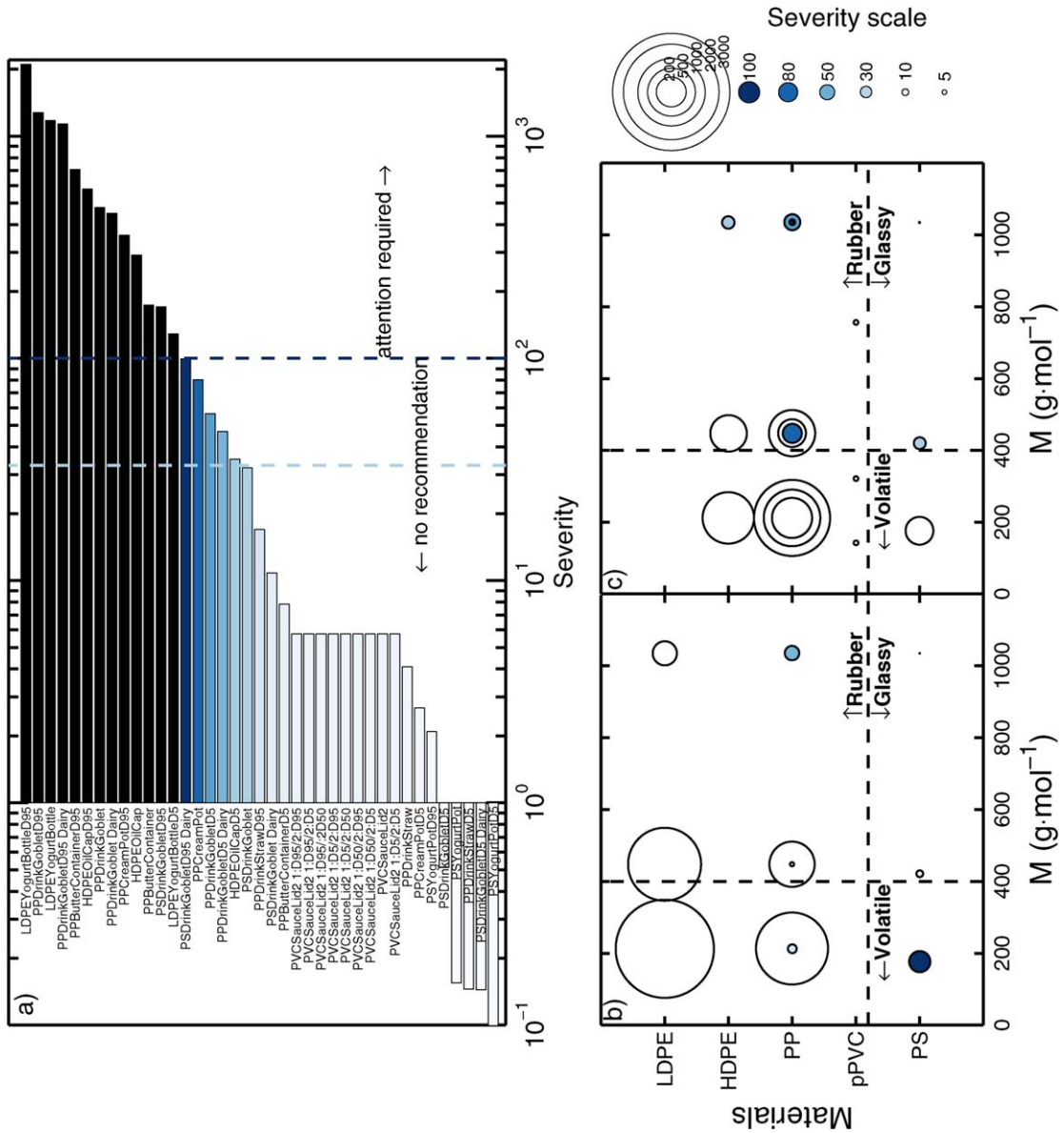

Figure 13. Results of the case study 3 "Risk-oriented screening" detailed in Table 7 and Figure 7.

(a) Pareto chart of severities associated with the nine real packaging systems and three diffusion coefficient ranges based on 5th, 50th, and 95th percentile (denoted D5, D50, and D95, respectively) extracted from the distribution of molecular masses of migrants in the tables "polymer" and "substance" and Eq. 18 (see Figure 7b). The 39 severity values represented in (a) are tabulated according to the molecular weight (M) of migrants and the types of polymer for the two food contact conditions: (b) dairy contact and (c) fatty contact. The surface area of each circle is proportional to the severity value with a corresponding scale represented on the right-hand side of the figure (values below 100 appear as colored disks). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

or scientific studies involve contacts with fatty or dairy products (see Table 9ii). Similarly, conditions of storage or use at ambient temperature or above are well identified as critical for food contamination (see Table 9iii). However, it is worth to notice that the conclusions are much more tricky to establish when several materials, steps, and substances have to be compared together. To illustrate the gain for the nonspecifically trained end-user, Figure 14 compares the previous semi-supervised approach with a possible human expert approach. The main issue for a trained expert is the high dimensionality of the mass-transfer problem even in the case of simple materials: (1) several potential migrants, several polymers, and various storage/use temperatures for determining diffusion coefficients, (2) various contact times, material thickness, food volumes, and chemical affinities controlling the final food contamination. For monolayer materials, dimensional analysis leads to plot the dimensionless food concentration $C_0(t)/C_0|_{t\to t_{eq}}$ vs. dimensionless time $Fo=D_1t/l_1^2$for some typical ratios of k_1/k_0 and l_1/l_0. As discussed in Ref. 1, an upper curve (worst-case leading to total substance extraction at equilibrium) is obtained with $k_1/k_0 \to \infty$ and/or $l_1/l_0 \to 0$. As a rule of thumb, 5, 10, 50, and 100% of $C_0(t)/C_0|_{t\to t_{eq}}$ (see the curve labeled "0" in Figure 4.6 of page 59 in Ref. 148) are approximately obtained under worst-case conditions (i.e., almost total extraction at equilibrium) for $Fo = 0.001$, $Fo = 0.01$, $Fo = 0.1$, and $Fo = 1$. From these considerations, the cumulative distribution of diffusion coefficients of likely additives in different polymers (using the distribution of molecular masses and Eq. 18) and for typical temperatures of use (i.e., chilled storage, room storage, and hot filling) can be

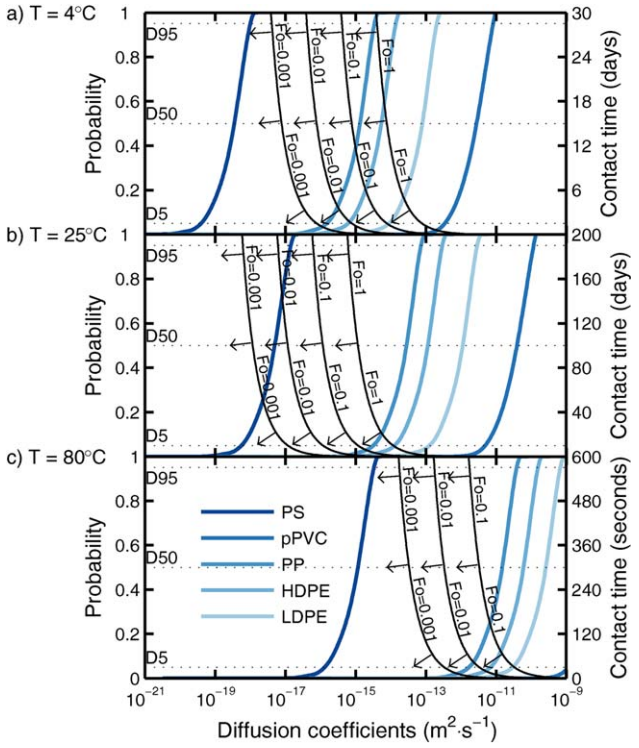

Figure 14. Cumulated distributions of diffusion coefficients (D_1) of common additives in different polymers at typical temperatures of use: (a) chilled food, (b) ambient storage, and (c) hot filling.

Isocontours of Fourier numbers ($Fo = D_1 t_1 / l_1^2$), calculated for $l_1 = 10^{-4}$ m and likely contact times, enable to identify the conditions for which the polymer is likely to lead to a time-dependent contamination of the food in contact. In monolayer materials, Fo values larger than 10^{-3}, 10^{-2}, 10^{-1}, and 1 lead roughly to a concentration in food close to 5, 10, 50, and 100% the value expected for an infinite contact time (thermodynamical equilibrium). The distribution of D_1 for likely additives was derived from the distribution of molecular masses of additives used for considered polymers (without accounting for their real occurrence on the market) and Eq. 18. A robust decision (whatever the real industrial practices) can be taken by considering a high percentile value (e.g., D95). List of presented polymers: HDPE: high-density polyethylene; LDPE: low-density polyethylene; PP: polypropylene; PS: polystyrene; pPVC: plasticized polyvinyl chloride (plasticization rate: 30 wt %). The Fo isocontours are plotted for a film thickness of 10^{-4} m, they can also be used for a rigid layer of 10^{-3} m but with contact times multiplied by a factor $10 \times 10 = 100$ s. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

compared with iso-Fo values obtained for different contact times and a reference material thickness of $l_1 = 10^{-4}$ m. Although the proposed approach does not integrate the market share of each substance, the percentiles plotted in Figure 14 illustrate unambiguously that plasticized PVC (i.e., cling film) presents the highest risk of migration whatever the considered migrant and application. Polyolefins (i.e., LDPE, HDPE, and PP) are intermediate with a higher risk for long-term storage. Polystyrene exhibits significant migration risk only, when it used at high temperature. Going into further details needs for the expert (1) to rescale Fo values of interest according to the real thickness of the packaging, and (2) to refine assumptions on $k_1/k_0$and l_1/l_0values when required. However, it is obvious that the presented manual approach cannot be generalized seamlessly to multisteps flowcharts and multimaterials.

Comparatively, the complicated "human expert" method, the semisupervised "automatic" method was shown to be superior to screen large amounts of conditions from basic input data entered in a human readable format (Figure 7a). From the simple syntax defined in Eq. 19 and illustrated in Figures 7b,c, the set of inference rules can be straightforwardly augmented with a text file or coded in a spread-sheet to fit specific purposes or applications. Databases will be extended to other materials with data originating from European or national projects and made available with the inference engine included in the current version of FMECAengine.[76]

Conclusions

Our modified FMECA approach prepares responses, scenarios, and possible ramifications of foreseen or unforeseen mass transfer of packaging constituents between thermoplastic components and food, which could develop into a major crisis. The approach relies on few specific prerequisites: the geometry and the assembling must be approximately known, the intended food-packaging chain must be described, the identity of materials must be available. According to needs, the method can be used to extract critical steps, components, substances, and so forth. Three case studies have been detailed to illustrate how the whole methodology could be applied through the different segments of the supply chain comprising the chemical industry, the packaging sector, the recycling industry, the food industry, and finally downstream retailers and consumers. The ability of the proposed method to integrate the multidimensionality of phenomena contributing to the final contamination of food (e.g., many substances, many components or materials, many process or storage steps in product life cycles, etc.) makes it a good response to the fragmentation of regulations based on a material-specific approach as enforced in the EU[44] or based on application-specific approaches as required in the US.[149,150] In EU, such a method and its future derivations might offer a harmonized framework for the implementation of good manufacturing practices under Regulation EC 2023/2006[151] for the 16 categories of food contact materials that are not currently covered by specific measures (e.g., no positive list, no limit of migration either overall or substance-specific).

Our FMECA approach is currently developed as an open-source project[76] that encourages the sharing of databases, numerical tools, inference engines, rule bases, and case study templates. The authors expect that such an initiative will promote cooperation between food packaging stakeholders and will contribute to increase consumer confidence in food contact materials developed with considerations of "safe design."

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Notation

Roman symbols

A = area, m^2
A'_P = polymer specific "diffusion conductance" parameter used in Eq. 18
Bi = mass-transfer Biot number

C = concentration, kg m^{-3}
D = diffusion coefficient, m^2 s^{-1}
de = distance between the interface and next node in "east direction" (see Figure 2b), m
dw = distance between the interface and next node in "west direction" (see Figure 2b), m
h = interface mass-transfer coefficient, m s^{-1}
he = equivalent conductance ("east direction"), m s^{-1}
hw = equivalent conductance ("west direction"), m s^{-1}
J = mass flux density, kg m^{-2} s^{-1}
je = normal mass flux in "east direction," kg m^{-2} s^{-1}
jw = normal mass flux in "west direction," kg m^{-2} s^{-1}
K = partition coefficient
k = Henry-like coefficient or equilibrium constant, J mol^{-3}
k^H = Henry coefficient, J mol^{-1}
l = thickness or characteristic dimension, m
M = molecular mass, g mol^{-1}
N = number control volumes
n = number of layers
p = partial pressure, Pa
$\mathbf{p}$ = vector of parameters in Eq. 13
t = time, s
T = temperature, K
V = volume, m^3
x = position, m

Greek symbols

ρ = density, kg m^{-3}
τ = activation parameter in Eq. 18, K

Subscripts

eq = equilibrium
F = food or food simulant
i = step index
j = layer or component index
j_{min} = layer index which minimizes $D_j\rho_j/k_jl_j$
k = modality index
n = layer index
P = packaging material
X = migrant X: benzophenone
Y = migrant Y: 1,2-benzoisothiazolin-3-one

Others

Criticality = dimensionless number defined in Eq. 17
NOAEL = no observable adverse effect level value for calculating severity
OML = overall migration limit as defined in European Regulation (EU) 10/2011
Severity = dimensionless number defined in Eq. 14
SML = specific migration limit value as defined in European Regulation (EU) 10/2011 of plastic materials for calculating severity
TDI = tolerable daily intake value for calculating severity
$\hat{X}$ = estimated value of X

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