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Safe food for infants: An EU-China project to enhance the control of safety risks raised by microbial and chemical hazards all along the infant food chains

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A B S T R A C T

The EU-project SAFFI targets food for EU's 15 million and China's 45 million children under the age of three. It aims at developing an integrated approach to enhance the identification, assessment, detection and mitigation of health risks raised by microbial and chemical hazards along EU and China infant food chains.

SAFFI will benchmark the main risks through an extensive hazard identification system based on multiple data sources and a risk ranking procedure. It will also develop procedures to enhance top-down and bottom-up hazard control by combining management options with a panel of technologies for the detection and mitigation of priority hazards. Furthermore, it will explore unexpected contaminants by predictive toxicology and improve risk-based food safety management of biohazards by omics and predictive microbiology. SAFFI will co-develop with and deliver to stakeholders a decision-support system (DSS) to enhance safety control all along the food chain. This DSS will integrate the databases, procedures and methods described above and will be a framework for a generic DSS dedicated to other food.

This overall methodology will also be implemented in a complementary Chinese side of the project, and exemplified for each side, with four case studies that were selected to cover priority hazards, main ingredients, processes and control steps of the infant food chain. Resulting databases, tools and procedures will be shared, cross-validated, concatenated, benchmarked and finally harmonized for further use in the EU and China.

This EU-China multi-actor consortium of 20 partners involves academia, food safety authorities, infant food companies, a paediatrics association and technological and data-science SMEs.

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1. Introduction

Due to the continuously increasing consumer demand for quality and transparency, larger-scale food production, more intensive food trade and increasing urbanisation that shape the food industry, the control of food safety is obviously a priority shared by both the EU and China. Food safety and quality assurance also address the need for trust, transparency and harmonization of practices, which is a prerequisite for the development of efficient domestic and international (EU-China) trade. However, implementing efficient food safety control is complex because of: (i) the variety of products due to the diversity of raw materials, processing, packaging and storage; (ii) the diversity and changes in consumer practices, which may put them at risk in some cases; (iii) the continuous product evolution driven by agri-food innovations, advances in human health knowledge and subsequent regulatory changes; (iv) the different regulatory contexts and health surveillance systems between countries with respect to intensive and/or global trade, resulting in a large set of potential hazards that need to be controlled.

The SAFFI project focuses on foods for infants and young children (which is the correct term according to EU legislation for what is designated as "infant food" in the rest of the text) because from the consumers' perspective this food sector is expected to adhere to the highest safety standards and must be strongly regulated given the vulnerability of its target population. Secondly, the wide international echoes of recent health scandals in this sector[1,2] are illustrations that food safety control is a focus point worldwide, with significant impact when not handled properly. The project is dedicated to the infant (below 3 years old) population. The focus on infant food of the most recent French Total Diet Study[3] was the world's first and demonstrated both the relevance of this issue for European public health authorities and the generic nature of this model; as such, this will allow a large transferability of its results to other food sectors and populations. Moreover, the growth of the infant food sector is particularly strong in China (+78% of the market value between 2010 and 2016). Infant food is also the second biggest food commodity in terms of import, specifically infant formulae from Europe due to its reputation of high quality in Chinese consumers' eyes and their trust in the product. Infant food is the third EU food and drink export product, with €6.6 million exports (+12% in 2017) and China is part of the top 3 export destinations of EU infant food. It is therefore valuable and timely to strengthen EU-China food safety cooperation as highlighted by Vytenis Andriukaitis, the EU Commissioner for Health and Food Safety, and to build an effective and harmonised food safety control system based on the infant food chain as a model.

Through four infant food chains - powdered infant formula, sterilized vegetable mixed with fish/meat, infant cereals and fruit puree- chosen as case studies to cover infant nutrition while encompassing very different hazards, ingredients, processing and control steps, SAFFI targets the control of the main priority hazards (see Table 1) pointed out by the French iTDS[3] and the recent infant food health crises.

The results of the French iTDS[3] and the recent health crises have shown the need to improve the levels of safety control and to identify bottlenecks impairing the effectiveness of the current systems. The aim of the present paper is to exemplify through a presentation of the main axes of the EU-China SAFFI project what research can do to help paediatricians and other actors in the area of infant food safety in order: (i) to have a better insight on microbiological and chemical hazards along the infant food chain; (ii) to identify the main known risks and provide new tools for their identification, detection, assessment and mitigation by both public health authorities and food industry; (iii) to anticipate unknown risks related to chemical contaminants not detected by current monitoring systems; (iv) to prevent public health crises related to foodborne microorganisms by proposing tools for predictive microbiology and risk management based no longer on hazards but on risks; (v) to further share data, practices and critical information in real time to ensure an overall food safety control.

2. Enhancement of food risk assessment

In order to provide paediatricians and other stakeholders with updated and comprehensive knowledge about both possible and priority hazards in infant food, one of the key issues is to refine risk assessment with advances in hazard identification and risk ranking (Fig. 1).

2.1. Hazard identification

Within Quantitative Risk Assessment for both microbiological and chemical hazards, the processes of hazard characterisation, exposure assessment, and risk characterisation are generally carried out following a structured procedure and are well documented. However, the initial part of risk assessment, namely hazard identification, is often not following a structured procedure and is mainly based on expert judgement, and considerations and decisions are not always well documented. Therefore, software prototypes can be developed to structurally identify hazards and rank the risks.[4–6]

In order to be able to evaluate and rank all risks (both chemical and microbiological), it is crucial to start broadly to not miss potential hazards but also being able to select the most relevant ones for further risk characterisation. Hazard identification requires the creation of underlying databases by collecting, aggregating, validating and analysing a wide range of available data. In the classical approaches of hazard identification these databases rely mainly on very specific, validated, defined but often limited data.[4] Thanks to the development of data sciences, these databases can now be extended to very broad, generic and not always directly related big data in order not to miss potential hazard. In the project initially the most relevant hazards (both microbiological and chemical) generally in infant foods will be identified. As a next step, a procedure for the selection of the specific hazards from this list will be developed, based on the ingredients, process, and characteristics of the specific food product.

2.2. Risk ranking

The hazard identification will generally result in a long list of hazards, therefore a next step is risk ranking, to then reduce the list of hazards to the most relevant ones in order to carry out for these, further more detailed exposure assessment and hazard characterization.[5] To

Table 1
List of priority infant food hazards targeted in SAFFI.

Origin in the Food Chain	Chemical or Microbial Hazard
Production environment	Persistant Organic Pollutants (including PolyChloroDibenzo-Dioxins/Furans (PCDD/Fs), PolyChloroBiphenyls (PCBs))
	Trace elements (As, Pb, Ni)
	Tropane alkaloids
	Mycotoxins
	Microbial pathogens*
	Per- and poly-fluoroalkyl substances (including PerFluoroOctanoic Acid (PFOA), PerFluoroOctane Sulfonate (PFOS))
Agricultural practices	Pesticides
	Pathogens from plants, animals or soils*
Industrial or domestic processes	Process Induced Toxicants (Acrylamide, Furans, HydroxyMethylFurfural (HMF))
	Pathogens from processing plant environment*
	Mineral Oil (Mineral Oil Saturated Hydrocarbons (MOSH), Mineral Oil Aromatic Hydrocarbons (MOAH)),
Packaging	Bisphenols
	Phthalates
	Photoinitiators
Storage	Food contact material migrants (see packaging)
	Pathogens*

*Pathogens include *Salmonella, Cronobacter, Listeria monocytogenes*, spore-formers like *Bacillus cereus* and *Clostridium botulinum*.

rank both chemical and microbiological risk, the first possibility is to convert the probability of illness and /or number of cases into Disability Adjust Life Year (DALY); this has been done for instance with arsenic in water[7] and *Listeria monocytogenes* in salmon.[8] However, for some hazards, particularly in the chemical field, it is difficult to go up to the probability of illness and number of cases while performing the risk assessment.

Moreover, consumer perception and political judgements are often also driven by other aspects, and for example will weigh the severity even more than in the DALY and additionally having a fear/fright factor for aspects where the real risk is very low but fear high.[9] Also, in certain cases, the public perception is more pronounced for one situation with 100 related cases than a situation with 1000 disperse cases. DALY's, but also other criteria as suggested by the FAO[9] can be assessed and combined in a multi-criteria decision approach (MCDA). These MCDA have been already used in food safety, for example to select effective health interventions.[10]

3. Enhancement of infant diet quality with innovative food processing technologies

Research can also help paediatricians a.o. by improving the overall quality of infant diet. One way is to propose new tools to enhance the effectiveness of food safety management options to better control the production process of infant food. Another way to improve the quality of infant diet may rely on the assessment of innovative food processing technologies which might advantageously replace classical preservation processes based on thermal treatments.

3.1. Effectiveness of the food management options

Validated hazard control options and risk mitigation strategies must be applied today all along the infant food supply chain, for the currently known hazards as well as for any emerging or new hazard derived from future events and developments. For this purpose, integrated approaches have to be developed enabling to prioritize and to design the most effective solutions combining control measures at critical points of the production process with up-to-date sampling and monitoring strategies along the food chain. This approach shall allow an efficient assurance of the food safety systems at both operational (including HACCP plans) and governmental level.

3.2. Innovative preservation technologies

As in the entire food industry, the infant food sector invests in the development of safer, fresher, healthier and more sustainable products with the implementation of new and emerging technologies like innovative processing and preservation technologies. These new technologies could represent a very attractive alternative to classical thermal treatments, which are known to have negative impacts on several dimensions of the food quality, such as nutritional or sensory properties, but also chemical safety. Pulse combustion drying (PCD) has been proven to efficiently dry chemical and pharmaceutical products, its potential has been also pointed out for some food (e.g. eggs[11]) and it could be promising for the production of dried infant food (powdered infant formula and cereals). The emerging thermal radiofrequency (RD) technology and non-thermal high-pressure processing (HPP) can be targeted for the production of infant food (sterilised and pasteurised). Compared to classical processing and preservation processes based on heat-treatment, RD and HPP should better preserve freshness, nutritional and sensory quality of infant food, while minimising the generation of process induced contaminants, assuring the microbiological safety standards and limiting environmental impact.[12]

The assessment of these innovative processing technologies that can be suspected to be more beneficial for the organoleptic and nutritional properties, more energy-efficient and environmentally-friendly needs to be carried out through the quantification of their impact on the microbiological and chemical relevant hazards for infant food listed in Table 1 (based on ANSES[3]; Bhunia et al.[13]; Mulder et al.[14]; Zwietering et al.[15]). It is necessary to check their preservation capacity towards pathogens in terms of growth, inhibition and inactivation but also to assess their impact on chemical food safety, given their potential influence on the fate of raw material contaminants,[16] on the generation of process-induced toxicants[17] and on the transfer of packaging migrants[13] (Fig. 2).

4. Enhancement of the surveillance of chemical hazards

Research can also help paediatricians through the development of analytical approaches in order to strengthen the surveillance of chemical hazard by both food safety authorities and infant food companies. To this end, two approaches based on both chemo- and bioanalytics can be undertaken. The first approach aims to improve the surveillance of known food chemical hazard while the second one deals with the discovery of unknown and / or unsuspected toxicants.

4.1. Strengthening the surveillance of known chemical hazard

Due to the very low Maximum Limits (ML) of most priority contaminants (e.g. pg/g range for PolyChloroBiphenyls-PCBs), their current detection and monitoring revolves around high-performance validated methods capable of detecting and quantifying key toxic contaminants at targeted ML. However, these methods are often expensive and low-throughput, thus limiting frequency and scope of surveillance by food safety authorities and dissuading routine preventive monitoring by the industry. Two complementary high-throughput, sensitive and cost-effective targeted tools can be developed in order to improve the coverage and the efficiency of non-conformity detection by food safety

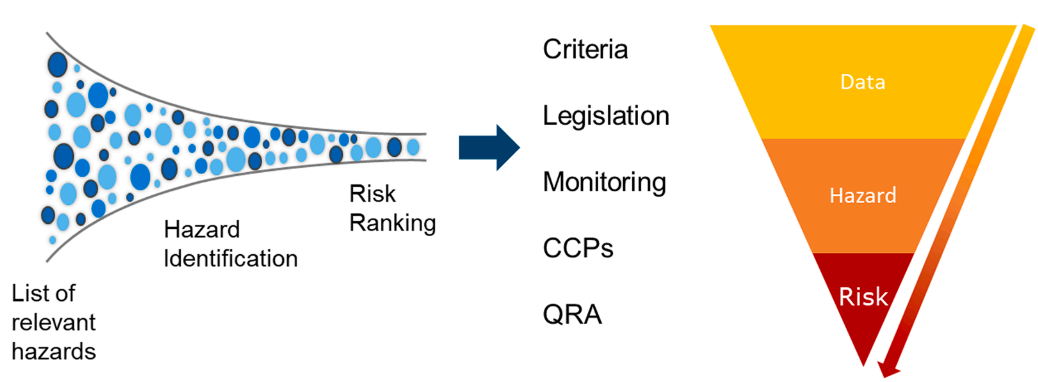

Fig. 1. Stages in hazard identification: initial list of relevant hazards in infant food, identification of hazards in a specific food product and ranking of the risks. Results are relevant to guide further actions in the management of the risks.

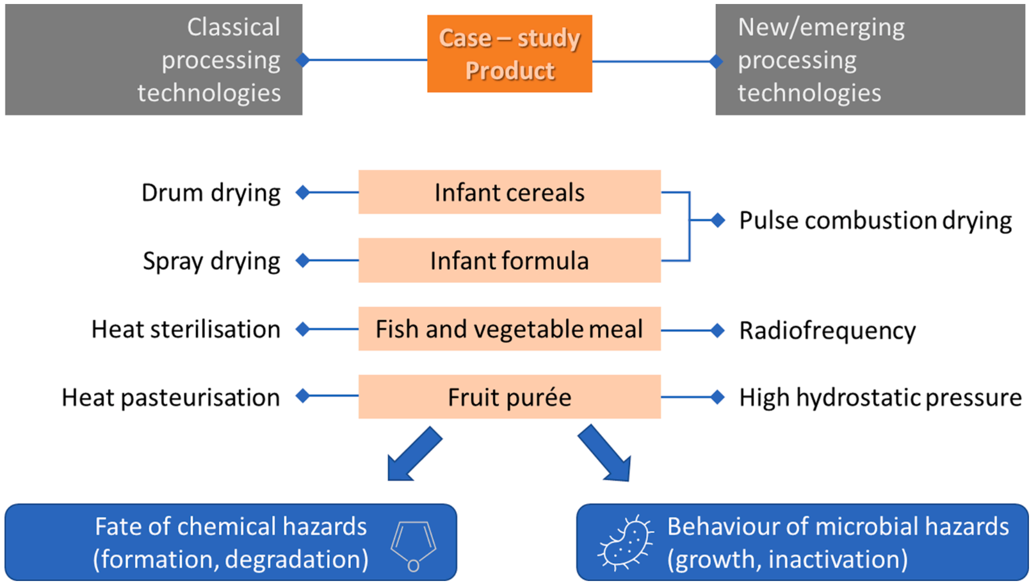

Fig. 2. Infant foods, classical and new/emerging processing technologies affecting the fate of chemical hazards and the behaviour of microbial pathogens.

authorities (top-down approach) and boost self-monitoring by the agri-food industry (bottom-up approach).

The first solution aims to reinforce the top-down surveillance by Food Safety Authorities. Based on chemoanalytics techniques, it consists in cutting the cost and low throughput of up-to-date mass spectrometry based-methods suitable for the detection of known priority contaminants with sample pooling strategy.[18] As shown in Fig. 3, pooling – also known as pool testing, group testing or pooled testing- means combining samples from several individuals or products and conducting one laboratory test on the combined pool of samples to detect the targeted contaminant. The rising interest for this strategy over the past years[19] enabled to clarify its prerequisites in terms of contamination prevalence, analytical cost and sensitivity and it suggests that these application conditions match with the implementation of pooling for the detection of priority chemical hazards in food. The second solution aims to develop the self-monitoring by private companies. Based on bioanalytics, it consists in implementing combinations of bioassays by coupling them to suitable extraction methods to modulate and refine bioassay selectivity.[20–22]

4.2. Discovery of unsuspected/unknown chemical hazard in food

Our knowledge of the chemical universe is very limited and most of the approximately 100,000 industrial chemicals that are in common use have undergone no or only limited safety testing only. This situation will improve significantly due to the REACH legislation, but still the majority of chemicals that surround us will remain untested. Recently, it has been recognized that contamination with unexpected food contaminants, both with known and unknown toxicity and often related to intended or unintended use of contaminated starting products (e.g. dioxin- or PCB-contaminated feed, melamine crisis, process-induced toxicants, packaging migrants) is an issue of concern.[23] Several of these contaminants will be picked up during routine screening in advanced quality control systems, but others (e.g. brominated dioxins, endocrine disruptors) may escape notice. Another complication is the fact that chemicals are present typically in complex mixtures, and that mixture effects need consideration as well. For these reasons, SAFFI will particularly focus on non-targeted methods to explore unsuspected and unknown contaminants. A first option is the non-targeted acquisition mode applied through full scan mass spectrometry analysis which has to be completed with specific filters to highlight chemical contaminants of interest based on 1/ the chemistry of the compounds (particular signatures, e.g. halogens[24]) or 2/ the research of specific patterns with chemometric tools.[25] Non-targeted approaches based only on chemo analytics would lead to limitation due to the complexity of the chemical universe, the lack of data on toxicity of most chemicals and the possibility of cocktail

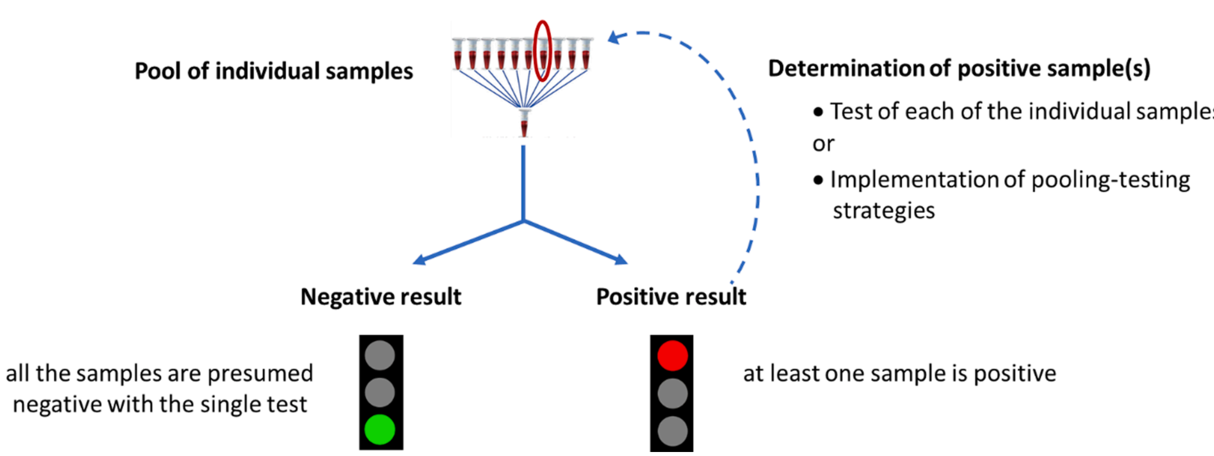

Fig. 3. Principle of the sample pooling strategy for the high-throughput detection of samples contaminated with a targeted chemical contaminant.

effects. A second option may consist in using bioassays to measure biological activity regardless of chemical structure, or prior knowledge. Bioassays, on the other hand cannot identify the chemical nature of individual compounds and a third option has to be considered. It will combine chemical and biological analytics using their complementary strengths and weaknesses in an effect-directed analysis (EDA)[26] to identify unknown or unexpected chemical hazards. In such a system, effect-based bioassays can best be used for comprehensive screening purposes, while chemical analytics can best be used for identification of chemicals in positive samples.

Despite EDA success in other fields like ecotoxicology, it has been hardly applied for contaminant discovery in food products until recently.[27,28] Recent advances in bioanalytics, chemoanalytics and chemo/bioinformatics could definitely boost this approach and enable the discovery of relevant "emerging" chemical hazards in the coming years.

5. Enhancement of microbial hazard characterization, detection and risk assessment

Research may also help paediatricians by enhancing the microbial safety of infant food through the development of holistic approaches namely omic approaches (Fig. 4). These new omics approaches may enable to refine the prediction of the pathogen behaviour in the food environment by highlighting the characteristics of the microbiota which may restrain or enhance the development or the persistence of pathogens.

Technological advances in DNA sequencing have resulted in a shift in the detection and monitoring of pathogens along food chains. Instead of only isolating pathogens from foods, microbiologists are also interested in capturing the bigger picture in which the pathogen is influenced by both the food environment and the other organisms present.[29] While metataxonomics or amplicon sequencing provides a taxonomic description of the food microbial community, metagenomics or shot-gun sequencing provides an overview of its collective function and metatranscriptomics indicate the genes that are actively transcribed by the community at sampling time.[30] In addition, recent works suggest that volatolomics may provide a promising alternative to more classical metabolomics platform to reveal significant changes in the metabolism of single culture[31] or microbiota.[32] Once integrated, this information provides an overview of microorganism associations and their metabolic and sense/response pathways within the food.[33]

These approaches offer an additional advantage as they are non-targeted and they by-pass the culturing step that may not always recover the targeted microorganism from the food. In infant food, these meta-omics approaches can be used to 1/ detect target foodborne pathogens in foods and their distribution in time and space, 2/ highlight the characteristics of the microbiota which may restrain or enhance persistence of pathogens and 3/ explore the behaviour of the target pathogens in samples or processing conditions that are relevant for food safety and propose predictive models. In parallel, a culture-dependent approach can be applied, coupled to WGS to enhance tracing of microbial hazards throughout the food chain and inferring associations with the microbiota or the environment.[34]

6. Enhancement of infant food safety standards

For raising food safety standards in the EU and China, the SAFFI project aims to develop decision support systems (DSS), recommendations and guidelines which are dedicated to be shared in Europe and China by food safety authorities and infant food companies for the management of safety risks all along the infant food chains.

These integrated approaches consist in collecting, connecting and combining pertinent knowledge and data from 1/ the entire food chain, 2/ the diversity of chemical and microbiological hazards, 3/ the different criteria contributing to risk ranking (including public health impact and perception impact), 4/ different sources of information (knowledge rules, structured databases and holistic data), 5/ different disciplines (risk assessment, food technology, toxicology, residue chemistry, predictive microbiology, paediatrics, data science, knowledge engineering), 6/ different criteria (safety, economic, regulatory, perception), 7/ different actors including stakeholders and academia, and 8/ different cultures.

Fig. 5 represents the integrative approach implemented in SAFFI which results in a project organisation that may be illustrated by an hourglass representing the broadness of the scope at the different steps. In the SAFFI strategy, hazard identification and risk ranking have to be as comprehensive as possible and this is the reason why corresponding DSS prototypes have to be developed with a broad scope that of being the whole infant food chain. The hazard identification and risk ranking procedures and related DSS prototypes have to be further applied and tested on a restricted scope to the four infant food chain defined as case studies, for demonstration purposes. The four case studies are first infant formula, sterilized vegetables with fish (or meat puree in China), infant cereals (infant dry noodles in China) and infant fruit puree. These same four case studies can then be used to develop innovative approaches and DSS prototypes for hazard control and mitigation together with a DSS module for detection of both chemical and microbial hazards. The different DSS prototypes or modules that are developed in SAFFI at the different steps of the risk management process are dedicated to be finally integrated to produce a single DSS which will further serve as a conceptual framework for further application to other infant food chains

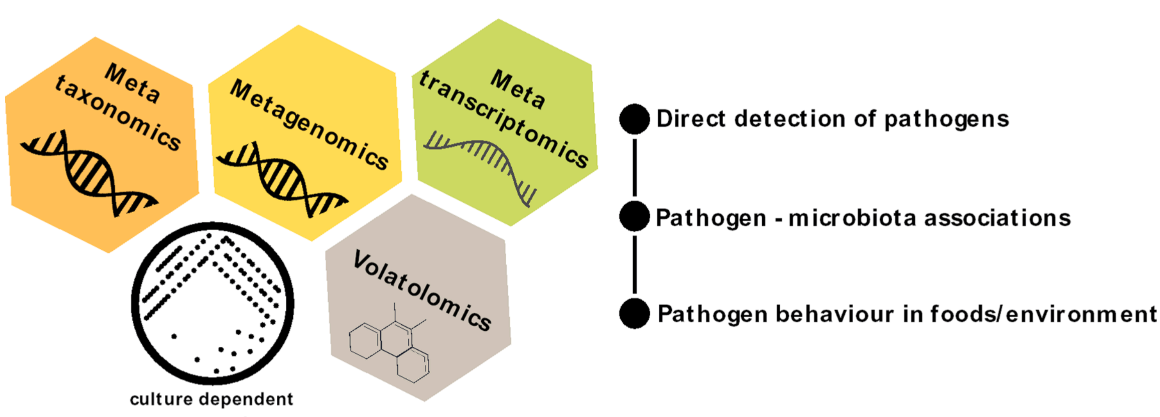

Fig. 4. Microbial communities' studies through omics approaches for infant food microbial safety. Microbial communities can be investigated in a culture independent manner, providing insights on microbial interactions and behaviour under "real" conditions. In parallel, a culture dependent approach may complement and integrate the findings of the omics applied directly in the samples.

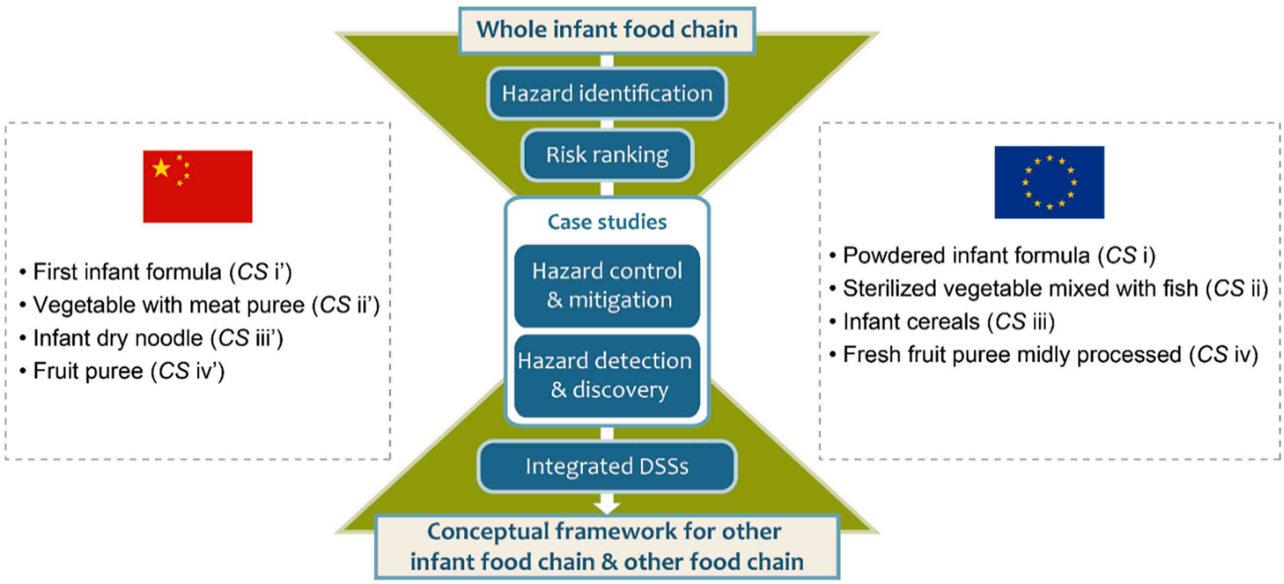

Fig. 5. Scheme of the integrative approach developed by SAFFI.

and beyond, to other food chains. Findings, including data, procedures and models will also enable to develop recommendations and guidelines for all stakeholders involved in the food chain.

7. Conclusion

Besides enhancing the current systems by improving targeted detection and assessing innovative preservation technologies, the SAFFI project is implementing several approaches enabling a real paradigm shift compared to practices currently implemented by food safety authorities and infant food companies: These cutting-edge approaches will more particularly focus on (i) enlarging the scope of food safety control to the wide range of unexpected or unknown chemical hazard that may occur in food and may pose a risk on consumers (ii) better predicting the behaviour and final assessment of the risk related to food-borne pathogens, (iii) refining hazard identification and risk-ranking to define the priority hazard to focus on.

The different knowledge, tools, databases, procedures and models collected and developed by the project will be integrated in a user-friendly and upgradable decision support system (DSS) for identification, detection, ranking and control of hazards and risk assessment. This will enable the rapid adoption by the DSS target end-users, that are food safety authorities and infant food companies, and will allow to overcome the complexity and the diversity of food chains. Besides the integration tools provided by data science and knowledge engineering, SAFFI's approach is multi-actor and interdisciplinary.

To reach its scientific, technological, socioeconomic and regulatory objectives, SAFFI's proof of concept will be exemplified on infant food chosen as model food chain. While hazard identification will deal with the infant food chain in its diversity, the case studies will focus on specific infant food products chosen to cover infant nutrition while encompassing very different hazards, ingredients, processing and control steps.

In order to make sure that the outcomes of the project will be adequately demand-driven, food safety authority experts, paediatrics, infant food companies and technological SMEs are involved, besides academia, in the construction, planning, implementation and dissemination of the project.

Finally, in order to create a frame to favour exchanges between the EU and China, SAFFI will set the basis to adapt food safety regulation, knowledge and practices through: 1/ EU-China co-construction of the project, structuration in two SAFFI mirror projects; 2/ training activities; 3/ standard setting, including good control practices; 4/regulation convergence; 5/ joint dissemination events. SAFFI refers to existing European risk assessment authorities (EFSA) and considers tools (e.g. alert system for food and feed (RASFF), animal tracing system (TRACES), European pesticides database) and their Chinese counterparts.

Declaration of Competing Interest

None.

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