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Microbial and chemical hazard identification in infant food chains

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ABSTRACT

To ensure foods are safe, food companies, food safety authorities, and governmental agencies work together to improve the control and prevent unwanted food contamination by either biological, chemical or physical agents, namely the hazards. Foodborne illnesses leading to diseases in humans are still frequently reported. To better protect infants and children from foodborne diseases, the SAFFI (Safe Food for Infant) project promoted by the European Union in collaboration with China, will develop an integrative approach to identify, assess, detect and mitigate risks associated with microbial hazards (MHs) and chemical hazards (CHs) in infant foods.

The first stage to tackle this issue was to identify relevant hazards in infant foods. By collecting data from the literature, scientific reports, existing databases, and clinical studies and using these data to compile a list of relevant foodborne hazards. These hazards caused major foodborne outbreaks, frequently contaminated foods, have large public health impacts, and/or are dangerous to young children.

After the initial identification of MHs and CHs in infant foods, we will prioritize the most relevant MHs or CHs present in specific food products and rank the risks associated with these hazards based on the probability of occurrence and severity of each hazard. Standardized and systematic hazard identification (HI) and risk ranking (RR) procedures will be developed and incorporated into HI and RR computational decision support tools that will serve to help food safety agencies, food companies, and risk assessors to identify and rank MHs and CHs in the entire infant food chain in Europe and China.

1. Introduction

Food is the basic nutrient source of life. Globally, a billion tonnes of primary crops are being produced,[1] and in the last two decades, the production of different food commodities has increased about 40–100% (primary crops: 53%, meat: 44%, fruits: 43%, and vegetables: 56%)[2] and may continue to increase in the years coming.[3] This is attributed to the sharp increase in food demand due to the growing population worldwide and the increment in per capita income also facilitates a higher spending power in developed countries. Taking the Netherlands as an example, on average, one kilogram of food is consumed per person per day,[4] and depending on the countries and personal habits, this number may even be higher.

As large amounts of foods are being produced and consumed daily worldwide,[2] and consumer's increasing awareness of the health aspects and product qualities of foods (i.e. nutritional values, presence of chemicals, or biological agents),[5] food safety from farm to fork is of crucial importance. Stimulated by the implementation of food law regulation (Regulation (EC) No 178/2002), there has been a continuing concerted effort from food companies and governmental agencies to monitor the quality and safety of foodstuffs.

1.1. Food contamination and foodborne illnesses

Despite the joined effort, cases of food contamination leading to human illnesses are still being reported frequently.[6,7] These contaminants can either be biological agents like bacteria, viruses, or parasites, or be chemicals like environmental contaminants, processing-induced compounds, agricultural products, veterinary drug residues, or physical objects like hairs, metals, plastics, glass, insects, or allergens that can trigger abnormal immune responses for a sensitive population.[8] Foods contaminated with biological or chemical agents can lead to more

Abbreviations: MH, Microbial Hazard; CH, Chemical Hazard; HI, Hazard Identification; RR, Risk Ranking; DSS, Decision Support System.

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than 200 human diseases, either mild diseases like diarrhea or life-threatening diseases like cancer.[9,10]

Foodborne outbreaks caused by biological or chemical contaminants lead to foodborne illnesses and result in a significant disease burden.[11] Examples of large foodborne outbreaks include: (1) fenugreek sprouts contaminated with Enterohemorrhagic *Escherichia coli* which killed 55 people and made more than 3000 people fell ill in 2011[12]; (2) polony processed meat contaminated with *Listeria monocytogenes* caused 216 deaths and more than 1000 illness cases in 2018 and many other *L. monocytogenes* outbreaks[13]; and (3) a fraud of adulteration of infant milk powder with melamine resulting in at least 294,000 children fell ill, 6 deaths and the hospitalization of 52,000 infants in 2008. After many years, these infants and children still suffer from renal damage (caused by urinary stone formation) and other long-term chronic effects.[14,15]

1.2. Foodborne diseases and estimated burden in children

In 2015, the World Health Organization (WHO) estimated that yearly, every 1 in 10 people fall ill due to consuming contaminated foods, and 420,000 lose their life due to foodborne illnesses.[11] Children under the age of five have relatively a larger burden. Young children have a high risk of foodborne illness and also of more severe effects and account for 1 out of 3 deaths from foodborne diseases.[11] This ratio is high when taking into consideration that children only make up about 10% of the total world population.[16] Therefore, it is important to strengthen food safety and ensure that foods that are fed to people particular infants or children are safe. This can be done by implementing systematic food safety management systems, like good hygiene practice (GHP) and good manufacturing practice (GMP), which are built further to the well-known Hazard Analysis Critical Control Point (HACCP) system.[17,18]

1.3. Food safety management system to ensure safe food

HACCP is a seven-principle science-based safety plan outlined to ensure the control of significant hazards in food businesses.[19] In the context of food safety, a hazard is defined as a biological, chemical, or physical agent in food that has the potential to cause adverse health effects in humans. Risk is the probability and severity of the health effects that consumers face after being exposed to a hazard.[20]

The first principle in HACCP is (1) hazard analysis, which is to collect and evaluate hazards identified in either raw materials, ingredients, environment, process, or foods to decide whether the identified hazards are significant. This is followed by (2) determining the critical control points (CCPs) to have essential measures to control significant hazards. The next step is (3) to establish validated critical limits for control measures set at CCPs and (4) to establish a system to monitor the control of CCPs. Following, when a deviation from the critical limit is observed at a CCP, (5) corrective actions are implemented, and (6) the HACCP plan is validated to confirm a working HACCP system. Lastly, (7) all procedures and records to the HACCP principles and their application are documented.[19]

The HACCP system is widely accepted by governmental agencies, trade organizations, and food companies.[19] It is implemented by food companies to establish the food safety goal, but there are also other systems to monitor food safety from farm to fork, starting from raw material production, procurement and handling, manufacturing, distribution, to consumption at the end. For example at the farm level, good agricultural practices (GAP) are implemented.

In addition, scientific evaluations of adverse effects caused by known biological or chemical hazards in various food commodities are also done to characterize the risk associated with the hazards and to give recommendations to control food safety. This process is called risk assessment and consists of 4 steps;

1 **Hazard identification;** In this step, hazards that may be present in a specific food commodity in given situations, have the potential to survive food processing techniques, and may cause disease in humans are identified.[19,21] This information is either collected based on scientific literature, surveillance/epidemiological data, existing expert knowledge, food analysis databases, or predefined knowledge of known pathogen/food associations,[22] for example, *Salmonella* in eggs.

2 **Hazard characterization;** In this step, the effects caused by hazards present in foods are evaluated, either based on qualitative data or quantitative data.[19,21] The relationship between hazard exposure (route, level, prevalence) and consequences of exposures are derived from foodborne outbreak data associated with illness, physico-chemical properties of hazards, hazard infectivity/virulence/ capability to produce toxins, toxicological studies, or human exposure studies[22]. Additionally, the immunological and physical statuses in humans of different age groups are considered, as the same hazard may have different effects for the young/-old/pregnant/immunocompromised populations.

3 **Exposure assessment;** is the stage in which the probability and quantity of hazard intake via foods are evaluated qualitatively or quantitatively, or exposures from other sources if relevant.[19,21] The number of microorganisms or the amount of chemicals/toxins consumed by a population in selected foods is quantified and the exposure to humans is assessed.

4 Lastly in **risk characterization**, based on the outcome of hazard characterization and exposure assessment, the probability of hazard occurrence and the severity of associated/potential adverse health effects caused by the hazard in a given population, including attendant uncertainties are estimated.[19] The risk of a specific hazard in foods is either expressed quantitatively with numerical outputs (e.g., annual illness incidence/100,000 population) or qualitatively with provided evidence and statements to show e.g. presence or absence of hazards.[22]

Notably, steps 2 and 3 can be done in the reverse order or parallel in risk assessment. When biological agents are examined, it is referred to as microbial risk assessment, and when chemicals are evaluated, it is referred to as chemical risk assessment.

2. Monitoring microbial and chemical hazards in foods

In Europe, different parties and local food safety authorities of each member state govern food safety. The European Food Safety Authority (EFSA) conducts scientific evaluations and risk assessments, the European Commission (EC) acts as the risk manager, and the Rapid Alert System for Food and Feed (RASFF) allows rapid sharing of information related to food safety between all member states whenever necessary.[23] RASFF provides notification concerning human health deriving from foods between the member states, EFSA, and the EC. EFSA analyzes the notification contents, conducts risk analysis and assessment, and communicates the scientific evaluation and technical information to the EC and other member states.[23] Each member state takes appropriate management control, reports food safety issues directly to EC, notifies RASFF when a foodborne hazard is encountered and is of international relevance, and provides foodborne outbreak data to the European Centre for Disease Prevention and Control (ECDC).

Annually, these authorities publish monitoring reports on detected foodborne hazards in different food categories, the total number of foodborne outbreaks caused by these hazards, their association with reported human diseases, and public health impacts (e.g. illness, hospitalization, and deaths).[6,24,25] These data are passed on to the International Food Safety Authorities Network (INFOSAN), managed jointly by WHO and the Food and Agriculture Organization (FAO). INFOSAN integrates the collected information gathered worldwide, conducts their evaluations, and also publishes estimations on the global burden of foodborne diseases and reports on corresponding foodborne hazards. Among all foodborne hazards, microbial hazards (MHs) and chemical hazards (CHs) are the main focuses in food safety.[11,26]

2.1. Microbial hazards

MHs can easily contaminate raw material, food products during processing (via contact surfaces or food handlers), or the end products because they are ubiquitous in the air, water, soil, animal, and humans.[8,27] Pathogenic MHs include bacteria, viruses, toxin-producing molds, and parasites. The difference in their physiologies accounts for aberrations in terms of epidemiology, virulence, and host association.[28,29] Therefore, surveillance and control of these MHs are challenging. While viruses and parasites cannot increase in foods, they are infectious. For some viruses (e.g., norovirus), ingesting just 1–10 virus particles is enough to cause illness in humans,[30,31] especially for young children as their immune systems are not fully developed.[32] For certain pathogenic organisms, a high number of cells need to be ingested to have a relevant probability of disease. However, given the right conditions, the outgrowth of pathogenic bacteria in foods is feasible and certain species can then also produce harmful toxins in the food or upon ingestion that hamper human health.[9] In the current legislation, presence/absence testing is laid down for some MHs, while other MHs are accepted to a certain level.

2.2. Chemical hazards

CHs are small or high molecular weight compounds that can be naturally present in the environment or manmade for specific purposes.[33,34] Their possible impact on human health is based on their physicochemical characteristics, exposure pathways (dermal, oral, or inhalation), and toxicological properties. Depending on their properties, they can contaminate food products at different levels. There are different families of CHs such as substances migrating from food contact materials, persistent organic pollutants (POPs), and naturally occurring substances such as marine biotoxins, mycotoxins, or trace elements and metals. Some chemical hazards (e.g., perfluoroalkyl substances or polychlorinated dibenzodioxins and dibenzofurans (PCDD/F)) can contaminate the soil, biomagnify in the trophic chain and bioaccumulate in the organism after consumption of food.[35,36] In 2001, The Stockholm convention determined some persistent organic pollutants that are closely monitored in Europe.[37] Another category of CHs, heat-induced contaminants such as furan, is produced at significant concentrations during thermal food processing and is associated with DNA damage and cancer.[38]

3. Safe food for infants (SAFFI) in the EU and China

To achieve the goal of reducing foodborne incidents in infants and children in the EU and China, an EU research project funded by Horizon Europe 2020, SAFFI (Safe Food or Infants in the EU and China) has been initiated, and the project group consists of 20 partners from different sectors i.e. academia, food safety authorities, infant food companies, paediatrics, technological and data-science companies.

3.1. SAFFI objective and approaches

The main objective of SAFFI is to develop an integrative approach to identify, assess, detect and mitigate risks associated with MHs and CHs for infants and children (< age of 3) in the EU and China. The first subobjective is the identification of hazards (similar to the first stage "hazard analysis" of HACCP and the first stage "hazard identification" of risk assessment). The specific ambition behind this project is to establish generic and standard procedures for hazard identification (HI) and risk ranking (RR) within the infant food chain, which will be achieved by the three-steps data-driven approach.

Firstly, data concerning MHs and CHs are collected based on literature, official reports published by governmental agencies, existing databases, clinical studies, and expert knowledge. These data are used to compile a list of relevant MHs and CHs that have the potential to be present in the food chain and cause adverse health effects to young children.

Secondly, the collected data are assembled and stored in structural databases that contain information like survival of MHs at different pH, temperatures, production of harmful toxins, or types of CHs generated during food processing procedures, etc. These specific pieces of information, namely the knowledge rules of the hazards, are prerequisites to understanding their relevant threat in a food product. Concomitantly, procedures for hazard identification are devised, which includes a second step to prioritize the hazards that are relevant for a specific food commodity. For MHs, this HI is based on the knowledge rules of selected organisms, i.e. the prevalence of an organism in a food commodity, survival during/after processing, and its growth opportunity in the specific food product. For CHs, HI is based on the knowledge rules of the hazards, i.e. the relevance in relation to the ingredients, processing conditions, and packaging materials. These devised generic procedures will serve to create a computational hazard identification decision support system (HI-DSS) (Fig. 1).

Lastly, the risk of the prioritized hazards associated with a food commodity will be evaluated, and similarly, procedures for risk ranking will be devised and a computational Risk Ranking Decision Support System (RR-DSS) will be constructed (Fig. 1). The HI-DSS and RR-DSS will be made flexible to easily incorporate newly acquired data in the future. The two DSS systems will be tested and validated with four case studies that represent four types of infant food products (powder infant formula, vegetable puree, infant cereals, and fresh fruit puree). These validated tools with integrated databases, procedures, and methods can be used by food safety agencies, food companies, and risk assessors to facilitate the assessment of either microbial or chemical risks in the infant food chain (see Fig. 1). Moreover, the data-driven approaches developed for infant food chains are also a conceptual, generic framework that can be modified and extrapolated for HI and RR in other food products in the future.

4. Hazard identification for microbial and chemical risks within infant food chains

4.1. Four important sources used for microbial hazards (MHs) identification

MHs in food products, with a special focus on infants and toddlers up to the age of 3 can be derived from public health databases, outbreak data, scientific literature, and expert knowledge. To obtain a list of relevant foodborne MHs in SAFFI, four different sources: (1) Outbreak data; (2) Recalled Foods; (3) public health impact; and (4) Expert knowledge of each MH were considered (see Fig. 2).

4.1.1. Foodborne outbreaks

Firstly, the occurrence and prevalence of MHs causing foodborne outbreaks in Europe were examined based on the data published in the most recent EFSA Zoonoses reports.[6] A total of 24 MHs associated with major foodborne outbreaks in Europe was found.

4.1.2. Recalled foods due to pathogen contamination

Secondly, ∼3500 serious alerts on foodborne pathogens, microorganisms, and parasites reported in the period from 1998-2021 in foods were analyzed and causative agents for each alert were manually defined.[25,39] Non-pathogenic organisms were excluded, giving rise to 35 MHs that caused either destruction, retraction, or withdrawal of foods from the market.

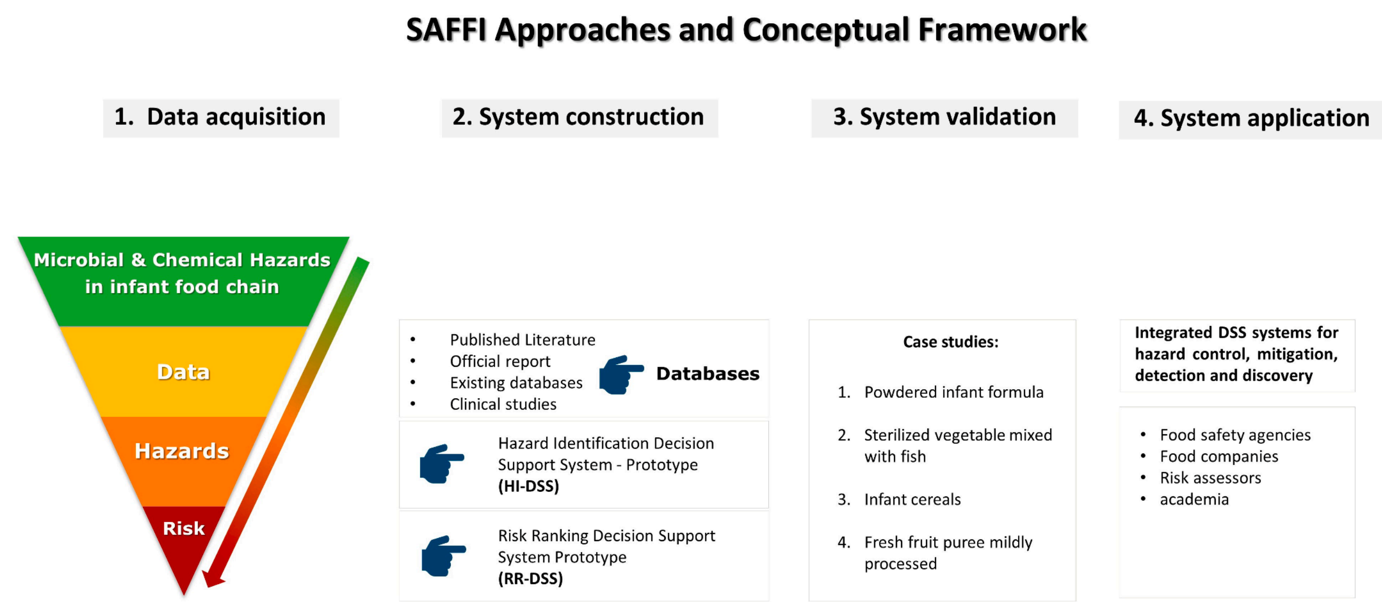

Fig. 1. General approaches of SAFFI and conceptual framework for hazard identification and risk ranking in the entire infant food chain.

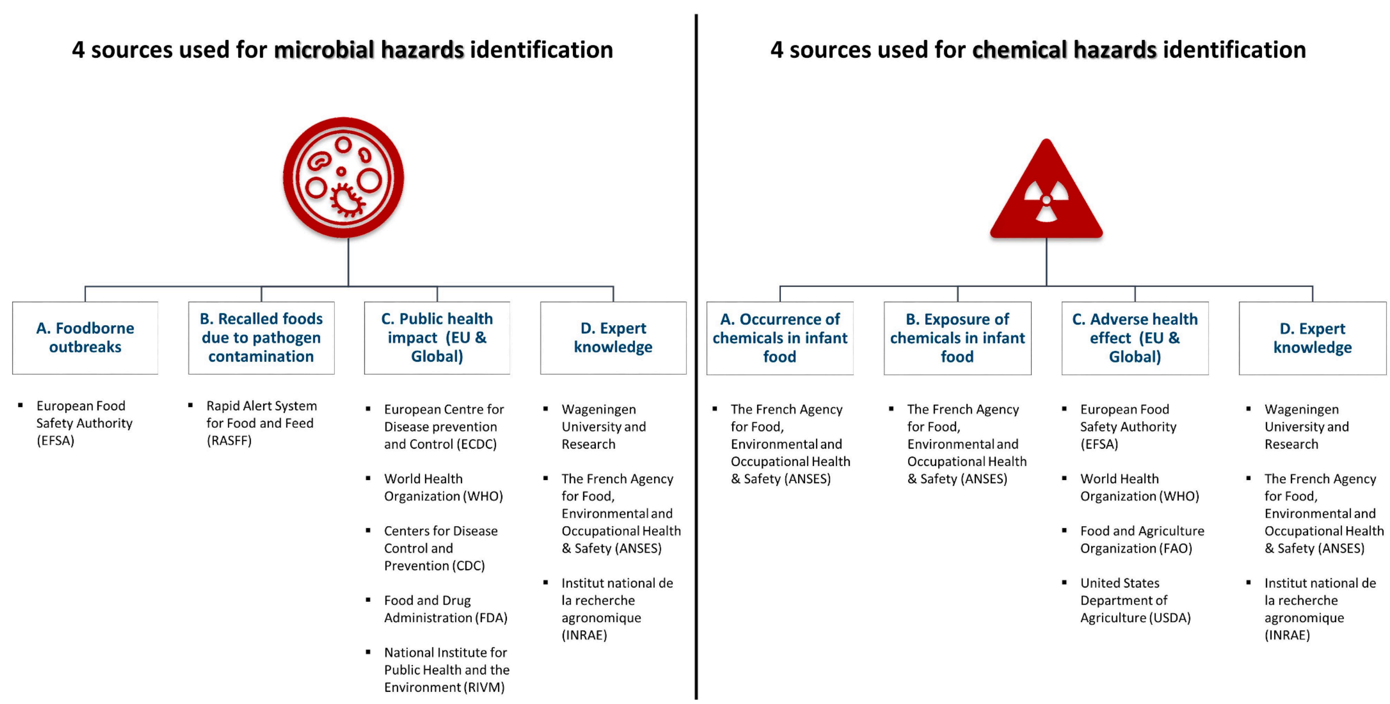

Fig. 2. Four important sources used for microbial and chemical hazards identification.

4.1.3. *Public health impact in EU and globally*

Thirdly, foodborne MHs that possessed large health impacts for humans in Europe were listed based on epidemiological reports. ECDC reported 22 foodborne MHs associated with human diseases,[24] the Dutch Institute for Public Health and the Environment (RIVM) showed 14 major MHs with large disease burden,[40] and WHO reported 15 MHs leading to major foodborne illnesses in Europe.[41] Moreover, the global public health impacts of MHs were also determined based on the MH health impact reports in the United States and worldwide. 31 pathogens were causing major foodborne diseases in the United States,[29] among these, 14 were estimated to have the largest overall disease burden.[42] Globally, 28 MHs are the main culprits of foodborne illnesses/death, and WHO also published 20 MHs that caused illnesses in children < 5 years.[32]

4.1.4. *Expert knowledge*

Other than that, some MHs usually do not cause major foodborne outbreaks, and neither are detected frequently in foods and do not have a large public health impact, but can still be a serious threat for infants and children. One such example would be the *Cronobacter* species. Therefore, expert knowledge was also taken as one of the important sources to identify relevant MHs for the young susceptible group.

All MHs identified in the above-mentioned reports were combined, and duplicates were removed. The occurrence of each MH in the reports was counted. Based on this, a list of 64 MHs that either cause major foodborne outbreaks, have relevant public health impacts, are frequently detected in foodstuffs, and are threatening to infants/children are identified. MHs that were reported in > 1 report were shortlisted, resulting in a total of 32 prioritized MHs, which include 18 bacteria, 6 parasites, 6 viruses, and 2 protozoa (Fig. 3). The identified 32 MHs are the most relevant hazards, after which a further prioritization has to be made by evaluating the food/process association for each of these MHs.

4.2. Four important aspects for chemical hazards (CHs) identification

Dietary exposure assessment reports are a major source for chemical hazard identification. When assessments of a risk associated with chemical hazards in food for a population are required, it is important to have representative contamination data. One of the most efficient methods to obtain this data is conducting a Total Diet Study (TDS). Indeed, contamination data and exposure calculations present in TDS reports give insight into the occurrence and contamination level of CHs in food products as consumed and representative of the whole diet. These reports can be found on food safety agencies' websites or scientific databases such as PubMed or Scopus.

Occurrence, exposure, adverse effects, and expert knowledge were the four important aspects considered to identify chemical hazards (Fig. 2).

4.2.1. Occurrence of chemicals in infant foods

When considering CHs, different types of data are needed. First, occurrence data provide information about the presence and the concentration of CHs in specific food matrices. From birth to the age of three, the diets of infants and toddlers become more and more diverse, going from a milk-based diet to a broader diet by introducing common foods. Infant food can be contaminated at every stage of food production from the raw materials to the consumed products. TDS are internationally recognized as efficient tools to have an overview of the contamination of food prepared as consumed and on which analyses are conducted to measure concentrations of CHs.[43] In 2011, the French Agency for Food, Environmental, and Occupational Health & Safety conducted an infant Total Diet Study (iTDS) with a list of 700 substances or groups of substances.[44] The global detection rate for each hazard listed in the iTDS was used to select the most relevant hazards present in infant foods. To complete the list of chemical hazards, searches in databases such as PubMed and Scopus were conducted to find occurrence data about the presence of some contaminants in infant food. Data from previous or recent assessments from EFSA were retrieved as well.

4.2.2. Exposure to chemicals in infant foods

In the iTDS, dietary exposure was assessed for 500 out of the 700 chemicals or groups of chemical hazards. Dietary exposure values for each age class from 1–4 to 13–36 months are obtained by combining food contamination data, food consumption data, and body weight. Based on these parameters, foods that contributed the most to the exposure were identified for each selected hazard when available. For most of the substances, the risk for infants and toddlers was negligible however for some chemicals such as acrylamide, furan, inorganic arsenic, and lead, the risk could not be excluded.[45,46]

4.2.3. Adverse health effects in the EU and globally

CHs in food can be associated with several adverse health effects. Knowledge of these effects is available from long-term toxicity studies conducted in animals or from epidemiological data. For this project, health-based guidance values (Tolerable Daily or Weekly intake) and toxicological references points (No Observed Adverse Effect Level or Benchmark dose limit) were identified in reports from different safety agencies or expert committees such as EFSA, Joint FAO/WHO Expert Committee on Food Additives (JECFA), Joint FAO/WHO Meeting on Pesticide Residues (JMPR), or WHO.

4.2.4. Expert knowledge

Some CHs were selected for the project even when they were not detected in infant food products in the iTDS, because of the severity of their adverse effects on humans, or when there were concerns in the available literature about the safety of their use. Some chemical hazards for which no health-based guidance value nor toxicological reference point have been established were also included. For example, emerging mycotoxins can be relevant because of the growing impact on climate change and identified effects *in vitro*.[47,48]

Based on the iTDS results and available literature, a list of 101 chemical hazards or groups of chemical hazards from 9 families has been established. One phytoestrogen, 11 substances migrating from food contact materials, 18 trace elements and metals, 28 persistent organic pollutants, 17 pesticide residues, 15 mycotoxins, 6 heat-induced compounds, 2 ionic compounds, and 3 food additives have been selected (Fig. 3).

The 32 MHs and 9 families of CHs were identified to be the most relevant hazards in infant food products, and in the following step, hazards will be prioritized for a specific food commodity as described in Section 3.1.

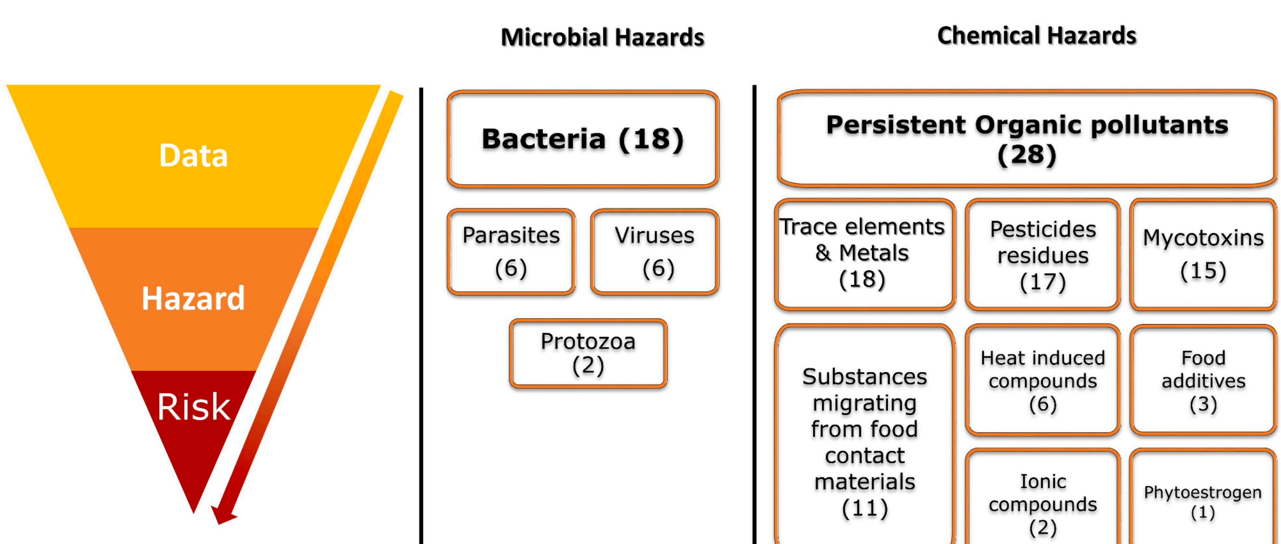

Fig. 3. Relevant microbial and chemical hazards identified in the infant food chain.

5. Criteria used in risk ranking

Following the initial identification of the most relevant MHs and CHs in infant food products, and subsequently, in specific food commodities, the risk of these hazards will be ranked systematically. For that, the probability of hazard occurrence/exposure and the severity of hazards associated with potential adverse health effects in infants and children will be estimated using selected criteria.

For the risk ranking of MHs, the severity of each MH will be estimated based on the disability adjusted life years (DALY) per case, and the probability of occurrence of each MH will be estimated based on hazard-food characteristics and hazard-food association strength. Hazard-food characteristics are determined using different elements, namely, growth opportunity of a hazard in a given food, processing effect on hazards, recontamination possibility of hazards, post-processing control of hazards, and the effect of meal preparation. Hazard-food association strengths are determined using the evidence of hazard-food alerts, hazard-food outbreaks, hazard-food prevalence, and food consumption data. For the risk ranking of CHs, the severity of each CH will be estimated based on the different toxic effects that a CH possesses, as described in ANSES.[49] The probability/likelihood of occurrence of each CH will be estimated based on the percentage of contribution to the total exposure as well as the corresponding percentage of the health-based guidance value.

6. Conclusion and future perspectives

In conclusion, 32 MHs consisting of bacteria, viruses, parasites, and protozoa and 9 families of CHs consisting of persistent organic pollutants, trace elements and metals, pesticides residues, mycotoxins, substances migrating from food contact materials, heat-induced compounds, phytoestrogen, ionic compounds, and food additives are identified to be the most relevant hazards in the food chain that can be dangerous for young children. In the next step, the identified MHs and CHs are prioritized for specific infant foods. These step-wise procedures will be implemented in the HI-DSS computational tool to identify MHs or CHs present in a specific infant food product. In a following up step, the risks of these prioritized MHs and CHs in infant foods will be evaluated using a structured risk-ranking approach, which takes into account the severity and probability of occurrence of each MH and CH mentioned above. Similarly, procedures for risk ranking will be devised and implemented in an RR-DSS computational tool.

The HI-DSS and RR-DSS tools will be validated using four case studies in following-up works and will be integrated and harmonized with the data obtained from the SAFFI mirror project in China. Together, these tools will be useful for food safety agencies, food companies, and risk assessors to identify and rank MHs and CHs in the entire infant food chain in Europe and China, and improve the control of these MHs and CHs.

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Statement

The corresponding author states on behalf of the co-authors that all Authors have no conflict or competing of interests to declare.

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References

[1] FAO. *World Food and Agriculture - Statistical Yearbook*. Rome, Italy: FAO; 2020. https://doi.org/10.4060/cb1329en, 2020.
[2] FAO. *FAO Statistical Yearbook 2021 - World Food and Agriculture*. World ReliefWeb; 2021. https://reliefweb.int/report/world/fao-statistical-yearbook-2021-world-food-and-agriculture (accessed December 8, 2021).
[3] van Dijk M, Morley T, Rau ML, Saghai Y. A meta-analysis of projected global food demand and population at risk of hunger for the period 2010–2050. *Nat Food*. 2021;2:494–501. https://doi.org/10.1038/s43016-021-00322-9.
[4] Geurts M, van Bakel A, van Rossum C, de Boer E, Ocke M. *Food consumption in the Netherlands and its determinants : background report to what is on our plate?. Safe, Healthy and Sustainable diets in the Netherlands*. Rijksinstituut voor Volksgezondheid en Milieu RIVM; 2017. https://www.rivm.nl/bibliotheek/rapporten/2016-0195.pdf (accessed 21 February 2022).
[5] Pinto VRA, Campos RF de A, Rocha F, et al. Perceived healthiness of foods: a systematic review of qualitative studies. *Future Foods*. 2021;4, 100056. https://doi.org/10.1016/j.fufo.2021.100056.
[6] European Food Safety Authority (EFSA) E. The European Union one health 2019 Zoonoses report. https://www.ecdc.europa.eu/en/publications-data/european-union-one-health-2019-zoonoses-reporthttps://www.efsa.europa.eu/en/efsajournal/pub/6406, 2019 (accessed April 14, 2021).
[7] European Food Safety Authority (EFSA) E. The European Union One Health 2018 Zoonoses Report.https://www.efsa.europa.eu/en/efsajournal/pub/5926, 2019 (accessed April 14, 2021).
[8] Schirone M, Visciano P, Tofalo R, Suzzi G. Editorial: biological hazards in food. *Front Microbiol*. 2017;7:2154. https://doi.org/10.3389/fmicb.2016.02154.
[9] Bintsis T. Foodborne pathogens. *AIMS Microbiol*. 2017;3:529–563. https://doi.org/10.3934/microbiol.2017.3.529.
[10] Mead PS, Slutsker L, Dietz V, et al. Food-related illness and death in the United States. *Emerg Infect Dis*. 1999;5:607–625. https://doi.org/10.3201/eid0505.990502.
[11] WHO. WHO estimates of the global burden of foodborne diseases: foodborne disease burden epidemiology reference group 2007-2015. https://apps.who.int/iris/bitstream/handle/10665/199350/9789241565165_eng.pdf, 2015 (accessed 21 February 2022).
[12] Köckerling E, Karrasch L, Schweitzer A, Razum O, Krause G. Public health research resulting from one of the world's largest outbreaks caused by entero-hemorrhagic *Escherichia coli* in Germany 2011: a review. *Front Public Health*. 2017;5:332. https://doi.org/10.3389/fpubh.2017.00332.
[13] Kaptchouang Tchatchouang CD, Fri J, De Santi M, et al. Listeriosis outbreak in South Africa: a comparative analysis with previously reported cases worldwide. *Microorganisms*. 2020;8:135. https://doi.org/10.3390/microorganisms8010135.
[14] Gossner CME, Schlundt J, Ben Embarek P, et al. The melamine incident: implications for international food and feed safety. *Environ Health Perspect*. 2009;117:1803–1808. https://doi.org/10.1289/ehp.0900949.
[15] Wen JG, Liu XJ, Wang ZM, Li TF, Wahlqvist ML. Melamine-contaminated milk formula and its impact on children. *Asia Pac J Clin Nutr*. 2016;25:697–705. https://doi.org/10.6133/apjcn.072016.01.
[16] United Nations, Department of economic and social affairs, population division. World population prospects 2019, custom data acquired via website. Dep Econ Soc Aff Popul Dyn 2019. https://population.un.org/wpp/DataQuery/, 2019 (accessed December 15, 2021).
[17] Varzakas T, Caballero B, Finglas PM, Toldrá F. *HACCP and ISO22000: risk assessment in conjunction with other food safety tools such as FMEA, Ishikawa diagrams and Pareto*. editors. *Encyclopedia of Food and Health*. Oxford: Academic Press; 2016:295–302. https://doi.org/10.1016/B978-0-12-384947-2.00320-2.
[18] Wallace CA, Mortimore SE, Lelieveld H, Holah J, Gabrić D. *Chapter 3 - HACCP*. editors. *Handbook of hygiene control in the food industry*. 2nd ed. San Diego: Woodhead Publishing; 2016:25–42. https://doi.org/10.1016/B978-0-08-100155-4.00003-0.
[19] Codex Alimentarius Commission. General principles of food hygiene CXC 1-1969. Adopted in 1969, amended in 1999. Revised in 1997, 2003, 2020. Codex Aliment CXC 1-1969 2020. https://www.fao.org/fao-who-codexalimentarius/sh-proxy/fr/?lnk=1&url=https%253A%252F%252Fworkspace.fao.org%252Fsites%252Fcodex%252FStandards%252FCXC%2B1-1969%252FCXC_001e.pdf, 2020 (accessed 18 January 2022).
[20] Food and Agriculture Organization of the United Nations. Definitions for the purposes of the codex alimentarius 2001. https://www.fao.org/3/y2200e/y2200e07.htm#fn4, 2001, (accessed December 15, 2021).
[21] FAO, WHO. Codex alimentarius commission – procedural manual twenty-seventh edition 2019. https://www.fao.org/publications/card/en/c/CA2329EN/, 2019 (accessed 21 February 2022).
[22] Mahoney D, McSweeney PLH, McNamara JP. *Safety and risk mitigation risk assessment in dairy processing - importance of food safety in the dairy processing sector*. editors. *Encyclopedia of Dairy Sciences*. 3rd ed. Oxford: Academic Press; 2022:776–784. https://doi.org/10.1016/B978-0-12-818766-1.00139-2.
[23] McEvoy JDG. Emerging food safety issues: an EU perspective. *Drug Test Anal*. 2016;8:511–520. https://doi.org/10.1002/dta.2015.

[24] European Centre for Disease Prevention and Control (ECDC) annual epidemiological reports (AERs) 2014 - 2020. (2020) online report. Available at https://www.ecdc.europa.eu/en/all-topics-z/surveillance-and-disease-data/annual-epidemiological-reports-aers (accessed April 14, 2021).

[25] Rapid alert system for food and feed (RASFF). RASFF annual report 2019. http://op.europa.eu/en/publication-detail/-/publication/2c5c7729-0c31-11eb-bc07-01aa75ed71a1/language-en/format-PDF,2020 (accessed April 14, 2021).

[26] Chammem N, Issaoui M, De Almeida AID, Delgado AM. Food crises and food safety incidents in European Union, United States, and Maghreb Area: current risk communication strategies and new approaches. *J AOAC Int*. 2018;101:923–938. https://doi.org/10.5740/jaoacint.17-0446.

[27] M.H. Zwietering and E.D. van Asselt, Wageningen University, the Netherlands. In Zwietering MH, Straver JM, van Asselt ED, Lelieveld H, Holah J, Gabrić D. *Chapter 4 - the range of microbial risks in food processing**this chapter is an updated version of: the range of microbial risks in food processing*. editors. *Handbook of Hygiene Control in the Food Industry*. 2nd ed. San Diego: Woodhead Publishing; 2016:43–54. https://doi.org/10.1016/B978-0-08-100155-4.00004-2.

[28] Havelaar AH, Haagsma JA, Mangen MJJ, et al. Disease burden of foodborne pathogens in the Netherlands, 2009. *Int J Food Microbiol*. 2012;156:231–238. https://doi.org/10.1016/j.ijfoodmicro.2012.03.029.

[29] Scallan E, Hoekstra RM, Angulo FJ, et al. Foodborne illness acquired in the United States—major pathogens. *Emerg Infect Dis*. 2011;17:7–15. https://doi.org/10.3201/eid1701.P11101.

[30] Food and Drug Administration. *Bad Bug Book, Foodborne Pathogenic Microorganisms and Natural Toxins*. 2nd ed. FDA; 2019. https://www.fda.gov/food/foodborne-pathogens/bad-bug-book-second-edition (accessed 21 February 2022).

[31] Robilotti E, Deresinski S, Norovirus PBA. *Clin Microbiol Rev*. 2015;28:134–164. https://doi.org/10.1128/CMR.00075-14.

[32] WHO. WHO estimates of the global burden of foodborne diseases. *PLoS Collect*; 2015. https://collections.plos.org/collection/ferg2015/, 2015 (accessed April 13, 2021).

[33] Groh KJ, Geueke B, Martin O, Maffini M, Muncke J. Overview of intentionally used food contact chemicals and their hazards. *Environ Int*. 2021;150, 106225. https://doi.org/10.1016/j.envint.2020.106225.

[34] Md Rahaman S, Md Ramaman M, Mise N, et al. Environmental arsenic exposure and its contribution to human diseases, toxicity mechanism and management. *Environ Pollut*. 2021;289, 117940. https://doi.org/10.1016/j.envpol.2021.117940.

[35] González N, Domingo JL. Polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/Fs) in food and human dietary intake: an update of the scientific literature. *Food Chem Toxicol*. 2021;157, 112585. https://doi.org/10.1016/j.fct.2021.112585.

[36] Pasecnaja E, Bartkevics V, Zacs D. Occurrence of selected per- and polyfluorinated alkyl substances (PFASs) in food available on the European market – a review on levels and human exposure assessment. *Chemosphere*. 2022;287, 132378. https://doi.org/10.1016/j.chemosphere.2021.132378.

[37] United Nations Treaty Collection (UNEP) 2001. https://treaties.un.org/pages/ViewDetails.aspx?src=TREATY&mtdsg_no=XXVII-15&chapter=27, 2001 (accessed January 28, 2022).

[38] Javed F, Shahbaz HM, Nawaz A, et al. Formation of furan in baby food products: identification and technical challenges. *Compr Rev Food Sci Food Saf*. 2021;20: 2699–2715. https://doi.org/10.1111/1541-4337.12732.

[39] RASFF. RASFF portal 2021. https://webgate.ec.europa.eu/rasff-window/screen/search 2021, (accessed December 15, 2021).

[40] Lagerweij G, Pijnacker R, Friesema I, Mughini Gras L, Franz E. *Disease burden of food-related pathogens in the Netherlands, 2019*. Rijksinstituut voor Volksgezondheid en Milieu; 2020. https://doi.org/10.21945/RIVM-2020-0117.

[41] WHO Europe. The burden of foodborne diseases in the WHO European Region (2017). https://www.euro.who.int/en/health-topics/disease-prevention/food-safety/publications/2017/the-burden-of-foodborne-diseases-in-the-who-european-region, 2017 (accessed December 15, 2021).

[42] Batz MB, Hoffmann S, Morris JG. Ranking the disease burden of 14 pathogens in food sources in the United States using attribution data from outbreak investigations and expert elicitation. *J Food Prot*. 2012;75:1278–1291. https://doi.org/10.4315/0362-028X.JFP-11-418.

[43] EFSA, FAO. Towards a harmonised total diet study approach: a guidance document. *EFSA J*. 2011;9:2450. https://doi.org/10.2903/j.efsa.2011.2450.

[44] Hulin M, Bemrah N, Nougadère A, Volatier JL, Sirot V, Leblanc JC. Assessment of infant exposure to food chemicals: the French total diet study design. *Food Addit Contam Part A*. 2014;31:1226–1239. https://doi.org/10.1080/19440049.2014.921937.

[45] Sirot V, Traore T, Guérin T, et al. French infant total diet study: exposure to selected trace elements and associated health risks. *Food Chem Toxicol*. 2018;120: 625–633. https://doi.org/10.1016/j.fct.2018.07.062.

[46] Sirot V, Rivière G, Leconte S, et al. French infant total diet study: dietary exposure to heat-induced compounds (acrylamide, furan and polycyclic aromatic hydrocarbons) and associated health risks. *Food Chem Toxicol*. 2019;130:308–316. https://doi.org/10.1016/j.fct.2019.05.009.

[47] Aichinger G, Krüger F, Puntscher H, Preindl K, Warth B, Marko D. Naturally occurring mixtures of Alternaria toxins: anti-estrogenic and genotoxic effects *in vitro*. *Arch Toxicol*. 2019;93:3021–3031. https://doi.org/10.1007/s00204-019-02545-z.

[48] Magan N, Medina A, Aldred D. Possible climate-change effects on mycotoxin contamination of food crops pre-and postharvest. *Plant Pathol*. 2011;60:150–163. https://doi.org/10.1111/j.1365-3059.2010.02412.x.

[49] ANSES opinion collective expert. Méthodologie de hiérarchisation des dangers biologiques et chimiques dans les aliments 2020. https://www.anses.fr/fr/system/files/BIORISK2016SA0153Ra.pdf, 2020, (accessed 18 December 2021).