Navigating the nexus: unraveling the impact of sustainability and the circular economy on food safety

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Abstract

Sustainable food production systems can be achieved through a circular economy, yet the whole system remains susceptible to various known, emerging, or even unknown/novel food safety hazards and contaminants. These upcycled foods can introduce related risks for human or animal health and ecological balance. These potential risks can be effectively mitigated by adopting integrated smart "safe-by-design" approaches. These multi-effective strategies can cascade far beyond consequences by addressing all potential food safety risks at each stage of the food supply chain, even at the post-consumption stage. Sustainability through circularity without harming food production systems can be achieved by integrating and harmonizing evidence-based risk control strategies, fostered with extensive and objective-oriented research and development, and preemptive ideological relationships with relevant stakeholders. The current review aimed at addressing the possible occurrence and risks associated with potential emerging or unknown hazards/contaminants linked to various production systems, along with relevant mitigation strategies. It also highlights the importance of implementing quality control measures and safety precautions throughout the food supply chain to prevent the occurrence and propagation of hazardous substances. Agricultural production systems can be transformed into sustainable entities by vigilant monitoring of end-product quality through the use of upcycled technologies.

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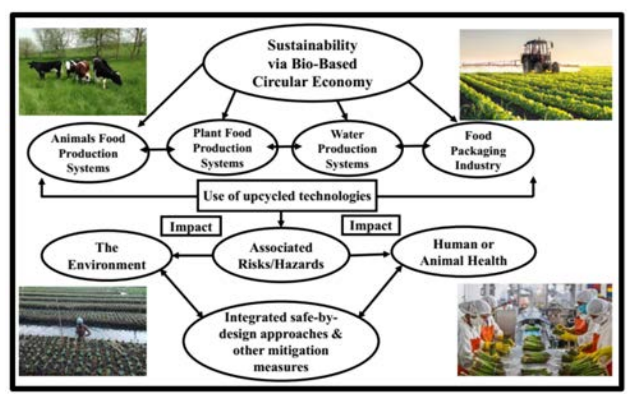

Graphical abstract.

Introduction

Exploring multidimensional food safety systems

Ensuring food safety entails implementing a rigorous regulatory framework at each stage of the food supply chain (FAO, 2006). However, if a country is still facing food safety issues despite formulating rigorous regulatory frameworks, then there can be an issue of a lack of effective implementation of those policy frameworks. Thus, tangible results of a policy framework can only be achieved through effective implementation and thorough monitoring at all levels, from farm to fork (consumer level). Food safety at the consumer level can be ensured through awareness and knowledge dissemination to create a sense of responsibility for eating safe and healthy food. Over recent decades, there has been a shift away from traditional food safety systems towards the adoption of rapid analytical food testing measures, as shown in Figure 1. These measures aim to align with the internationally recognized food regulatory standards applicable from farm to fork (WHO, 2021). This shift in the approach to food safety can be achieved by embracing smart agricultural practices across the food production systems. Incorporation of new technologies and approaches in food sciences for sustainability can yield multidimensional effects, including the reduction, exacerbation, or introduction of emerging food safety hazards; thereby compromising the overall food safety scenario (FAO and WHO, 2002). Alarmingly, Food and Agriculture Organization of the United Nations (FAO) statistics from 2020 revealed that a significant portion of the global population (approximately 768 million) faced severe food insecurity and 9.9% encountered deadly hunger due to the COVID-19 pandemic, despite the United Nations (UN) commitment to "Zero-Hunger" in the Sustainable Development Goals (SDGs) (Godenau *et al.*, 2020; UNEP, 2021). This condition can be associated with the developmental state of a country and its level of commitment to "Zero-Hunger". Based on these associations, comparative analysis can be drawn between different countries, *e.g.*, the European Union (EU) *vs.* Africa, North America *vs.* South America, *etc*. After complete analysis, solid conclusive evidence in statistical form can be achieved, explaining the actual scenario of each region of the world. Communities grappling with various knock-over deadly situations, such as floods, earthquakes, pandemic outbreaks like COVID-19, or state bankruptcy, become more vulnerable to food security and food safety issues, along with the price volatility (Yildirim and Yildirim, 2020). Consequently, the overall state concerned with food safety/security is severely compromised and can be reinstated only after applying cost-effective, easily implementable, and comprehensive risk-based food safety approaches as outlined in Figure 1.

Classification of food waste and food systems

According to FAO's slogan, "whenever there is a use of water, there will be waste". This statement seems fit for all other food and livelihood commodities. A sustainable food system can be achieved by ensuring stepwise food safety and food security measures. It is an intricate and multifaceted task that demands equilibrium between the goals and needs of both food safety and security. The prime objective of applying all management strategies related to the food sector is to comprehend the concept of food safety, consumer health, and sustainability. Modern holistic "One-Health" approach can be a suitable problem-solving option to recognize the trade-offs and ease of access towards sustainability for these complex and intervened opaque units of food supply chains (Hernando *et al*., 2019). Food waste can be a deciding factor in achieving sustainability as it tops the pyramid, accounting for approximately 17% of global food production, and is the most significant contributor to vulnerable food distribution systems. It results in potential destruction of the natural ecosystem by creating imbalances between renewable and non-renewable energy resources.

The EU has proposed a simple and self-explanatory food waste hierarchy in which waste prevention is on top at the first tier. The second tier relates to the reuse of waste, followed by waste recycling and waste recovery, respectively. Bottom of the pyramid is occupied by proper waste disposal statement as illustrated in Figure 2 (Salemdeeb *et al*., 2017).

According to General Food Law Regulation (EC-178/2002), safe food is defined as "any prepared, processed, and stored food item that, when consumed, does not cause harm and adheres to the legal limits for food safety hazards (chemical or microbiological)". Moreover, the availability of safe food can only be ensured through the implementation of a multifaceted food safety approach, which encompasses all the activities starting from farm to fork as outlined in Figure 3 (FAO, 2023). While unsafe food is that which is potentially unfit for consumer consumption due to contamination (European Parliament and Council of the European Union, 2002).

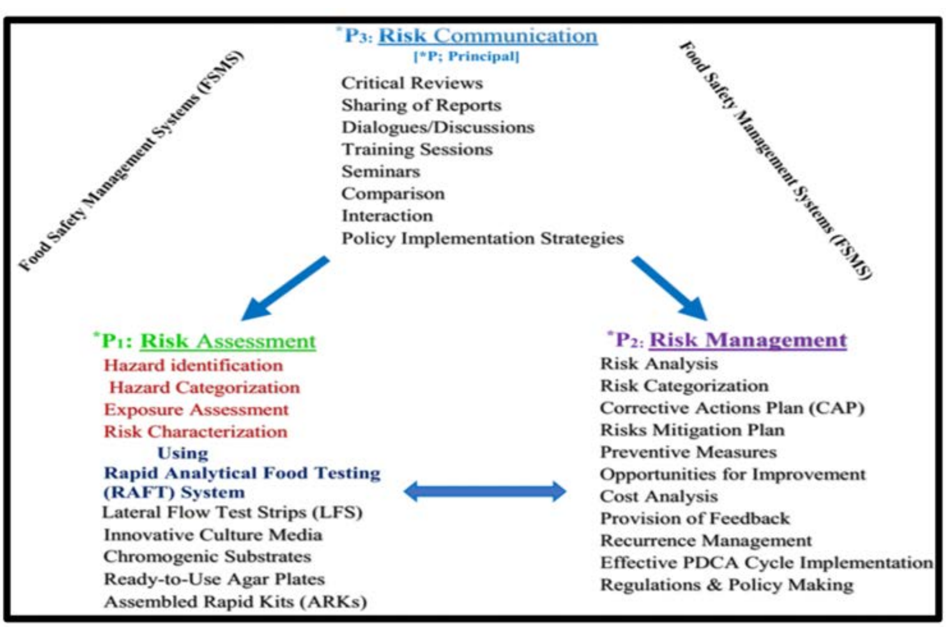

Figure 1. Risk-based food safety analysis approach to mitigate food safety hazards.

It is pertinent to maintain ecological poise coupled with compliance of end-products to international standards for customer health and safety during sustainability achievement *via* circularity. However, novel food safety hazards can emerge and enter food production systems due to the use of various by-products or upcycling technologies. These new and less common pathogens can cause chaos because no specific EU regulations/guidelines are available to cure and control them (European Parliament and Council of the European Union, 2008). Recently, the government of the United Arab Emirates (UAE) has launched a nationwide campaign to reduce food waste by 50% by 2030 under the "Nema Food Loss and Waste Reduction Roadmap" project to achieve the goals of zero food waste and hazard-free food and feed production. It is a joint public-private venture involving the UAE government and private stakeholders, including Jumeirah Group, Hilton Group, Rotana Group, and Expo City. This initiative prioritizes the reduction of food loss/waste and aligns with the upcoming COP-28 food systems, highlighting the commitment of the UAE government to address climate change, particularly in the transformation of food and agricultural systems. Through the COP-28 food systems and agricultural summit, the UAE aims to make food loss and food waste reduction a global strategic imperative.

Animal and plant-based food production systems generate many by-products, secondary materials, and food wastes (Ominski *et al*., 2021). Food waste is an act of intentional discarding of food products that are fit for consumption or fit to proceed in the food supply chain. It mostly occurs at later stages of the food supply chain, *i.e*., retail and consumer households, and often relates to human behavior (Parfitt *et al*., 2010). Food waste can be reduced by applying various control measures, while the reuse of by-products in feed and food production systems can be enhanced through awareness and literacy drives. These efforts can lead to the accumulation and distribution of conventional and novel food safety hazards in food production systems (Bodar *et al*., 2018; Garrett *et al.*, 2020; Lange and Meyer, 2019). Entry of potential food safety hazards sources can be restricted, and their dispersion can be controlled by revising and following proper standard operating procedures for the reuse of by-products. Previous incidents of food mishandling have proved fatal, *i.e*., the Belgian polychlorinated biphenyls (PCB) incident of 1999, where animal feed was prepared with recycled oil/fat containing transformer oil (a rich source of PCB). Another such failure was noticed in Ireland (2008), where recycled mineral oil was accidentally added to animal feed, causing many farm animal casualties and substantial economic losses and social mistrust (Hoogenboom *et al.*, 2007; Heres *et al*., 2010). Such incidents should be critically monitored and managed with the help of smart hazards-based mitigation strategies to lessen their occurrence frequency in food supply chains.

Potential food safety hazards associated with the circular bio-based economy

The basic concept of circular economy (CE) revolves around the mitigation of food waste and food loss through smart recycling and reuse of existing natural and man-made resources, along with a reduction in environmental impact. However, mistakes in the analysis of recycled and reused food products are the main cause of the health hazards involved with their consumption in the existing food operation systems. For readers' ease, the current review topic discussing the whole food supply chain has been subdivided into three primary production and supplementary (secondary) production domains.

Primarily plant-based food production (flora), animal-based food production (fauna), and water-based food production (aquaculture) domains have been discussed, while food packaging systems and the utilization of seaweeds are documented as secondary production systems. Every system's input and output undergo a series of chemical and structural changes to form various by-products and secondary supplements during recycling and reusing steps, so as to develop a circular system. Inputs of one system are the outputs of the other, similarly, by-products of one production system can become potential reactants/inputs for the other system. Each system has been explained to elaborate on its connectivity with circularity, sustainability, and potential connectivity with conventional and emerging food safety hazards.

Plant-based food production systems

In these systems, the input materials consist of soil and water (irrigation source). Potential hazards can infiltrate into this system into the soil through waste-derived soil enrichment compounds, *e.g*., animal manure and composts prepared from biodegradable wastes. Hazards can also enter through water in the form of bio solids extracted from sewage systems.

Animal manure

While animal manure serves as a viable alternative to artificial

Figure 2. Food waste management pyramid.

Figure 3. A multifaceted food safety approach can guarantee "safe food". Reproduced from: FAO, 2023.

fertilizers, it concurrently poses a potential threat as a source of multiple food safety hazards, particularly of chemical and microbiological nature. Notably, studies have demonstrated that application of manure to nutrient-deprived soils significantly elevates the concentration levels of heavy metals like chromium (Cr), copper (Cu), cadmium (Cd) and zinc (Zn) (Nomeda *et al.*, 2008; Lu *et al.*, 2014; Zhen *et al*., 2020), thus contaminating the soil with rich reservoirs of heavy carcinogenic metals. Furthermore, manure can also carry varying levels of highly persistent antimicrobials like tetracycline, macrolides, quinolones, and pleuromutilins attributed to the administration of pharmaceuticals to farm animals (Berendsen *et al*., 2018). Experimental findings on farm animals support the fact that more than half of the administered doses (55% in swine and 75% in calves) are excreted as such through urine and feces (Berendsen *et al*., 2015). Varying concentrations of these antimicrobials, *e.g*., tetracycline, macrolides, quinolones, and pleuromutilins, are absorbed by plants and lead to the development of bacterial resistance and dissemination of antibiotic resistance genes (ARG) (Chitescu *et al*., 2013; Sun *et al*., 2021). Besides chemical hazards, animal manure can serve as a vector for the spread of multiple microbial hazards like pathogenic bacteria, *i.e.*, *Campylobacter coli* and *jejuni*, *Bacillus anthracis*, *Brucella abortus*, and *Escherichia coli*. Apart from bacterial invasions, some viruses like *avian-swine influenza* and *Hepatitis-E virus* can also be hosted by animal manure. A variety of human parasites like *Balatidium coli, Cryptosporidium parvum*, and *Giardia spp*. can also infiltrate the food systems through animal manure (Millner *et al*., 2009).

Composts and vermicomposts

Composts, just like animal farm-yard manure, can become carriers of different chemical contaminants such as dioxins, per and polyfluoroalkyl substances (PFAS), polycyclic aromatic hydrocarbons (PAHs), PCB, and polychlorinated dibenzop-dioxins, as well as heavy metals into the food supply chain (Costello and Lee, 2020). Biosolids (sludge), extracted from civil (waste) water, industrial effluents, and other bio-wastes, are utilized as soil improvers and may be loaded with a vast variety of organic contaminants. A recent study by Gustavsson *et al*. (2022) identified approximately 2000 nos. of hazardous contaminants in the wastewater of Sweden. These hazardous substances eventually enter the food supply chain, compromising food safety and putting consumer health at risk. Despite its numerous drawbacks, there are certain advantages associated with the use of green manure, particularly Vermicompost - a type of compost produced by the worms, especially earthworms. Mitigating effects of green compost on rocket salad were observed by reduction in uptake levels of different hydrophobic contaminants like boscalid, imidacloprid, metribuzin, *etc*., and some endocrine disruptors, *e.g*., 4-tert-octylphenol and bisphenol-A (Parlavecchia *et al.*, 2020). Besides chemical hazards, green waste/manure, which is mainly composed of wastes from public and private gardens, does not support the growth of pathogenic organisms, but still some pathogens, *e.g*., *Salmonella enteritidis*, *E. coli*, and *Listeria monocytogenes*, can survive in fresh green manure (Lemunier *et al*., 2005).

Water (irrigation/treated)

Irrigation water can also serve as a conduit for chemical/microbial and human pathogens to enter the food systems. Hazards pertaining to aquatic biocycle may include cyanobacteria/blue-green algae, which produce cyanotoxins, can accumulate and dissolve in prevailing food systems (Miller and Russel, 2017). When considering human pathogens, those originating from the Gastrointestinal tract (GIT), such as *Salmonella* spp., can accumulate in surface water (rivers, lakes/ponds) through feces and later be used for irrigation purposes (Islam *et al.*, 2004; Liu *et al*., 2018). Treated water, often derived from sewage, is utilized for crop irrigation; however, it carries water-soluble contaminants, including heavy metals and chemical hazards such as persistent organic pollutants (POPs), including PAHs (Zhen *et al*., 2020).

The concept of persistent mobile organic contaminants remains a subject of debate among researchers, necessitating a comprehensive study to fully comprehend its impacts on agricultural production (Reemtsma *et al*., 2016). Supporting evidence was gathered by Blum *et al*. (2018), who identified several persistent aromatic chemicals in industrial effluents. Similarly, Aro *et al*. (2021) discovered a wide range of short-chain PFAS during their examination of industrial effluents.

The use of irrigation water can present major hazards in the form of human pathogens (bacteria/viruses/fungi) which permanently reside within these water systems and multiply insanely. As a result, this water will contaminate the irrigated soil and serve as a source of transmission for related pathogens. Their mode of proliferation may differ depending on their nature and type, *e.g.*, *Salmonella* spp. have been frequently reported in surface water of rivers/lakes, where they come from human/animal GIT and are eventually used for irrigation purposes (Liu *et al*., 2018). Similarly, *C. jejuni* and *E. coli* O157 are also normally present in surface water, originating from animals/wild bird feces, or poultry (Mulder *et al*., 2020). Severity and dispersion of these microbial pathogens may be vastly affected due to sudden and obvious climate change patterns around the globe. As summers are moving towards increased periods of hard dryness, resulting in moisture loss and increase in hydrophobicity of the soil. It will enhance the occurrence of soil runoff events, causing wide dispersion of pathogens (Sterk *et al*., 2013). Pathogenic microbes can spread and contaminate crops through irrigation water, with their distribution varying based on the type of irrigation methods or systems used and the sophistication of the technologies employed. As per the latest findings, those irrigation systems exposing direct water contact with the edible parts of the plants (sprinkler) are more vulnerable to pathogenic attacks than their counterparts (drip and surface furrow) (Alegbeleye *et al*., 2018).

Biosolids (sludge)

Sludge containing different biological forms is mainly extracted from wastewaters and effluents from industries/civil societies/ mixed water systems. Treated sludge is commonly used as a soil enhancer or compost in plant production systems. A wide variety of organic pollutants/contaminants are still typically bound with the treated sewage water/sludge. Recent evidence from studies conducted by Gustavsson *et al.* (2022) further supports this concept, as they investigated wastewater in Sweden and identified over 2000 hazardous chemicals in these sources. These included detergents, surfactants, lakes/dyes, pigments, brominated flame retardants, and certain other dangerous chemical groups which can compromise the safety of agricultural produce. Organic carbon in biosolids can adhere to the POPs persisting within wastewater sources and thereby cause their entry into the food chain (Brambilla *et al*., 2016). A wide range of familiar pesticides like Aldrin, Chlordane, and DDT, and other industrial effluents, *e.g.*, perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluoroalkyl acids, sulfonates, sulfonamides, and a few pharmaceutical residual contaminants constitute the ever-green

POPs due to their high retention and penetration power (Aro *et al*., 2021). In addition to this, biosolids can also introduce heavy metals, *i.e.*, lead (Pb) and Cd, into the food supply chains. Concentrations of these heavy metals can rise during the treatment of biosolids due to the degradation of organic matter in residual content (Thakali and MacRae, 2021).

Sewage sludge can also pose different microbiological hazards to the food systems owing to the presence of different pathogenic bacteria and parasites. Bacterial species can include *C. jejuni*, *E. coli*, *L. monocytogenes*, *Salmonella* spp., while the parasitic community is mainly comprised of *Cryptosporidium* spp. Moreover, biosolids are a potential source of ARGs, having lower levels than manure, but are still more prone to their increased concentrations upon usage/treatment (Hamilton *et al*., 2020). The worst part of it is the potential existence of lethal viral infectious pathogens among biosolids, which can introduce adenovirus, enterovirus, and norovirus into the food safety systems (Hamilton *et al*., 2020; Tozzoli *et al*., 2017).

Agricultural soil (the ultimate safe house for food safety hazards)

Agricultural soil is considered the main storage chamber for the accumulation and dispersion of all potential and actual food safety hazards because all the inputs are directly applied to the soil. So, the most important and critical link in determining and controlling the food safety hazards is agricultural land/soil, which can become a habitat for several safety hazards, especially heavy metals and different types of pharmaceuticals. These hazardous compounds can withstand harsh and unfavorable surrounding circumstances for several years and amass inside living organisms by infecting both humans and animal species (Costello and Lee, 2020). Potential sources responsible for these hazards may include artificial fertilizers, industrial effluents, pesticides, polluted irrigation water, *etc*. (Thakali and MacRae, 2021).

Heavy metals, such as mercury (Hg), arsenic (As), nickel (Ni), Cr, Cu, Cd, Pb, and Zn, tend to deposit in the soil (Thakali and MacRae, 2021). Their mode of entry into the food systems is by adsorption and deposition in edible and nonedible plant tissues during growth periods (Zhou *et al*., 2016). Pb- or As-based pesticides were mostly used in fruit orchards at the start of the 20^{th} century, leaving behind their residues in fruit crops and soil. Although their concentrations were below threshold levels in orchard fruits but a significant rise in the levels of these hazardous compounds was noted in edible plant parts when these old orchards were used in the production of roots of leafy crops (McBride *et al*., 2015).

Likewise, the menace of pharmaceuticals enters the soil through sewage biosolids, wastewater, industrial effluents, or manure. These are either retained in the surface layers of the soil or leached down to the groundwater. This mode of action is purely derived from the physico-chemical properties and molecular and granular structure of pharmaceuticals and soil. This is evident from the fact that plants grown in sandy soils contain higher levels of pharmaceutical residues compared to those grown in soils with high organic matter content (Gworek *et al*., 2021).

The highly resistant nature of these hazards leads to prolonged soil contamination, which ultimately affects plants. Organochlorine pesticides, dioxins, polybrominated diphenyl ethers, hexabromocyclododecane (HBCD), and some PFAS, including PFOS and PFOA, are some of the renowned POPs that can gather in the soil from where they can proliferate and become part of the food safety systems (Thakali and MacRae, 2021).

Major outputs of plant-based production systems

Plant by-products

By-products from plants are further utilized either as animal feed, green manure, compost, substrate for insects, or cover crops in plant production, thereby ensuring that all the accumulated food safety hazards remain intact within the food supply chain (Devarajan *et al*., 2021). Despite providing numerous benefits, such as improving organic matter, soil fertility, microbial diversity, and crop yield, these by-products pose significant risks to food safety by introducing hazardous chemicals and microbes, including heavy metals, POPs, and various harmful viruses and bacteria (Mason *et al*., 2020). Therefore, before utilizing these by-products, their safety standards should be carefully assessed to prevent further complications in food production systems.

Animal-based food production systems

Animal by-products are envisioned as the linchpin in the CE, yet their sustainability is compromised by the substantial expulsion of greenhouse gases (GHGs). Currently, nearly 40% of total farmland is underutilized, dedicated solely to feed production, emphasizing the imperative to seek alternative feed sources (Van Zanten *et al*., 2018). Several potential alternatives are explored here, including plant- and animal-based by-products, feed materials derived from wastes, and insect rearing by-products.

Animal production systems inputs

Feed based on plant by-products

By-products of the food industry are mostly used as animal feed if they adhere to the legal limits for contaminants. These may include sugar-beet pulp from the sugar industry, brewers' spent grains, germs, and rootlets from the brewing industry, and by-products from the olive oil industry (European Commission, 2013; Boudra *et al*., 2015; Mastanjevic *et al*., 2019). However, these by-products can harbor potential food safety hazards including mycotoxins including aflatoxins, patulin, gliotoxin, zearalenone, mycophenolic acid, roquefortine-C and ochratoxin-A (Wang *et al*., 2019; Gullon *et al*., 2020).

Mycotoxins can be detrimental to human and animal health and productivity. A large number of these toxins are metabolized by the animals and thereby nullify their presence forwarding into the food supply chain, but still can be excreted by the animals. Most of the metabolites have not been regulated, and toxicity levels have not been monitored perfectly. Aflatoxin M1 is a milk-based excretory metabolite derived from aflatoxin B1, produced in the cow's body fed upon aflatoxin B1-contaminated feed (Van der Fels-Klerx and Bouzembrak, 2016). Besides mycotoxins, plant-based by-products can also introduce pesticide residual threats as food safety hazards into the food production systems, just like the application of Cu residues after harvesting to mitigate fungal and bacterial infections (Hammann *et al*., 2019). Water-insoluble pesticides are more likely to accumulate in brewer's spent grains. Pesticide residues possess unbelievable stability and degrade only to a small extent (Navarro and Vela, 2009). The scope of hazards posed by the plant by-products can be widened due to the presence of antibiotic residues, which can be taken up from the soil and end up in animal production systems after being used as by-products (van der Fels-Klerx *et al*., 2019).

Feed based on animal by-products

Animal based by-products used as feed matrix in animal production systems are defined as "forms, entire bodies, or parts of animals, products of animal origin or other products obtained from animals, which are not intended for human consumption, including oocytes, embryos, and semen" (European Parliament and Council of the European Union, 2009). These may pose potential hazards such as prions, pharmaceutical residues, antibiotic residues, and household food waste, potentially transmitting diseases such as foot and mouth disease, African swine fever, *etc*. (Gale, 2004; Jansen *et al*., 2017; Ominski *et al*., 2021). Processed animal proteins (PAP) comprise by-products, including blood meal, meat meal, bone meal, horn meal, feather meal, and fish meal, collected from slaughterhouses of healthy animals. EU regulations must be followed while using these PAPs in animal production systems. As per EU guidelines, PAPs from farmed insects can be used on poultry and porcine animals (European Commission, 2021). One major concern in adopting animal by-products is the inter-transmission of some viruses between species because of their fluctuating virulence behavior (Ma *et al*., 2009). Additionally, pharmaceutical and antibiotic residues are the other potential hazards in animal by-products, as evident in different studies on chicken feathers involving heat treatment as well (Jansen *et al*., 2017). Therefore, strict regulations have been made by the EU to lessen the impact of these hazards on consumer health, according to which only specific food wastes can be used as animal feed for specific animal species (Salemdeeb *et al*., 2017). As per these rules, food waste containing meat is strictly prohibited from being used as animal feed (European Commission, 2021).

Feed from insects

Insects have emerged as a highly suitable, cost-effective and nutritionally rich alternative to conventional protein sources, as seen from the FAO's food safety perspective, which considers edible insects a means to achieve food value chain sustainability, as highlighted in Figure 4 (FAO, 2023; Van der Heide *et al*., 2021; Veldkamp *et al.*, 2021). Processed animal proteins from specific species of farmed insects can be used in poultry and porcine animals, pet food, and fish feed as per EU Regulation (EU) No 1372/2021. However, it is important to note that insects can carry heavy metals (As, Pb, Hg), pesticide residues, pharmaceuticals, hormones, dioxins and PCBs, and bacterial pathogens, typically sourced from their rearing substrates (Meyer *et al*., 2021; Van der Fels-Klerx *et al*., 2018). Different types of risks are associated with these contaminants/toxicants depending upon their origin, chemistry, and mode of action inside the body. The presence of toxic heavy metals above safe levels can cause cancer, while residues of pesticides, pharmaceuticals, hormones, and bacterial pathogens can bring various biochemical and structural body changes among consumers, leading to several complications and syndromes. Substrates used for insect rearing can become a carrier for contaminants to the insects and ultimately to the animals fed on these insects. In addition to these, insects can also act as a vector of prions; therefore, by-products of plants are considered a safe substrate for insect rearing, but consumer waste containing meat needs extra precautionary measures (Van Raamsdonk *et al*., 2017).

Outputs of animal production systems

Animal by-products

Regulation (EC) No 1069/2009 classifies animal by-products in three distinguished categories based upon their severity and lethality in causing health hazards to humans. These categories are further subdivided into the highest risk category (category 1), encompassing contaminated animal products with contaminants or pesticide/antibiotic residues within legal limits. Category 2 consists of products like manure and by-products containing contaminants more than the upper threshold level. Such products are not allowed to be used as animal feed and must be destroyed on-site. However, some by-products of this category can be used for the production of organic fertilizers or in a certified composting plant. By-products present in category 3 can be used as organic fertilizers or in the production of pet food due to their low-risk and mild nature, based on the origin, processing treatment, and intended use (European Parliament and Council of the European Union, 2009).

Multiple food safety hazards including viruses, protozoa, bacteria, prions, parasites, various pharmaceuticals and other chemical substances *e.g*., heavy metals/dioxins are found in animal carcasses especially in cattle tissues such as eyes, brain, spleen, spinal cord and some gut parts might contain transmissible spongiform encephalopathy (TSE) prions (European Parliament and Council of the European Union, 2009; Gooding and Meeker, 2016; Lee *et al*., 2021). These animal by-products can be hazardous in animal and plant feeds, as leguminous and land plants like corn, alfalfa, and tomato can take up prions from land (Pritzkow *et al*., 2015). Prions are protein-based infectious agents responsible for prion diseases. Infectious prion proteins (PrPSc) exhibit strong binding affinity and prolonged retention in plants. Even trace amounts of PrPSc, present in diluted brain homogenates or excretory materials (urine and feces), can bind to wheatgrass roots and leaves. Additionally, leaves sprayed with a prion-containing solution retained PrPSc for several weeks while the plant remained alive. Prions can also be absorbed from contaminated soil and transported to the aerial parts of the plant, such as stems and leaves. This ability of plants to efficiently bind infectious prions and act as carriers of infectivity highlights their potential role in the environmental transmission of prion diseases through horizontal pathways. Research has shown that infectious prions bind tightly to soil and remain infectious for years, suggesting that soil contamination may contribute to the spread of TSEs (Johnson *et al*., 2006; Johnson *et al.*, 2007). Prion diseases can be transmitted between animals and humans, but the mechanisms and factors governing their spread remain unclear. Naturally acquired forms like variant Creutzfeldt-Jakob disease, kuru, and bovine spongiform encephalopathy are linked to consuming meat or meat-derived products from infected individuals. Studies show that infectious prions enter the environment *via* bodily fluids, placenta, or decay-

Figure 4. Food and Agriculture Organization's slogan to achieve food value chain sustainability. Reproduced from: FAO, 2023.

ing carcasses of infected animals (Terry *et al*., 2011). The uncertain behavior and complex nature of prions remain challenging to understand, partly due to various biological, chemical, and physical changes occurring during composting. While Xu *et al*. (2013) did not detect prions in samples after 2 or 4 weeks of composting, the composting matrix complicates their detection, leaving the study unable to confirm whether prions were entirely degraded during the process. Other studies have found that pathogens can survive composting, even when recommended time–temperature conditions are met. This complexity makes the detection and decontamination of prions during composting particularly difficult, as contrasting findings about their nature and chemistry have been reported by scientists (Gooding and Meeker, 2016).

Water-based food systems (aquaculture)

The animal food manufacturing industry is one of the fastest-growing sectors and contributes to approximately 50% of global seafood production (Campanati *et al.*, 2022). Aquaculture by-products consist of body parts, damaged fish, shells, carapaces, or trimmings from processing. These by-products are further processed for the preparation of fish meal and oil and reused as feed ingredients for pets and aquatic life (Campanati *et al.*, 2022). However, the presence of food safety hazards in aquaculture by-products, including bacterial pathogens, obligate/facultative parasites, dioxins, heavy metals, bio-toxins, pesticide residues, and antibiotics from pharmaceuticals, along with other disinfectants, is a permanent source of worry (Bodin *et al*., 2007). The final destination of these hazards is the end-consumers, and their transport is certainly aided by some carriers like mussels (the fish meal), which may not be the direct human diets but can serve as potential feed ingredients for fish, pigs, and poultry (Suplicy, 2020; Van der Heide *et al*., 2021). The primary use of mussels is aimed at reducing the nitrogen and phosphorus levels in urban water sources by pumping and filtering the water and capturing the hazardous enemies such as water-borne pathogens, viruses, bacteria, antimicrobials, parasites, chemical contaminants (*e.g*., PFAS, bio-toxins), and heavy metals (Pb, Cd, Hg) (Zhelyazkov *et al*., 2018; Lopez Cabo *et al*., 2020). So, overall, the main inputs in the aquaculture production domain are fish feed and water, with a major focus on finding alternative feed sources for fish. The system's outputs focus on seaweeds and aquaculture wastewater.

Seaweeds

Seaweeds, often called "aquaculture novel food", offer a viable and sustainable nutrient source for farmed fish, oysters, and poultry feeds (Morais *et al*., 2020). Edible groups of seaweeds include *Rhodophyta* (red), *Phaeophyta* (brown), and *Chlorophyta* (green) (Banach *et al*., 2020). Despite their multifold benefits, the main hindrance to their use is the ability to accumulate a large number of contaminants from the surrounding environment. Potential contaminants can include heavy metals (As, Cd, iodine), *Salmonella* spp., micro-plastics, POPs, marine biotoxins, pharmaceuticals, norovirus, and hepatitis-E virus (Banach *et al.*, 2020).

Aquaculture wastewater

In a circular system, animal feed can be manufactured by using single-cell proteins, which are derived from aquaculture wastewater and can be a potential source of multiple enteric pathogens, including *Salmonella* and *Campylobacter* (Klase *et al*., 2019; Asiri and Chu, 2020). Beyond health complications, wastewater can induce adverse ecological and pathological impacts, such as increased ammonia levels, algal blooms, water acidification, eutrophication, and lethal concentrations of bacteria and viruses (Campanati *et al*., 2022). Generally, aquaculture wastewater/sludge contains fewer contaminants than industrial sludges or municipal wastes, but it still cannot be directly used as land fertilizers due to the high concentrations of pathogenic bacteria, viruses, and antibiotic residues (Van Rijn, 2013). This issue can be addressed by treating and replenishing the aquaculture wastewater using various techniques. One such technique is the sedimentation/mechanical filtration method in which solid wastes in wastewater can be retained within the matrix, resulting in the omega-3 rich aqua feeds. Another suitable water treatment technique is vermicomposting (employing worms to decompose waste and produce nutrient-rich compost). Resultant earthworm biomass can be used further as fish, pets, or even livestock feed. Although wastewater treated with vermicomposting might contain contaminants (heavy metals) either in the vermicompost or in the earthworms, their concentration will be far below the EU legal limits, which render it fit for irrigation purposes (Kouba *et al*., 2018). Wastewater can be treated and reused by applying different treatments like recirculating aquaculture systems or integrated multitrophic aquaculture, or aqua-ponics. In all these techniques, wastewater is first treated to lessen the burden of contaminants and then reused either within the system or for other beneficial purposes (Wirza and Nazir, 2021).

Food packaging industry (reuse and recycle)

The food waste hierarchy, addressed under the EU's Circular Economy Action Plan and waste management directives such as the Packaging and Packaging Waste Directive, can only be achieved when packaging waste is reduced, reused, and recycled to the maximum extent. The primary goal of this plan is to minimize packaging waste, promote recycling, and encourage sustainable packaging practices. Although food waste and packaging waste are often interlinked, they are addressed under separate frameworks in EU policies. This practice can result in the accumulation and migration of different hazards in the resultant packaging material and the final food product. Recycling removes a considerable proportion of microbial hazards, while chemical contaminants present in the raw materials tend to persist in the final packaged product. These contaminants float in the system from previous packaging material to the new one because a proportion of the old packaging material is recycled (Geueke *et al*., 2018). Recycling of packaging materials is, although a sustainable technology, still it should be safe to use, *e.g.*, Regulation (EC) 282/2008 about the use of recycled plastic materials states that the recycled packing should comply with the same food safety standards just like the original virgin materials (European Parliament, Council of the European Union, 2008). Recently "bamboo cups" issue originated from the packaging where bamboo fibers were added to melamine plastic, due to which the migration rate of melamine and formaldehyde towards the food product was changed and resulted in several rapid alert systems for food and feed notifications (Bouma *et al*., 2022).

Conventional plastic, being non-sustainable due to its non-renewable resource origin, prioritizes a bio-based, biodegradable food packaging alternative. However, their cost-effectiveness and ability to protect and preserve the food product from different contaminants remain notable areas for using these alternatives. In terms of cost analysis, biodegradable packaging materials propose high prices and have found very limited market value (Nilsen-Nygaard *et al.*, 2021). Therefore, the reuse and recycle of conventional food packaging, including aluminum/steel cans, glass packaging, paper, and conventional plastic, will be discussed in the next section.

Reuse and recycling (aluminum, steel, glass)

The primary focus is on the reuse and recycling of conventional food packaging materials such as aluminum or steel cans, glass, paper, and conventional plastic to create hazard-free novel packaging products. The presence of heavy metals should be critically observed and controlled in the recycling of food packaging containing metals. For example, recycling of aluminum or steel cans can lead to accumulation of heavy metals/metalloids like Mn and Cr originating from alloying materials, which are used to enhance the strength of cans. Sn, Zn, Cd, and Pb coming from the coating residues left from previous use may also amass in the final food packaging products (Geueke *et al*., 2018). On the other hand, glass packaging is considered safe to be reused or recycled due to its inertness and easy-to-sanitize properties. However, it is pertinent to mention the potential presence of heavy metal Pb in glass packaging originating from the sand used in glass production which may leach down to food as food contact material (FCM) or can become a part of food due to traces of heavy metals coming from pesticide residues or heavy metals which remain intact for indefinite time (Marsh and Bugusu, 2007). Recycling of both metal and glass packaging is potentially safe because almost all microorganisms and organic compounds are completely abolished, while the material properties do not alter during the re-melting process.

Paper packaging

According to Geueke *et al.* (2018), there is a number of potential sources of food safety hazards in paper and board, which include retention aids, sizing agents, coatings, fillers, plasticizers, pigments, solvents, printing inks, *etc*. Moreover, contaminants particularly related to paper and board are heavy metals, bisphenol-A, diisopropylnaphthalenes, phthalates, mineral oil hydrocarbons, PAHs, and PFAS. Furthermore, two other types of contaminants termed as intentionally added substances during production and non-intentionally added substance (NIAS) due to reaction of by-products, oligomers, chemical reactions between packaging materials and foodstuff or as impurities from the raw materials used for the FCM production; might be present in paper and board as well (Peters *et al*., 2019). More research is needed to address the issue of NIAS and promote safety measures during the recycling of paper and board, as these contaminants tend to accumulate in the recycled paper packaging products, leading to potential food system hazards. The use of recycled paper and board can be conditionally recommended after minimizing the risks of potential contaminants and food safety hazards based on their lag times and application of effective simulation models (Pivnenko *et al.*, 2016).

Use of plastics

Strict EU regulations and limitations have been imposed for the effective use of recycled plastic as FCM due to food safety concerns, because plastic recycling as FCM is much more challenging and difficult to handle. To achieve a sustainable CE, EU's policy is very clear that by the end of 2030, all plastic packaging should be either reusable or it should be recycled in a cost-effective manner. Recycling of plastic can result in the formation of multiple food safety hazards including degradation polymers products (oligomers and monomers), additives such as phthalates [di (2-ethylhexyl) phthalate, dibutyl phthalate, benzyl butyl phthalate], flame retardants (PBDE, HBCD), fuel oils and heavy metals (Cd, Ni, Pb). Levels of oligomers formed during the synthesis or recycling of plastic are of major concern because their levels are much higher in the recycled product than virgin. Poor waste management practices can result in the absorption of these chemicals by plastic, where food-grade and non-food-grade plastics are not differentiated for further usage. Comprehensive Research and Development (R & D) is required to devise and implement cost-effective and target-oriented risk mitigation strategies for the eradication of these contaminants due to their innate ability to migrate into the food, thereby imposing serious threats to food safety systems. Another notable point is that the polyethylene terephthalate-based packaging can be recycled and reused as FCM as per EU regulations in place of other recycled polymers, *e.g.*, polyethylene, polypropylene, *etc*., mainly due to product properties retention and food safety problems. Extensive R & D is required to elaborate on the nature and impact of recycled plastic packaging usage in FCM to achieve sustainability.

Relative risks associated with emerging hazards/contaminants

CE is a transitional cognitive approach of transforming a linear economic model designed on the consumption of limited resources and producing surplus wastes with an alternative close-loop economic model primarily based on sharing, leasing, reuse, repair, and recycle. This affirmative strategy can assist in the attainment of the UN's SDGs, especially SDG-12 (responsible consumption and production), which in turn will lead to the accomplishment of SDG-3 (good health and well-being). CE may lead to sustainability, but, at the same time, can also reinvigorate the menace of new/emerging hazards into the food supply chain due to the use of upcycling technologies. Multiple risks associated with these emerging contaminants may arise and, if not properly addressed through smart mitigation strategies, can severely thwart the progression of human and animal safety. The most critical step to encounter these unpredictable is to evaluate the evidence for vulnerabilities in the CE approach for food/feed safety, plant, animal, human health, and the environment.

Emerging risks may be defined as "a susceptible risk linked to a known hazard or newly identified hazard with significant exposure, or from an unexpected new or increased significant exposure" (EFSA, 2024). These risks may result from primary or secondary production sites and may originate from biological (*e.g*., microbial), chemical (*e.g*., heavy metals) and physical (*e.g*., glass, plastic fragments) hazards to affect plants, animals, human health and the environment.

Risks to human or animal health

Human or animal health is significantly affected due to risks arising from emerging pathogens and other contaminants. Different food/feed products cause various types of hazards, including biological, chemical, or physical. Entry of these newly emerged contaminants into the food supply chain can occur at any stage, *e.g*., procurement, preparation, processing, transportation, or storage. These upcycled foods are more prone to contamination because of their delicate and vulnerable chemical and biological structures. These foods are often pre-treated so as to become an easy target for any new pathogen/contaminant. The inadequate use of these contaminated foods or feeds can import foreign hazardous chemicals into the consumer's body and may result in adverse health effects and even deaths in some cases.

Environmental risks arising from insects reared on waste

Eco-friendly food conservation techniques are generally prioritized in the modern food world. Ecological effects of upcycled foods are strictly monitored to assess their compatibility with the existing food supply chain management strategies. Novel risks affecting the overall global environment and resulting in phenomenal changes like global warming, GHG emissions, eutrophication, and an increase in carbon dioxide concentration have been linked with the use of upcycled technologies to transform food waste into upcycled foods. *Supplementary Table 1* (Nordentoft *et al*., 2014; Charlton *et al*., 2015; Tschirner and Simon, 2015; Boccazzi *et al*., 2017; Thévenot *et al*., 2018; Wynants *et al*., 2018; Conti *et al*., 2019; Truzzi *et al*., 2019; Varotto Tedesco *et al*., 2019; Campos *et al*., 2020; Mancini *et al*., 2020; Truzzi *et al*., 2020; Milanović *et al*., 2021; Osimani *et al*., 2021; Parodi *et al*., 2021) explains the detailed lists of relative risks associated with the use of innovative technologies, type of risk, causative agent or potential contaminant and mitigation measures. Regardless of the type or source of food/feed ingredients, there is no single method or sole approach which is sufficient to address possible food and feed contamination threats (Colovíc, Rakita, *et al*., 2019; Colovíc, Puvača, *et al.*, 2019). However, more sophisticated and safe approach can be ensured through the implementation of established food/feed safety protocols (*e.g*., hazard analysis and risk-based preventive controls; FDA, 2022) when transforming the food waste into animal feed. Strategic integration of de-risking strategies with good management practices, coupled with proper regulatory and technical control mechanisms, can help attain the desired objectives and make the use of food waste in animal feeds safe and viable.

Discussions and Conclusions

The intersection of sustainability and the CE significantly shapes the landscape of food safety. As industries strive to create more sustainable practices and adopt CE principles, their impacts on the safety of our foods become pivotal considerations. In sustainable food production systems, the emphasis is on minimizing the environmental impact, reducing food waste, and ensuring long-term viability. However, such complacent transitions within or

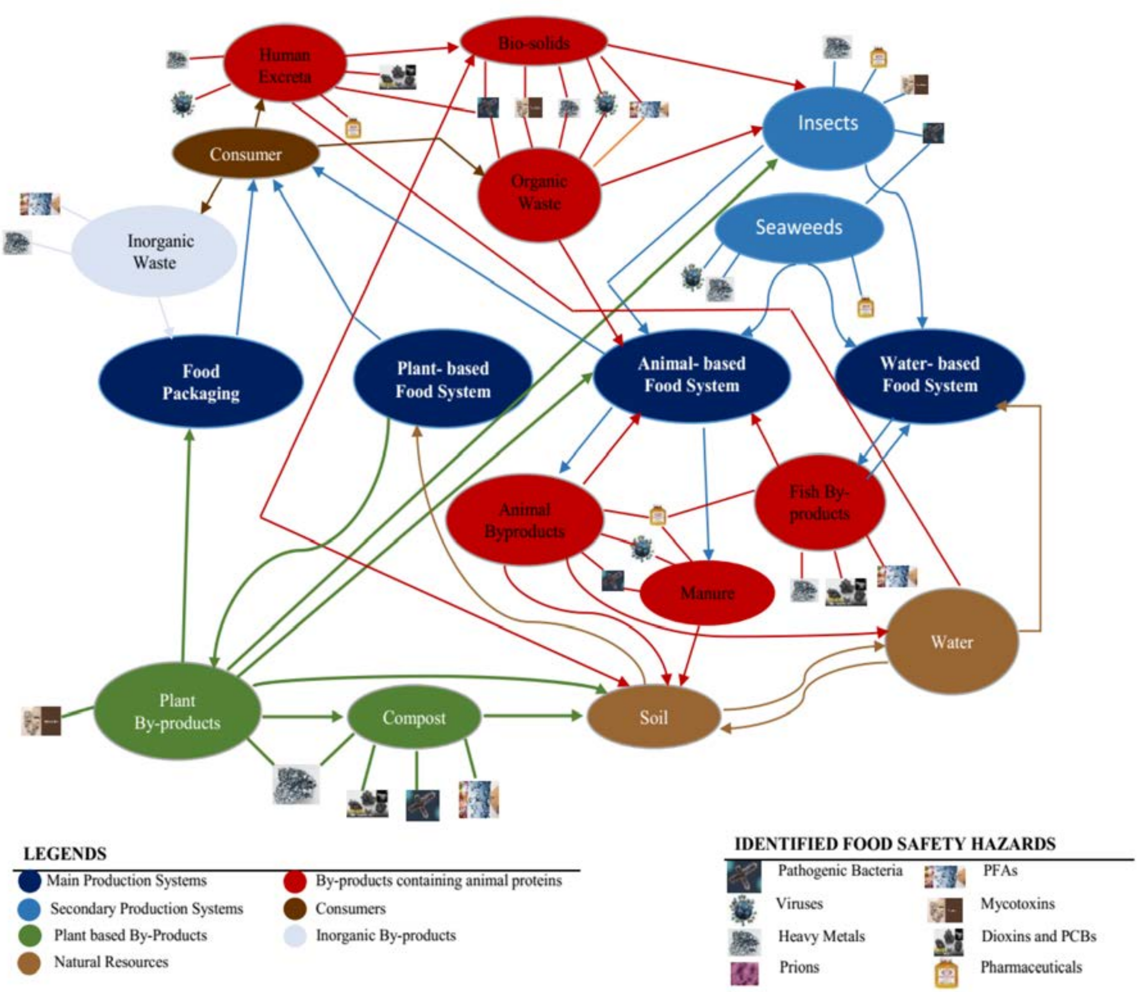

Figure 5. Potential food safety hazards in the circular bio-based economy showing their expected accumulation pathways in main production domains as well as in the secondary production system through reuse of by-products. Reproduced from: Focker *et al.*, 2022.

between food systems can bring new challenges and unpredictable vulnerabilities, particularly concerning food safety. Sustainable practices may involve the use of relatively newer alternative inputs, unfamiliar novel techniques and technologies, and modified and newly crafted supply chain models. As a result of these recently adopted practices, multiple novel and unfamiliar risks/hazards in addition to conventional risks may appear throughout the main line stream from farm-to-fork. The CE largely deals with the closing of resource loopholes while minimizing waste and tends to introduce circularity in production and consumption patterns. While this approach contributes to environmental stewardship, concurrently, it necessitates careful attention towards potential food safety hazards strictly associated with these intricate efforts. The reuse, recycling, or repurposing of raw materials, primary products, and their by-products should be managed meticulously to prevent contamination or introduction of harmful substances into the food supply systems.

Fostering the reader's knowledge about the nexus of circular bio-based economy with the food safety, the current review discusses main production domains (plants, animals, aquaculture and food packaging) of food supply chain, use of primary/secondary inputs and out puts and reuse of by-products produced in each production system to flow back into the food-nutrients cycle. Information about potential hazards at each step of the circular bio-based economic model can help to understand and investigate the sensitivity and specificity of every causative agent and elucidation of an effective mitigation plan to ensure food safety at all levels of the food supply chain. Figure 5 (Focker *et al*., 2022) transcribes the potential food safety hazards, domain-wise distribution patterns, and secondary production systems by reuse of different by-products in a circular bio-based economy. Similarly, *Supplementary Table 2* (Focker *et al*. 2022) enlists the main food safety hazards associated with relevant inputs and outputs within the main production domains of animals, plants, and aquaculture, which are ultimately linked with the CE. Most of the hazards enter the food system due to the reuse of by-products or during the recycling of waste materials. It is evident from previous studies that the main point of concern was the presence of pharmaceuticals, dioxins and PCBs, heavy metals, and microbial pathogens in the main production domains. However, in addition to these, several other novel hazards can also appear during the exploration of circular food production systems. These might include microbial, bio-medical, biological, chemical, physical, and physiological hazards with very little or zero knowledge about their origin, occurrence, mode of action, and other physico-chemical attributes. Therefore, more research work is required to investigate and discover such novel/emerging type of food safety hazards to close the loopholes in the feed and food production units/cycles. Other important points to foresee while applying these closing loophole strategies are the temporal and spatial effects of contaminants and chemical hazards. Temporal effects can be better explained with the help of an example of using hazardous pesticides or pharmaceuticals in the past, which might still be present in the soil or the food packaging materials. This is because of prolonged retention capacity of these substances enabling them to withstand the mortalities of extreme environmental conditions and such immortal behavior confiscates the complete wipe out of these agents from the system. Similarly, spatial effects are to cover a local region or become a part of it after passing through a transition period. Such effects provide a necessary safety shield to the hazards to survive within the production systems through a circular chain of the feed and being fed. It may result in mass scale localization of these hazards under indigenous circumstances when integrated with the in-house local production.

Conclusively, mitigation of these risks requires the implementation of a holistic "safe-by-design" approach combined with prevailing smart strategies addressing the potential food safety issues at each level of circular bio-based food supply chains. This approach aims at comprehensive goal-oriented R & D annexed with relevant stakeholder engagement and then assessing and re-assessing the efficiency of applied strategies by connecting with the evidence-based risk control techniques to ensure the safety of CE-driven food production (Van der Berg *et al*., 2020). As sustainability efforts have evolved over time, it is crucial to strike a balance between ecological sustainability and food safety. Adapting agricultural systems to these changes involves minimizing the potential food safety hazards associated with modern-day economic practices. Achieving a harmonious coexistence between sustainability, the CE, and food safety essentially needs ongoing collaboration, innovation, and a commitment to safeguarding the well-being of consumers and the planet (Barros *et al*., 2020). Overall, a circular redesign of our economy model is mandatory, which is more concentrated on "Safe Food" rather than producing "Surplus Food", just like the theme of being "Health conscious" and "Diet conscious".

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Online supplementary material:
Supplementary Table 1. Related risks associated with potential contaminants and mitigation measures due to use of upcycling technologies.
Supplementary Table 2. List of selected inputs and outputs and their corresponding identified hazards related to circular economy. Reproduced from: Focker et al., 2022.