Emerging risks from novel foods and feeds of relevance to the circular economy framework: Extensive Literature Review

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Background

Circular economy (CE) is an approach that decouples economic activity from the consumption of finite resources, designs out waste, opposes the take-make-consume-waste linear economic model and replaces it with an economic model based on sharing, leasing, reuse, repair, refurbishment and recycling, in an (almost) closed loop. During the transition to a circular economy, it is crucial to identify potential emerging risks for the environment and food and feed safety in a holistic and integrated fashion in order to achieve an optimal balance between opportunities, benefits and risks. EFSA is undertaking a 2-year project on "Food and feed safety vulnerabilities in circular economy". One aspect of this project is to conduct a literature review to gather and evaluate the evidence for vulnerabilities in the circular economy approach for food/feed safety, plant, animal and human health and the environment.

The literature review has three specific objectives:

- Objective 1: to identify and categorise current and envisaged circular economy practices within all stages of the food and feed chain in Europe.

- **Objective 2: to identify emerging risks for plant, animal and human health and the environment from novel food and feed within the CE framework.**

- Objective 3: to characterise the identified emerging risks from novel food and feed within the CE framework by providing the available information justifying the definition of emerging risk, relevant for EFSA's prioritisation and risk assessment activities.

Objective 1 is now complete and was used to identify the topic area for Objective 2. Twenty-six CE practices were identified in Objective 1 and stakeholders were asked in an online survey to prioritise them in terms of: (1) importance to CE; (2) ease of implementation of practice; (3) likelihood of risk from practice; (4) ease of overcoming risk; (5) current state of knowledge regarding risk from CE practice. The survey results indicated that current knowledge was considered particularly low for novel sources of food and feed and potential likelihood of risk was high. In consultation with EFSA, it was decided that this practice would be the focus of Objective 2.

This report documents the methodology and outcomes for Objective 2, to conduct an extensive literature search and monitoring on-going research projects to:
'identify emerging risks for plant, animal and human health and the environment resulting from new hazards and new exposure pathways leading to increased exposure from novel foods and feeds of relevance to the circular economy'

For the purposes of this review we have used the European Commission's definition of CE:
'where the value of products, materials and resources is maintained in the economy for as long as possible, and the generation of waste minimised' (EC, 2015).

The scope of the review focuses on using waste, former food products (FFP), and side streams (by-products and co-products) as a resource to develop novel foods and feeds, so contributing to CE. Novel foods for humans are defined in EU regulations as: 'any food that was not consumed "significantly" in the EU prior to May 15 1997 (Regulation (EU) 2015/2283)'. For the purposes of this review we consider 'novel feeds' to be new sources of feed from the food industries, biofuel industries and industrial processes and new types of ingredients such as processed animal proteins (PAPs) derived from farmed insects, marine resources and aquatic plants (FAO/WHO 2019). Whilst EU regulation for novel food is specific to food only, we have taken a broader approach and also include for example, food (and feed) additives and flavourings that aim to minimise waste and contribute towards CE.

The review considers novel foods and feeds arising from waste, FFP and side streams (i.e. by-product and co-products) from all stages of food/feed production and supply chains and the emerging risks to plant, animal and human health and the environment. Included are all emerging risks, resulting from biological (e.g. microbial), chemical (e.g. heavy metals) and physical (e.g. glass, plastic fragments) hazards.

Method

The literature search strategy and selection criteria (inclusion/exclusion) follow EFSA Systematic Review Guidance to address the following primary question: 'What are the emerging risks for plant, animal and human health and the environment resulting from new hazards and new exposure pathways leading to increased exposure, from novel food and feeds of relevance to circular economy?'

Studies included in the review were based on the following elements of the primary question:

- **Population**; Humans, plants, animals and environment
- **Exposure**; Novel food and feeds of relevance to CE and originating from food/feed production and supply chains
- **Comparator**; Use of novel foods and feeds compared to their counterparts used currently or no comparator
- **Outcome**; Emerging risks (resulting from biological, chemical, physical hazards) for plant, animal and human health and the environment resulting from production or consumption of novel foods and feeds

Primary research and reviews and on-going research projects from Europe were captured.

The search string below was used to collate relevant evidence:
"lab-grown meat" OR "test tube meat" OR "artificial meat*" OR "cultured meat*" OR "in vitro meat*" OR "synthetic meat*" OR "novel food*" OR "novel feed*" OR "alternative food*" OR "alternative feed*" OR "edible insect*" OR "insect food*" OR "insects as food" OR "insect feed*" OR "alternative protein*" OR "cell-based meat*" OR "insect protein*" OR "novel plant protein*" OR "cell-based protein*" OR "innovative food*" OR "innovative feed*" OR "sustainable protein*" OR "recycled protein*" OR "novel by-product*" OR "agri-food side stream*" OR "processed animal protein*" OR "mycoprotein*" OR upcycle* OR "new dietary ingredient*" OR "former food*" AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR "*nutrient*" NOT psychology OR accept* OR attitud* OR behav*

In addition, shorter search strings were used for some specific topic areas.

A comprehensive search to capture an un-biased sample of published and grey literature was undertaken using multiple information sources including: bibliographic databases, websites of relevant organisations and research funding platforms.

Articles retrieved from grey literature searches (i.e. from organisational web site searches and research funding platforms) were screened on a case by case basis for inclusion during the searching of websites.

A total of 51,235 articles were retrieved in the bibliographic database searches. Following duplicate removal using EndNote™ and EPPI-Reviewer4, a total of 26,669 articles remained for screening on title and abstract. DistillerSR Artificial Intelligence (AI) algorithm was used to automatise the identification of relevant documents.

The following meta-data were extracted from primary research studies: full reference; study type; food or feed type; relationship of food or feed to CE framework; population at risk; hazard type (biological, chemical, physical); study design; study endpoints measured; authors conclusions. This information was used to create summaries of the included studies and draw preliminary conclusions about the results.

Results

A total of 24 primary research articles were included for meta-data extraction at full text to inform the review. The main findings of these 24 studies were summarised and key findings and concluding remarks drawn.

Nearly all of the studies (n=23) investigated the rearing of invertebrates for food or feed on substrate arising from waste or side streams: (*Hermetia illucens* (black soldier fly) n=11; *Musca domestica* (house fly) n= 5; *Tenebrio molitor* (yellow mealworm) n=3; *Eisenia fetida* (earthworm) n=3; *Alphitobius diaperinus* (lesser mealworm) n=1; *Calliphora vomitoria* (bluebottle fly) n=1). One of these (23) studies investigated both *M. domestica* larvae reared on waste and rapeseed meal for swine feed. The remaining study investigated poultry by product (poultry fat, poultry by-product meal and steam hydrolysed feather meal) for animal feed.

No studies were found that investigated the risk of novel foods stemming from side streams or waste that are fed directly to humans.

Twelve studies were about risks to human or animal health. All of these studies investigated the risks of consuming invertebrates reared on side streams or waste. Seven of the 12 studies reported potential biological hazards and five studies reported potential chemical hazards.

Fourteen studies carried out an assessment of the environmental risks of producing novel food or feed from waste or side streams. The majority (n=12) of these studies investigated the environmental impact of rearing insects. One of these (12) studies investigated *M. domestica* larvae reared on food waste and rapeseed meal compared to traditional feed for

swine. The remaining studies investigated poultry by product (poultry fat, poultry by-product meal and steam hydrolysed feather meal) for animal feed and the rearing of the earthworm *E.fetida*.

A wide range of potential biological and chemical hazards, and hazards for the environment were reported in the 24 studies. No primary research studies reported physical hazards. The authors identified risks to human or animal health from biological hazards such as antibiotic resistance genes, mycotoxinogenic fungi and allergens (e.g. gluten) and chemical hazards such as pesticides, PCBs, dioxins and heavy metals. Of the 14 studies that investigated potential risks to the environment, 11 used life cycle assessment (LCA) methodology to determine environmental impacts. The majority of these investigated the production of insects reared on waste in comparison to conventional production systems for animal feed. The overarching conclusion from these studies was that the main environmental risk arises from the high energy requirement of the system and therefore an increase in global warming potential (GWP). Other risks to the environment identified in the studies were increases in emissions of carbon dioxide, methane, dinitrogen monoxide and ammonia.

Key findings from authors of reviews and reports about potential hazards and emerging risks was varied and included:

- Physical hazards: safety standards for producing feed from FFP in the EU means that the risk of contamination with packaging material is low.
- Edible insects: the risk of transmitting zoonotic infections to humans through edible insects appears to be low and the topic requires further investigation.
- Slaughterhouse by-products are a source of substrate that needs detailed safety investigation.
- The safety of thermally generated carbohydrate degradation products from biomass pretreatment should be investigated in relation to using yellow and green biomass biorefinery products in food or feed.
- Anaerobic digestion and post-treatment of agro-industrial wastes and wastewater can lower the risks associated with heavy metals and pathogens, but that it is unclear for certain persistent xenobiotics.
- Pre-treatments of side streams substrates for insects can potentially have both positive and negative effects on substrate microbial load and currently used preparation technologies has not been thoroughly investigated.
- There are many uncertainties and data gaps when considering chemical and microbiological risks associated with FFP such as the lack of epidemiological data on incidents and outbreaks of disease caused by the use of insect larvae as animal feed.

In addition to the 24 articles that were included at full text and the reviews and research projects, a further 1911 primary research articles were reviewed at abstract only. Of these there were 835 primary research articles that investigated the risks to animal production performance (e.g. growth, digestibility, development) from the direct feeding of waste, FFP and side streams to animals. The focus of these studies was predominantly farmed livestock. Many of these studies concluded that waste, FFP or side streams can only be fed to animals when combined with traditional feeds or with additives because these feeds alone do not provide the full nutritional requirements of the animal under investigation.

A further 172 articles originated from outside of Europe. These were mainly concerned with investigating the risk to animal production parameters. Again, a significant proportion of the literature related to the risks to animal production performance.

Sixty articles examined risks associated with insects used as feed or food but it was unclear if these insects had been reared on waste, FFP or side streams. These articles covered a wide range of risks of producing and consuming insects including: risk of allergy from consuming insects for food or feed (e.g. pet food) and risk of chemical or biological contamination of larvae via substrates.

Of all of the articles read at abstract only all conclusions are inferred only and have not been confirmed.

Conclusions

A large and growing volume of research and development is being carried out not only in Europe but on a global scale on novel food and feeds in relation to the CE framework. The key findings from this review suggest:

- The volume of research investigating emerging risks for animal, human, plant health and the environment is small, particularly when compared to the volume of research investigating the suitability of novel feeds in terms of productivity parameters.
- Primary research about risks is focused on insects as food or feed and the substrate that they are reared on. Primary research about the risks of other novel foods and feeds arising from the CE framework are limited.
- The focus of primary research is on biological and chemical hazards and risks to health, and environmental impacts. Potential physical hazards have been discussed in reviews.
- Emerging risks for animal and human health and environment regarding the production and consumption of invertebrates are strongly correlated to the type of rearing substrate. Specific hazards identified in primary research in this review include the presence of: (i) antibiotic resistance genes in substrates, larvae and insect frass (ii) high levels of the heavy metals cadmium and nickel in prepupae (iii) uptake of allergens from the substrate e.g. gluten
- Some studies reported that insect production when compared to conventional feed production has a higher global warming potential because of the energy intensive processing requirements and use of non-renewable energy resources.
- Many authors researching invertebrates reared on side streams in Europe reported that: although some biological and chemical contaminants that may pose a hazard to animal or human health or the environment are present in substrate, larvae or frass, they are at levels below European recommended safety limits for food or feed. This is perhaps unsurprising considering the current strict food and feed safety legislation in Europe. Authors also highlighted that pre-treatments (e.g. heat treatment, freeze drying) to deactivate biological hazards can reduce or eliminate some risks. Future emerging risks are likely to arise should there be changes in food and feed legislation resulting from a transition towards CE to allow substrates that are currently not authorised for rearing substrate (e.g. animal manure, catering waste, slaughterhouse products, FFP containing meat and fish).

- Topics for future primary research identified by authors of reviews include investigating: the safety of thermally generated carbohydrate degradation products from biomass pretreatment in relation to using yellow and green biomass biorefinery products in food or feed; the biological hazards associated with pre-treatments of side streams substrates for insects.
- Given the large amount of research and development occurring globally particularly regards novel feeds vigilance is needed for foods imported into the EU.

1.0 Background

Circular economy (CE) is an approach that decouples economic activity from the consumption of finite resources, designs out waste, opposes the take-make-consume-waste linear economic model and replaces it with an economic model based on sharing, leasing, reuse, repair, refurbishment and recycling, in an (almost) closed loop. Such change from a linear economy to a circular one is expected to significantly support the attainment of the United Nations Sustainable Development Goals (SDGs), particularly SDG 12 (Responsible consumption and production). However, the design and implementation of circular economy requires a careful consideration of the numerous trade-offs that may emerge. This is a pre-requisite for the attainment of the SDG 3 (Good health and well-being).

During the transition to a circular economy, it is crucial to identify potential emerging risks for the environment and for food and feed safety in a holistic and integrated fashion in order to achieve an optimal balance between opportunities, benefits and risks. It is necessary to ensure that food and feed safety and environmental health considerations are incorporated at an early stage of research or policy initiatives linked to recycling and the circular economy.

In the framework of enabling regulatory and policy drivers (e.g. Circular Economy Action Plan, Integrated Nutrient Management Plan, Farm to Fork strategy, new Water Reuse Regulation, the European Bioeconomy Strategy, Single Use Plastics Directive etc), EFSA is undertaking a 2-year project on "Food and feed safety vulnerabilities in circular economy".

One aspect of this project is to conduct a literature review to gather and evaluate the evidence for vulnerabilities in the circular economy approach for food/feed safety, plant, animal and human health and the environment. As a new driver, implementation of circular economy approaches might bring about a set of emerging risks, understood as risks resulting from a newly identified hazard to which significant exposure may occur, or from an unexpected new or increased significant exposure and/or susceptibility to a known hazard.

The literature review has three specific objectives:

Objective 1: to identify and categorise current and envisaged circular economy practices within all stages of the food and feed chain in Europe.

Objective 2: to identify emerging risks for plant, animal and human health and the environment from novel food and feed within the CE framework

Objective 3: to characterise the identified emerging risks from novel food and feed within the CE framework by providing the available information justifying the definition of emerging risk, relevant for EFSA's prioritisation and risk assessment activities.

Objective 1 is now complete. **This report documents the methodology and preliminary outcomes for Objective 2.**

Objective 1 was used to identify the topic area for Objective 2. Twenty-six CE practices were identified in Objective 1 and stakeholders were asked in an online survey to prioritise them in terms of: (1) importance to CE; (2) ease of implementation of practice; (3) likelihood of risk

from practice; (4) ease of overcoming risk; (5) current state of knowledge regarding risk from CE practice. The survey results indicated that current knowledge was considered particularly low for novel sources of food and feed and potential likelihood of risk was high. In consultation with EFSA, it was decided that this practice would be the focus of Objective 2.

2.0 Objective

To conduct an extensive literature search and monitoring on-going research projects to:

*'identify emerging risks for plant, animal and human health and the environment resulting from new hazards and new exposure pathways leading to increased exposure from novel foods and feeds of relevance to the circular economy'**

**The scope of the review, and definitions of criteria outlined in the objective are discussed in the following section.*

3.0 Scope of the review and definitions

This review aimed to capture literature about risk from novel foods and feeds that fit with the circular economy (CE) approach.

3.1 Circular economy

In recent years, the CE concept has gained significant momentum, but no singular definition of CE exists, and the concept has been widely reported to be interpreted differently by different societal actors, seeking to influence its meaning and understanding, resulting in a diversity of conflicting approaches (e.g. Kirchherr, Reike and Hekkert, 2017; Friant, Vermeulen and Salomone, 2021). CE is most frequently depicted as reducing waste to a minimum through a combination of reduce, reuse and recycle activities (e.g. Kirchherr, Reike and Hekkert, 2017).

The geographical focus of this review is Europe and therefore for the purposes of this review we have used the European Commission's definition of CE, which concurs with the most frequently used definitions of CE.

'where the value of products, materials and resources is maintained in the economy for as long as possible, and the generation of waste minimised' (EC, 2015).

In March 2020, the European Commission adopted the new circular economy action plan (EC, 2020). This action plan is one of the main building blocks of the European Green Deal, Europe's new agenda for sustainable growth. The aim of the EU's transition to a circular economy is to reduce pressure on natural resources and create sustainable growth and jobs. It is also fundamental to achieving the EU's 2050 climate neutrality target and halting biodiversity loss.

Transition to the circular economy is also a prerequisite to the EU's is commitment to achieving the global Sustainable Development Goal Target 12.3 to halve per capita food waste at the retail and consumer level by 2030, and reduce food losses along the food production and supply chains. To accelerate the EU's progress, the Commission will propose legally

binding targets for food waste reduction by 2023, as called for by the Farm to Fork Strategy (EC, 2020). Innovative strategies for food within the CE framework will contribute to reaching this target.

The scope of the review focuses on using waste, former food products (FFP), and side streams (by-products and co-products) as a resource to develop novel foods and feeds, so contributing to CE.

3.2 Novel foods and feeds

Novel foods for humans are defined in EU regulations as: 'any food that was not consumed "significantly" in the EU prior to May 15 1997 (Regulation (EU) 2015/2283)'. 'Novel Food' can be newly developed, innovative food, food produced using new technologies and production processes, as well as food which is or has been traditionally eaten outside of the EU.

To our knowledge 'novel feed' for animals has yet to be defined in EU regulation. For the purposes of this review we consider 'novel feeds' to be new sources of feed from the food industries, biofuel industries and industrial processes and new types of ingredients such as processed animal proteins (PAPs) derived from farmed insects, marine resources and aquatic plants (FAO/WHO 2019). In addition to 'novel' sources of PAPs, we have also considered the EU's re-introduction (in August, 2021) of the use of PAPs from poultry for pigs and the use of PAPs from pigs for poultry, that was previously banned in 2001 in the wake of the bovine spongiform encephalopathy crisis (Boffey, 2021; EC, 2021). The drivers for re-introduction of these previously banned specific PAPs includes: the growing demand for protein sources, and their potentially valuable contribution to creating a CE, the European Green Deal and farming's net zero goals for greenhouse gas emissions (Driver, 2021). Although these previously banned PAPs may not technically be classed as 'novel' feed because historically they have been fed to animals, there is concern about the health risks of their re-introduction (e.g. Moran, 2021) and the ban will not, for example, be lifted in the United Kingdom (Boffey, 2021). For this reason, we have decided to include these previously banned PAPs (from poultry for pigs and from pigs for poultry) in the review.

European Commission regulations (EC 999/2001; EC 1774/2002; EC 767/2009) prohibits the use of some materials for animal feed for example, wastes including faeces, and catering and household waste. This review considered the inclusion of studies that investigated these prohibited materials as feeds within the CE framework. The rationale for including these studies is that there may be changes in regulation in the future in the transition to CE in Europe.

Whilst EU regulation for novel food is specific to food only, we have taken a broader approach and also include for example, food (and feed) additives and flavourings that aim to minimise waste and contribute towards CE.

Examples of novel foods and feeds that fit with the CE approach to reduce waste include: different types of biorefineries that aim to reduce waste by using processing of various biomass streams to create novel food and feed (e.g. Lange and Meyer, 2019); alternative primary production of sources of animal protein such as insects reared on bio-waste substrate

(e.g. EEA 2020, SAPEA 2020). Novel foods and feeds that are not related to minimising waste but that have wider sustainability benefits were not included e.g. foods grown in laboratories (and not using waste, former food stuffs or side streams as a substrate) that aim to reduce carbon footprint associated with conventional farming practices.

The review considers novel foods and feeds arising from waste, FFP and side streams (i.e.by-product and co-products) from all stages of food/feed production and supply chains (Figure 1.)

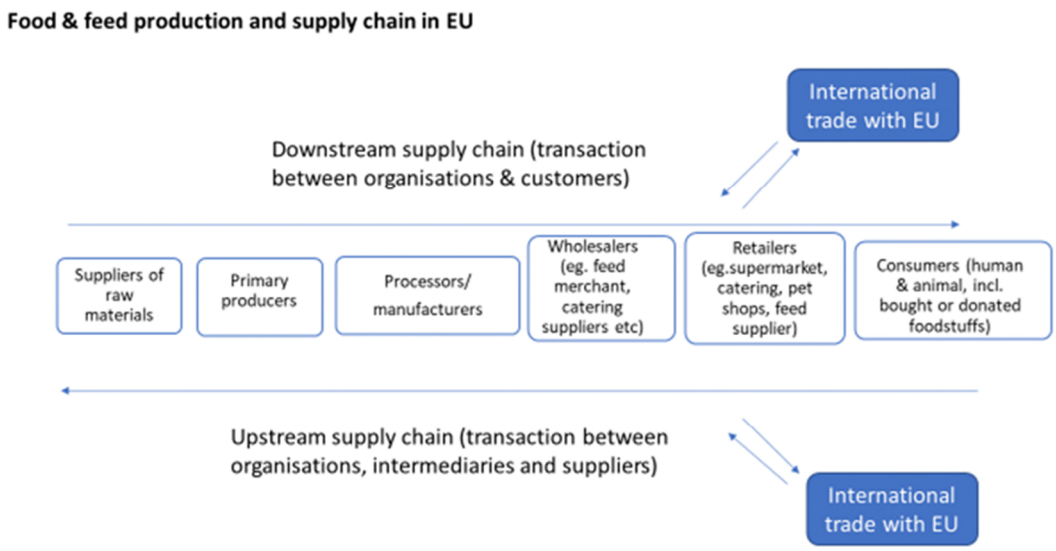

Figure 1. Food and feed production and supply chains from which novel foods and feeds may arise

3.3 Population at risk

The review considers emerging risks from novel foods and feeds to *plant, animal and human health and the environment.* In the context of this review, 'animal' refers to farmed animals (food producing and non-food producing animals) and companion animals (including working or service animals). Wild plants and animals are considered to be part of the environment. All animal species have been considered (including vertebrates and invertebrates). Non-wild plants are considered to be crops.

The environment is defined as the 'natural environment' and it encompasses all living (i.e. wild -animals, plants, algae and fungi) organisms and non-living natural resources (i.e. soil, air and water).

3.4 Emerging risks

Included are all emerging risks, resulting from biological (e.g. microbial), chemical (e.g. heavy metals) and physical (e.g. glass, plastic fragments) hazards, to plant, animal and human health and the environment.

Emerging risks are defined by EFSA as "a risk resulting from a newly identified *hazard* to which a significant *exposure* may occur, or from an unexpected new or increased significant exposure and/or susceptibility to a known hazard." (EFSA, undated https://www.efsa.europa.eu/en/topics/topic/emerging-risks)

We include risks arising both in the production/manufacture (e.g. environmental pollution arising from primary or secondary production) and consumption of novel foods and feeds.

4.0 Method

The literature search strategy and selection criteria (inclusion/exclusion) follow EFSA Systematic Review Guidance (EFSA, 2010).

4.1 Primary question

'What are the emerging risks for plant, animal and human health and the environment resulting from new hazards and new exposure pathways leading to increased exposure, from novel food and feeds of relevance to circular economy?'

Table 1. shows the population (P), exposure (E), comparator (C) and outcome (O) key elements (PECO) of the primary question. *The definitions for the components of the key elements are provided in the section above 'scope of the review and definitions'*

Table 1. Components of the PECO key elements

Key element	**Description**
Population	Humans, plants, animals and environment
Exposure	Novel food and feeds of relevance to CE and originating from food/feed production and supply chains
Comparator	Use of novel foods and feeds compared to their counterparts used currently or no comparator
Outcome	Emerging risks (resulting from biological, chemical, physical hazards) for plant, animal and human health and the environment resulting from production or consumption of novel foods and feeds

4.2 Inclusion criteria

Inclusion criteria (what a study must contain to be included in the review) were formulated based on the PECO elements of the primary question. Please refer to the 'scope of the review and definitions' for specific detail.

4.2.1 Populations at risk

Humans, animals, plants and the environment as defined in the 'scope of the review and definitions' section.

4.2.2 Exposure route

Novel foods and feeds (as defined in the scope of the review) arising from all stages of food/feed production and supply chains (as defined in the scope of the review) so long as they fit into the CE approach to minimise waste.

We considered emerging risks arising both in the production (e.g. environmental pollution arising from primary or secondary production) and consumption of novel foods and feeds.

4.2.3 Study comparators

Use of novel foods and feeds compared to their counterparts used currently or no comparator.

4.2.4 Study outcomes

Any biological (e.g. microbes, mycotoxins, allergens, antibiotic resistance genes) chemical (e.g. heavy metals, dioxins, pesticides, pharmaceuticals) and physical (e.g. plastic, card, glass packaging) hazards that constitute emerging risks for plant, animal and human health and the environment originating from production or consumption of novel foods and feeds.

Primary research studies about the risk of animal feeds derived from waste, FFP, and side streams on biological animal production parameters (e.g. live weight, digestibility of product, organ development) were excluded where the authors reported **no risk if the product was included in the diet within the recommendations of the study findings**. These studies have been categorised and saved in the systematic reviewing software should they be of future interest. However, during the screening of these articles at title and abstract some potentially useful trends in the evidence were noted.

Primary research studies about invertebrates and potential risk for plant, animal, human health and the environment **but where there was no clear relationship to the CE framework** were excluded. Again, these studies were categorised and saved in the systematic reviewing software should they be of future interest but some trends in the evidence were noted during the screening out of these articles.

4.2.5 Study designs

Primary research and reviews and on-going research projects were captured. Reviews were categorised separately and screened for relevant articles to ensure that these have not been missed in searches for literature. Useful inferences made by the authors of reviews about hazards and emerging risks were noted.

Books, Book chapters and MSc theses were excluded from the review.

Study designs were highly heterogenous and it is difficult to carry out any formal critical appraisal of studies. However, we extracted study design quality indicators (e.g. use of

control, replication, randomisation) to provide an indication of the reliability of the evidence base.

4.2.6 Geographical limitations for inclusion of evidence

Primary studies, reviews and on-going research projects from Europe were included.

Studies, reviews and projects from outside Europe were excluded from the review but have been categorised separately and saved in the systematic reviewing software, should they be of future interest.

4.2.7 Date restrictions

Literature was included from 1997 onwards following the European Union regulation for novel food May 15 1997 (Regulation (EU) 2015/2283).

4.2.8 Languages

Only literature in English language was searched for and included due to limited resources for translating non-English language texts.

4.3 Search string development

Scoping searches were conducted to test the specificity and sensitivity of keywords relevant to the scope of the review, to develop the search string that was used to search for literature in bibliographic databases (and where appropriate other online sources of literature). The scoping searches showed that inclusion of outcome terms (e.g. risk, hazard, safety, exposure etc) reduced the number of results returned significantly as expected. However, there were concerns that unless the outcome terms are comprehensive relevant literature may be missed and therefore the decision was made not to include them.

The search string below was used to collate relevant evidence. Exposure (blue) keywords, qualifiers (green) and limiters (orange) were used to ensure relevance to food and feed and prevent the capture of irrelevant literature (e.g. experiments about how animals behave towards novel feed, people's attitudes towards novel food). The search string was applied to title and abstract in bibliographic database searches for literature.

"lab-grown meat" OR "test tube meat" OR "artificial meat*" OR "cultured meat*" OR "in vitro meat*" OR "synthetic meat*" OR "novel food*" OR "novel feed*" OR "alternative food*" OR "alternative feed*" OR "edible insect*" OR "insect food*" OR "insects as food" OR "insect feed*" OR "alternative protein*" OR "cell-based meat*" OR "insect protein*" OR "novel plant protein*" OR "cell-based protein*" OR "innovative food*" OR "innovative feed*" OR "sustainable protein*" OR "recycled protein*" OR "novel by-product*" OR "agri-food side stream*" OR "processed animal protein*" OR "mycoprotein*" OR upcycle* OR "new dietary ingredient*" OR "former food*" AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR "*nutrient*" NOT psychology OR accept* OR attitud* OR behav*

Note: *Following searches for literature using the search string above, it was decided with the EFSA team that cultured meats (i.e. "lab-grown meat", "test tube meat", "artificial meat*", "cultured meat*", "in vitro meat*", "synthetic meat*") would not be included in the review. This is because the production of these meats is not related to minimising waste but instead may have wider sustainability benefits compared to conventional farming. These articles picked up by the search string above were subsequently screen out at the title and abstract screening stage and not included in the review.*

The scoping searches showed that it was not possible to include some keywords for specific novel foods or feeds or sources of novel foods and feeds, without returning very large volumes of evidence. Given the time and resources allocated to this project it was not feasible to screen all these additional articles for relevance. We therefore developed shorter limited search strings for these specific keywords, applied at title only in bibliographic database searches. The shorter search strings to be used are shown below:

- “by-catch” AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR nutrient*
- algae AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR nutrient*
- “aquatic plant*” OR “aquatic protist*” AND Food* OR Feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR nutrient*
  algae OR microalgae OR macroalgae OR seaweed AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR nutrient*
- biorefiner* OR bioprocess OR biowaste* OR "by-product*" and "novel food*" OR "novel feed*" OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR *nutrient*
- biofuel OR biodiesel OR bioethanol AND "co-product*" AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR "*nutrient*"

4.4 Searching for literature

A comprehensive search to capture an un-biased sample of published and grey literature was undertaken using multiple information sources including: bibliographic databases, websites of relevant organisations and research funding platforms. Table 2 documents which sources were searched.

The searches endeavoured to be as thorough as possible within the timescale of this project. The search string was adapted to the syntax of each source searched and a record of each search was made: date the search was conducted; database name; search term; number of hits; and notes. Database and repository searches were conducted in the English language.

Any publications provided by team experts and the wider stakeholder network was considered for inclusion.

Some relevant literature for this review was collated from a previous review conducted by our review team for EFSA 'The current degree of uptake of circular economy within all stages of food/feed production chains in Europe'. This literature was added to this review.

Historical and ongoing research project pages (Horizon 2020, SUSFOOD, UKRI) were also searched for relevant literature.

Table 2. Sources searched for published and grey literature and on-going research projects

Bibliographic databases	Pubmed
	Web of Science – including Web of Science TM Core collection
	Scopus
	DART E-Thesis
	EBSCO (including: CAB Abstracts, Food Science Source, GreenFILE, Business Source Complete, eBook Collection (EBSCOhost), Harper Adams Library Catalogue, Regional Business News, Teacher Reference Center, Library, Information Science & Technology Abstracts)
Organisation Websites	Food Navigator https://www.foodnavigator.com/ SAPEA
	Fédération Européenne des Fabricants d'Adjuvants pour la Nutrition Animal
	World Health Organisation
	Food and Agriculture Organisation of the United Nations
	International Platform of Insects for Food and Feed
	PROteINSECT https://www.proteinsect.eu/
	European Feed Manufacturer's Federation
	Joint Research Centre EU Science Hub
	Pet Food Manufacturers Association
	Nordic Council of Ministers
	Susinchain - Sustainable Insect Chain
	Luonnonvarakeskus
	National Institute for Public Health and the Environment Ministry of Health Welfare and Sport Netherlands
	Netherlands Food and Consumer Product Safety Authority. Ministry of Agriculture, Nature and Food Quality
	Health and Environment Alliance
	Department for Environment Food and Rural Affairs
	EFSA
	PBL Netherlands Environmental Assessment Agency
	Joint Research Centre Publication Repository
	United Nations Environment Programme
	European Centre for Disease Prevention and Control
	EC Europa
	EFFPA (European Former Foodstuff Processors Association)
	Ellen MacArthur Foundation
	ETP food for life
	EU Platform on Food Losses and Food Waste
	Interreg Europe
	OECD i Library

	The European Aquaculture Technology and Innovation Platform
	Waseabi
Research funding platforms	Horizon 2020
	SUSFOOD
	UKRI

Further details of the searches and databases used for the grey literature searches is included in Appendix I.

4.5 Screening literature for inclusion in the review

Articles retrieved from grey literature searches (i.e. from organisational web site searches and research funding platforms) were screened on a case by case basis for inclusion during the searching of websites (a summary of the number of articles retrieved in grey literature searches and where the articles were sourced from is provided in Appendix II).

All articles retrieved from the bibliographic database searches (see list of databases in Table 2), were first collated in a reference management program (EndNote™) and duplicate articles removed using the automated duplicate removal function. The remaining articles, following duplicate removal, were exported from EndNote™ into EPPI-Reviewer4 a specialised systematic reviewing software. A second round of duplicate removal was conducted using EPPI-Reviewer4 automated duplicate removal function.

A total of 51,235 articles were retrieved in the bibliographic database searches. Following duplicate removal using EndNote™ and EPPI-Reviewer4, a total of 26,669 articles remained for screening on title and abstract (a summary of the number of articles retrieved from each bibliographic database and the total number of duplicates removed using reviewing software is provided in Appendix II).

In order to reduce the burden of screening, due to time constraints, of the articles retrieved from the bibliographic database search, DistillerSR Artificial Intelligence (AI) algorithm was used to automatise the identification of relevant documents.

4.5.1 Training the DistillerSR AI algorithm

A set of 1334 articles (5%) of the total corpus (26,669 articles) was randomly selected for manual screening at title and abstract against pre-defined inclusion criteria by two independent reviewers. A Cohens Kappa result of 0.58 indicated moderate agreement (Landis and Koch, 1973) between reviewers in screening at title and abstract of this 5%. After resolving possible conflict between reviewers' judgment, the human labelled set was used to train DistillerSR AI screening (a SVM classifier). DistillerAI was trained using a percentage (80%) of manually reviewed references and then the trained algorithm was applied to unreviewed references to automatically determine if references should be included or excluded, providing a measure of the probability of relevance. The remaining 20% of manually screened articles was used to calculate performance measures of DistillerAI, namely accuracy (number of all correct predictions divided by the total number of references),

sensitivity/recall (the number of correct positive predictions divided by the total number of relevant references) and specificity (number of correct negative predictions divided by the total number of irrelevant references). Those measures were calculated for different values of threshold, the cut-off value of predicted probability of relevance. When setting the threshold, there is a trade-off between recall and specificity, that is the ability of the classifier to identify all the relevant papers and the ability to identify irrelevant paper. Setting a threshold with low value, leads to inclusion of many irrelevant articles (high false positive) with consequent low value of specificity, but leads to inclusion of many relevant articles with consequent high value of sensitivity. Setting a threshold with high value, leads to exclusion of many irrelevant articles but also the potential exclusion of relevant articles, with consequent low value of sensitivity and high value of specificity.

To benefit from the workload reduction property of active learning, an additional 5% of the 26,669 articles, ranked according to predicted relevance, were again manually screened by the two independent reviewers. DistillerAI was trained again using (80%) of total manually reviewed references and performance measures were re-calculated on the remaining 20% (Fig.2). A value of threshold equal to 0.3 was selected, corresponding to sensitivity of 87% and specificity of 62%. The estimated percentage of relevant articles missed with the selected threshold is 13%.

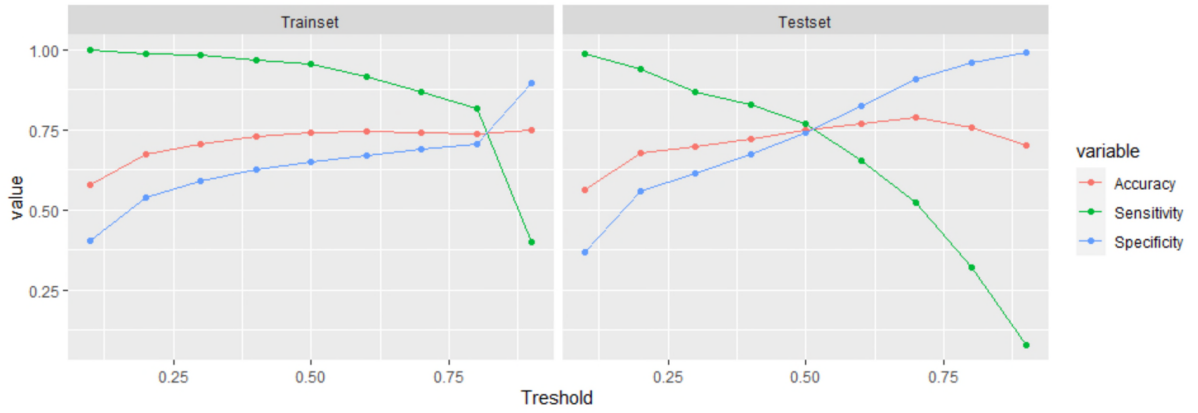

Figure 2 Performance measures of trained classifier for training set and test set, based on 10% manually screened articles, (5% random selection and 5% active learning)

4.5.2 Screening the literature selected by the DistillerSR AI algorithm

Using the threshold of 0.3 two independent reviewers screened the 1,457 articles considered by the AI to be of relevance. Following screening of these articles using a threshold of 0.3, it was decided that to benefit again from the AI an additional 603 articles would be screened at title and abstract using the threshold of 0.5. A threshold of 0.5 was used this time due to time constraints to screen literature, as the threshold of 0.5 returned fewer articles.

Articles included following title and abstract screening stage were then screened against pre-defined inclusion criteria at full text.

4.6 Preliminary meta-data extraction

4.6.1 Primary research

The following meta-data were extracted from primary research studies: full reference; study type; food or feed type; relationship of food or feed to CE framework; population at risk; hazard type (biological, chemical, physical); study design; study endpoints measured; authors conclusions. This information was used to create summaries of the included studies and draw preliminary conclusions about the results.

4.6.2 Other evidence

Useful author and reviewer inferences from primary research not within the scope of the review and reviews screened for primary research were noted and discussed separately. No meta-data was extracted from these sources.

5.0 Results and discussion

5.1 Articles included and excluded from the review

A total of 24 primary research articles were included for meta-data extraction at full text to inform the review. The main findings of these 24 studies have been summarised and key findings and concluding remarks drawn.

Twenty-eight reviews/reports and one PhD thesis (listed in Appendix III) were found in the searches of: (i) bibliographic databases; (ii) grey literature searches (including searching websites of relevant Horizon 2020, SUSFOOD and UKRI funded research projects (see Appendix IV for list of projects searched) and literature captured in our previous review for EFSA ('The current degree of uptake of circular economy within all stages of food/feed production chains in Europe'). .

Screening of these reviews/reports and thesis, identified an additional 4 primary research articles. These additional articles are included in the total of 24 articles cited above. Useful inferences from the authors of the reviews and reports about potential hazards and emerging risks are presented and discussed in the section '***Inferences from authors of reviews and reports about potential hazards and emerging risks'.***

A total of 835 primary research articles investigated the risks to animal production performance (e.g. growth, digestibility, development) from the direct feeding of waste, FFP and side streams to animals. It was often difficult to decipher what country the study originated from by only reading the abstracts, therefore this category may include articles that are outside of geographical Europe.

A further 172 articles originated from outside of Europe were found, which were mainly concerned with investigating the risk to animal production parameters. Sixty articles examined risks associated with insects used as feed or food but it was unclear if these insects had been reared on waste, FFP or side streams.

As mentioned in the methods section, these articles (animal performance, studies outside of Europe and non-CE insect studies) were not examined at full text and were not used to formulate conclusions for this review. These studies have been categorised and saved in the systematic reviewing software should they be of future interest. However, during the screening of these articles at title and abstract some trends in the evidence were noted and these are presented in the section '***General trends and reviewer inferences from literature excluded from the review'.***

A flow diagram of the processes involved in the capture and screening of literature and the number of articles included and excluded at each stage is shown in Figure 3.

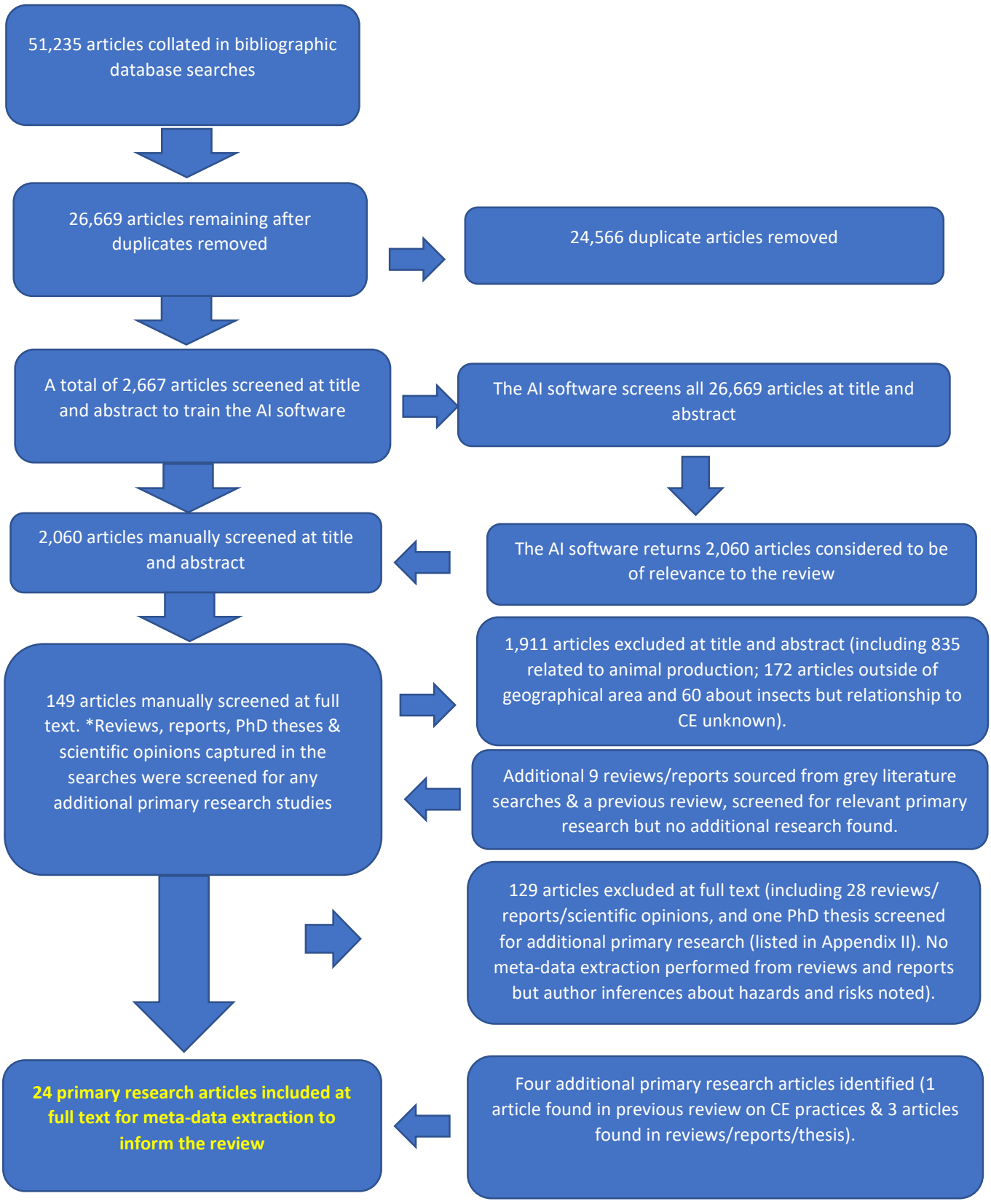

Figure 3. A flow diagram of the processes involved in the capture and screening of literature and the number of articles included and excluded at each stage

5.2 Evidence from the 24 primary research articles

A total of 24 primary research articles were identified that investigated potential risks for animals, human health or the environment, of novel food or feed arising from waste or side streams (a list of all 24 references are provided in Appendix V). The earliest study was published in 2014 and the latest in 2021 (Figure 4.). With the exception of two conference publication all other studies were published in peer-reviewed journals.

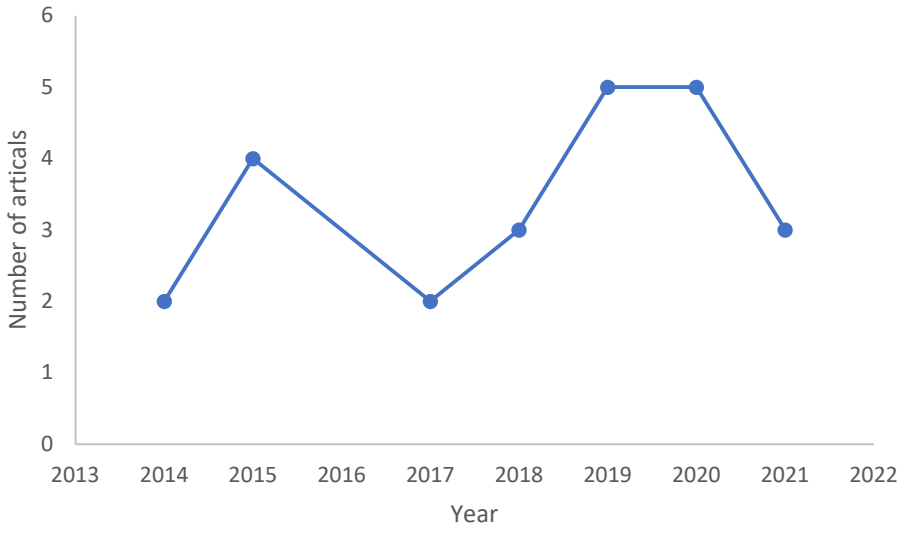

Figure 4. Number of articles published per year investigating the risk for the environment or animals or human health of novel food or feed arising from waste or side streams (i.e. by-product and co-products).

5.2.1 Overview of food and feed investigated in the 24 primary research studies

Nearly all of the studies (n=23) investigated the rearing of invertebrates for food or feed on substrate arising from waste or side streams: (*Hermetia illucens* (black soldier fly) n=11; *Musca domestica* (house fly) n= 5; *Tenebrio molitor* (yellow mealworm) n=3; *Eisenia fetida* (earthworm) n=3; *Alphitobius diaperinus* (lesser mealworm) n=1; *Calliphora vomitoria* (bluebottle fly) n=1). One of these (23) studies investigated both *M. domestica* larvae reared on waste and rapeseed meal compared to traditional soybean meal feed for swine. The remaining study investigated poultry by product (poultry fat, poultry by-product meal and steam hydrolysed feather meal) for animal feed. No studies were found to investigate FFP for feed.

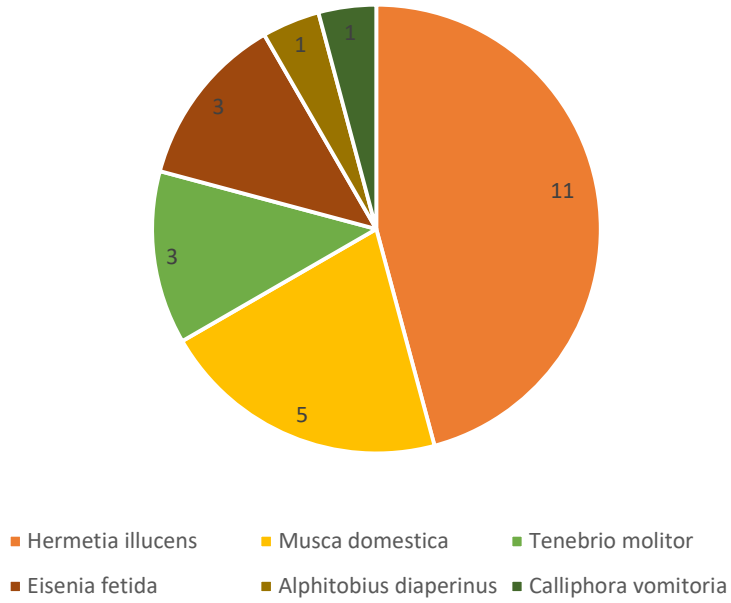

Figure 5. Number of studies investigating different invertebrate species for food or feed reared on substrate arising from waste or side streams

No studies were found that investigated the risk of novel foods stemming from side streams or waste that are fed directly to humans (i.e. not indirect consumption for example food insects fed on waste).

Table 3 summarises the waste or side stream (i.e. by-product and co-products) investigated and the animal it was fed to. The studies are labelled 1-24 and the corresponding study reference is provided as a footnote at the bottom of the table.

Table 3. Waste or side stream investigated in the 24 included primary research studies and the animal it was fed to. The corresponding study reference is provided as a footnote at the bottom of the table for studies labelled 1-24.

Substrate/Animal fed	***Hermetia illuncens***	***Calliphora vomitoria***	***Eisenia fetida***	**Generic animal feed**	***Musca domestica***	***Alphitobius diaperinus***	**Pig**	***Tenebrio molitor***
Cereal by-product	14							
Cereal flours (wheat, maize),								8
Coffee silverskin (roasting by-product)	18,19							
Distillers' grain	6,9,11,22							
Feather meal				15				
Fish feed waste					11			
Food waste	6,13				5, 7, 3			
Fruit waste	6		1, 4					
Maize distiller	9							
Manure - bovine	6,12,21							
Manure - porcine	6,21				11			
Manure - poultry	6,21				5,7,11,23			
Municipal organic waste	6							
Olive-pomace								16
Pig offal		11						
Poultry by-product				15				
Rapeseed meal							3	8
Soybean by-product	6,9							8
Sugar beet by-product	6							
Sunflower meal								8
Unknown side stream						17		

Vegetable waste	2,6		1, 4, 24					
***M. domestica* larval meal fed on food waste**							3	
Wheat bran								8
Wheat flour								16
Wheat meal								16
Wheat middlings	6,10							

1. Tedesco *et al.* (2020), 2. Boccazzi *et al.* (2017), 3. van Zanten *et al.* (2018), 4. Tedesco *et al.* (2019), 5. van Zanten *et al.* (2014), 6. Bosch *et al.* (2019), 7. van Zanten *et al.* (2015), 8. Thévenot *et al.* (2018), 9. Bava *et al.* (2019), 10. Tschirner and Simon (2015), 11. Charlton *et al.* (2015), 12. Parodi *et al.* (2021), 13. Salomone *et al.* (2017), 14. Maiolo *et al.* (2020), 15. Campos *et al.* (2020), 16. Truzzi *et al.* (2019), 17. Wynants *et al.* (2018), 18. Truzzi *et al.* (2020), 19. Milanović *et al.* (2021), 20. Osimani *et al.* (2021), 21. Oonincx *et al.* (2015), 22. Mancinia *et al.* (2020), 23. Nordentoft *et al.* (2014), 24. Conti et al. (2019)

5.2.2 Overview of hazards and risks investigated in the 24 primary research studies

Twelve studies were about risks to human or animal health. All of these studies investigated the risks of consuming invertebrates reared on side streams or waste. Seven studies reported potential biological hazards (Varotto Boccazzi et al., 2017; Wynants et al., 2018; Conti et al., 2019; Tedesco et al., 2019; Mancinia et al., 2020; Milanović et al., 2021; Osimani et al., 2021) and five studies reported potential chemical hazards (Nordentoft et al., 2014; Charlton et al., 2015; Tschirner and Simon, 2015; Truzzi et al., 2019; Truzzi et al., 2020).

Fourteen studies carried out an assessment of the environmental risks of producing food or feed from waste or side streams. The majority (n=12) of these studies investigated the environmental impacts of rearing insects (van Zanten et al., 2014; Oonincx et al., 2015; van Zanten et al., 2015; Salomone et al., 2017; Thévenot et al., 2018; van Zanten et al., 2018; Bava et al., 2019; Bosch et al., 2019; Maiolo et al., 2020; Milanović et al., 2021; Osimani et al., 2021; Parodi et al., 2021). One of these (12) studies investigated both *M. domestica* larvae reared on food waste and rapeseed meal compared to a traditional feed for swine (van Zanten et al., 2018). The remaining studies investigated poultry by product (poultry fat, poultry by-product meal and steam hydrolysed feather meal) for animal feed (Campos et al., 2020) and the rearing of the earthworm *E.fetida* (Tedesco et al., 2019).

A wide range of potential biological and chemical hazards, and hazards for the environment were reported in the 24 studies as illustrated in Figure 6. No primary research studies reported physical hazards (e.g. glass, plastic, cardboard packaging remnants in feed).

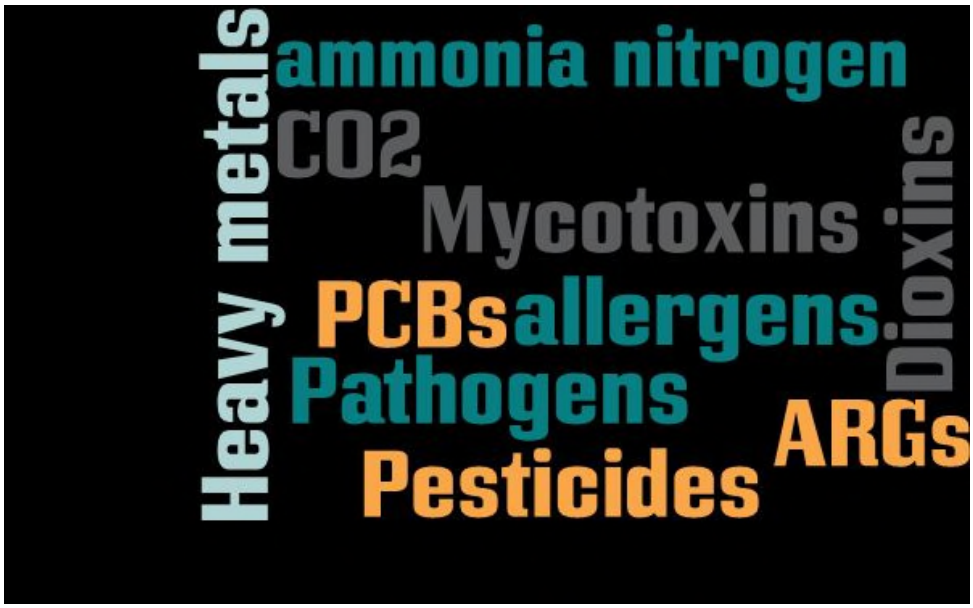

Figure 6. Examples of biological and chemical hazards and hazards for the environment reported in the 24 primary research studies (antibiotic resistance genes (ARGs); carbon dioxide (CO_2); polychlorinated biphenyls (PCBs))

5.2.3 Risks to human or animal health

Food product: T. molitor reared on brewers spent grain.
Biological hazard: Allergen - gluten

Mancinia et al. (2020), investigated whether *T. molitor* larvae reared on brewers spent grain (and other substrates containing gluten) contain gluten. Gluten was detected in the larvae. Washing and fasting decreased the quantity of gluten, with the authors concluding that gluten was present on the surface of the mealworms and in their gut. Washing and fasting the larvae resulted in a gluten content below 20 ppm (the level for gluten free products in the EU). However, the authors cautioned that the final risk of contamination is not zero, and testing of mealworms for the presence of gluten is advised.

Feed product: H. illucens reared on dried distillers' grains with solubles, dried sugar beet pulp or middlings
Chemical hazard: heavy metals

Tschirner and Simon (2015) fed *H. illucens* larvae destined for animal feed on middlings (control group), dried distillers' grains with solubles (protein group), and dried sugar beet pulp (fibre group). The authors looked for the presence of heavy metals and reported considerable accumulation of Pb and Cd in the larvae from the substrates (including the control) but only larvae fed on dried sugar beet pulp had a Cd content (2.24mg/kg recorded in larvae) that exceeded the EC limit for Cd by 12% (Directive 2002/32/EG (EC, 2002) the maximum levels for Cd 2 mg/kg). Larval survival and yield was also lower on the two experimental substrates compared to the control

Food product: A. diaperinus reared on vegetables and unknown side stream source
Biological hazard: Mycotoxinogenic fungi, opportunistic pathogenic yeasts

Wynants et al. (2018), studied the microbial dynamics during production of *A. diaperinus* for human consumption at industrial scale. Mealworms were reared on dry feed (standard lesser mealworm feed) based on vegetable raw materials which are suitable and allowed for animal feed, and a moist product based on a side stream from food industry, also allowed for animal feed. Fusarium spp. were found in the substrates and *Aspergillus flavus* was detected in the larvae and substrate. These are mycotoxinogenic species. The study also recorded the presence of *Trichosporon asahi* in the larvae and *Diutina rugosa* and *Issatchenkia orientalis* in both the larvae and substrate. These are opportunistic pathogenic yeasts that are known causes of candidemia or trichosporonosis. The authors reported that generally, health hazards due to these species only apply to immunocompromised patients.

A blanching treatment significantly reduced all bacterial counts, but a bacterial spore count of 4.0 log cfu/g remained. The authors concluded that future research is needed on possible hazards caused by the remaining bacterial spores, as well as on the possible presence of mycotoxins.

Food product: T. molitor reared on olive pomace
Chemical hazard: heavy metals

Truzzi et al. (2019) investigated the presence of the heavy metals, cadmium (Cd), lead (Pb), nickel (Ni), arsenic (As) and mercury (Hg) in larvae of *T. molitor* fed on olive pomace and the

risk for human consumption. The authors reported that although toxic metals were present in the substrate they were below the legal limit of undesirable substances in animal feed (2002/32/EC). Toxic metals were also present in the larvae and a statistically significant correlation between metal content in feeding substrates and in larvae was evidenced for Hg, which bioaccumulates. Overall, the authors concluded that the risk of exposure to metals from consumption of the mealworm larvae is relatively low and in compliance with European Union regulations. This study however exemplifies that Hg can accumulate in larvae and that heavy metal accumulation is related to the substrate they are reared on.

Feed product: M. domestica reared on poultry manure and C. vomitoria reared on pig offal
Chemical hazards found: pesticides, PCBs, dioxins, heavy metals

Nordentoft et al. (2014) examined the accumulation of dioxins and polychlorinated biphenyls (PCBs) in *M. domestica* reared on poultry manure and used as feed for organic laying hens, compared to hens fed on conventional compound feed. Samples of fly larvae, poultry manure, compost and compound feed as well as egg samples were analysed for dioxin and PCB contamination.

The authors found that the larvae had a content of dioxins plus dioxin-like PCB four times higher than the poultry manure, suggesting accumulation in the larvae from the rearing substrate. However, the authors concluded that although the levels of dioxins and PCB in the larvae were four times the levels in the compound feed, the added exposure of the hens when feed with 15g larvae per day constitute only a minor amount compared to the exposure from the compound feed alone. No difference was found between the content of dioxins and dioxin-like PCB in the eggs from layers receiving larvae in the feed compared to chickens fed the conventional feed. Whilst this study indicates that the hazard of dioxins and PCB accumulation in eggs is no greater than conventional feed, it does illustrate that larvae are able to accumulate these chemicals.

Charlton et al. (2015) explored the chemical safety of *M. domestica* reared on manure and *C. vomitoria* reared on pig offal (in the UK) as a source of protein for animal feed (this study also carried out experiments with other insect species and substrates in Africa and China but the results are not reported here). The authors examined the presence of veterinary pharmaceuticals, pesticides, heavy metals, dioxins, polychlorinated biphenyls and polyaromatic hydrocarbons (PAHs) and mycotoxins in the larvae.

Cd in *M. domestica* samples (723 µg/kg) was above the legal EU limit for cadmium in animal feed (500 µg/kg) specified in directive 2002/32/EC (EC, 2002). PAHs were also present in both larvae but a value was not provided by the author.

Piperonyl butoxide an insecticide synergist was found in *C. vomitoria* (200 µg/kg). The authors reported that this chemical does not have a widely adopted recommended maximum concentration, but Codex advise that pea fodder should contain less than 2,000 µg/kg (Codex Alimentarius, 2014), suggesting that there is unlikely to be a significant safety concern. The pesticide Chlorpyrifos was found in *M. domestica* larvae (at a level thought by the authors to be safe) but since this study was published, this pesticide has now been banned in the EU.

Food or feed product: H. illucens or E. fetida reared on fruit and vegetable waste
Biological hazards: Opportunistic pathogenic yeasts, pathogenic bacteria

Varotto Boccazzi et al. (2017), studied the fungal microbiota of *H. illucens* reared on vegetable waste for animal feed and the potential risks for food and feed safety. As Wynants et al. (2018) reported for *A. diaperinus*, *T. asahii* was also detected in this study in black soldier fly larvae. Varotto Boccazzi et al (2017) suggested that further investigations should be conducted to characterize this opportunistic yeast and its presence in insect-based feed or food. As Tedesco et al. (2019) highlighted, Varotto Boccazzi et al. (2017) also cautioned that the thermal treatments of insects as well as the choice of substrate have a great impact on the occurrence and levels of biological contaminants, and the type of thermal treatment is important because not all treatments are effective for complete inactivation of microorganisms and their toxins.

Conti et al. (2019) investigated the microbial food safety of fresh, drying at 50^0C or freeze dried *E. fetida* reared on fruit and vegetable waste. *Salmonella* spp. and *Listeria monocytogenes* were absent from the substrate and fresh, heat dried and freeze dried worms. Fresh earthworm microbial contamination was considered acceptable for all parameters except for *Enterobacteriaceae* when compared to Center for Research and Documentation on Food Safety for minced meat (CeIRSA). Heat drying and freeze drying resulted in a reduction of all microbial parameters considered by CeIRSA, and were comparable to satisfying category reported for minced meat. The authors highlighted the importance of a heat drying or freeze-drying step in earthworm production for food to reduce microbial contamination to a level safe for food.

Tedesco et al. (2019) studied the risk of biological (bacteria, mycotoxins) and chemical (pesticides, heavy metals, antibiotic residues, volatile organic compounds (VOCs)) contamination of *E. fetida* fed on fruit and vegetable waste from processing industries. The authors also investigated mitigating the risk of bacterial contamination through freeze drying and sterilisation (steam autoclave) of the larvae. Mesophilic aerobic bacteria, Enterobacteriaceae, *Bacillus cereus*, sulphite reducing clostridia and spores of sulphite reducing clostridia were found in fresh, freeze dried and sterilised worms. Overall, bacterial contamination was highest in fresh worms followed by freeze dried worms and all bacteria were <1 Log CFU/g for the sterilised worms. Specifically, *Escherichia coli* and coagulase-positive staphylococci were found in fresh, freeze dried and sterilised samples but at <1 Log CFU/g so were considered safe. The authors reported that whilst freeze drying reduced *B. cereus*, sulphite reducing clostridia and spores of reducing clostridia only sterilisation reduced risk completely. *Salmonella* spp. and *Listeria monocytogenes* were not present in any of the samples taken. This study highlights the industrial processes required to produce a microbiologically safe end-product. The author cautioned that some bacteria and emetic toxin of *B. cereus* can develop resistance to conventional heat treatments and that time and temperature variables should be carefully considered in order to obtain a safe product to include in human food.

In this study no residues of antibiotics, pesticides or mycotoxins were found and heavy metals were below detection levels. The authors concluded that the non-presence of these types of residue was probably due to the fact that the larvae had been fed food grade fruit and

vegetables that have therefore undergone strict controls in order to ensure an adequate health and hygiene profile.

Feed product: H. illucens reared on coffee silverskin with or without addition of microalgae
Biological hazards: Antibiotic resistance genes, multidrug-resistant bacteria able to spread ARGs horizontally
Chemical hazards: Heavy metals

Truzzi et al. (2020), Milanović et al. (2021) and Osimani et al. (2021) investigated the chemical and biological hazards of rearing *H. illucens* on a diet containing coffee silverskin (a coffee roasting by-product) fed alone or in combination with the microlagae (*Schizochytrium limacinum* or *Isochrysis galbana*). The rationale for adding microalgae to the diets was to increase the relative quantity of lipids and proteins in the larvae, to improve their nutritional value for animal feed. All three studies investigated contamination of the substrates, larvae and frass.

Truzzi et al. (2020) looked for the presence of Cd, Pb, As, Ni and Hg in the substrates, prepupae and frass. Prepupae accumulated Cd, Pb and Hg from all growth substrates: coffee silverskin alone or coffee silverskin plus 5, 10, 20, 25% of either *Schyzochytrium sp* or *Isochrysis sp*. The authors stated that this highlights the importance that safe production of the larvae as ingredient for feed or food needs a strict control of these undesirable contaminants both in the initial substrate as well as in the final product. In this study all heavy metals in all growth substrates, prepupae and frass were below EU legal limits for Cd, Pb, As and Hg, although Cd content of prepupae (Cd 0.077 mg kg^{-1} ww) was close to the legal limit for food (0.05 to 0.2 mg kg^{-1} ww Directive 1881/2006/EU and amending regulations 420/2011/EU respectively). The authors reported the concentration of Cd in the substrate feed was mainly influenced by its content in coffee silverskin.

Prepupae reared on substrates based on 100% coffee silverskin and 5 % of *Schizochytrium* sp. or *Isochrysis* sp. showed the high Ni concentration (0.76, 0.54 and 0.49 mg kg^{-1} ww). The authors suggested that considering the high level of Ni in the prepupae, its toxicity, and the limited number of studies for bioaccumulation in insects, that this potential risk requires more attention in future research.

The authors concluded that even if prepupae bioaccumulate Cd, Pb or Hg the risk is low to animals or humans consuming them and that levels are in compliance with EU regulation. In accordance with other studies cited in this review, the authors also stated that contamination depends on the growth substrate and that it would be useful in the future to create a specific list of tested growth substrates for safe edible-insect production.

Milanović et al. (2021) examined the presence of 12 antibiotic resistance genes (ARGs) conferring resistance to the antibiotics erythromycin (erm), tetracycline (tet), vancomycin (vam), β-lactams (bla, mec), and aminoglycosides (aac-aph). The tet(M) and tet(S) genes were widely present in all analysed substrates, with the tet(K) gene also found in coffee silverskin. Larvae reared on the basal coffee silverskin substrate resulted positive for the erm (B) and tet (O) genes. However, no significant effect of rearing substrates (i.e. with and with microalgae added at different proportions to the coffee silverskin) on the distribution of the AR genes in

the *H. illucens* larvae was found. In contrast, the authors observed that the frass samples were characterised by a significant accumulation of ARGs, and this was particularly evident for the frass after rearing larvae on substrates supplemented with high percentages (>20%) of *I. galbana*. The authors concluded that this raises concern since this waste can be used as a biofertilizer and that chitosan is used as a fish supplement posing risks to both the environment and humans.

Osimani et al. (2021) investigated the microbial dynamics in rearing trials of *H. illucens* larvae fed coffee silverskin and microalgae. In this study the inclusion of *I. galbana* was characterised by the presence of bacteria from the Morganella genus in the larvae. Milanović et al. (2021) pointed out that multidrug-resistant species from the Morganella genus are able to spread ARGs horizontally among the same or different species. These studies highlight that careful consideration is required to assess the potential risks not only of side stream when used alone as substrate for rearing insects but also when combined with other ingredients that may further increase hazards. They also illustrate the importance of a holistic experimental approach to investigating hazards, in this case showing that not only are ARG present but bacteria with the potential to spread ARGs are also present.

5.2.4 Risks to the environment

Of the 14 studies that investigated potential risks to the environment, 11 used life cycle assessment (LCA) methodology to determine environmental impacts (Van Zanten et al., 2014; van Zanten et al., 2015; Salomone et al., 2017; Thévenot et al., 2018; van Zanten et al., 2018; Bava et al., 2019; Bosch et al., 2019; Tedesco et al., 2019; Campos et al., 2020; Maiolo et al., 2020; Parodi et al., 2021)

The remaining studies were laboratory experiments, investigating the suitability of chicken, pig, and cow manure as feed for insect larvae which included an assessment of nitrogen loss (Oonincx et al., 2015) and the occurrence of ARGs (Milanović et al., 2021) and the microbial dynamics (Osimani et al., 2021) in the rearing of *H. illucens* on coffee by-products.

Environmental risks arising from insects reared on waste

The majority of these LCA studies (n=8) investigated the production of insects reared on waste in comparison to conventional production systems for animal feed. A wide range of hazard endpoints were measured and reported in these studies including: greenhouse gas emissions, energy use, land use, global warming potential, cumulative energy demand, climate change, carbon dioxide emissions, acidification potential, eutrophication potential, ozone depletion, particulate matter, photochemical ozone formation, acidification, terrestrial eutrophication, freshwater eutrophication, marine eutrophication, water resource depletion, and mineral and fossil renewable resource depletion.

The overarching conclusion from these studies was that the main environmental risk arises from the high energy requirement of the system. For example, Thévenot et al. (2018) considered the environmental performance of *T. molitor* larvae meal reared on side streams (sugar beet pulp, wheat bran, sunflower meal, rapeseed meal) compared to feed production using soybean meal and fish meal. For both systems they assessed cumulative energy

demand, CO_2 equivalent for climate change, SO_2 equivalent for acidification potential, PO_4 equivalent for eutrophication potential and (LU). The authors reported that *T. molitor* meal production had higher environmental impacts, especially the energy required, compared to the other animal feed protein production systems. Van Zanten et al. (2015) found similar results from the production of *M. domestica* larvae meal reared on food waste and poultry manure compared to compared to conventional fishmeal and soybean meal. The authors reported an increase in energy use (EU) and therefore an increase in global warming potential (GWP) but also a reduction in land use (LU). They concluded that insect production for animal feed to be trade-off between decreased LU and increased GWP and EU. Van Zanten et al (2018), also investigated *M. domestica* larvae meal reared on food waste (using data from van Zanten et al., 2015) and rapeseed meal compared to traditional soybean meal for swine. Using consequential LCA the results indicated that using co-products and waste-fed larvae meal currently does not reduces the net environmental impact of pork production when compared to soybean meal. Rapeseed meal resulted in an increased GWP, EU and LU whereas waste fed larvae had an increased GWP and EU although LU was decreased (as per van Zanten et al., 2015 results for waste fed larvae), when compared to soybean meal.

Oonincx et al. (2015) and Parodi et al. (2021) studied the environmental risks of rearing *H. illucens* on animal manures. Ooincx et al. (2015) reported that a large proportion of the nitrogen from the manure (23-78%) was lost in the production system. Parodi et al. (2021) quantified and compared nutrient balances, nutrient levels in residual materials and emissions of greenhouse gases and ammonia between manure incubated with and without *H. illucens*. The authors found that more carbon dioxide and ammonia-nitrogen were emitted from the system with *H. illucens* larvae compared to when larvae were absent. Oonincx et al. (2015) suggested that mitigation measures such as an air washer would be required to make the system ecologically sound.

Bava et al. (2019) proposed that it is the careful selection of rearing substrate that is important for optimising the growth and reducing the environmental impact of the production of insects for animal nutrition. Bava et al. (2019) evaluated the production of *H. illucens* fed on okara, maize distiller brewer's grains, and a hen diet (control) and found the most sustainable product was obtained from larvae grown on the maize distiller brewer's grains.

As reported in the previous section regarding health risks, insect larvae reared on side streams have been found to contain ARGs and bacteria that are able to spread ARGs horizontally among the same or different species. ARGs have also been shown to be present in insect frass (Milanović et al., 2021; Osimani et al., 2021). This presents an emerging risk for contamination of the environment by ARGs when the frass is used as biofertiliser or if ARGs are subsequently excreted into the environment when larvae are used as animal feed.

Environmental risks arising from poultry by-products as animal feed

Campos et al. (2020) conducted an LCA for poultry fat, poultry by-product meal and steam hydrolyzed feather meal, compared to traditional fishmeal or fish oil as fish feed. The authors assessed global warming (CO_2), abiotic depletion, acidification (SO_2) and eutrophication potential of the systems. The authors highlighted points in the life cycle where the main

hazards occur: the rendering process of poultry by-products is mainly responsible for global warming and abiotic depletion (mainly due to process heat), while the poultry production is the main contributor for acidification and eutrophication. However, overall the LCA indicated that poultry by product has a lower environmental impact compared to tradition fish feeds based on fishmeal/oil.

Environmental risks arising from earthworms reared on vegetable waste

Food waste is a sustainability issue of the modern food chain due to the associated waste of natural resources and the production of greenhouse gas emissions (GHG). The valorisation of fruit and vegetable waste (FVW) by vermicomposting can be seen as a method to reduce food waste. Tedesco et al. (2019) evaluate the environmental impact of the bioconversion of FVW into earthworm meal to be used as a food/feed source. The main areas of environmental concern were the emissions of methane, dinitrogen monoxide and ammonia from the vermicomposting and the energy requirements of FVW transport and fresh earthworm processing (freeze drying for food and oven drying for feed, the latter is more energy consuming). Tedesco et al. (2019) suggested that a move to renewable energy sources to improve the sustainability of the production of earthworm meal.

5.3 Key findings from authors of reviews and reports about potential hazards and emerging risks

- Physical hazards resulting from the use of FFP in animal feed were highlighted by Pinotti et al. (2019) and Luciano et al. (2020) but Pinotti et al. (2019) concluded that safety standards for producing feed from FFP in the EU means that the risk of contamination with packaging material is low.
- Authors of a recent report by the FAO (2021) investigating edible insects from a food safety perspective concluded:
    - While the risk of transmitting zoonotic infections to humans through edible insects appears to be low the topic requires further investigation.
    - Slaughterhouse by-products are a source of substrate that needs detailed safety investigation
- Lange and Meyer (2019) reviewed the potentials and possible safety issues of using biorefinery products in food value chains. The authors suggested that:
    - The safety of thermally generated carbohydrate degradation products from biomass pretreatment should be investigated in relation to using yellow and green biomass biorefinery products in food or feed.
- Markou et al. (2018) reviewed the contamination and safety of using agro-industrial wastes and wastewater (WaW) for the cultivation of microalgae and duckweeds. The authors reported that anaerobic digestion and post-treatment of WaW can lower the risks associated with heavy metals and pathogens, but that it is unclear for certain persistent xenobiotics.
- Vandeweyer et al. (2021) highlighted that pre-treatments (e.g. mixing, concentration by a heat or alternative treatment, milling, acidification) of side streams substrates for insects can potentially have both positive and negative effects on substrate microbial load. They

concluded that the impact on food pathogens that can occur in (mixtures of) organic side streams of the currently used preparation technologies is not yet thoroughly investigated.

- A risk assessment 'Advice on animal and public health risks of insects reared on former foodstuffs as raw material for animal feed' (Anon, 2019) highlighted that there are many uncertainties and data gaps when considering chemical and microbiological risks associated with FFP including such as the lack of epidemiological data on incidents and outbreaks of disease caused by the use of insect larvae as animal feed.
- Varelas (2019) reviewed food wastes as a substrate for insect mass production for food and feed. The author highlighted that: many trials are applied with simple food mixtures of wastes and safety aspects such as microbial stability are usually not referred to; compilation of a standardised artificial diet for mass insect production based on household waste that contains highly heterogenous substrate will be highly complicated compared to simpler food industry mixtures of wastes; clinical trials of insects reared on food materials and wastes have not been performed in humans and animals and are lacking.

5.4 General trends and reviewer inferences from literature excluded from the review

The following findings are based on abstracts read during the screening process. The findings therefore come with the caveat that full text have not been read and critically analysed.

5.4.1 Literature excluded on production parameter criteria

A total of 835 primary research articles investigated the risks to animal production performance (e.g. growth, digestibility, development) from the direct feeding of waste, former food products and side streams to animals. The focus of these studies was predominantly farmed livestock, although a limited number of articles were relevant to companion animals. Many of these studies concluded that waste, FFP or side streams can only be fed to animals when combined with traditional feeds or with additives because these feeds alone do not provide the full nutritional requirements of the animal under investigation. The authors of the studies provided recommendations for the proportion of the diet the feedstuff should constitute to ameliorate negative impacts on performance parameters. These studies did not investigate potential biological, chemical or physical contamination of waste, FFP and side streams for animal feed or their environmental impact.

Examples of this type of literature include:

- House fly fed on broiler manure as a source of nutrition for poultry production (Hall et al., 2018)
- Algal biomass obtained from the pig manure treatment as feed for rainbow trout (Tomás-Almenar et al., 2018)
- Black Soldier Fly (Hermetia illucens) reared on roasted coffee by-product and Schizochytrium sp. as a sustainable terrestrial ingredient for aquafeeds production (Zarantoniello et al., 2020)

- Black soldier fly larvae (Hermetia illucens) reared on media containing organic waste streams as feed for Atlantic salmon (Belghit et al., 2018)
- Microorganisms (single cell proteins) cultivated on residual streams from wood-based biorefineries for fish feed (Alriksson et al., 2014; Smárason, Alriksson & Jóhannsson 2019)

It was often difficult to decipher what country the study originated from by only reading the abstracts, therefore this category may include articles that are outside of geographical Europe.

5.4.2 Studies from non-European countries

A large volume of literature (n=172) originated from outside of Europe, notably Brazil. Again, a significant proportion of the literature related to the risks to animal production performance (e.g. growth, digestibility, development) from the direct feeding of waste, former food products and side streams to animals, with authors investigating the proportion of feed the material can constitute without compromising production parameters. Examples of animal feeds based on wastes and side streams for different animals are shown in Table 4.

In a study from the United States of America, Miranda et al. (2021), found that *H. illucens and M. domestica* larvae can efficiently and effectively manage livestock manure to produce feed and compost. They showed that *H. illucens and M. domestica* reduce manure waste and heavy metal pollutants prior to land application, and thus insect management procedures need to be congruent with production emphases of the insects for waste management or protein products.

Table 4. Examples of animal feeds based on wastes or side streams for different animals from experiments conducted in countries outside of Europe.

Animal fed to	**Animal waste, side stream feed**
Fish	Shrimp waste meal
	Tuna viscera
	Poultry by product meal
	Blood meal
	Scallop mid-gut glands
	Squid viscera meal
	Coconut meal
	Groundnut meal
Ruminants	Crambe meal
	Crude glycerin
	Groundnut meal
	Feather meal
	Poultry by-product meal
Goats and sheep	De-toxified castor bean cake
	Cocoa meal
	Cottonseed cake
Swine	Cassava by-product e.g. peelings

	Cottonseed cake
	Coconut meal
	Poultry by-product meal
Poultry	Acai meal
	Babassu meal
	Cashew nut meal
	Crayfish waste meal
	Food waste
	Almond hulls
	Poultry by-product meal
	Feather meal
	Fish waste meal
Insects	Poultry, dairy, swine, sheep, horse manure
	Restaurant food waste
	Almond by-product

5.4.3 Studies about invertebrates and potential risk for plant, animal, human health and the environment but where there was no clear relationship to the CE framework

For sixty articles the relationship between invertebrates, mainly insects, for food or food and the CE framework was unclear. These articles covered a wide range of risks of producing and consuming insects including: risk of allergy from consuming insects for food or feed (e.g. pet food) and risk of chemical or biological contamination of larvae via substrates (spiking of substrates or natural). Some of the findings from these studies may be useful for inferring risks when insects are reared on substrates within the CE framework, however it was not possible to look at all of these articles within the time constraints of this review.

6.0 Key findings and concluding remarks

A large and growing volume of research and development is being carried out not only in Europe but on a global scale on novel food and feeds in relation to the CE framework. The key findings from this review suggest:

- The volume of research investigating emerging risks for animal, human, plant health and the environment is small, particularly when compared to the volume of research investigating the suitability of novel feeds in terms of productivity parameters.
- Primary research about risks is focused on insects as food or feed and the substrate that they are reared on. Primary research about the risks of other novel foods and feeds arising from the CE framework are limited.
- The focus of primary research is on biological and chemical hazards and risks to health, and environmental impacts. Potential physical hazards have been discussed in reviews.
- Emerging risks for animal and human health and environment regarding the production and consumption of invertebrates are strongly correlated to the type of rearing substrate. Specific hazards identified in primary research in this review include the presence of: (i)

ARGs in substrates, larvae and insect frass (ii) high levels of the heavy metals Cd and Ni in prepupae (iii) uptake of allergens from the substrate e.g. gluten

- Some studies reported that insect production when compared to conventional feed production has a higher global warming potential because of the energy intensive processing requirements and use of non-renewable energy resources.
- Many authors researching invertebrates reared on side streams in Europe reported that: although some biological and chemical contaminants that may pose a hazard to animal or human health or the environment are present in substrate, larvae or frass, they are at levels below European recommended safety limits for food or feed. This is perhaps unsurprising considering the current strict food and feed safety legislation in Europe. Authors also highlighted that pre-treatments (e.g. heat treatment, freeze drying) to deactivate biological hazards can reduce or eliminate some risks. Future emerging risks are likely to arise should there be changes in food and feed legislation resulting from a transition towards CE to allow substrates that are currently not authorised for rearing substrate (e.g. animal manure, catering waste, slaughterhouse products, FFP containing meat and fish).
- Topics for future primary research identified by authors of reviews include investigating: the safety of thermally generated carbohydrate degradation products from biomass pretreatment in relation to using yellow and green biomass biorefinery products in food or feed; the biological hazards associated with pre-treatments of side streams substrates for insects.
- Given the large amount of research and development occurring globally particularly regards novel feeds vigilance is needed for foods imported into the EU.

The aim of this review was to 'horizon scan' for emerging risks of novel food and feed within the CE framework. Limitations of the review are that: (i) literature reviews inherently look backwards at existing evidence and the evidence gathered does not always 'look forward' and into the future for emerging risks (ii) the searches for evidence were bias towards gathering academic research, but there is a growing commercial research and development (R&D) regards novel foods and feeds within the CE framework, however much of this R&D will be unobtainable due to commercial sensitivity. Literature reviews are only one tool for identifying emerging risks and other tools such as stakeholder elicitation will help to inform this topic area. Emerging risks may be identified by monitoring upcoming projects, for example, the H2020 projects 'Demonstrable and replicable cluster implementing systemic solutions through multilevel circular value chains for eco-efficient valorization of fishing and fish industries side-streams' and 'The power of grape extracts: antimicrobial and antioxidant properties to prevent the use of antibiotics in farmed animals.' The next stage of this project aims to engage stakeholder to identify and further characterise emerging risks. This is discussed in the following section.

7.0 Next steps

The next step in this project will be to characterise the identified emerging risks from novel food and feed within the CE framework by providing the available information justifying the definition of emerging risk, relevant for EFSA's prioritisation and risk assessment activities.

Using the evidence sourced in this review in combination with expert elicitation we aim to address the following questions:

- What are the emerging risks, new hazards, increased exposures?
- What are the biological, physical and chemical hazards in food, feed or in the environment?
- What type, amount and frequency of application of products are applied in/on environmental matrices?
- Which food/feed products could pose a risk and which plants or animals species are at risk?
- Which locations within a supply chain are where new and emerging risks are most likely to emerge?
- Identify which scientific areas (E.g. Plant Health, Animal Health, Biological Hazards, Chemical contaminants (including biotoxins, etc.) within EFSA's remit that this might relate to.
- What is the availability of data underpinning the definition of emerging risk:
    - (eco)toxicological, bioaccumulation and environmental accumulation, epidemiological, biomonitoring, consumption and occurrence data in line with EFSAs environmental risk assessments remit
    - severity, duration and frequency of the expected effects on human, plant and animal health
    - descriptions of exposure pathways
    - interactions with other contaminants and possible additive effects
- What evidence is there for risk management and reduction measures:
    - monitoring systems/programs, practices to lower or eliminate the contamination risks,
    - possible solutions to achieve a safe CE practice/technology etc.
    - existing international/national regulations/guidelines,
- What are the impacts on economy, environment, social aspects, and food and feed security?
- At what scale (local, national, regional, European, global) is the available evidence?
- How is the evidence base characterised?
- What is the availability of detection methods?
- What is the strength of the association with CE?
- What is the imminence of these impacts? (How quickly might the risk materialise? How urgent is the response?)
- What are the parallels and interactions with other areas and emerging issues?
- What are the data gaps and research needs, including needs for new analytical approaches?

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Appendices

Appendix I Searching for literature from organisational websites

Table 1 shows the organisational websites searched for relevant publications relating to novel food or feed (highlighted in bold). Where included, these websites generally had basic search functions that only allowed search by keywords. Search terms included "Novel Food", "Novel Feed", "Edible Insect" and “Insect” depending upon the functionality of the search feature. These searches were supplemented with a manual search. For those websites without a search function, publications were searched manually. The results from these searches were reviewed for potential articles/datasets and downloaded (results are shown in Table 1)

EFSA publishes all of its scientific outputs, including its scientific opinions, in the EFSA Journal on Wiley. The abstract search used was: "lab-grown meat" OR "test tube meat" OR "artificial meat*" OR "cultured meat*" OR "in vitro meat*" OR "synthetic meat*" OR "novel food*" OR "novel feed*" OR "alternative food*" OR "alternative feed*" OR "edible insect*" OR "insect food*" OR "insects as food" OR "insect feed*" OR "alternative protein*" OR "cell-based meat*" OR "insect protein*" OR "novel plant protein*" OR "cell-based protein*" OR "innovative food*" OR "innovative feed*" OR "sustainable protein*" OR "recycled protein*" OR "novel by-product*" OR "agri-food side stream*" OR "processed animal protein*" OR "mycoprotein*" OR upcycle* OR "new dietary ingredient*" OR "former food*" AND food* OR feed* OR ingredient* OR additive* OR supplement* OR mineral* OR vitamin* OR "*nutrient*" NOT psychology OR accept* OR attitud* OR behav* The results were downloaded as RIS files and loaded into Endnote™ for review (results are shown in Table 1)

The potential articles from the organisational websites were then reviewed for those that investigated potential risks for animals, human health or the environment, from novel food or feed arising from waste, FFP or side streams.

Table 1 Organisational websites searched for relevant publications relating to novel food or feed.

Organisation	Number of potential articles/datasets
Department for Environment Food and Rural Affairs	0
EC Europa	2
EFFPA (European Former Foodstuff Processors Association)	0
EFSA	142
Ellen MacArthur Foundation	8
ETP food for life	0
EU Platform on Food Losses and Food Waste	0
European Centre for Disease Prevention and Control	1
European Feed Manufacturer’s Federation	7
Fédération Européenne des Fabricants d’Adjuvants pour la Nutrition Animal	1
Food and Agriculture Organisation of the United Nations	8

Food Navigator	0
Health and Environment Alliance	0
Horizon 2020	1
International Platform of Insects for Food and Feed	5
Interreg Europe	16
Joint Research Centre EU Science Hub	3
Joint Research Centre Publication Repository	12
Luonnonvarakeskus	9
National Institute for Public Health and the Environment Ministry of Health Welfare and Sport Netherlands	5
Nordic Council of Ministers	4
OECD i Library	1
PBL Netherlands Environmental Assessment Agency	5
Pet Food Manufacturers Association	1
PROteINSECT	5
SAPEA	6
SUSFOOD2	1
Susinchain - Sustainable Insect Chain	3
The European Aquaculture Technology and Innovation Platform	6
UKRI	4
United Nations Environment Programme	7
Waseabi	0
World Health Organisation	1

A dataset from the Horizon 2020 website identified nine research projects relating to novel food and feed as shown in Appendix IV Table 1. None of the other publications/datasets retrieved from these organisational websites investigated potential risks for animals, human health or the environment, from novel food or feed arising from waste, FFP or side streams.

The grey literature obtained during Objective 1 (Table 1 not highlighted in bold) was also reviewed for those that investigated potential risks for animals, human health or the environment, from novel food or feed arising from waste, FFP or side streams. No relevant publications were found.

Appendix II Number of articles retrieved from bibliographic databases and grey literature searches

Table 1. Summary of the number of articles retrieved from bibliographic databases, the total number of duplicate articles removed using Endnote and Eppi Reviewer software and the total number of articles remaining to be screened against inclusion criteria.* [*Bibliographic databases searched: Pubmed, Web of Science, Scopus and EBSCO (CAB Abstracts, Food Science Source, GreenFILE, Business Source Complete, eBook Collection (EBSCOhost), Harper Adams Library Catalogue, Regional Business News, Teacher Reference Centre, Library, Information Science & Technology Abstracts)]

Bibliographic database	**Total**
EBSCO	14,022
Pubmed	8,400
WOS	12,478
Scopus	16,335
Total number of articles retrieved from bibliographic databases before duplicates removed	51,235
Total imported into Endnote software	51,235
Duplicates removed in Endnote	9,177
Total number of articles imported into Eppi Reviewer software	42,058
Duplicates removed using Eppi Reviewer software	15,389
Total number of articles to screen title & abstract	26,669

*Table 2. Number of articles sourced from grey literature searches (*primary research)*

Source	**Number of articles**	**Reference**
FAO	2	1. FAO and WHO. 2019. Hazards associated with animal feed. Report of the Joint FAO/WHO expert meeting – 12–15 May 2015, FAO headquarters, Rome, Italy. FAO Animal Production and Health Report No. 13. Rome. 2. FAO. 2021. Looking at edible insects from a food safety perspective. Challenges and opportunities for the sector. Rome. https://doi.org/10.4060/cb4094en
Previous review conducted by	5	1. Stroka J., Robouch P., Goncalves C. (2021). Aspects of Food and Feed Safety regarding insects and the flow of commodities. JRC, Geel JRC124260

our review team		2. *Conti C., Castrica M., Balzaretti C. M., Tedesco D. E. A. (2019). Edible earthworms in a food safety perspective: Preliminary data. Italian Journal of Food Safety 8:7695 3. Lange L., Meyer A. S. (2019). Potentials and possible safety issues of using biorefinery products in food value chains. Trends in Food Science & Technology 84:7-11 4. Pinotti L., Luciano A., Ottoboni M., Manoni M., Ferrari L., Marchis D., Tretola M. (2021). Recycling food leftovers in feed as opportunity to increase the sustainability of livestock production. Journal of Cleaner Production 294: 126290 5. Markoua G., Wang L., Ye J., Unc A. (2018). Using agro-industrial wastes for the cultivation of microalgae and duckweeds: Contamination risks and biomass safety concerns. Biotechnology Advances 36: 1238-1254
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Appendix III Reviews, reports, PhD theses and scientific opinions screened for additional primary research

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Appendix IV Historical and ongoing (Horizon 2020, SUSFOOD2, UKRI) projects investigating food and feed in relation to the CE framework

Table 1. Historical and ongoing research (Horizon 2020, SUSFOOD2, UKRI) projects investigating food and feed in relation to the CE framework

Project title	Start date	End date	Funding framework
Development and market launch of novel technology for production of nutritionally complete plant proteins called FIDOs - "Functional (Protein) Isolates Derived from Oilseeds".	2015-10-01	2016-01-31	Horizon 2020
Industrial symbiosis for valorising whey and banana wastes and by-products for the production of novel foods	2016-10-01	2018-09-30	Horizon 2020
Insects for a Sustainable Aquaculture	2017-01-01	2017-06-30	Horizon 2020
Investigating the commercial feasibility of a novel biological enhancement technology for creating a sustainable, high value, insect-derived protein supplement for the EU aquaculture market	2017-05-01	2017-09-30	Horizon 2020
Sustainable mass production of Hermetia illucens in controlled environments to produce protein feeds for aquaculture, poultry	2017-08-01	2018-01-31	Horizon 2020

and livestock industries.			
Hexafly Black Soldier Fly Protein and Oils for Fishfeed	2018-05-01	2018-09-30	Horizon 2020
INSECTS FOR A SUSTAINABLE AQUACULTURE 2	2018-08-01	2020-07-31	Horizon 2020
SCALABLE TECHNOLOGIES FOR BIO-URBAN WASTE RECOVERY	2018-11-01	2022-10-31	Horizon 2020
Value chains for disruptive transformation of urban biowaste into biobased products in the city context (WaysTUP!)	2019-09-01	2023-02-28	Horizon 2020
Demonstrable and replicable cluster implementing systemic solutions through multilevel circular value chains for eco-efficient valorization of fishing and fish industries side-streams	2021-10-01	2026-09-30	Horizon 2020
The power of grape extracts: antimicrobial and antioxidant properties to prevent the use of antibiotics in farmed animals.	2021-10-01	2025-09-30	Horizon 2020
PROREF	2014		SUSFOOD
BerryPom	2014		SUSFOOD
OATPRO	2014		SUSFOOD
SUSMEATPRO	2014		SUSFOOD
SUNNIVA	2013		SUSFOOD
Sustainable & Healthy	2013		SUSFOOD
BIOPROT	2013		SUSFOOD
InProVe	2018		SUSFOOD2

FUNBREW	2018		SUSFOOD2
DISCOVERY	2018		SUSFOOD2
AVARE	2018		SUSFOOD2
SPAREC	2018		SUSFOOD2
ImPrOVE	2018		SUSFOOD2
SUSPUFA	2018		SUSFOOD2
FERBLEND	2019		SUSFOOD2
Bio4Food	2019		SUSFOOD2
ALL-IN	2019		SUSFOOD2
Poultrynsect	2019		SUSFOOD2
PROVIDE	2019		SUSFOOD2
Valorisation of cold press rapeseed oil processing by products as feedstock for insect farming	Oct 21	Sep 2025	UKRI
Development of integrated sustainable processes for food waste valorisation	Nov 20	October 2024	UKRI
A modular insect food waste management concept	May 2017	October 2017	UKRI
Wheat straw valorisation	November 2012	March 2013	UKRI

Appendix V References of the 24 primary research studies included in the review

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