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EXTERNAL SCIENTIFIC REPORT

Extensive literature searches on bromine and ochratoxin A in feed

Daniele Urbani[1], Diego Centonze[2], Greta Varchi[3], Martina Evangelisti[1], Marco Daniele Parenti[3], Alberto Del Rio[1]

[1]Innovamol Consulting Srl; [2]University of Foggia, Foggia, Italy; [3]Consiglio Nazionale delle Ricerche (CNR) Istituto per la Sintesi Organica e Fotoreattività, Bologna, Italy

Abstract

Two Extensive Literature Searches (ELSs) by using PubMed, Web of Science (WoS) and SciFinder for relevant studies on Ochratoxin A (OTA) and bromine, bromate and bromide (BRs) in feed were performed. Search queries allowed to obtain a total number of 8,953 and 34,183 references for OTA and BRs, respectively. The relevance analysis of the documents was performed by screening titles and abstracts against inclusion and exclusion criteria. Relevant references accounted in each Area, for OTA and BRs, were respectively: Area 1 (Information on analytical techniques for quantification) 117 and 117 documents, respectively; Area 2 (Information on occurrence/concentrations and formation) 176 and 176 documents, respectively; Area 3 (Information on exposure of farm and companion animals) 31 and 3 documents, respectively; Area 4 (Information on toxicokinetics (absorption, distribution, metabolism, excretion) in farm and companion animals) 37 and 8 documents, respectively; Area 5 (Information on toxicity of OTA/BRs in farm and companion animals) 249 and 23 documents, respectively; Area 6 (Information on the transfer of OTA/BRs from feed to animal derived food) 18 and 4 documents. A total number of 618 and 100 relevant non-redundant documents was found for OTA and BRs, respectively. Those results were obtained after the full text analysis of all the document previously labelled as relevant.

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Summary

The overall purpose of this project was the identification and selection of relevant literature to gather information on ochratoxin A (OTA) and bromine, bromate and bromide (BRs) in feed. This information will support the preparatory works for a first opinion that will be an update of a previous EFSA risk assessment of OTA in feed and a second opinion that will be an assessment on the risks for animal health and transfer from feed to food of animal origin related to the presence of BRs in feed. The project was developed to pursue three major objectives explained below.

Objective 1

Two protocols for tailored search strategies to retrieve studies including reviews and grey literature pertinent to the risk assessment of OTA and BRs were developed. The selection of keywords and the query syntax were customised for PubMed, Web of Science and SciFinder databases and for the different areas of interest which were the following for the two searches:

- Area 1: Information on analytical techniques for quantification of OTA/BRs in feed
- Area 2: Information on occurrence/concentrations and formation of OTA/BRs in feed
- Area 3: Information on exposure of farm and companion animals to OTA/BRs via feed
- Area 4: Information on toxicokinetics (absorption, distribution, metabolism, excretion) in farm and companion animals
- Area 5: Information on toxicity of OTA/BRs in farm and companion animals
- Area 6: Information on the transfer of OTA/BRs from feed to animal derived food.

Inclusion and exclusion criteria were thoroughly defined to allow the selection of relevance. In addition, data reporting methodology and summary tables were defined and agreed with EFSA.

Objective 2

The extensive literature search (ELS) was carried out using the protocol devised in Objective 1. Three different databases were interrogated, namely, PubMed, Web of Science and SciFinder. In parallel, a literature search specific for grey documents from regulatory agencies and other authorities was also performed. PubMed, Web of Science, SciFinder and the grey literature allowed to identify 24,569 documents for the OTA search and 115,632 for the BRs search. The removal of references that appeared simultaneously in more than one database allowed to obtain a final list of 8,953 non-redundant references for OTA search and 34,183 for BRs search.

Objective 3

A screening of titles and abstracts for relevance to the risk assessment was performed keeping into account inclusion and exclusion criteria. The experts of the team analysed references divided by areas of interest and full-text examination was performed only in case of doubts or where a missing consensus about the relevance was present among experts. A subsequent analysis of the full text allowed to remove additional irrelevant documents and compile summarizing tables with high-level information in each area. The relevance analysis allowed to retrieve the following relevant documents in each Area for the OTA and the BRs searches, respectively:

- Area 1 – 117 documents for OTA and 42 documents for BRs
- Area 2 - 176 documents for OTA and 21 documents for BRs
- Area 3 - 31 documents for OTA and 3 documents for BRs
- Area 4 - 37 documents for OTA and 8 documents for BRs
- Area 5 - 249 documents for OTA and 23 documents for BRs

- Area 6 - 18 documents for OTA and 4 documents for BRs

A total number of 618 and 100 relevant non-redundant documents was found for OTA and BRs. Files compatible with EndNote (RIS file) with the relevant literature were exported and provided as well as tables divided by area information. In addition, a summary table reporting included/excluded selection with the reason(s) of exclusion and high-level information for each relevant paper were provided.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

This contract was awarded by EFSA to a consortium with Innovamol Consulting Srl in the lead:

Contractor: Innovamol Consulting Srl

Members of the consortium are:

- Innovamol Consulting Srl, Modena, Italy

- Università di Foggia, Foggia, Italy, Italy

- Consiglio Nazionale delle Ricerche (CNR) Istituto per la Sintesi Organica e Fotoreattività, Bologna, Italy

Contract: NP/EFSA/FEEDCO/2022/01

1.2. Background as provided by EFSA

The Feed and Contaminants Unit (FEEDCO Unit) supports the Panel on Contaminants in the Food Chain (CONTAM Panel), which provides scientific advice on contaminants in the food chain and undesirable substances such as natural toxicants, mycotoxins and residues of unauthorised substances.

EFSA has received mandates from the European Commission for a scientific opinion on ochratoxin A (OTA) in feed and for a scientific opinion on bromine, bromate, bromide (BRs) in feed. At the time when the contract was awarded, these mandates were both allocated to the EFSA CONTAM Panel which will establish two working groups to be tasked with developing these opinions. The first opinion will be an update of the previous EFSA risk assessment of OTA in feed (EFSA CONTAM Panel, 2004) taking into account new scientific information that has since become available on the risks for animal health and transfer from feed to food of animal origin related to the presence of ochratoxin A in feed. The scope of the second opinion, initially relating only to risks for animal health and transfer from feed to food of animal origin related to the presence of BRs in feed, in particular in algae and seaweed and derived products, was subsequently expanded to include risk to human health for the presence of bromide in feed. The ELS described in the report relates to the animal health aspect of the mandate.

To support the preparatory work for these opinions, EFSA outsourced two Extensive Literature Searches (ELSs) as well as the selection of relevant studies by screening of title and abstract. The compounds considered for the searches and evaluations were as follows:

Ochratoxin A in feed (1st opinion):

- Ochratoxin A

BRs in feed (2nd opinion):

- Bromine

- Bromate

- Bromide

A final list of compounds for the two different opinions was agreed with EFSA at the first project meeting.

1.3. Objectives as provided by EFSA

The objectives of the contract resulting from this procurement procedure were as follows:

➢ Objective 1): To develop tailored search strategies to retrieve studies (including reviews and grey literature) pertinent to:

    ○ the risk assessment of OTA in feed published since 01/01/2003, and

- o the risk assessment of BRs in feed (no time limit).

The information was to be organised according to the following information fields or research areas and also organised separately for their relevance for the two different opinions:

- o Area 1: Information on analytical techniques for quantification of OTA/BRs in feed,
- o Area 2: Information on occurrence/concentrations and formation of OTA/BRs in feed,
- o Area 3: Information on exposure of farm and companion animals to OTA/BRs *via* feed,
- o Area 4: Information on toxicokinetics (absorption, distribution, metabolism, excretion) in farm and companion animals,
- o Area 5: Information on toxicity of OTA/BRs in farm and companion animals,
- o Area 6: Information on the transfer of OTA/BRs from feed to animal derived food.

➢ Objective 2: To carry out the ELS using the tailored search strings developed by the contractor and agreed by EFSA for identifying studies.

➢ Objective 3: To screen the titles and abstracts for relevance to the risk assessment. To prepare a file compatible with EndNote (RIS file) with the relevant literature and a table summarising the relevant studies. These should contain the studies considered as relevant applying the eligibility criteria (for inclusion/exclusion of studies) that have to be developed by the contractor. Files compatible with EndNote (RIS file) with the relevant literature searches and selection of relevant were exported and provided divided by area of information. In addition, summary tables reporting included/excluded selection with the reason(s) of exclusion and high-level information for each relevant paper were provided.

2. Data and Methodologies

2.1. Objective 1: Develop tailored search strategy

2.1.1. Preparation of the literature search

The protocol for the developed of tailored searches included the definition of the following points:

- Definition of PICO/PECO. The definition of population (P), intervention/exposure (I/E), comparators (C) and outcomes (O) was essential to develop the eligibility criteria as well as inclusion and exclusion criteria at the beginning of the project.

- Definition of Boolean searches. All the database and data sources were able to support automated queries that were managed as specified below with query syntax suitable to obtain output files. Searches were performed with Boolean queries, in particular by using the Boolean operators "AND" and "OR" and parenthesis combinations involving keywords or chemical structures agreed with EFSA during the preparatory meeting. The Boolean operators "NOT" was not used for queries in order to avoid automatic rejection of potentially relevant documents.

- Keywords and query syntax for PubMed and Web of Science. The selection of keywords and the query syntax were customised and agreed with EFSA by keeping into account different area of interest

- Keywords and query syntax for SciFinder. For this search queries required a different strategy that is dictated by the different search engine capability of the database itself and the information related to chemical substances. After different test queries performed with SciFinder, the team of experts devised a strategy composed by different steps that is presented in the result section.

- Definition of searches for grey literature.
- Definition of inclusion criteria.
- Definition of exclusion criteria.
- Definition of reporting methodology and summary tables.

All the above-mentioned points were agreed with EFSA before proceeding to actual searches.

2.1.2. Database

The database used for this project were PubMed, Web of Science, SciFinder and, in the case of the grey literature, direct access to websites of agencies and authorities in EU and outside EU was performed. Because of the intrinsic differences in each website, tailored searches were applied for each source. Queries and date of searches are reported in the result section.

2.1.3. Software and IT tools

Raw results were collected by exporting references from PubMed, Web of Science and SciFinder in CSV, NBIB or RIS formats. Zotero V. 6.0.13, Mendeley V.1.19.08 and EndNote 20 were used to manage references, including the creation of RIS files. Innovamol Literature DB V.1.0 was used to merge data and perform the selection of relevance. Microsoft Word and Microsoft Excel were used to report data in text and table format.

2.2. Objective 2: Carry out the extensive literature search

Each ELS was carried out using the protocol devised in Objective 1. PubMed, Web of Science and SciFinder Documents retrieved from PubMed, Web of Science and SciFinder were collected in reference manager software (see 2.1.3) as a repository.

The repository of data was post-processed in order to:

i) merge data from the different databases,

ii) remove duplicates,

iii) perform integrity check of each entry, and

iv) correct reference citations if needed.

Query syntax, date of performance of searches and hits obtained are reported in the results section. The result of this post-processing returned a non-redundant list of entries that were imported in Excel where custom variables related to Areas and Exclusion Codes (EC) were added.

2.3. Objective 3: Screening of titles and abstract

Data were imported in the Innovamol Literature DB where a screening of titles and abstracts for relevance was performed keeping into account inclusion and exclusion criteria. The experts of the team analysed references divided by area of interest and full-text examination was performed only in case of doubts or where a missing consensus about the relevance was present among experts.

The work was organised in such a way that two experts with different expertise could review independently documents. A decision on the relevance was made for each record/document if at least one expert judged it relevant as respect to the specific questions of the tender (i.e. inclusion and exclusion criteria). For each document, the following actions were performed:

➢ The relevance of each document was evaluated by checking if relevant keywords describe a real scientific relationship between OTA/BRs and feed,

➢ The relevance of each document was evaluated against inclusion criteria,

> ➢ The relevance of each document was evaluated against exclusion criteria.

In many cases, based on the evaluation against exclusion criteria, papers were judged irrelevant and excluded without further action. In many other cases the screening of the title and abstract was sufficient to judge the article relevant. In this case the appropriate checkbox of relevance was applied to the record and no further action was performed at this stage. Full-text examination was performed only in case of doubts or where a missing consensus about the relevance was present among experts. In most of the cases, the full-text examination allowed to judge documents to be mainly irrelevant, but it is worth to emphasise that in case of borderline documents a conservative approach was used to ensure the completeness and the document were marked as relevant.

Relevant studies were gathered for extraction of bibliographic information and concerned area of interest in both Excel summary tables and RIS files.

Files that were provided at the end of the project included:

- The final protocol and project plan implemented to carry out the project including the report of the ELS and the selection process (the present document),

- The results of the ELS for both OTA and BRs searches divided by database and combined in RIS files (i.e. EFSA_OTA_SciFinder_ELS.RIS, EFSA_OTA_PubMed_ELS.RIS, EFSA_OTA_Grey literature_ELS.RIS, EFSA_OTA_General_ELS.RIS, EFSA_BRs_SciFinder_ELS.RIS, EFSA_BRs_PubMed_ELS.RIS, EFSA_BRs_Grey literature_ELS.RIS, EFSA_BRs_General_ELS.RIS),

- The results of the selection for relevance for both OTA and BRs searches in RIS files (i.e. EFSA_OTA_Relevant_ELS.RIS, EFSA_BRs_Relevant_ELS.RIS),

- The summarising table and reference list for both OTA and BRs searches divided by area and combined in Excel format (i.e. Area1_OTA.xlsx, Area2_OTA.xlsx, Area3_OTA.xlsx, Area4_OTA.xlsx, Area5_OTA.xlsx, Area6_OTA.xlsx, Summarizing table_OTA_FINAL.xlsx, Area1_BRs.xlsx, Area2_BRs.xlsx, Area3_BRs.xlsx, Area4_BRs.xlsx, Area5_BRs.xlsx, Area6_BRs.xlsx, Summarizing table_BRs_FINAL.xlsx),

Results of relevant assessment are reported in the Result section.

3. Results

3.1. Objective 1: Develop tailored search strategy

3.1.1. PICO/PECO definition

The definition of PICO and PECO is essential to define and develop the eligibility criteria as well as inclusion and exclusion criteria. The following table describes the adopted definition.

Table 1. Definition of PICO and PECO.

	Ochratoxin A (OTA) search	Bromine, bromate and bromide contaminants (BRs) search
P	Populations (P) will identify farm and companion animals.	Populations (P) will identify farm and companion animals.
I/E	Interventions and exposure (I and E) will identify any intervention and/or exposure to which the P is exposed by OTA.	Interventions and exposure (I and E) will identify any intervention and/or exposure to which the P is exposed by BRs.
C	Comparators (C) will identify control or reference group in experimental studies or documents not exposed to I or E and information on regulatory documents. For the scope of this tender, we	Comparators (C) will identify control or reference group in experimental studies or documents not exposed to I or E and information on regulatory documents. For the scope of this tender, we

		propose the use of non-contaminated products in animal feed, in particular, cereal grains.	propose the use of non-contaminated products in animal feed, in particular, algae.
O		Outcomes (O) will identify: i) adverse effects of OTA animals relating to acute toxicity, repeated-dose toxicity, reproductive or developmental toxicity; ii) adverse effects of OTA animals resulting from different routes of exposure (e.g. inhalation, dermal, ingestion, intravenous and other parenteral administration routes).	Outcomes (O) will identify: i) adverse effects of BRs animals relating to acute toxicity, repeated-dose toxicity, reproductive or developmental toxicity; ii) adverse effects of BRs animals resulting from different routes of exposure (e.g. inhalation, dermal, ingestion, intravenous and other parenteral administration routes).

3.1.2. Keywords and query syntax for PubMed and Web of Science (WoS)

3.1.2.1. OTA search

For OTA search, a time limitation was imposed and only documents published from 01-01-2003 to 14 - 07-2022 were extracted.

Area 1 - Analytical Techniques Area

Search query - PubMed

("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (chem* OR analy* OR identi* OR charact* OR detect* OR determin* OR method* OR form* OR degrad* OR hydroly* OR reaction* OR "GC-MS*" OR "HPLC" OR "LC-MS" OR "ICP-MS") AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR pet food)

Search query - WoS

TS=(("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (chem* OR analy* OR identi* OR charact* OR detect* OR determin* OR method* OR form* OR degrad* OR hydroly* OR reaction* OR "GC-MS*" OR "HPLC" OR "LC-MS" OR "ICP-MS") AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR pet food))

Area 2 - Occurrence Area

Search query - PubMed

("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR "pet food")

Search query - WoS

TS=(("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR "pet food"))

Area 3 – Exposure Area

Search query - PubMed

("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (exposure) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=(("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (exposure) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

Area 4 – Toxicokinetics Area

Search query - PubMed

("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (absor* OR tissue* OR metaboli* OR excret* OR kinetic* OR toxicokinetic* OR pharmacokinetic* OR degrad* OR biotrans* OR eliminat* OR biomark* OR ADME) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=(("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (absor* OR tissue* OR metaboli* OR excret* OR kinetic* OR toxicokinetic* OR pharmacokinetic* OR degrad* OR biotrans* OR eliminat* OR biomark* OR ADME) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

Area 5 – Toxicity Area

Search query - PubMed

("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (toxi* OR poison* OR cancer* OR carcino* OR tumor* OR tumour* OR organ* OR tissue* OR immun* OR neuro* OR developmental OR teratogen* OR repro* OR liver OR kidney* OR brain* OR lung* OR cardiovascular OR health OR clinical OR growth OR weight) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=(("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (toxi* OR poison* OR cancer* OR carcino* OR tumor* OR tumour* OR organ* OR tissue* OR immun* OR neuro* OR developmental OR teratogen* OR repro* OR liver OR kidney* OR brain* OR lung* OR cardiovascular OR health OR clinical OR growth OR weight) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

Area 6 – Transfer From Feed To Animal Derived Food

Search query - PubMed

("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (administration OR absorption OR distribution OR "tissue distribution" OR bioavailab* OR metaboli* OR biotransform* OR activat* OR half-li* OR excret* OR clearance OR eliminat* OR bioconcentrat* OR kinetic* OR PBPK OR PBK OR transfer OR carry-over OR carryover OR "carry over") AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=(("ochratoxin" OR "ochratoxins" OR "ochratoxin A" OR "ochratoxins A" OR 303-47-9 OR "OTA") AND (administration OR absorption OR distribution OR "tissue distribution" OR bioavailab* OR metaboli* OR biotransform* OR activat* OR half-li* OR excret* OR clearance OR eliminat* OR bioconcentrat* OR kinetic* OR PBPK OR PBK OR transfer OR carry-over OR carryover OR "carry over") AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR

piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

3.1.2.2.   BRs search

For BRs search no time limit was imposed. The search was performed on 18/07/2022.

Area 1 - Analytical Techniques Area

Search query - PubMed

(bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (chem* OR analy* OR identi* OR charact* OR detect* OR determin* OR method* OR form* OR degrad* OR hydroly* OR reaction* OR "GC-MS*" OR "HPLC" OR "LC-MS" OR "ICP-MS") AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR pet food)

Search query - WoS

TS=((bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (chem* OR analy* OR identi* OR charact* OR detect* OR determin* OR method* OR form* OR degrad* OR hydroly* OR reaction* OR "GC-MS*" OR "HPLC" OR "LC-MS" OR "ICP-MS") AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR pet food))

Area 2 - Occurrence Area

Search query - PubMed

(bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR "pet food")

Search query - WoS

TS=((bromine OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (intake OR feed* OR fodder OR diet* OR meal OR cereal* OR corn OR maize OR Zea mays OR wheat OR "Triticum aestivum" OR rye OR "Secale cereale" OR barley OR "Hordeum vulgare" OR oat OR Avenasativa OR grain* OR seed* OR forage OR silage OR grass OR Poaceae OR hay OR rape OR Brassicanapus OR soybean OR "Glycine max" OR DDGS OR WDG OR seaweed OR algae OR "pet food")

Area 3 – Exposure Area

Search query - PubMed

(bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (exposure) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream"

OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=((bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (exposure) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

Area 4 – Toxicokinetics Area

Search query - PubMed

(bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (absor* OR tissue* OR metaboli* OR excret* OR kinetic* OR toxicokinetic* OR pharmacokinetic* OR degrad* OR biotrans* OR eliminat* OR biomark* OR ADME) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=((bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (absor* OR tissue* OR metaboli* OR excret* OR kinetic* OR toxicokinetic* OR pharmacokinetic* OR degrad* OR biotrans* OR eliminat* OR biomark* OR ADME) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

Area 5 – Toxicity Area

Search query - PubMed

(bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (toxi* OR poison* OR cancer* OR carcino* OR tumor* OR tumour* OR organ* OR tissue* OR immun* OR neuro* OR developmental OR teratogen* OR repro* OR liver OR kidney* OR brain* OR lung* OR cardiovascular OR health OR clinical OR growth OR weight) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR

salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=((bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (toxi* OR poison* OR cancer* OR carcino* OR tumor* OR tumour* OR organ* OR tissue* OR immun* OR neuro* OR developmental OR teratogen* OR repro* OR liver OR kidney* OR brain* OR lung* OR cardiovascular OR health OR clinical OR growth OR weight) AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish))

Area 6 – Transfer From Feed To Animal Derived Food

Search query - PubMed

(bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (administration OR absorption OR distribution OR "tissue distribution" OR bioavailab* OR metaboli* OR biotransform* OR activat* OR half-li* OR excret* OR clearance OR eliminat* OR bioconcentrat* OR kinetic* OR PBPK OR PBK OR transfer OR carry-over OR carryover OR "carry over") AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow OR cows OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe OR ewes OR ram OR rams OR lamb OR goat* OR caprine OR ovine OR pig OR pigs OR swine* OR hog OR hogs OR sow OR sows OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen OR hens OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet OR pets OR cat OR cats OR kitten* OR dog OR dogs OR bitch* OR pup OR puppies OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)

Search query - WoS

TS=((bromine OR Br2 OR bromate OR bromide OR 7726-95-6 OR 15541-45-4 OR 24959-67-9) AND (administration OR absorption OR distribution OR "tissue distribution" OR bioavailab* OR metaboli* OR biotransform* OR activat* OR half-li* OR excret* OR clearance OR eliminat* OR bioconcentrat* OR kinetic* OR PBPK OR PBK OR transfer OR carry-over OR carryover OR "carry over") AND (farm animals OR horse* OR stallion* OR mare* OR foal* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle OR bull* OR calf OR calves OR heifer* OR bovine OR sheep* OR ewe* OR ram* OR lamb OR goat* OR caprine OR ovine OR pig* OR swine* OR hog* OR sow* OR gilt* OR boar* OR porcine OR mink* OR poultry OR chicken* OR hen* OR cock* OR rooster* OR broiler* OR duck* OR goose OR geese OR gosling* OR turkey* OR quail* OR guinea OR rabbit* OR fish* OR salmon OR trout* OR piscine OR zebrafish OR pet* OR cat* OR kitten* OR dog* OR bitch* OR pup*OR "sea bream" OR seabream OR "sea bass" OR seabass OR turbot OR carp OR sturgeon OR eel OR eels OR tilapia OR cod OR halibut OR cobia OR "milk fish" OR tuna OR "tuna fish" OR tunafish)) WoS hits: 20941

3.1.3. Keywords and query syntax for SciFinder

SciFinder queries requires a different strategy that is dictated by the different search engine capability of the database and the information related to chemical substances. Different test queries were

performed in order to keep into account the general objective of both searches by performing the following steps:

- Chemical structure identified by means of CAS numbers.
- Refine substances to retrieve only chemical substances that:
  a. Have references
  b. Are a single component
  c. Are in specific substance classes: organics, and others not listed
  d. Are in specific types of studies: analytical and biological
- Refine substances to exclude chemical substances that:
  a. Contain isotopes
- Refine substances to exclude chemical substances that:
  o Contain metals.
- Get references from substances limiting results to:
  o Adverse effect, including toxicity
  o Analytical studies
  o Biological studies
- Refine references to retrieve only studies with the following research topic:
  o Food and feed
  o Agricultural use
  o Adverse effect
- Refine references to retrieve only studies with the following language:
  o English
- Refine references to retrieve only the following study type:
  o Biography
  o Book
  o Clinical trial
  o Commentary
  o Conference
  o Dissertation
  o Editorial
  o Historical
  o Journal
  o Letter
  o Report
  o Review
- Removal of duplicate using the SciFinder tool

Both searches were performed on 18/07/2022.

23978325, 2023, 3, Downloaded from https://efsa.onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2023.EN-7938 by Cochrane Italia, Wiley Online Library on [22/06/2024]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

3.1.4.   Other database

Grey literature searches were performed by accessing websites of agencies and authorities in EU and outside EU (see Table 2) and by searching guidance, regulations and scientific opinions. Because of the intrinsic differences in each website, a tailored search was applied for each source. In general, relevant documents are searched by using the internal search engine of the website and different combinations of the search terms as described above.

3.1.5.   Inclusion criteria

As a general rule, articles describing occurrence, characterization, or toxicity data of OTA and BRs consistent with the PICO/PECO definition above were included as relevant; in particular in relation to the areas detailed in Table 2. In order to comply with inclusion criteria, each reference documents needed to involve at least one of the areas.

Table 2. Relevant areas for both OTA and BRs searches

Area number	Information fields and research areas
Area 1	Information on analytical techniques for quantification of OTA/BRs in feed.
Area 2	Information on occurrence/concentrations and formation of OTA/BRs in feed.
Area 3	Information on exposure of farm and companion animals to OTA/BRs via feed.
Area 4	Information on toxicokinetic (absorption, distribution, metabolism, excretion) in farm and companion animals.
Area 5	Information on toxicity of OTA/BRs in farm and companion animals.
Area 6	Information on the transfer of OTA/BRs from feed to animal derived food.

3.1.6.   Exclusion criteria

To allow accounting in an efficient and unambiguous manner the reasons for excluding a particular document, we devised the scheme detailed in Table 3 where we encoded exclusion criteria, *i.e.* a codification of the reasons explaining why a specific document needed to be excluded.

Table 3. Exclusion criteria defined for both OTA and BRs

Exclusion code	Description of exclusion criteria
EC1	Documents describing solely OTA/BRs preparations, manufacturing and/or synthesis.
EC2	Articles describing data, analytical techniques, occurrence/concentrations, exposure that are not test item related (i.e., no clear link with OTA/BRs).
EC3	No clear link with feed, farm and companion animals. (e.g. toxicity study in mice and on humans).
EC4	Document with general speculation, general description, or historical description of OTA/BRs or any other documents that cannot be categorized in inclusion criteria and cannot be excluded with EC1-EC3 codes.

3.2.   Objective 2: Carry out the extensive literature search

ELS was performed on the requested database with the methodology described in the previous chapter (Objective 1). Individual results of database searches are reported below divided by area of interest.

3.2.1.   PubMed searches

PubMed searches were performed on 14/07/2022. Table 4 below shows the list of identified documents in PubMed searches divided by area of interest for both searches.

Table 4. List of identified documents for PubMed searches.

Area number	Hits - OTA search	Hits - BRs search

The present document has been produced and adopted by the bodies identified above as author(s). This task has been carried out exclusively by the author(s) in the context of a contract between the European Food Safety Authority and the author(s), awarded following a tender procedure. The present document is published complying with the transparency principle to which the Authority is subject. It may not be considered as an output adopted by the Authority. The European Food Safety Authority reserves its rights, view and position as regards the issues addressed and the conclusions reached in the present document, without prejudice to the rights of the author(s).

Area 1	2,313	5,234
Area 2	2,497	5,718
Area 3	267	1,172
Area 4	916	7,909
Area 5	1,826	11,297
Area 6	1,064	8,683

3.2.2.   Web of Science searches

Web of Science searches were performed on 15/07/2022. Table 5 below shows the list of identified documents in Web of Science searches divided by area of interest for both searches.

Table 5. List of identified documents for Web of Science searches.

Area number	Hits - OTA search	Hits - BRs search
Area 1	4,010	7,784
Area 2	4,916	8,951
Area 3	550	1,293
Area 4	948	13,748
Area 5	2,239	22,006
Area 6	1,027	20,941

3.2.3.   SciFinder searches

SciFinder searches were performed on 18/07/2022 by following the procedure specified in previous sections. The total number of hits identified with SciFinder were 1,978 for the OTA search and 896 for the BRs search.

3.2.4.   Combined database

The number of cumulative references identified with ELS are depicted in Table 6. Several references were simultaneously present in different databases, and this explains why the sum of hits from the three databases plus the grey literature is greater than the total number of non-redundant references. According to these searches, ELS allowed to obtain 8,953 non-redundant references for the OTA search and 34,183 non-redundant references for the BRs search.

Table 6. List of identified documents for the combined database.

	Hits - OTA search	Hits - Bromine search
PubMed+WoS+SciFinder – with duplicates	24,569	115,632
PubMed without duplicates	3,811	17,659
WoS without duplicates	5,976	41,978
SciFinder without duplicates	1,978	896
Grey literature	5	2
Total without duplicates	8,953	34,183

3.2.5.   Additional filtering for the BRs search

Due to the high number of hits obtained for the BRs search, a filtering out step was performed for documents containing specific keywords that were expected to be out of the scope of the present assignment. Keywords were identified during the selection of relevance. For each keyword as depicted in Table 7, a pilot check was performed to assess the not relevance of articles, i.e. 100 documents per keyword were checked. In case no articles were found to be relevant among these sample of documents, the keyword was used to remove all the other documents from the amount generated by the BRs search, which contained such keyword. On the contrary, when one or more papers were identified as relevant within the sample of documents, then the keyword was not used to filter the overall output of

the ELS. This is the case of the following keywords which were not used to apply this filtering: investigation, chlorine, ultraviolet, process, removal, reduce, injury, assay, reaction, preparation and water.

Table 7. Filtering out keywords for the BRs search and results of the sampling test.

Filter keyword(s)	Number of documents found	Results of the test (sampling of at least 100 documents per keyword)
Human	3,471	Documents mostly describing bromide for flame retardants, MTT assays, tetrabromobisphenol, polybrominated diphenyl ethers.
Rat OR rats	1,888	Documents describing bromide referring to pinaverium bromide, MTT assays, flame retardants or brominated vegetable oil (BVO) as food additives.
Mouse OR mice	1,576	Documents describing bromide referring to potassium bromide not in the context of companion animals, MTT assays or pyridostigmine bromide.
MTT or XTT or MTS or WST	2,072	Documents describing bromide referring mainly to MTT assays in various studies.
perovskite	79	All documents have been checked and none of them were found to be relevant.
additive	283	Documents describing bromide as additive but not in the context of this procurement.
flame OR retardant OR PBDEs OR BDE-28 OR BDE-47 OR BDE-49 OR BDE-99 OR BDE-100 OR BDE-138 OR BDE-153 OR BDE-154 OR BDE-183 OR DDE-209 OR HBCDDs OR alpha-HBCDD OR beta-HBCDD OR gamma-HBCDD OR TBBPA OR TBBPA-bOHEE OR TBBPA-bAE OR TBBPA-bDiBPrE OR TBBPA-bGE OR TBBPA-bAcr OR TBBPA-bOAc OR TBBPA-bOHEE-bAcr OR TBBPA-bME OR TBBPA-bOPr OR 2,4-DBP OR 2,4,6-TBP OR PBP OR TBPD-TBP OR TBP-AE OR PBP-AE OR TBP-DBPE OR BEH-TEBP OR BTBPE OR DBDPE OR DBE-DBCH OR DBHCTD OR EH-TBB OR HBB OR HCTBPH OR OBTMPI OR PBB-Acr OR PBEB OR PBT OR TBNPA OR TDBP-TAZTO OR TBCO OR TBX OR TDBPP OR BDBP-TAZTO OR DBNPG OR DBP-TAZTO OR DBS OR EBTEBPI OR HBCYD OR HEEHP-	1,494	Documents describing bromide as additive for flame retardant, thus not in the context of this procurement.

TEBT OR 4'-PeBPO-BDE208 OR TTBNPP OR TTBP-TAZ		
Seizure	135	All documents have been checked and none of them were found to be relevant.
Lead OR Copper OR zinc OR platin	889	A selection of 100 documents was checked and none of them were found to be relevant.
Semiconductor OR Solar or TiO2	108	All documents have been checked and none of them were found to be relevant.
Cataly	1,026	A selection of 100 documents was checked and none of them were found to be relevant. Most of the documents are related to organic synthesis, bromine K-edge X-ray absorption, brominated pharmacologically active compounds, reactive brominating species and flame retardants.
Purification	2,338	A selection of 100 documents was checked and none of them were found to be relevant. Most of the documents are related to organic synthesis, bromine derivatives with pharmacological activity, cetyltrimethylammonium bromide (CTAB)-aided in coagulation-filtration processes and lithium bromide as widely used water-absorbent material.

The additional filtering as depicted above allowed to remove a total of 15,359. The remaining 18,822 documents were screened by title and abstract ad described in the next section.

3.3. Objective 3: Screening of titles and abstract

The selection for relevance was performed following the methodology reported in the previous sections. A subsequent screening of the full text allowed to remove additional not relevant documents and compile summarising tables with high-level information in each area.

3.3.1. Summary of the results of screening

The table below reports the number of relevant documents that were identified divided by area of interest.

Table 8. Results of the selection of relevance for OTA and BRs searches

Area number	Information fields and research areas	N° relevant document – OTA search	N° relevant document – BRs search
Area 1	Information on analytical techniques for quantification of OTA/BRs in feed.	117	42
Area 2	Information on occurrence/concentrations and formation of OTA/BRs in feed.	176	21
Area 3	Information on exposure of farm and companion animals to OTA/BRs via feed.	31	3
Area 4	Information on toxicokinetic (absorption, distribution, metabolism, excretion) in farm and companion animals.	37	8
Area 5	Information on toxicity of OTA/BRs in farm and companion animals.	249	23
Area 6	Information on the transfer of OTA/BRs from feed to animal derived food.	18	4

3.3.2. Summary of provided files

The files listed in Table 9 were provided together with the present report.

Table 9. Provided files

Item	File name – OTA search	File name – BRs search

Final protocol implemented by the contractor to carry out the project and the report of the ELS and selection process in MS Word format (this file)	NP EFSA FEEDCO 2022 01 final deliverable 15 10 2022_final version	NP EFSA FEEDCO 2022 01 final deliverable 15 10 2022_final version
Results of the ELS – PubMed in RIS files	EFSA_OTA_PubMed_ELS	EFSA_BRs_PubMed_ELS
Results of the ELS – WoS in RIS files	EFSA_OTA_WoS_ELS	EFSA_BRs_WoS_ELS
Results of the ELS - SciFinder in RIS files	EFSA_OTA_SciFinder_ELS	EFSA_BRs_SciFinder_ELS
Results of the ELS - Grey literature in RIS files	EFSA_OTA_Grey literature_ELS	EFSA_BRs_Grey literature_ELS
Results of the ELS – combined without duplicates in RIS files	EFSA_OTA_General_ELS	EFSA_BRs_General_ELS
Results of the selection of relevance in EndNote files	EFSA_OTA_Relevant_ELS	EFSA_BRs_Relevant_ELS
Results of the selection of relevance in RIS files	EFSA_OTA_Relevant_ELS	EFSA_BRs_Relevant_ELS
Relevant in Area 1 (Excel)	Area1_OTA	Area1_BRs
Relevant in Area 2 (Excel)	Area2_OTA	Area2_BRs
Relevant in Area 3 (Excel)	Area3_OTA	Area3_BRs
Relevant in Area 4 (Excel)	Area4_OTA	Area4_BRs
Relevant in Area 5 (Excel)	Area5_OTA	Area5_BRs
Relevant in Area 6 (Excel)	Area6_OTA	Area6_BRs
Summarizing table with reference list and high level information in Excel	Summarizing table_OTA_FINAL	Summarizing table_BRs_FINAL

4. Conclusions

For this call, two Extensive Literature Searches (ELSs) by using PubMed, Web of Science and SciFinder for relevant studies on Ochratoxin A (OTA) and bromine, bromate and bromide (BRs) in feed were performed. In conformity to the needs of EFSA, literature searches were organised by following the general principles for systematic reviews as specified by the EFSA guidance (EFSA, 2010). The methodology was implemented and tailored in order to address the tasks underlined in the tender specifications in a realistic and well-structured way.

For the OTA search the ELS and the selection of relevant documents allowed to identify the following relevant articles divided by area of interest:

➢ Area 1 (Information on analytical techniques for quantification) 117 relevant documents.

➢ Area 2 (Information on occurrence/concentrations and formation) 176 relevant documents.

➢ Area 3 (Information on exposure of farm and companion animals) 31 relevant documents.

➢ Area 4 (Information on toxicokinetics (absorption, distribution, metabolism, excretion) in farm and companion animals) 37 relevant documents have been identified.

➢ Area 5 (Information on toxicity of OTA in farm and companion animals) 249 relevant documents.

➢ Area 6 (Information on the transfer of OTA from feed to animal derived food) 18 relevant documents.

The total number of non-redundant and relevant document found was 618 for OTA search.

For the BRs search the ELS and the selection of relevant documents allowed to identify the following relevant articles divided by area of interest:

➢ Area 1 (Information on analytical techniques for quantification) 42 relevant documents.

➢ Area 2 (Information on occurrence/concentrations and formation) 21 relevant documents.

➢ Area 3 (Information on exposure of farm and companion animals) 3 relevant documents.

➢ Area 4 (Information on toxicokinetics (absorption, distribution, metabolism, excretion) in farm and companion animals) 8 relevant documents have been identified.

➢ Area 5 (Information on toxicity of BRs in farm and companion animals) 23 relevant documents.

➢ Area 6 (Information on the transfer of BRs from feed to animal derived food) 4 relevant documents.

The total number of non-redundant and relevant document found was 100 for BRs search.

References

EFSA Panel on Contaminants in the Food Chain (CONTAM Panel), 2004. Opinion of the Scientific Panel on contaminants in the food chain [CONTAM] related to ochratoxin A (OTA) as undesirable substance in animal feed, EFSA Journal 2004; 2(10):101, pp. 36 doi:10.2903/j.efsa.2004.101.

European Food Safety Authority (EFSA), 2010. Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA Journal 2010; 8(6):1637. pp. 90 doi:10.2903/j.efsa.2010.1637.

EFSA, 2010. Application of systematic review methodology to food and feed safety assessments to support decision making. EFSA J. 8. https://doi.org/10.2903/j.efsa.2010.1637.

EFSA, 2004. Opinion of the Scientific Panel on contaminants in the food chain [CONTAM] related to ochratoxin A (OTA) as undesirable substance in animal feed. EFSA J. https://doi.org/10.2903/j.efsa.2004.101.

Abbreviations

ELS	Extensive Literature Search
WoS	Web of Science
OTA	Ochratoxin A
BRs	Bromine, bromate, bromide
EFSA	European Food Safety Authority
FEEDCO	Feed and Contaminants (Unit)
CONTAM	Contaminants in the Food Chain (Panel)
PICO	Populations, Interventions, Comparators, Outcomes
PECO	Populations, Exposure, Comparators, Outcomes
EC	Exclusion criteria
EU	European Union
MTT	3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide

Annexes

Annex A – Results of the ELS

The results of the ELS for both OTA and BRs searches divided by database and combined in RIS files (namely EFSA_OTA_SciFinder_ELS.RIS, EFSA_OTA_PubMed_ELS.RIS, EFSA_OTA_WoS_ELS EFSA_OTA_Grey literature_ELS.RIS, EFSA_OTA_General_ELS.RIS, EFSA_BRs_SciFinder_ELS.RIS, EFSA_BRs_PubMed_ELS.RIS, EFSA_BRs_WoS_ELS EFSA_BRs_Grey literature_ELS.RIS, EFSA_BRs_General_ELS.RIS), are available on EFSA's Knowledge Junction community on Zenodo at: https://doi.org/10.5281/zenodo.7755479

Annex B – Selection for relevance

The results of the selection for relevance for both OTA and BRs searches in RIS files (namely EFSA_OTA_Relevant_ELS.RIS, EFSA_BRs_Relevant_ELS.RIS, Area1_OTA.RIS, Area2_OTA.RIS, Area3_OTA.RIS, Area4_OTA.RIS, Area5_OTA.RIS, Area6_OTA.RIS, Area1_BRs.RIS, Area2_BRs.RIS, Area3_BRs.RIS, Area4_BRs.RIS, Area5_BRs.RIS, Area6_BRs.RIS.), are available on EFSA's Knowledge Junction community on Zenodo at: https://doi.org/10.5281/zenodo.7755479

Annex C – Summarising table

The summarising table and reference list for both OTA and BRs searches divided by area and combined in Excel format (namely Area1_OTA.xlsx, Area2_OTA.xlsx, Area3_OTA.xlsx, Area4_OTA.xlsx, Area5_OTA.xlsx, Area6_OTA.xlsx, Summarizing table_OTA_FINAL.xlsx, Area1_BRs.xlsx, Area2_BRs.xlsx, Area3_BRs.xlsx, Area4_BRs.xlsx, Area5_BRs.xlsx, Area6_BRs.xlsx, Summarizing table_BRs_FINAL.xlsx), are available on EFSA's Knowledge Junction community on Zenodo at: https://doi.org/10.5281/zenodo.7755479