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Nielsen, Elsa Ebbesen; Egebjerg, Mikael Mandrup; Olesen, Pelle Thonning; Sharma, Anoop Kumar; Nørby, Karin Kristiane; Beltoft, Vibe Meister; Rasmussen, Peter Have; Bredsdorff, Lea; Hansen, Max; Eriksen, Folmer Damsted; Pilegaard, Kirsten; Ravn-Haren, Gitte; Jørgensen, Kevin

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Extensive literature search for studies related to fumonisins and their modified forms

National Food Institute, Technical University of Denmark

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Abstract

An extensive literature search to identify and collect all studies related to fumonisins and their modified forms was performed in the two databases PubMed and Web of Science for nine Areas. After combination of the searches from the two databases and removal of the duplicates, the total number of hits for Area 1 was 4456, for Area 2 was 2261, for Area 3 was 1649, for Area 4 was 3555, for Area 5 was 1632, for Area 6 was 2424, for Area 7 was 5087, for Area 8 was 3284, and for Area 9 was 3283. The evaluation of all retrieved references for relevance by screening the title and abstract (if available) and applying eligibility criteria (inclusion/exclusion) resulted in a total number of relevant references for Area 1 of 532, for Area 2 of 114, for Area 3 of 273, for Area 4 of 87, for Area 5 of 138, for Area 6 of 38, for Area 7 of 270, for Area 8 of 709, and for Area 9 of 270.

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Key words: fumonisins, toxicity, occurrence in food and feed, chemistry, extensive literature search

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Summary

The overall aim of this assignment was to identify and collect all relevant literature related to fumonisins and their modified forms to support preparatory work for the human and animal risk assessment of these substances.

Initially, nine tailored search strings were designed to retrieve all potentially relevant studies within the following nine areas:

- **Area 1**: Data on chemistry and analysis (substance identification and characterisation, analytical detection and determination, formation).
- **Area 2**: Data on toxicokinetics (absorption, distribution, metabolism, excretion) in experimental animals, farm and companion animals, humans and from *in vitro* studies and on biomarkers.
- **Area 3**: Data on *in vitro* and *in vivo* mode of action (MoA) of toxicity.
- **Area 4**: Data on toxicity *in vivo* (e.g. acute, subacute, subchronic, chronic toxicity; genotoxicity, carcinogenicity, toxicity to specific organs) in laboratory animals.
- **Area 5**: Data on toxicity *in vitro*.
- **Area 6**: Data on observations in humans (e.g. epidemiological studies, case reports, intervention studies).
- **Area 7**: Data on adverse effects in farm and companion animals (studies in the different species e.g. ruminants, pigs, poultry, rabbits, fish, cats, dogs etc.).
- **Area 8**: Data on occurrence in food.
- **Area 9**: Data on occurrence in feed and animal exposure (including feed occurrence in the different feed commodities, feed intake and animal exposure).

The search strings were tailored to the databases PubMed and Web of Science and consisted of two major steps each designed to search titles and abstracts in PubMed and Web of Science, as well as full text in PubMed. Combinations of search terms were used, starting with a broad search for fumonisins and their modified forms, synonyms and abbreviations (step 1) and followed by an Area specific step with the addition of search terms relevant to each Area (step 2).

Then the nine tailored search strings were employed to retrieve all relevant studies from the two databases. Data published since year 2000 were retrieved for Area 1-6 and Area 8-9. Data published since year 1980 were retrieved for Area 7. All retrieved references were exported as separate files into EndNote™. Duplicate studies were then removed after combining the two EndNote™ files per Area into one single combined file per Area.

The total number of hits from each database, as well as the total number of hits (combined total) and total number of hits after removal of the duplicates (combined) are summarised in the table below.

<table>
<thead>
<tr>
<th>Area</th>
<th>PubMed</th>
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<th>Combined total</th>
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<td>3283</td>
</tr>
</tbody>
</table>
All retrieved references were then evaluated for relevance by applying eligibility criteria (inclusion/exclusion). The selection for relevance was conducted by screening the title and abstract (if available) and all the retrieved studies were ultimately sorted into one of the following three categories:

- **Relevant to the research objectives**: References ultimately evaluated to be relevant were included in this category.

- **Maybe relevant to the research objectives**: In case the relevance could not be evaluated because e.g. of missing or vague abstracts or because the reference addressed and discussed mycotoxins in general and fumonisins could not be excluded based on the title and abstract of the reference, the references were included in this category, as a conservative approach.

- **Not relevant to the research objectives**: References ultimately evaluated not to be in-scope were included in this category.

The results of the reference selection process were reported in summary tables (Excel files), one table per Area. The summary tables include all pertinent information for each of the references in the 'Relevant’ category as identified by the eligibility criteria and which could be retrieved from the title and abstract (when available). The summary tables also include references in the 'Maybe relevant’ and the 'Not relevant’ categories, but without any study details except for including the reason for exclusion for the 'Not relevant’ references, i.e. not target compound or not relevant for the specific Area is presented.

The evaluation for relevance resulted in a total number of relevant references for Area 1 of 532, for Area 2 of 114, for Area 3 of 273, for Area 4 of 87, for Area 5 of 138, for Area 6 of 38, for Area 7 of 270, for Area 8 of 709, and for Area 9 of 270.
Table of contents

Abstract .............................................................................................................................................1
Summary ...............................................................................................................................................3
1. Introduction ........................................................................................................................................6
1.1. Background and Terms of Reference as provided by the requestor .............................................6
1.1.1. Background as provided by EFSA .......................................................................................6
1.1.2. Objectives as provided by EFSA ..........................................................................................6
2. Methodologies ......................................................................................................................................7
2.1. Objective 1 .....................................................................................................................................7
2.1.1. Task 1 Developing tailored search strategies and search strings for collecting relevant studies 7
2.2. Objective 2 ......................................................................................................................................8
2.2.1. Task 2 Execution of the extensive literature searches using the tailored search strings developed in task 1 .....................................................................................................................8
2.3. Objective 3 .....................................................................................................................................8
2.3.1. Task 3 Selection of all relevant studies retrieved by the extensive literature searches ..........8
3. Results ...............................................................................................................................................9
3.1. Objective 1 .....................................................................................................................................9
3.1.1. Task 1 Developing tailored search strategies and search strings for collecting relevant studies 9
3.2. Objective 2 ....................................................................................................................................11
3.2.1. Task 2 Execution of the extensive literature searches using the tailored search strings developed in task 1 .....................................................................................................................11
3.3. Objective 3 ....................................................................................................................................12
3.3.1. Task 3 Selection of all relevant studies retrieved by the extensive literature searches ........12
4. Conclusions .......................................................................................................................................14
References ..........................................................................................................................................14
Abbreviations ......................................................................................................................................15
Appendix A – Log file for the tailored search strings to retrieve all relevant data on fumonisins and their modified forms ........................................................................................................16
Appendix B – Identified relevant references for each area .................................................................21
1. Introduction

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

This contract/grant was awarded by EFSA to:
Contractor: National Food Institute, Technical University of Denmark
Contract title: Extensive literature search for studies related to fumonisins and their modified forms
Contract number: RC/EFSA/BIOCONTAM/2016/03

1.1.1. Background as provided by EFSA

The Unit on Biological Hazard and Contaminants (BIOCONTAM 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.

In April 2015 EFSA received from the European Commission a mandate for a scientific opinion on the appropriateness to set a group health based guidance value for fumonisins and their modified forms (EFSA-Q-2015-00227) and a mandate for a scientific opinion on the risks for animal health related to the presence of fumonisins and their modified forms in feed (EFSA-Q-2015-00248). These mandates were allocated to the CONTAM Panel. Working Groups have been established to develop these scientific opinions.

To support preparatory work for the hazard identification and characterization steps in the human and animal risk assessment, EFSA wishes to outsource an extensive literature search (ELS) related to fumonisins and their modified forms.

The present Call is based on EFSA’s 2016 Work Programme for Grants and operational Procurements Financing Decision found in Annex II of the Programming Document 2016-2018, available on EFSA’s website.

1.1.2. Objectives as provided by EFSA

The overall aim of the assignment is to identify and collect all relevant literature related to fumonisins and their modified forms to support preparatory work for the human and animal risk assessment of these substances.

The three specific objectives in this assignment include:

Objective 1:

To design a tailored search strategy to retrieve all potentially relevant studies on fumonisins and their modified forms as defined by EFSA (2014) in the following areas:

- Area 1: Data on chemistry and analysis (substance identification and characterisation, analytical detection and determination, formation).
- Area 2: Data on toxicokinetics (absorption, distribution, metabolism, excretion) in experimental animals, farm and companion animals, humans and from in vitro studies and on biomarkers.
- Area 3: Data on in vitro and in vivo mode of action (MoA) of toxicity.
- Area 4: Data on toxicity in vivo (e.g. acute, subacute, subchronic, chronic toxicity; genotoxicity, carcinogenicity, toxicity to specific organs) in laboratory animals.
- Area 5: Data on toxicity in vitro.

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Objective 2:
To retrieve all potentially relevant studies for fumonisins and their modified forms by execution of an extensive literature search (ELS) using the tailored search strings for the nine areas developed under objective 1.

Objective 3:
To determine the relevance of the retrieved studies by screening titles and abstracts according to preselected eligibility criteria and prepare the outcome of the project for presentation to EFSA.

2. Methodologies
The methodology for systematic reviews including guidance for development and optimisation of a search strategy and for selecting relevant studies has been described by EFSA (2010). This methodology was implemented as appropriate in the Tasks described below.

2.1. Objective 1

2.1.1. Task 1 Developing tailored search strategies and search strings for collecting relevant studies

A tailored search string for each of the nine areas described above was developed for identifying all potentially relevant studies for the human and animal risk assessment of fumonisins and their modified forms.

The search strings are driven by eligibility criteria for each Area (1-9) developed by the Contractor and agreed with EFSA. The eligibility criteria contained both inclusion and exclusion criteria. The search strings were tailored to the databases PubMed and Web of Science\(^2\). Therefore the search strings consisted of two major steps each designed to search titles and abstracts in PubMed and Web of Science, as well as full text in PubMed. Combinations of search terms were used. Use of the Boolean operator “NOT” is generally to be avoided as a relevant reference can contain discussions on both relevant and excluded search terms.

Step 1 consisted of a broad search for fumonisins and their modified forms, synonyms and abbreviations. The dominant fumonisins found as contaminants in food and feed belong to the B group (FB) and comprise FB1 to FB6. Modified forms of fumonisin B (FB) include hydrolysed fumonisin B (HFB), partially hydrolysed fumonisin B (PHFB), N-deoxyfructos-1-yl fumonisin B (NDF-FB) and N-carboxymethyl fumonisin B (NCM-FB) (EFSA 2014). The search strategies were designed to capture the fumonisin B group and their modified forms, as well as to capture other fumonisin groups (e.g. A, C and P) and their modified forms, if any.

Step 2 was Area specific with the addition of search terms relevant to each specific Area.

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\(^2\) Including the following databases: Web of Science™ Core Collection, BIOSIS Citation IndexSM, CABI: CAB Abstracts®, Current Contents Connect®, Data Citation Index SM, FSTA® - the food science resource, MEDLINE®, SciELO Citation Index and Zoological Recored®.
Search terms were identified in collaboration with the entire project team to identify as many relevant as possible. The search terms were developed in order to retrieve the largest number of potentially relevant studies on fumonisins and their modified forms within Area 1-9. The search strings were presented and discussed with EFSA at the kick-off meeting.

2.2. Objective 2

2.2.1. Task 2 Execution of the extensive literature searches using the tailored search strings developed in task 1

The tailored search strings developed in Task 1 and agreed upon by EFSA were employed to retrieve all relevant studies from the databases PubMed and Web of Science on fumonisins and their modified forms.

Data published since year 2000 were retrieved for Area 1-6 and Area 8-9. Data published since year 1980 were retrieved for Area 7.

All references located in the extensive literature searches in PubMed and Web of Science were exported as separate files into EndNote™. Title, author, journal, year of publication and abstract were included for each study imported to EndNote™ and the number of hits resulting from each of the tailored search strings in each of the two databases were recorded in a log file. Duplicate studies were then removed after combining the two EndNote™ files per Area into one single combined file per Area.

2.3. Objective 3

2.3.1. Task 3 Selection of all relevant studies retrieved by the extensive literature searches

All studies retrieved by the extensive literature searches and imported into the combined EndNote™ files, one file per Area (Task 2), were evaluated for relevance by applying eligibility criteria (inclusion/exclusion) for each subject Area (1-9) developed by the Contractor and agreed upon by EFSA. The selection for relevance was conducted by screening their title and abstract (if available) and all the retrieved studies were ultimately sorted into one of the following three categories:

- Relevant to the research objectives: References ultimately evaluated to be relevant were included in this category.
- Maybe relevant to the research objectives: In case the relevance could not be evaluated because e.g. of missing or vague abstracts or because the reference addressed and discussed mycotoxins in general and fumonisins could not be excluded based on the title and abstract of the reference, the references were included in this category, as a conservative approach.
- Not relevant to the research objectives: References ultimately evaluated not to be in-scope were included in this category.

To ensure a uniform understanding of the eligibility criteria in each Area, these were discussed in an internal meeting before all references were assessed for relevance.

According to the original protocol proposed by the Contractor, “Each reference will be individually assessed by two reviewers in order to prevent the introduction of errors and personal bias. In the possible event of disagreements between reviewers a third member of the project team will assist in solving the specific issue as recommended by EFSA (2010).” However, as a result of the very broad search strings for each Area, a huge number of irrelevant hits were retrieved in the ELS for each Area. Furthermore, as a result of the many Areas, a great number of references appeared in more than one area. It was therefore decided that one principal team member for each Area performed an initial sorting of the hits into one of the following four categories: 1) Relevant, 2) Maybe relevant, 3) Not relevant, and 4) to be further assessed. All the references in the fourth category (“to be further
were then evaluated by a principal team member eventually in collaboration with another team member and the references were then included either in the ‘Relevant’, the ‘Maybe relevant’ or in the ‘Not relevant’ category. The project coordinator also assisted in this evaluation. In case relevance still remained uncertain, the references were included in the ‘Maybe relevant’ category, as a conservative approach. This deviation from the original protocol is not considered to invalidate the outcome of the selection for relevance of the studies retrieved from the ELSs because of the control measures and quality check taken in the execution of this task.

During the selection of relevance process the principal team member for a specific Area also identified references of potential relevance for other Areas. After the selection of relevance process was finalised for each Area a cross check was made between one specific Area and all other Areas to ensure that all relevant references have been captured for each Area. References that were identified in another Area / other Areas as being potential relevant for the specific Area, but not retrieved in the Area specific literature searches in PubMed and Web of Science were included in both the Area specific summary table (in an additional sheet) and in the Area Specific EndNote file (in a separate folder).

To ensure a uniform reporting in the summary tables, representative references within each Area were assessed for relevance by all principal team members and discussed in an internal meeting before all references were assessed for relevance. These described measures were implemented to avoid the introduction of time-consuming mistakes.

The results of the reference selection process were reported in summary tables (Excel files), one table per Area. The summary tables included all pertinent information from each of the relevant studies as identified by the eligibility criteria developed by the Contractor and agreed with EFSA. The information included in the summary tables ensures that all eligibility criteria of the studies were considered. Additional fields for relevance (answered by yes/no based on the eligibility criteria), indication of other potential Areas, the person(s) responsible for the screening and comments were also included in the summary tables.

All references found relevant for the human and animal risk assessment of fumonisins and their modified forms within Area 1-9 were collected in a single EndNote file including all indexed fields per reference (i.e. title, author, publication year, journal and abstract).

All relevant studies were collected in a reference list, one list per Area, see Appendix B.

3. Results

3.1. Objective 1

3.1.1. Task 1 Developing tailored search strategies and search strings for collecting relevant studies

The tailored search strings were developed in order to retrieve the largest number of potentially relevant studies for the human and animal risk assessment of fumonisins and their modified forms within Area 1-9.

The proposed search strings were submitted to EFSA on 7 July 2016 (email) as part of Deliverable 1, and were discussed, revised and agreed with EFSA at the kick-off meeting on 11-12 July. The agreed search strings for Step 1 and Step 2, for Area 1-9 are presented below.

The search string for step 1 was developed in order to capture all known fumonisin groups (e.g. A, B, C and P) by using the search term fumonisin*. Regarding modified forms of fumonisins the search terms have been restricted to include the known modified forms of the fumonisin B group defined in the EFSA CONTAM Panel (2014) opinion as modified forms of other fumonisin groups are not known to the Contractor.

The search strings for step 2, Area 2-6 were developed based on the experiences obtained in a similar procurement recently carried out for EFSA ‘Identifying and collecting relevant literature related to the
oral toxicity of furan and its methyl analogues, 2-methylfuran and 3-methylfuran, final report submitted to EFSA on 14 June 2016. In that procurement, the search terms were combined and tested in the databases PubMed and Web of Science to develop the most sensitive and appropriate search string. The search strings were also tested by assessing whether they retrieved relevant papers already known to the project team as recommended in EFSA (2010).

The search strings for step 2, Area 1 and 7-9 were deliberately developed as very broad and detailed in order to capture all potentially relevant data within these Areas. For Area 7, many of the search terms regarding farm and companion animal species were suggested as it is known to the Contractor that fumonisins cause adverse effects in these species; other search terms regarding species were suggested in order to achieve completeness regarding major farm and companion animal species. For Area 8 and 9, many of the search terms regarding food (Area 8) and feed (Area 9) were suggested as it is known to the Contractor that fumonisins have been detected in these foods/feeds; other search terms were suggested in order to achieve completeness regarding major foods/feeds.

In the proposed search strings, “OR” is the Boolean operator that expands the amount of references returned when used in a search string as just one of the search terms need to be present in the returned references. “*” symbolises truncation and is used for finding singular and plural forms of words and various endings. Both PubMed and Web of Science use an asterisk as their truncation symbol.

**Step 1:**
The search string agreed for step 1 is as follows:

- Fumonisin*
- OR HFB*
- OR PHFB*
- OR NDF-FB*
- OR NDF/FB*
- OR NCM-FB*
- OR NCM/FB*

**Step 2:**
The Area specific search strings agreed for step 2 are as follows:

**Area 1:** Data on chemistry and analysis (substance identification and characterisation, analytical detection and determination, formation).

(\textit{Fusarium} OR chem* OR analy* OR identi* OR charact* OR detect* OR determin* OR method* OR form* OR degrad* OR hydroly* OR reaction* OR GC* OR HPLC OR LC-MS OR ICP-MS)

**Area 2:** Data on toxicokinetics (absorption, distribution, metabolism, excretion) in experimental animals, farm and companion animals, humans and from \textit{in vitro} studies and on biomarkers.

(\textit{in vitro} OR absor* OR tissue* OR metabol* OR excret* OR kinetic* OR toxicokinetic* OR pharmacokinetic* OR degrad* OR biotrans* OR eliminat* OR biomark*)

**Area 3:** Data on \textit{in vitro} and \textit{in vivo} mode of action (MoA) of toxicity.

(\textit{in vitro} OR \textit{in vivo} OR mode OR action OR mechanism* OR glycol* OR sphingolipid* OR apoptosis OR oxidative)

**Area 4:** Data on toxicity \textit{in vivo} (e.g. acute, subacute, subchronic, chronic toxicity; genotoxicity, carcinogenicity, toxicity to specific organs) in laboratory animals.

(\textit{in vivo} OR acute OR chronic OR tox* OR genotox* OR muta* OR DNA OR damage OR repair OR clastogen* OR aneugen* OR chromosom* 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...
Extensive literature search for fumonisins and their modified forms

kidney* OR brain* OR lung* OR cardiovascular OR rat* OR mouse OR mice OR rabbit* OR guinea OR hamster* OR primate* OR monkey*)

Area 5: Data on toxicity in vitro.
(in vitro OR cytotox* OR genotox* OR muta* OR DNA OR damage OR repair OR clastogen* OR aneugen* OR chromosom* OR culture)

Area 6: Data on observations in humans (e.g. epidemiological studies, case reports, intervention studies).
(epidemio* OR intervention OR exposure* OR case* OR poison* OR cohort* OR cross-sectional OR random* OR work*)

Area 7: Data on adverse effects in farm and companion animals (studies in the different species e.g. ruminants, pigs, poultry, rabbits, fish, cats, dogs etc.).
(tox* 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 OR farm animals OR horse* OR stallion* OR equine OR ruminant* OR livestock OR herd OR cow* OR cattle 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 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 geese 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 pupp*)

Area 8: Data on occurrence in food.
(Fusarium OR concentration* OR occurrence OR food* OR diet* OR commod* OR fruit* OR pineapple OR Ananas comosus OR vegetable* OR garlic OR Allium sativum OR asparagus 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 Avena sativa OR rice OR Oryza sativa OR soya bean OR Glycine max OR sorghum OR sugar cane OR Saccharum officinarum OR millet OR Eleusine sp. OR Pennisetum glaucum OR starch OR flour OR bran OR germ OR dairy OR milk OR egg* OR meat OR liver OR kidney* OR offal OR coffee)

Area 9: Data on occurrence in feed and animal exposure (including feed commodities, feed intake and animal exposure).
(Fusarium OR concentration* OR occurrence OR feed* OR diet* OR commod* OR fruit* OR pineapple OR Ananas comosus OR vegetable* OR garlic OR Allium sativum OR asparagus 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 Avena sativa OR rice OR Oryza sativa OR soya bean OR Glycine max OR sorghum OR sugar cane OR Saccharum officinarum OR millet OR Eleusine sp. OR Pennisetum glaucum OR starch OR flour OR bran OR germ OR dairy OR milk OR egg* OR meat OR liver OR kidney* OR offal OR coffee)

DDGS: Dried Distillers Grains with Solubles
WDG: Wet Distillers Grains

3.2. Objective 2

3.2.1. Task 2 Execution of the extensive literature searches using the tailored search strings developed in task 1

The number of hits resulting from each of the tailored search strings in each of the two databases PubMed and Web of Science were recorded in a log file, see Appendix A.

The total number of hits from each database, as well as the total number of hits after removal of the duplicates (combined) are summarised in the table below. The duplicates in the combined file for each Area 1-9 were removed by the EndNote tool; however, duplicates may still be present in the combined
files as the EndNote tool for various reasons is not able to remove all duplicates. These duplicates were identified during the execution of Task 3 and then removed manually. The revised versions of the combined files were submitted as part of the final deliverable.

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The search terms NDF-FB*, NDF/FB* and NCM/FB* gave no hits in Web of Science and NDF-FB* gave no hits in PubMed.

The search term GC* in the Area 1 search string gave no hits. The search term GC alone gave 88295 hits, which have been included in the final search for Area 1.

The results of the ELS on fumonisins and their modified forms for Area 1-9 were submitted to EFSA on 29 July (Interim report N2 by email, EndNote files uploaded to the DMS) as Deliverable 2.

For each of Area 1-9, three EndNote files were submitted: One including all hits from PubMed (named: My EndNote Library_AREA X_PubMed.enlx), one including all hits from Web of Science (named: My EndNote Library_AREA X_WoS.enlx), and one including the combined hits from PubMed and Web of Science with duplicate records removed (named: My EndNote Library_AREA X_combined.enlx).

3.3. Objective 3

3.3.1. Task 3 Selection of all relevant studies retrieved by the extensive literature searches

The total number of relevant references for Area 1 was 532, for Area 2 114, for Area 3 273, for Area 4 87, for Area 5 138, for Area 6 38, for Area 7 270, for Area 8 709, and for Area 9 270.

The final protocol and project plan implemented by the Contractor to carry out the project was submitted to EFSA on 7 November (uploaded to the DMS and by email) as part of the draft final deliverable, the final version was submitted to EFSA on 21 November (uploaded to the DMS and by email), and the revised final version was submitted to EFSA on 2 December (uploaded to the DMS and by email) as part of the final deliverable.

Summary tables

A proposal for the information (eligibility criteria) to be included in the summary tables for each area (combined pdf) was submitted to EFSA on 7 July (email) as part of Deliverable 1. The proposed summary tables were discussed with EFSA at the kick-off meeting on 11-12 July. EFSA had a few suggestions for revisions which were agreed at the kick-off meeting, and reflected in the revised version of the summary tables submitted to EFSA on 20 July (email), and again on 27 July (email).

Summary tables (Excel files) were prepared, one table for each Area 1-9. The summary tables include all pertinent information for each of the references in the ‘Relevant’ category as identified by the eligibility criteria suggested by the Contractor and agreed by EFSA, which could be retrieved from the title and abstract (when available).
According to the tender specifications, the summary tables should only include the relevant studies. However, for transparency reasons, it was agreed at the kick-off meeting also to include the ‘Maybe relevant’ and ‘Not relevant’ studies, but without any study details. For the ‘Not relevant’ studies, the reason for exclusion, i.e. not target compound or not relevant for the specific Area is presented. In addition, there is also an indication if a specific reference is considered of potential relevance for other Area(s).

All references included in the ‘Relevant’ category appear on a green background; all references included in the ‘Maybe relevant’ category appear on a yellow background; and all references included in the ‘Not relevant’ category appear on a white background. An additional sheet has been added in the summary tables for all Areas, except for Area 7. This additional sheet includes the references that were identified in another Area / other Areas as being potential relevant for the specific Area, but not retrieved in the Area specific literature searches in PubMed and Web of Science.

The summary tables were submitted to EFSA on 7 November (uploaded to the DMS) as part of the draft final deliverable and the final versions were submitted to EFSA on 21 November (uploaded to the DMS) as part of the final deliverable.

**EndNote™ files**

In the EndNote files, one file per Area (named: My EndNote Library_AREA X_deliverable 3.enlx), all hits were separated into 5 or 6 folders and named as follows:

- ‘Relevant’: Containing hits evaluated to be of relevance for this procurement
- ‘Maybe relevant’: Containing hits for which the relevance could not be evaluated because e.g. of missing or vague abstracts or because the reference addressed and discussed mycotoxins in general and fumonisins could not be excluded based on the title and abstract of the reference
- ‘Not relevant’: Containing hits evaluated not to be in-scope for this procurement
- ‘Relevant from other areas’: Containing hits evaluated to be of relevance for this procurement that were identified in another Area / other Areas than the specific Area, but not retrieved in the Area specific literature searches in PubMed and Web of Science.
- ‘May-be relevant from other areas’: Containing hits that may be relevant that were identified in another Area / other Areas that the specific Area, but not retrieved in the Area specific literature searches in PubMed and Web of Science.
- ‘Trash’: Containing the removed duplicates.

The EndNote files were submitted to EFSA on 7 November (uploaded to the DMS) as part of the draft final deliverable, the final versions were submitted to EFSA on 21 November (uploaded to the DMS), and the revised final versions were submitted to EFSA on 2 December (uploaded to the DMS) as part of the final deliverable.

**Reference lists**

All relevant references were collected in a reference list (Word file), one file per Area. The reference lists are included in Appendix B to this report.
4. Conclusions

An extensive literature search to identify and collect all studies related to fumonisins and their modified forms was performed in the two databases PubMed and Web of Science for nine Areas. The total number of hits from each database, as well as the total number of hits (combined total) and total number of hits after removal of the duplicates (combined) are summarised in the table below.

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</table>

The evaluation of all retrieved references for relevance by screening the title and abstract (if available) and applying eligibility criteria (inclusion/exclusion) resulted in a total number of relevant references for Area 1 of 532, for Area 2 of 114, for Area 3 of 273, for Area 4 of 87, for Area 5 of 138, for Area 6 of 38, for Area 7 of 270, for Area 8 of 709, and for Area 9 of 270.

References


Abbreviations

DDGS  Dried Distillers Grains with Solubles
EFSA  European Food Safety Authority
ELS  Extensive literature search
FB  Fumonisin B
GC  Gas Chromatography
HFB  Hydrolysed fumonisin B
HPLC  High Performance Liquid Chromatography
ICP-MS  Inductively Coupled Plasma Mass Spectrometry
LC-MS  Liquid Chromatography Mass Spectrometry
MoA  Mode of Action
NCM-FB  N-carboxymethyl fumonisin B
NCM/FB  N-carboxymethyl fumonisin B
NDF-FB  N-deoxyfructos-1-yl fumonisin B
NDF/FB  N-deoxyfructos-1-yl fumonisin B
PHFB  Partially hydrolysed fumonisin B
WDG  Wet Distillers Grains
Appendix A – Log file for the tailored search strings to retrieve all relevant data on fumonisins and their modified forms

The search terms NDF-FB*; NDF/FB* and NCM/FB* gave no hits in Web of Science and NDF-FB* gave no hits in PubMed.

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<thead>
<tr>
<th>Date of search</th>
<th>Substance name</th>
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Appendix B – Identified relevant references for each area

Appendix B contains the systematic review of the relevant literature. Versions in excel format are available for all nine areas in the online version of this output (in the “Supporting information” section): http://dx.doi.org/10.2903/sp.efsa.2018.EN-1148

AREA 1 CHEMISTRY AND ANALYSIS

Reference list with all relevant references identified for AREA 1: Data on chemistry and analysis (substance identification and characterisation, analytical detection and determination, formation) published in English since year 2000.

Relevant references retrieved in the literature searches for Area 1 CHEMISTRY AND ANALYSIS:


Bansal, J.; Pantazopoulos, P.; Tam, J.; Cavlovic, P.; Kwong, K.; Turcotte, A. M.; Lau, B. P. Y.; Scott, P.


Bergmann, D.; Hubner, F.; Humpf, H. U., 2013. Stable isotope dilution analysis of small molecules...


Bian, Y. N.; Huang, X. Y.; Ren, J. C., 2016. Sensitive and homogenous immunoassay of fumonisin in foods using single molecule fluorescence correlation spectroscopy, Analytical Methods, 8, 1333-1338.


Extensive literature search for fumonisins and their modified forms


Extensive literature search for fumonisins and their modified forms


Extensive literature search for fumonisins and their modified forms


Extensive literature search for fumonisins and their modified forms


Ezekiel, C. N.; Abia, W. A.; Ogara, I. M.; Sulyok, M.; Warth, B.; Krsk, R., 2015. Fate of mycotoxins in two popular traditional cereal-based beverages (kunu-zaki and pito) from rural nigeria, Lwt-Food Science and Technology, 60, 137-141.


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Extensive literature search for fumonisins and their modified forms


Guo, W. B.; Han, Z.; Yang, J. H.; Rao, Q. X.; Zhao, Z. H., 2016. Simultaneous preparation and characterization of three high-purity type B fumonisins from maize culture. Analytical Methods, 8, 2737-2742.


Ho, J. A. A.; Durst, R. A., 2000. Development of a flow-injection liposome immunoanalysis system for...
fumonisins B1, Analytica Chimica Acta, 414, 61-69.


Extensive literature search for fumonisins and their modified forms


Extensive literature search for fumonisins and their modified forms


Lino, C. M.; Silva, L. J. G.; Pena, A. L. S.; Silveira, M. I., 2006. Determination of fumonisins b1 and b2 in portuguese maize and maize-based samples by hplc with fluorescence detection, Analytical and Bioanalytical Chemistry, 384, 1214-1220.


Extensive literature search for fumonisins and their modified forms


Extensive literature search for fumonisins and their modified forms


Extensive literature search for fumonisins and their modified forms


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**AREA 5 IN VITRO TOXICITY**

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AREA 7 TOXICITY IN FARM ANIMALS

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