

APPENDIX 3

LITERATURE SEARCH FOR ANNUAL MONITORING ON THE GENERAL SURVEILLANCE OF MON 88017 MAIZE IN THE EU

TABLE OF CONTENTS

1. INTRODUCTION.....	3
2. IDENTIFYING THE REVIEW QUESTION AND PURPOSE FOR UNDERTAKING THE LITERATURE SEARCH.....	3
3. SEARCHING FOR IDENTIFYING RELEVANT STUDIES	4
3.1. SEARCH TERMS AND THEIR COMBINATION	4
3.2. LIMITS APPLIED.....	7
3.3. LANGUAGE	7
3.4. TIME PERIOD	7
3.5. REFERENCE STUDIES	8
3.6. INFORMATION SOURCES	14
3.6.1. ELECTRONIC BIBLIOGRAPHIC DATABASES.....	14
3.6.2. RELEVANT KEY ORGANISATIONS	15
4. SELECTING STUDIES	15
4.1. PROCESS	15
4.2. QUALITY ASSURANCE	16
4.3. ELIGIBILITY/INCLUSION CRITERIA TO ESTABLISH RELEVANCE	16
5. SUMMARISING AND REPORTING THE DATA, AND CONSIDERING THE IMPLICATIONS OF THE FINDINGS.....	16
5.1. SEARCH OUTCOMES	16
5.1.1. <i>Outcomes of literature search in electronic bibliographic databases.....</i>	<i>16</i>
5.1.2. <i>Outcomes of literature search in internet pages of relevant key organisations ..</i>	<i>17</i>
5.2. RESULTS OF THE STUDY SELECTION PROCESS FOR ELECTRONIC BIBLIOGRAPHIC DATABASES.....	21
5.3. IMPLICATIONS OF THE RETRIEVED RELEVANT STUDIES FOR THE RISK ASSESSMENT ..	22
6. CONCLUSION	24
REFERENCES.....	25

1. INTRODUCTION

As part of the general surveillance requirements for MON 88017 genetically modified (GM) maize authorised in the European Union (EU) market under regulation (EC) No 1829/2003, Bayer Agriculture BVBA¹ has actively monitored scientific literature related to MON 88017 maize covering the time span between June 2018 and May 2019.

The publications that resulted from this literature search have been analysed in detail according to the relevance for the risk assessment of this product and are presented here.

The completeness literature search checklist (EFSA's Annex 2) is provided as **Attachment I**.

2. IDENTIFYING THE REVIEW QUESTION AND PURPOSE FOR UNDERTAKING THE LITERATURE SEARCH

This literature search has been conducted to address the review question “Do MON 88017 maize derived food/feed products and the introduced insect protection and herbicide tolerance traits have adverse effects on human and animal health and the environment?”

The purpose for undertaking this literature search is to ensure compliance with the 2017 EFSA explanatory note on literature searching for annual post-market environmental monitoring (PMEM) on GM maize products authorised in the EU under regulation (EC) No 1829/2003 (EFSA, 2017).

Key elements used for the review question are humans, animals, and/or the environment (= population), MON 88017 maize, derived food/feed products and the introduced insect protection and herbicide tolerance traits (= intervention/exposure), conventional counterpart or non-GM maize (= comparator), and adverse effect on human and animal health, and the environment (= outcomes). Accordingly, the eligibility criteria for assessing the relevance of studies for inclusion in the literature review are provided in **Table 1**.

¹ Hereafter, referenced as Bayer

Table 1. Eligibility/inclusion criteria to establish the relevance of retrieved studies

Key elements	Criteria
Population	Humans, animals and the environment (taking into account the scope of the application <i>i.e.</i> authorisation for all uses as any other maize but excluding the cultivation of MON 88017 maize are addressed as general protection goals.
Intervention/exposure	MON 88017 maize, derived food/feed products and the introduced insect protection and herbicide tolerance traits addressed in the study are identical or similar to those under scientific review by the EFSA.
Comparator	In case of a comparative study that uses the GM plant material as test material, eligible studies must report a non-GM maize as a comparator.
Outcomes	Adverse effects on human and animal health and the environment are addressed (taking into consideration the scope of the application).
Additional key elements	
Information/ data requirements, including source of studies data	The study potentially contributes to the knowledge of the risk assessment of MON 88017 maize intended for all uses as any other maize, but excluding cultivation. Original/primary data are presented in the study.

3. SEARCHING FOR/IDENTIFYING RELEVANT STUDIES

The approach used to develop the search strategy follows the lumping method and a wide range of free-text terms to define search terms in accordance with the 2010 EFSA Guidance on application of systematic review methodology to food and feed safety assessments to support decision making (EFSA, 2010) and the 2017 EFSA Explanatory note on literature searching (EFSA, 2017).

3.1. Search terms and their combination

The intervention/exposure key elements were defined and translated into search terms. Based on the key elements of the review question, the search terms, the field and the Boolean operators used to combine them were defined as shown in **Table 2**. These search terms considered possible synonyms, related terms, abbreviations and truncations, old and new as well as lay and scientific terminologies, brand and generic names, and spelling variants. Where available, the search was also adapted to controlled vocabulary (subject indexing). The search terms were designed to give an excellent coverage and retrieve the broadest possible number of articles related to MON 88017 maize.

Table 3 shows the translation of the intervention key elements into search terms and, when available, the reference publications used to test the search terms. The table includes lists of search terms that are representative of each key element based on the criteria described above and the free-text terms and spelling variants representative of the indicated search terms. As shown in the table, the free-text terms and spelling variants are used to build the search string in the Web of ScienceTM and EBSCOhost platforms. Where available, controlled vocabularies based on Descriptors which are also representative of the indicated search terms are used to build the search string in EBSCOhost platform. The search terms, free-text terms, controlled vocabularies and the search strings are updated upon identification of a new search term.

Table 2. List of search terms and Boolean operators used to search for MON 88017 related publications

Set	Field	Search string	Key elements (Intervention/Exposure)
Web of Science™ platform			
#11	Combination	#10 OR #9 OR #7 <i>DocType=All document types;</i> <i>Language=All languages;</i>	
#10	Topic	(TS=(MON88017 OR "MON 88017")) <i>DocType=All document types;</i> <i>Language=All languages;</i>	Event
#9	Combination	#8 AND (#2 OR #1) <i>DocType=All document types;</i> <i>Language=All languages;</i>	The newly expressed proteins in GM organisms, including maize
#8	Topic	(TS=((Cry3Bb* OR "Cry3 Bb*" OR "Cry 3 Bb*" OR "Cry 3Bb*" OR CryIIIBb* OR "CryIII Bb*" OR "Cry III Bb*" OR "Cry IIIBb*")) AND (cp4epsps OR "cp4 epsps")) <i>DocType=All document types;</i> <i>Language=All languages;</i>	Newly expressed proteins
#7	Combination	#6 OR #5 <i>DocType=All document types;</i> <i>Language=All languages;</i>	GM maize displaying the introduced insect protection and herbicide tolerance traits OR GM maize with the indicated trade names
#6	Combination	#4 AND #2 AND #1 <i>DocType=All document types;</i> <i>Language=All languages;</i>	GM maize with the indicated trade names
#5	Combination	#3 AND #2 AND #1 <i>DocType=All document types;</i> <i>Language=All languages;</i>	GM maize displaying the introduced insect protection and herbicide tolerance traits
#4	Topic	(TS=("Yield Gard VT Rootworm RR2" OR "YieldG* VT Rootworm RR2" OR "Yield Gard VT Rootworm Roundup Ready 2" OR "YieldG* VT Rootworm Roundup Ready 2" OR CCR)) <i>DocType=All document types;</i> <i>Language=All languages;</i>	Trade names
#3	Topic	(TS=((TOLERAN* OR RESISTAN* OR PROTEC*) NEAR/5 (GLYPHOSATE OR ROUNDUP OR Rootworm* OR "Root worm*" OR Coleoptera OR Chrysomel* OR Diabrotica))) <i>DocType=All document types;</i> <i>Language=All languages;</i>	Introduced insect protection and herbicide tolerance traits
#2	Topic	(TS=(maize* OR corn* OR "Zea mays" OR "z mays")) <i>DocType=All document types;</i>	Plant species

Set	Field	Search string	Key elements (Intervention/Exposure)
		<i>Language=All languages;</i>	
#1	Topic	(TS=(GMO* OR LMO* OR GM OR GE OR transgen* OR ((genetic* OR living OR biotech*) NEAR/5 (modif* OR transform* OR manipul* OR improv* OR engineer* OR deriv*)))) <i>DocType=All document types;</i> <i>Language=All languages;</i>	GMO general
EBSCOhost platform (<i>All document types and all languages</i>)			
S14	Combination	S9 OR S11 OR S12	
S13	All Text	TX (MON88017 OR "MON 88017")	Event
S12	Combination	S11 AND (S2 OR S1)	The newly expressed proteins in GM organisms, including maize
S11	All Text	TX ((Cry3Bb* OR "Cry3 Bb*" OR "Cry 3 Bb*" OR "Cry 3Bb*" OR CryIIIBb* OR "CryIII Bb*" OR "Cry III Bb*" OR "Cry IIIBb*") AND (cp4epsps OR "cp4 epsps"))	Newly expressed proteins
S10	Combination	S8 OR S9	GM maize displaying the introduced insect protection and herbicide tolerance traits OR GM maize with the indicated trade name
S9	Combination	S1 AND S2 AND S7	GM maize with the indicated trade name
S8	All Text	S1 AND S2 AND S6	GM maize displaying the introduced insect protection and herbicide tolerance traits
S7	All Text	TX ("Yield Gard VT Rootworm RR2" OR "YieldG* VT Rootworm RR2" OR "Yield Gard VT Rootworm Roundup Ready 2" OR "YieldG* VT Rootworm Roundup Ready 2" OR CCR)	Trade name
S6	Combination	S3 AND (S4 OR S5)	
S5	Descriptor	DE "glyphosate"	Controlled vocabularies (subject indexes) offered by the database for introduced insect protection and herbicide tolerance traits
S4	Descriptor	DE "Coleoptera"	
S3	Descriptor	DE "insect control" OR DE "weed control"	
S2	Descriptor	DE "Zea mays" OR DE "maize"	Controlled vocabularies (subject indexes) offered by the database for plant species. Note that the term 'corn' is covered by the term 'maize'.
S1	Descriptor	DE "genetic engineering" OR DE "genetic transformation" OR DE "genetically engineered foods" OR DE "genetically engineered organisms"	Controlled vocabularies (subject indexes) offered by the database for GMO general term

3.2. Limits applied

An advanced literature search was conducted in the Web of Science™ Core collection database using the Web of Science™ platform² and in the CAB Abstracts® database³ using the EBSCOhost platform⁴ (see section 3.6.1). Each platform enables searching in the specified electronic database by making use of pre-defined fields, set combinations based on Boolean operators or a combination of both^{5,6}.

The literature search strategy utilises the “Topic” (TS) field in Web of Science™ platform and the “TX” field in EBSCOhost platform which have the broadest coverage of search terms and enable comprehensive searching within a record^{7,6} (see **Table 2**). In the case of the Web of Science™ Core collection database, the “TS” field searches for topic terms in the following fields within a record: Title, Abstracts, Author Keywords and Keywords Plus®. The Keywords Plus® facility maximises the possibility of retrieving relevant records in the advanced search⁸. In the case of the CAB Abstracts® database, the “TX” field searches for the search terms “*within the full text of all articles for your term*”⁶.

In this literature search, the search strategy utilised also the controlled vocabulary (subject indexing) facility offered by the CAB Abstracts® database. Accordingly, the search string was refined by using the CAB Thesaurus-Descriptors field, which is assigned by subject specialists to CAB records to represent the content of the source documents. The Descriptor (“DE”) field enables selection of one or more controlled terms from the CAB Thesaurus to add to the search query. More importantly, having a controlled vocabulary allows users to use only one term to search for a concept rather than using lots of terms⁹. The most relevant, broad and controlled search terms in the hierarchy of CAB Thesaurus terms that were listed as preferred terms by CAB for the search query were selected and added to the search string in combination with the “DE” field (see **Table 2**).

3.3. Language

The search terms and their combination are established in English; hence, the search is expected to result in a list of articles written in English and/or articles written in other languages with at least a title, abstract or keywords in English. Also, technical terms like proteins names, MON codes, Latin names, ... are common in all languages and therefore, articles in all languages, as specified in **Table 2**, will be retrieved.

3.4. Time period

This literature search covered the reporting period from June 2018 until May 2019.

²http://apps.webofknowledge.com/UA_GeneralSearch_input.do?product=UA&SID=X1sK9uHnF5WXHkLGpbw&search_mode=GeneralSearch - Accessed on 03 October 2019

³http://support.ebsco.com/help/?int=ehost&lang=en&feature_id=Databases&TOC_ID=Always&SI=0&BU=0&GU=1&PS=0&ver=live&db=lah - Accessed on 03 October 2019

⁴<https://help.ebsco.com/interfaces/EBSCOhost> - Accessed on 03 October 2019

⁵http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hp_advanced_examples.html - Accessed on 03 October 2019

⁶https://help.ebsco.com/interfaces/EBSCOhost/training_promotion/Advanced_Searching_EBSCOhost_Tutorial - Accessed on 03 October 2019

⁷http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hs_advanced_fieldtags.html - Accessed on 03 October 2019

⁸<http://clarivate.libguides.com/woscc/searchtips> - Accessed on 03 October 2019

⁹<https://www.cabi.org/Uploads/CABI/publishing/training-materials/resources-by-interface/cab-direct-user-guides/advanced-searching-cab-abstracts.pdf> - Accessed on 03 October 2019

3.5. Reference studies

In accordance with the 2017 EFSA Explanatory note on literature searching (EFSA, 2017), a list of reference publications, complying with the eligibility/inclusion criteria, to test, fine-tune and validate the search strategy as part of the protocol development was used whenever available (**Table 3**).

Table 3. Translation of intervention/exposure key elements into search terms for MON 88017 literature search in the Web of Science™ Core Collection and CAB Abstracts® databases

Key elements		Search terms	Comments
GMO general			
<i>Reference publications</i>		Not applicable.	<p>This step is to focus the search on GM related papers.</p> <p>The search terms, free-text terms, controlled vocabularies and the search strings are updated upon identification of a new search term.</p>
<i>Search terms</i>		Genetically modified organism (GMO, GM); Living modified organism (LMO); biotechnology-derived organism (biotech-derived); Genetic engineering (GE); transgenesis (transgene); genetic transformation; genetic manipulation; genetic improvement.	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=(GMO* OR LMO* OR GM OR GE OR transgen*OR ((genetic* OR living OR biotech*) NEAR/5 (modif* OR transform* OR manipul* OR improv* OR engineer* OR deriv*))))	
	<i>Truncations and spelling variants used and their meanings</i>	GMO* = GMO, GMOs, GMO's GM = GM crop, GM plant, GM crops, GM plants GE = GE crop, GE plant, GE crops, GE plants LMO* = LMO, LMOs, LMO's Transgen* = transgene, transgenic, transgenesis Genetic* = genetic, genetically Biotech* = biotech, biotechnology, biotechnological Modif* = modify, modified, modification Transform* = transform, transformed, transformation Manipulat* = manipulate, manipulated, manipulation Improv* = improve, improved, improvement Engineer* = engineer, engineered, engineering Deriv* = derive, derived	
<i>EBSCOhost platform</i>	<i>Search string based on controlled vocabularies using the Descriptors (DE) field</i>	DE "genetic engineering" OR DE "genetic transformation" OR DE "genetically engineered foods" OR DE "genetically engineered organisms"	

Key elements		Search terms	Comments
Crop name			
<i>Reference publications</i>		Not applicable.	<p>This step is to focus the search on maize related papers.</p> <p>The search terms, free-text terms, controlled vocabularies and the search strings are updated upon identification of a new search term.</p>
<i>Search terms</i>		Maize, corn, <i>Zea mays</i> , <i>Z mays</i>	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=(maize* OR corn* OR " <i>Zea mays</i> " OR "z mays"))	
	<i>Truncations and spelling variants used and their meanings</i>	Maize* = maize, maizes, maize's Corn* = corn, corns, corn's	
<i>EBSCOhost platform</i>	<i>Search string based on controlled vocabularies using the Descriptors (DE) field</i>	DE " <i>Zea mays</i> " OR DE "maize"	
Intended trait			
<i>Reference publications</i>		<p>1) Healy <i>et al.</i> 2008. Results of a 13-week safety assurance study with rats fed grain from corn rootworm-protected, glyphosate-tolerant MON 88017 corn. Food and Chemical Toxicology, 46, 2517-2524.</p> <p>2) Curran <i>et al.</i> 2015. Kernel compositions of glyphosate-tolerant and corn rootworm-protected MON 88017 sweet corn and insect-protected MON 89034 sweet corn are equivalent to that of conventional sweet corn (<i>Zea mays</i>). Agricultural and Food Chemistry, 63, 3046-3052.</p>	
<i>Search terms</i>		Glyphosate/ Roundup tolerance, Protection against corn rootworm/ coleopteran pests/ <i>Chrysomelidae</i> spp/ <i>Diabrotica</i> spp.	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=((TOLERAN* OR RESISTAN* OR PROTEC*) NEAR/5 (GLYPHOSATE OR ROUNDUP OR Rootworm* OR "Root worm*" OR Coleoptera OR Chrysomel* OR Diabrotica)))	

Key elements		Search terms	Comments
	<i>Truncations and spelling variants used and their meanings</i>	Toleran* = tolerance, tolerant Resistan* = resistance, resistant Protect* = protection, protected Rootworm* = rootworm, rootworms, rootworm's Root worm* = root worm, root worms, root worm's Chrysomel* = <i>Chrysomelidae</i> spp	
<i>EBSCOhost platform</i>	<i>Search string based on controlled vocabularies using the Descriptors (DE) field</i>	DE "glyphosate" DE "Coleoptera" DE "insect control" OR DE "weed control"	
Trade names			
<i>Reference publications</i>		1) Healy <i>et al.</i> 2008. Results of a 13-week safety assurance study with rats fed grain from corn rootworm-protected, glyphosate-tolerant MON 88017 corn. Food and Chemical Toxicology, 46, 2517-2524.	
<i>Search terms</i>		YieldGard VT Rootworm Roundup Ready 2/RR2	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=("Yield Gard VT Rootworm RR2" OR "YieldG* VT Rootworm RR2" OR "Yield Gard VT Rootworm Roundup Ready 2" OR "YieldG* VT Rootworm Roundup Ready 2" OR CCR))	
	<i>Truncations and spelling variants used and their meanings</i>	"YieldG* VT Rootworm RR2" = YieldGard VT Rootworm Roundup Ready 2/RR2 "YieldG* VT Rootworm Roundup Ready 2" = YieldGard VT Rootworm Roundup Ready 2/RR2 CCR = Control of Corn Rootworm	
<i>EBSCOhost platform</i>	<i>Search string based on free-text terms using the All Text (TX) field</i>	TX ("Yield Gard VT Rootworm RR2" OR "YieldG* VT Rootworm RR2" OR "Yield Gard VT Rootworm Roundup Ready 2" OR "YieldG* VT Rootworm Roundup Ready 2" OR CCR)	
	<i>Truncations and spelling variants used and their meanings</i>	"YieldG* VT Rootworm RR2" = YieldGard VT Rootworm Roundup Ready 2/RR2 "YieldG* VT Rootworm Roundup Ready 2" = YieldGard VT Rootworm Roundup Ready 2/RR2 CCR = Control of Corn Rootworm	

Key elements		Search terms	Comments
Newly expressed protein			
Reference publications		1) Healy <i>et al.</i> 2008. Results of a 13-week safety assurance study with rats fed grain from corn rootworm-protected, glyphosate-tolerant MON 88017 corn. Food and Chemical Toxicology, 46, 2517-2524. 2) Curran <i>et al.</i> 2015. Kernel compositions of glyphosate-tolerant and corn rootworm-protected MON 88017 sweet corn and insect-protected mon 89034 sweet corn are equivalent to that of conventional sweet corn (<i>Zea mays</i>). Agricultural and Food Chemistry, 63, 3046-3052	
Search terms		CP4 EPSPS, Cry3Bb1	
Web of science™ platform	Search string based on free-text terms using the Topic (TS) field	(TS=((Cry3Bb* OR "Cry3 Bb*" OR "Cry 3 Bb*" OR "Cry 3Bb*" OR CryIIIBb* OR "CryIII Bb*" OR "Cry III Bb*" OR "Cry IIIBb*") AND (cp4epsps OR "cp4 epsps")))	
	Truncations and spelling variants used and their meanings	Cry3Bb*, "Cry3 Bb*", "Cry 3 Bb*","Cry 3Bb*", CryIIIBb*, "Cry III Bb*", "Cry IIIBb*" = Cry3Bb1	
EBSCOhost platform	Search string based on free-text terms using the All Text (TX) field	TX ((Cry3Bb* OR "Cry3 Bb*" OR "Cry 3 Bb*" OR "Cry 3Bb*" OR CryIIIBb* OR "CryIII Bb*" OR "Cry III Bb*" OR "Cry IIIBb*") AND (cp4epsps OR "cp4 epsps"))	
	Truncations and spelling variants used and their meanings	Cry3Bb*, "Cry3 Bb*", "Cry 3 Bb*","Cry 3Bb*", CryIIIBb*, "Cry III Bb*", "Cry IIIBb*" = Cry3Bb1	
Event			

Key elements		Search terms	Comments
<i>Reference publications</i>		<p>1) Healy <i>et al.</i> 2008. Results of a 13-week safety assurance study with rats fed grain from corn rootworm-protected, glyphosate-tolerant MON 88017 corn. Food and Chemical Toxicology, 46, 2517-2524.</p> <p>2) Curran <i>et al.</i> 2015. Kernel Compositions of glyphosate-tolerant and corn rootworm-protected MON 88017 sweet corn and insect-protected mon 89034 sweet corn are equivalent to that of conventional sweet corn (<i>Zea mays</i>). Agricultural and Food Chemistry, 63, 3046-3052</p>	
	<i>Search terms</i>	MON 88017	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=(MON88017 OR "MON 88017"))	
	<i>Truncations and spelling variants used and their meanings</i>	The options shown in the search string above are spelling variants. Truncations are not applicable.	
<i>EBSCOhost platform</i>	<i>Search string based on free-text terms using the All Text (TX) field</i>	TX (MON88017 OR "MON 88017")	
	<i>Truncations and spelling variants used and their meanings</i>	The options shown in the search string above are spelling variants. Truncations are not applicable.	

3.6. Information sources

3.6.1. Electronic bibliographic databases

Based on the coverage and relevance of the journals included, Bayer selects the Web of Science™ Core Collection database¹⁰ and the CAB Abstracts® database¹¹ for performing the literature searches. The advanced literature search was conducted using the Web of Science™ platform⁴ for the Web of Science™ Core collection database and using the EBSCOhost platform⁶ for the CAB Abstracts® database³.

The Web of Science™ Core Collection database¹⁰ includes literature captured under the following two catalogues: 1) the Science Citation Index Expanded (1995-present); and 2) the Conference Proceedings Citation Index-Science (1990-present). These catalogues offer a complete view of item from a journal, including original research articles, reviews, editorials, chronologies, conference proceedings, bulletins, monographs, and technical reports. This database is “*indisputably the largest citation database available, with over 1 billion cited reference connections indexed from high quality peer reviewed journals, books and proceedings. Each cited reference is meticulously indexed to ensure that it is searchable and attributes credit to the appropriate publication.*”¹⁰. Further, The Web of Science™ Core Collection database is connected to Google Scholar to allow a seamless movement between the open web and the Web of Science™ Core Collection for the literature search¹⁰.

The CAB Abstracts® database¹¹ includes literature capture under the CAB Abstracts (1972-present) catalogue. This catalogue offers a complete view of items from a journal, including original research articles, reviews, books, conference proceedings/ papers, correspondences, editorials, patents, thesis, reports, and bulletins on international agricultural literature, including plant protection, animal husbandry, animal and plant breeding, genetics, and nutrition.

All journals included in the two databases must go through a verification process and as a minimum requirement, non-English language journals must include English-language bibliographic information (title, abstract, keywords) and be peer-reviewed. In general, English is considered the universal language of science¹². For this reason, the journals most important to the international research community will publish either full text or a minimum of bibliographic information in English, which is especially true in the scientific domain of natural sciences. Full text in English is highly desirable if the journal intends to serve an international community of researchers. Therefore, it is expected that even if there is a relevant article for the food and feed safety of GM plants in a language different than English, the article will include title/abstract/keywords in English, which will guarantee the retrievability of these articles when using keywords and keyword combinations in English.

Based on the above, the selected databases are, to our knowledge, comprehensive, multidisciplinary, conservative sources for literature searching and offer the broadest coverage to retrieve a largest breadth of possible relevant studies. Therefore, additional search sources are not deemed necessary.

¹⁰ Web of Science Core Collection; <https://clarivate.com/products/web-of-science/web-science-form/web-science-core-collection/> - Accessed on 03 October 2019

¹¹ CABI CAB Abstracts® database; <http://www.cabi.org/cab-direct/> - Accessed on 03 October 2019

¹² Web of Science™; <http://wokinfo.com/essays/journal-selection-process/> - Accessed on 03 October 2019

3.6.2. Relevant key organisations

In accordance with the 2017 Explanatory note on literature searching (EFSA, 2017) and additional EFSA recommendations, the search in electronic bibliographic databases has been complemented with literature search in internet pages of relevant key organisations involved in the risk assessment of GM plants.

Of the 13 key organisations cited in the 2017 Explanatory note on literature searching (EFSA, 2017), nine¹³ are involved in risk assessment of single GM maize products. Two of the remaining four (CIBIOGEM and Environment and Climate Change Canada) are not involved in GM risk assessment while the other two (OGTR and GEAC), for the time being, only assess GM cotton and oilseed rape. Therefore, the internet search focused on the nine key organisations relevant for MON 88017.

For the selection of studies, all records concerning GMO applications and approvals published in the webpages of each relevant key organisation were screened based on 'limits applied' as shown **Table 4**. Afterwards, all the records within the specified limits were assessed for their relevance to MON 88017 and the results are presented in **Section 5.1.2**.

4. SELECTING STUDIES

Studies retrieved from the literature search were screened for their relevance first and then the selected ones were evaluated for their reliability through detailed assessments. Relevance to the search scope and scientific reliability were rigorously assessed by internal and external technical experts.

4.1. Process

The process of selecting relevant studies was undertaken in two stages:

- **Rapid assessment** for the relevance based on information in the title and abstract of the studies, to exclude publications that are obviously irrelevant.
- **Detailed assessment** of full-text document if required. Experts with a solid experience in the risk assessment of GM plants and experts with technical experience in the specific area of the selected publication performed this analysis. This stage was conducted to formally assess the identified studies (methodological quality) and the result has then been used to assess if the conclusions on the food/feed safety of the risk assessment, based on the comprehensive weight of evidence, are still valid.

¹³ Internet pages of the relevant key organisations for MON 88017 maize:

US EPA (<https://www.epa.gov/environmental-topics/science-topics>) - Accessed on 03 October 2019;

USDA (<https://www.usda.gov/media>) - Accessed on 03 October 2019;

US FDA (<https://www.fda.gov/>) - Accessed on 03 October 2019;

CFIA (<http://www.inspection.gc.ca/eng/1297964599443/1297965645317>) - Accessed on 03 October 2019;

Health Canada (<https://www.canada.ca/en/health-canada.html>) - Accessed on 03 October 2019;

FSANZ (<http://www.foodstandards.gov.au/Pages/default.aspx>) - Accessed on 03 October 2019;

CTNBio (<http://ctnbio.mcti.gov.br/>) - Accessed on 03 October 2019;

CONABIA (<https://www.argentina.gob.ar/>) - Accessed on 03 October 2019;

Japan MAFF (<http://www.maff.go.jp/e/>) - Accessed on 03 October 2019

4.2. Quality assurance

All publications that were identified by the search described in Section 3 have been screened by three different reviewers (one internal and two external experts) with solid experience in the risk assessment of GM plants.

In case of disagreements on eligibility for the inclusion of studies, the reviewers discuss together. If uncertainty remains, the study is *de facto* included for further consideration.

4.3. Eligibility/inclusion criteria to establish relevance

From the full reference list of retrieved hits, taking into account i) the review question, ii) the scope of the application, *i.e.* authorisation of MON 88017 maize for all uses as any other maize but excluding cultivation in the EU and iii) the eligibility criteria to establish the relevance of retrieved studies, an assessment was conducted in order to conclude whether a certain publication was considered relevant or not. When a publication was considered relevant, the category the publication belongs to is indicated. The following is a non-exhaustive list of categories publications can belong to:

Food/Feed safety assessment

- Molecular characterisation
- Protein expression
- Crop composition
- Agronomic and phenotypic characteristics
- Toxicology - Animal feeding / *In vitro*
- Allergenicity of the protein or the whole food/feed
- Nutrition
- Protein / DNA/ RNA fate in digestive tract

Environmental safety assessment

- Spillage and consequences thereof

It should be noted that the selection criteria are well defined and reassessed annually.

5. SUMMARISING AND REPORTING THE DATA, AND CONSIDERING THE IMPLICATIONS OF THE FINDINGS

5.1. Search outcomes

5.1.1. Outcomes of literature search in electronic bibliographic databases

The literature search was run using Web of ScienceTM Core Collection and the CAB Abstracts[®] databases on a monthly basis, covering the time span June 2018–May 2019. As a result, 25 hits were identified using Web of ScienceTM Core Collection database and 9 hits using the CAB Abstracts[®] database.

5.1.2. Outcomes of literature search in internet pages of relevant key organisations

The literature search in the internet pages of the relevant key organisations was conducted on 03 October 2019. The links to the results of the literature search and the summary of the retrieved data are shown in **Table 4**. There was no publication based on primary/original data that needed further assessment.

Table 4. Results of literature search in internet pages of relevant key organisations for MON 88017 maize

Relevant key organisations	Link to the relevant information and summary of the retrieved data
US EPA	<p>https://www.epa.gov/ingredients-used-pesticide-products/current-and-previously-registered-section-3-plant-incorporated – Accessed on 03 October 2019. The webpage dedicated to PIP registrations was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> 24/10/2018</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list of PIP active ingredients registered was sorted by ‘Year Registered’ and those registered starting from 2018 were assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “1”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved record is not relevant to MON 88017.</p>
USDA	<p>https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/petitions/petition-status - Accessed on 03 October 2019. The webpage dedicated to petitions for determination of nonregulated status was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> 26/09/2019</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list of the petitions was sorted by ‘Effective Date’ and those completed/ released starting from 01/01/2018 were assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “5”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017.</p>
US FDA	<p>https://www.accessdata.fda.gov/scripts/fdcc/?set=Biocon – Accessed on 03 October 2019. The webpage dedicated to biotechnology consultations on food from GE plant varieties was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> 05/09/2019</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list of the consultations starting from the ‘FDA Letter Date’ of Jan 1, 2018 was assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “7”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017.</p>

Relevant key organisations	Link to the relevant information and summary of the retrieved data
CFIA	<p>http://www.inspection.gc.ca/plants/plants-with-novel-traits/approved-under-review/decision-documents/eng/1303704378026/1303704484236 - Accessed on 03 October 2019. The webpage dedicated to decision documents – determination of environmental and livestock feed safety was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> 28/05/2019</p> <p><i>Date span of the search:</i> 2018 – 2019</p> <p><i>Limits applied:</i> The list of decision documents starting from the DD No. = DD2018 was assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “2”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017.</p>
Health Canada	<p>https://www.canada.ca/en/health-canada/services/food-nutrition/genetically-modified-foods-other-novel-foods/approved-products.html - Accessed on 03 October 2019. The webpage dedicated to approved products of genetically modified (GM) foods and other novel foods was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> 26/06/2019</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list of novel food decisions starting from the ‘Decision Date’ of 01/01/2018 was assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “7”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017.</p>
FSANZ	<p>http://www.foodstandards.gov.au/consumer/gmfood/applications/Pages/default.aspx - Accessed on 03 October 2019. The webpage dedicated to current GM applications and approvals was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> August 2019</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list for GM applications and approvals with ‘Status’ approved or under assessment starting from 2018 was assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “5”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017.</p>

Relevant key organisations	Link to the relevant information and summary of the retrieved data
CTNBio	<p>http://ctnbio.mcti.gov.br/liberacao-comercial#/liberacao-comercial/consultar-processo – Accessed on 03 October 2019. The webpage dedicated to commercial releases (= Liberações Comerciais) was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> Not clear (several dates mentioned)</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list of commercial releases for plants (= plantas) starting from 2018 was assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “11”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017</p>
CONABIA	<p>https://www.argentina.gob.ar/agroindustria/alimentos-y-bioeconomia/ogm-comerciales – Accessed on 03 October 2019. The webpage of the national advisory commission on agricultural biotechnology (= Comisión Nacional Asesora de Biotecnología Agropecuaria) was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> Not available</p> <p><i>Date span of the search:</i> 2018-2019</p> <p><i>Limits applied:</i> The list of decision documents open for public comment was assessed. Note: decision documents are available for 60 days to allow the public to give comments and are removed afterwards.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “17”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017</p>
MAFF	<p>http://www.maff.go.jp/j/syouan/nouan/carta/torikumi/attach/pdf/index-189.pdf - Accessed on 03 October 2019. The weblink dedicated to list of approved genetically modified agricultural crops was checked.</p> <p><i>Date of the most recent website update at the time of the search:</i> 30/05/2019</p> <p><i>Date span of the search:</i> 2018 – 2019</p> <p><i>Limits applied:</i> The list of GM agricultural crops with approval date (‘承認日’) starting from January 01, 2018 was assessed.</p> <p><i>Number of records retrieved matching the abovementioned criteria:</i> “17”.</p> <p><i>Number of relevant records or full-text documents retrieved:</i> The retrieved records are not relevant to MON 88017.</p>

5.2. Results of the study selection process for electronic bibliographic databases

The results of the study selection process are provided in **Table 5**. The one relevant study retrieved after detailed assessment of the full text document (ordered by category of information) is listed in **Table 6**. Excluded studies after detailed assessment of the full text documents for relevance are listed in **Table 7**. A copy of the full-text document listed in Table 6 is provided as a pdf file in the references folder of this document.

Table 5. Results of the study selection process.

Review question captured in the search	Number of studies	
	Web of Science™ Core Collection database	CAB Abstracts® database
Total number of <i>studies</i> retrieved after all searches of the scientific literature (excluding duplicates)	25	9
Number of <i>studies</i> excluded from the search results after rapid assessment for relevance	21	8
Total number of <i>full-text documents</i> assessed in detail (excluding duplicates)	5	
Number of <i>studies</i> excluded from further consideration after detailed assessment for relevance	4	
Total number of unobtainable/unclear studies	0	
Total number of relevant studies	1	

Table 6. Report of all relevant studies retrieved after detailed assessment of full-text documents for relevance: ordered by category of information.

Study (author(s) and year)	Title	Source
Food/Feed safety assessment		
Nutrition		
Chrenková <i>et al.</i> (2012)	The influence of diet with genetically modified maize on growth, nutrient digestibility and health status of broiler rabbits.	Folia Veterinaria
Environmental safety assessment		
No relevant studies identified		

Table 7. Report of studies excluded from the risk assessment after detailed assessment of full-text documents (classified by authors)

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
Mesnage, R <i>et al.</i>	2018	An integrated multi-omics analysis of the NK603 roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process (vol 25, pg 455, 2018)	Scientific reports	The hybrid used to conduct the study is not MON 88017
Wechsler, S and Smith, D	2018	Has resistance taken root in us corn fields? Demand for insect control	American Journal of Agricultural Economics	It is not a food/feed safety study on MON 88017
Signorini, AM <i>et al.</i>	2018	Management of field-evolved resistance to Bt maize in Argentina: a multi-institutional approach	Frontiers in Bioengineering and Biotechnology	It is not a food/feed safety study on MON 88017
Liu, MM <i>et al.</i>	2018	Molecular characterization and efficacy evaluation of a transgenic corn event for insect resistance and glyphosate tolerance	Journal of Zhejiang University-Science B	The hybrid used to conduct the study is not MON 88017

5.3. Implications of the retrieved relevant studies for the risk assessment

Table 8 reports the reliability and implications for the risk assessment of all the relevant studies. The relevant study did not identify any new information that would require further consideration in the risk assessment of MON 88017 which found no adverse effects on human, animal health and the environment.

The literature search conducted by Bayer provides a comprehensive analysis of reliable scientific publications that are relevant to the food, feed, and environmental safety of MON 88017. Therefore, a systematic review would not add value to the risk assessment of this product.

Table 8. Report of the reliability and implications for the risk assessment of all relevant studies retrieved after detailed assessment of full-text documents for relevance: ordered by category of information.

Study author(s) and year	Reliability appraisal ¹	Implications for the risk assessment ²
Nutrition		
Chrenková <i>et al.</i> (2012)	Not reliable	None, because no new hazards, modified exposure, or new scientific uncertainties are reported

¹ **High** (use as key study); **Moderate** because the study reported is subject to some limitations (useable as key study depending on the limitations of the study); **Low** because the study reported is subject to several limitations (limited use or not useful; generally not to be used as key study, but depending on the limitations of the study, it may be useful in weight of evidence approaches or as supporting information); **Not reliable** because the study reported does not comply with minimum reliability criteria carrying a high level of uncertainty (not useful); **Not assignable** because no or insufficient information is reported in the study (EFSA, 2017).

² Identification of a new hazard, modified exposure, or new scientific uncertainty requiring further consideration in the risk assessment; **None**, because no new hazards, modified exposure, or new scientific uncertainties are reported; **None**, because the findings reported in the study are not reliable; Implications for risk assessment were previously considered by EFSA and/or its GMO Panel, and are therefore not addressed further here (EFSA, 2017).

6. CONCLUSION

Taking into consideration all the above, Bayer confirms that this literature search, conducted in accordance with the 2017 EFSA explanatory note on literature searching (EFSA, 2017) and within the context of general surveillance for MON 88017 in the EU, identified no relevant publications that would invalidate the initial conclusions of the MON 88017 risk assessment. Therefore, the conclusions of the risk assessment as presented in the initial application remain unchanged. No adverse effects are to be expected from authorised uses of MON 88017 in the EU.

REFERENCES

References in grey are EFSA publications and are therefore not provided with this response.

Chrenková M, Chrastinová L, Poláciková M, Formlová Z, Plachá I, Szabóová R, Ondruska L, Parkányi V, Vasicek D, Pogány Simonová M and Strompfová V, 2012. The influence of diet with genetically modified maize on growth, nutrient digestibility and health status of broiler rabbits. *Folia Veterinaria*, 56, 28-30.

EFSA, 2010. Application of systematic review methodology to food and feed safety assessments to support decision making *The EFSA Journal*, 1637, 1-90.

EFSA, 2017. Explanatory note on literature searching conducted in the context of GMO applications for (renewed) market authorisation and annual post-market environmental monitoring reports on GMOs authorised in the EU market. *EFSA journal*, 2017:EN-1207, 1-48.