

APPENDIX 3

LITERATURE SEARCH FOR ANNUAL MONITORING ON THE GENERAL SURVEILLANCE OF MON 87427 × MON 89034 × NK603 AND ITS SUB-COMBINATIONS IN THE EU

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1. INTRODUCTION

As part of the general surveillance requirements for MON 87427 × MON 89034 × NK603 and three related GM maize combining two different single GM events (MON 89034 × NK603, MON 87427 × MON 89034, MON 87247 × NK603) authorised in the European Union (EU) market under regulation (EC) No 1829/2003, Bayer Agriculture BVBA¹ has actively monitored scientific literature related to MON 87427 × MON 89034 × NK603 maize and its sub-combinations 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 87427 × MON 89034 × NK603 maize and its sub-combinations derived food/feed products and the introduced insect protection and/or 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 87427 × MON 89034 × NK603 maize and its sub-combinations, derived food/feed products and the introduced insect protection and/or 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 87427 × MON 89034 × NK603 maize and its sub-combinations are addressed as general protection goals.
Intervention/exposure	MON 87427 × MON 89034 × NK603 maize and its sub-combinations, 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	
Stacked events/sub-combinations	The single events addressed in the study are the single events in MON 87427 × MON 89034 × NK603 maize and its sub-combinations. MON 87427 × MON 89034 × NK603 maize or its sub-combinations are addressed in the study
Information/ data requirements, including source of studies data	The study potentially contributes to the knowledge of the risk assessment of MON 87427 × MON 89034 × NK603 maize and its sub-combinations 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 87427 × MON 89034 × NK603 maize and its sub combinations.

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 87427 × MON 89034 × NK603 and its sub combinations related publications

Set	Field	Search string	Key elements (Intervention/Exposure)
Web of Science™ platform			
#14	Combination	#13 OR #9 OR #7 <i>DocType=All document types; Language=All languages;</i>	
#13	Combination	#10 OR #11 OR #12 <i>DocType=All document types; Language=All languages;</i>	
#12	Topic	(TS=((NK603 OR "NK 603") AND (MON87427 OR "MON 87427" OR MON89034 OR "MON 89034"))) <i>DocType=All document types; Language=All languages;</i>	Events
#11	Topic	(TS=((MON89034 OR "MON 89034") AND (MON87427 OR "MON 87427" OR NK603 OR "NK 603"))) <i>DocType=All document types; Language=All languages;</i>	Events
#10	Topic	(TS=((MON87427 OR "MON 87427") AND (MON89034 OR "MON 89034" OR NK603 OR "NK 603"))) <i>DocType=All document types; Language=All languages;</i>	Events
#9	Combination	#8 AND (#2 OR #1) <i>DocType=All document types; Language=All languages;</i>	The newly expressed proteins in GM organisms, including maize
#8	Topic	(TS=((Cry1A105 OR "Cry1A 105" OR "Cry 1A 105" OR "Cry 1A105" OR CryIA105 OR "CryIA 105" OR "Cry IA 105" OR "Cry IA105" OR Cry1A.105) AND (Cry2Ab* OR "Cry2 Ab*" OR "Cry 2 Ab*" OR "Cry 2Ab*" OR CryIIAb* OR "CryII Ab*" OR "Cry II Ab*" OR "Cry IIAb*")) OR (cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P")) <i>DocType=All document types; Language=All languages;</i>	Newly expressed proteins
#7	Combination	#6 OR #5 <i>DocType=All document types; 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; Language=All languages;</i>	GM maize with the indicated trade names
#5	Combination	#3 AND #2 AND #1 <i>DocType=All document types; Language=All languages;</i>	GM maize displaying the introduced insect protection and herbicide tolerance traits

Set	Field	Search string	Key elements (Intervention/Exposure)
#4	Topic	(TS=("VT Double Pro" OR "VT DoublePro" OR VT2Pro OR "VT2 Pro" OR "VT?2?Pro" OR Yieldg* VT Pro OR "Yield Gard VT Pro" OR RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2")) <i>DocType=All document types; Language=All languages;</i>	Trade names
#3	Topic	(TS=((TOLERAN* OR RESISTAN* OR PROTEC*) NEAR/5 (Borer* OR Lepidoptera OR Ostrinia OR Sesamia OR GLYPHOSATE OR ROUNDUP))) <i>DocType=All document types; 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; Language=All languages;</i>	Plant species
#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; Language=All languages;</i>	GMO general
EBSCOhost platform (<i>All document types and all languages</i>)			
S17	Combination	S10 OR S12 OR S16	
S16	Combination	S13 OR S14 OR S15	
S15	All Text	TX ((NK603 OR "NK 603") AND (MON87427 OR "MON 87427" OR MON89034 OR "MON 89034"))	Events
S14	All Text	TX ((MON89034 OR "MON 89034") AND (MON87427 OR "MON 87427" OR NK603 OR "NK 603"))	Events
S13	All Text	TX ((MON87427 OR "MON 87427") AND (MON89034 OR "MON 89034" AND NK603 OR "NK 603"))	Events
S12	Combination	S11 AND (S2 OR S1)	The newly expressed proteins in GM organisms, including maize
S11	All Text	TX (((Cry1A105 OR "Cry1A 105" OR "Cry 1A 105" OR "Cry 1A105" OR CryIA105 OR "CryIA 105" OR "Cry IA 105" OR "Cry IA105" OR Cry1A.105) AND (Cry2Ab OR "Cry2 Ab" OR "Cry 2 Ab" OR "Cry 2Ab" OR CryIIAb OR "CryII Ab" OR "Cry II Ab" OR "Cry IIAb")) OR cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P")	Newly expressed proteins

Set	Field	Search string	Key elements (Intervention/Exposure)
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	Combination	S1 AND S2 AND S6	GM maize displaying the introduced insect protection and herbicide tolerance traits
S7	All Text	TX ("Yieldg* VT Pro" OR "Yield Gard VT Pro" OR RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2" OR "VT Double Pro" OR "VT DoublePro" OR VT2Pro OR "VT2 Pro" OR "VT?2?Pro")	Trade name
S6	Combination	S3 AND (S4 OR S5)	
S5	Combination	DE "glyphosate"	Controlled vocabularies (subject indexes) offered by the database for introduced insect protection and herbicide tolerance traits
S4	Descriptor	DE "Lepidoptera"	
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 ScienceTM Core collection database using the Web of ScienceTM 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 ScienceTM 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 ScienceTM 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 are 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 14 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&dbs=.lah - Accessed on 14 October 2019

⁴<https://help.ebsco.com/interfaces/EBSCOhost> - Accessed on 14 October 2019

⁵http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hp_advanced_examples.html - Accessed on 14 October 2019

⁶https://help.ebsco.com/interfaces/EBSCOhost/training_promotion/Advanced_Searching_EBSCOhost_Tutorial - Accessed on 14 October 2019

⁷http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hs_advanced_fieldtags.html - Accessed on 14 October 2019

⁸<http://clarivate.libguides.com/woscc/searchtips> - Accessed on 14 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 14 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 87427 × MON 89034 × NK603 and its sub-combinations 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 manipulat* 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 "zea mays" 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 "Zea mays" OR DE "maize"	
Intended trait			
<i>Reference publications</i>		Taylor, M., Lucas, D., Nemeth, M., Davis, S., Hartnell, G. (2007). Comparison of broiler performance and carcass parameters when fed diets containing combined trait insect-protected and glyphosate-tolerant corn (MON 89034 x NK603), control, or conventional reference corn. POULTRY SCIENCE, 86(9), 1988-1994, DOI: 10.1093/ps/86.9.1988	
<i>Search terms</i>		Protection against corn borer/ lepidopteran pests/ <i>Ostrinia</i> sp./ <i>Sesamia</i> sp., Glyphosate/ roundup tolerance	
<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 (Borer* OR Lepidoptera OR Ostrinia OR Sesamia OR GLYPHOSATE OR ROUNDUP)))	
	<i>Truncations and spelling variants used and their meanings</i>	Toleran* = tolerance, tolerant Resistan* = resistance, resistant Protect* = protection, protected Borer* = borer, borers, borer's	

Key elements		Search terms	Comments
<i>EBSCOhost platform</i>	<i>Search string based on controlled vocabularies using the Descriptors (DE) field</i>	DE "glyphosate" DE "Lepidoptera" DE "insect control" OR DE "weed control"	
Trade names			
<i>Reference publications</i>		Not available.	There are no reference publications complying with the eligibility/inclusion criteria to test this set of keywords for the trade name.
<i>Search terms</i>		YieldGard VT Double PRO, Roundup Ready2	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	TS=("VT Double Pro" OR "VT DoublePro" OR Yieldg* VT Pro OR "Yield Gard VT Pro" OR RoundupReady* OR "Roundup Ready 2"))	
	<i>Truncations and spelling variants used and their meanings</i>	"VT Double Pro" = Yield Gard VT Double PRO "VT DoublePro" = Yield Gard VT Double PRO Yieldg* VT Pro OR = Yield Gard VT Double PRO "Yield Gard VT Pro" = Yield Gard VT Double PRO RoundupReady* = Roundup Ready2 "Roundup Ready 2" = Roundup Ready2	
<i>EBSCOhost platform</i>	<i>Search string based on free-text terms using the All Text (TX) field</i>	TX ("Yieldg* VT Pro" OR "Yield Gard VT Pro" OR RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2" OR "VT Double Pro" OR "VT DoublePro" OR VT2Pro OR "VT2 Pro" OR "VT?2?Pro")	
	<i>Truncations and spelling variants used and their meanings</i>	"Yieldg* VT Pro" = Yield Gard VT Double PRO "Yield Gard VT Pro" = Yield Gard VT Double PRO "VT Double Pro" = Yield Gard VT Double PRO VT2Pro = Yield Gard VT Double PRO "VT2 Pro" = Yield Gard VT Double PRO "VT?2?Pro" = Yield Gard VT Double PRO RoundupReady* = Roundup Ready2 RR, RR2, "RR 2" = Roundup Ready2	

Key elements		Search terms	Comments
Newly expressed protein			
Reference publications		Taylor, M., Lucas, D., Nemeth, M., Davis, S., Hartnell, G. (2007). Comparison of broiler performance and carcass parameters when fed diets containing combined trait insect-protected and glyphosate-tolerant corn (MON 89034 x NK603), control, or conventional reference corn. POULTRY SCIENCE, 86(9), 1988-1994, DOI: 10.1093/ps/86.9.1988	
Search terms		Cry1A.105, Cry2Ab2, CP4 EPSPS L214P	
Web of science™ platform	Search string based on free-text terms using the Topic (TS) field	(TS=(((Cry1A105 OR "Cry1A 105" OR "Cry 1A 105" OR "Cry 1A105" OR CryIA105 OR "CryIA 105" OR "Cry IA 105" OR "Cry IA105" OR Cry1A.105) AND (Cry2Ab* OR "Cry2 Ab*" OR "Cry 2 Ab*" OR "Cry 2Ab*" OR CryIIAb* OR "CryII Ab*" OR "Cry II Ab*" OR "Cry IIAb*")) OR (cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P"))))	
	Truncations and spelling variants used and their meanings	Cry2Ab*, "Cry2 Ab*", "Cry 2 Ab*", "Cry 2Ab*", CryIIAb*, "CryII Ab*", "Cry II Ab*", "Cry IIAb*" = Cry2Ab2 "CP4?EPSPS?L214P" = CP4 EPSPS L214P	
EBSCOhost platform	Search string based on free-text terms using the All Text (TX) field	TX (((Cry1A105 OR "Cry1A 105" OR "Cry 1A 105" OR "Cry 1A105" OR CryIA105 OR "CryIA 105" OR "Cry IA 105" OR "Cry IA105" OR Cry1A.105) AND (Cry2Ab OR "Cry2 Ab" OR "Cry 2 Ab" OR "Cry 2Ab" OR CryIIAb OR "CryII Ab" OR "Cry II Ab" OR "Cry IIAb")) OR cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P")	
	Truncations and spelling variants used and their meanings	"CP4?EPSPS?L214P" = CP4 EPSPS L214P	
Event			
Reference publications		Taylor, M., Lucas, D., Nemeth, M., Davis, S., Hartnell, G. (2007). Comparison of broiler performance and carcass parameters when fed diets containing combined trait insect-protected and glyphosate-tolerant corn (MON 89034 x NK603), control, or conventional reference corn. POULTRY SCIENCE, 86(9), 1988-1994, DOI: 10.1093/ps/86.9.1988	

Key elements		Search terms	Comments
	<i>Search terms</i>	MON 87427, MON 89034, NK603	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=((MON87427 OR "MON 87427") AND (MON89034 OR "MON 89034" OR NK603 OR "NK 603"))) (TS=((MON89034 OR "MON 89034") AND (MON87427 OR "MON 87427" OR NK603 OR "NK 603"))) (TS=((NK603 OR "NK 603") AND (MON87427 OR "MON 87427" OR MON89034 OR "MON 89034")))	
	<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 ((MON87427 OR "MON 87427") AND (MON89034 OR "MON 89034" AND NK603 OR "NK 603")) TX ((MON89034 OR "MON 89034") AND (MON87427 OR "MON 87427" OR NK603 OR "NK 603")) TX ((NK603 OR "NK 603") AND (MON87427 OR "MON 87427" OR MON89034 OR "MON 89034"))	
	<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 item 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 14 October 2019

¹¹ CABI CAB Abstracts® database; <http://www.cabi.org/cab-direct/> - Accessed on 14 October 2019

¹² Web of Science™; <http://wokinfo.com/essays/journal-selection-process/> - Accessed on 14 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), two (Environment and Climate Change Canada and CIBIOGEM) are not involved in the risk assessment of GM plants. Six (USDA, FDA, CFIA, Health Canada, FSANZ and MAFF) do not regulate stack products. Two (OGTR and GEAC), for the time being, only assess cotton and oilseed rape. From the remaining three, US EPA regulates only stacks with Plant-Incorporated Protectants (PIP) combinations while CTNBio and CONABIA regulate stack products. Therefore, the internet search focused on the last three organisations (US EPA, CTNBio and CONABIA)¹³ relevant for MON 87427 × MON 89034 × NK603 and/or its sub-combinations.

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 in **Table 4**. Afterwards, all the records within the specified limits were assessed for their relevance to MON 87427 × MON 89034 × NK603 and/or its sub-combinations 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.

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.

¹³ Internet pages of the relevant key organisations:

US EPA (<https://www.epa.gov/environmental-topics/science-topics>) - Accessed on 14 October 2019;

CTNBio (<http://ctnbio.mcti.gov.br/>) - Accessed on 14 October 2019;

CONABIA (<http://www.agroindustria.gob.ar/>) - Accessed on 14 October 2019

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

Taking into account i) the review question, ii) the scope of the application, *i.e.* authorisation of MON 87427 × MON 89034 × NK603 maize and/or its sub-combinations 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 Science™ Core Collection and the CAB Abstracts® databases on a monthly basis, covering the time span June 2018 – May 2019. As a result, 100 hits were identified using Web of Science™ Core Collection database and 49 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 14 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 87427 × MON 89034 × NK603 maize and/or its sub-combinations

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 14 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 87427 × MON 89034 × NK603.</p>
CTNBio	<p>http://ctnbio.mcti.gov.br/liberacao-comercial#/liberacao-comercial/consultar-processo – Accessed on 14 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 record is not relevant to MON 87427 × MON 89034 × NK603 and/or its sub-combination.</p>
CONABIA	<p>https://www.argentina.gob.ar/agroindustria/alimentos-y-bioeconomia/ogm-comerciales/ – Accessed on 14 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> One of the retrieved records is relevant to MON 87427 × MON 89034 × NK603 and/or its sub-combinations (RESOL-2019-61-APN-SAYBI#MPYT, 2019¹⁴). It does not have any implication on the risk assessment, because no new hazards, modified exposure, or new scientific uncertainties are reported.</p>

¹⁴ <https://www.boletinoficial.gob.ar/detalleAviso/primera/213597/20190816> - Accessed on 17 December 2019

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 two relevant studies retrieved after detailed assessment of the full text document (ordered by category of information) are listed in **Table 6**. Excluded studies after detailed assessment of the full text documents for relevance are listed in

Table 7. Copies of the full-text documents listed in **Table 6** are provided as pdf files 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)	100	49
Number of <i>studies</i> excluded from the search results after rapid assessment for relevance	88	43
Total number of <i>full-text documents</i> assessed in detail (excluding duplicates)	16	
Number of <i>studies</i> excluded from further consideration after detailed assessment for relevance	14	
Total number of unobtainable/unclear studies	0	
Total number of relevant studies	2	

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		
Agronomic and phenotypic characteristics		
Hrčková <i>et al.</i> (2018)	Agronomic and economic performance of genetically modified and conventional maize	Agriculture (Pol'nohospodárstvo)
Crop composition		
Oliveira <i>et al.</i> (2018)	Nutritional composition and aerobic stability of wheat and corn silages stored under different environmental conditions.	Londrina:Universidade Estadual de Londrina,
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
Mesnager, R <i>et al.</i>	2016	An integrated multi-omics analysis of the NK603 Roundup-tolerant GM maize reveals metabolism disturbances caused by the transformation process	Scientific Reports	The hybrid used to conduct the study is not MON 87427 × MON 89034 × NK603 or its sub-combinations
Sharma, HC and Dhillon, MK	2018	Bio-safety of <i>Helicoverpa</i> -resistant transgenic chickpea with <i>Bacillus thuringiensis</i> genes in the environment	Indian Journal of Agricultural Sciences	The hybrid used to conduct the study is not MON 87427 × MON 89034 × NK603 or its sub-combinations
Bernillon, S <i>et al.</i>	2018	Characterization of GMO or glyphosate effects on the composition of maize grain and maize-based diet for rat feeding	Metabolomics	The hybrid used to conduct the study is not MON 87427 × MON 89034 × NK603 or its sub-combinations
Shabbir, MZ <i>et al.</i>	2018	Characterization of the Cry1Ah resistance in Asian corn borer and its cross-resistance to other <i>Bacillus thuringiensis</i> toxins	Scientific Reports	The hybrid used to conduct the study is not MON 87427 × MON 89034 × NK603 or its sub-combinations

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
Ncube, E <i>et al.</i>	2018	Fusarium ear rot and fumonisins in maize kernels when comparing a <i>Bt</i> hybrid with its non- <i>Bt</i> isohybrid and under conventional insecticide control of <i>Busseola fusca</i> infestations	Crop Protection	The hybrid used to conduct the study is not MON 87427 × MON 89034 × NK603 or its sub-combinations
Campagne, P <i>et al.</i>	2017	Genetic hitchhiking and resistance evolution to transgenic <i>Bt</i> toxins: insights from the African stalk borer <i>Busseola fusca</i> (<i>Noctuidae</i>)	Heredity	The hybrid used to conduct the study is not MON 87427 × MON 89034 × NK603 or its sub-combinations
de Vos, CJ and Swanenburg, M	2018	Health effects of feeding genetically modified (GM) crops to livestock animals: A review	Food and Chemical Toxicology	It is not a food/feed safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations
Gressel, J <i>et al.</i>	2017	How well will stacked transgenic pest/herbicide resistances delay pests from evolving resistance?	Pest Management Science	It is not a food/feed safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations
Dolezel, M <i>et al.</i>	2018	Limits of concern: suggestions for the operationalisation of a concept to determine the relevance of adverse effects in the ERA of GMOs	Environmental Sciences Europe	It is not a food/feed safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations
Signorini, AM <i>et al.</i>	2018	Management of field-evolved resistance to <i>Bt</i> maize in Argentina: A multi-institutional approach	Frontiers in Bioengineering and Biotechnology	It is not a food/feed safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
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 87427 × MON 89034 × NK603 or its sub-combinations
Sun, H <i>et al.</i>	2017	Processing and targeting of proteins derived from polyprotein with 2A and LP4/2A as peptide linkers in a maize expression system	PLOS ONE	It is not a safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations
Strydom, E <i>et al.</i>	2019	Resistance status of <i>Busseola fusca</i> (<i>Lepidoptera: Noctuidae</i>) populations to single- and stacked-gene <i>Bt</i> maize in South Africa	Journal of Economic Entomology	It is not a food/feed safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations
Buso, WHD and Borges e Silva, L	2017	Use of technology to increase the productivity of corn in Brazil	Maize Germplasm: Characterization and Genetic Approaches for Crop Improvement London: Intech Open Limited	It is not a food/feed safety study on MON 87427 × MON 89034 × NK603 or its sub-combinations

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 studies did not identify any new information that would require further consideration in the risk assessment of MON 87427 × MON 89034 × NK603 and/or its sub-combinations 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 87427 × MON 89034 × NK603 and/or its sub-combinations. 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
Agronomic and phenotypic characteristics		
Hrčková <i>et al.</i> (2018)	Low/Not reliable	None, because no new hazards, modified exposure, or new scientific uncertainties are reported
Crop composition		
Oliveira <i>et al.</i> (2018)	Low	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 87427 × MON 89034 × NK603, three related GM maize combining two different single GM events (MON 89034 × NK603, MON 87427 × MON 89034, MON 87247 × NK603) in the EU, identified no relevant publications that would invalidate the initial conclusions of the MON 87427 × MON 89034 × NK603 and its sub-combinations 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 87427 × MON 89034 × NK603, three related GM maize combining two different single GM events (MON 89034 × NK603, MON 87427 × MON 89034, MON 87247 × NK603) in the EU.

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

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