

## **APPENDIX 3**

### **LITERATURE SEARCH FOR ANNUAL MONITORING ON THE GENERAL SURVEILLANCE OF NK603 × MON 810 MAIZE IN THE EU**

## TABLE OF CONTENTS

<b>1. INTRODUCTION.....</b>	<b>3</b>
<b>2. IDENTIFYING THE REVIEW QUESTION AND PURPOSE FOR UNDERTAKING THE LITERATURE SEARCH.....</b>	<b>3</b>
<b>3. SEARCHING FOR IDENTIFYING RELEVANT STUDIES .....</b>	<b>4</b>
3.1. SEARCH TERMS AND THEIR COMBINATION .....	4
3.2. LIMITS APPLIED.....	9
3.3. LANGUAGE .....	9
3.4. TIME PERIOD .....	9
3.5. REFERENCE STUDIES .....	10
3.6. INFORMATION SOURCES .....	16
3.6.1. ELECTRONIC BIBLIOGRAPHIC DATABASES.....	16
3.6.2. RELEVANT KEY ORGANISATIONS .....	17
<b>4. SELECTING STUDIES .....</b>	<b>17</b>
4.1. PROCESS .....	17
4.2. QUALITY ASSURANCE .....	17
4.3. ELIGIBILITY/INCLUSION CRITERIA TO ESTABLISH RELEVANCE .....	18
<b>5. SUMMARISING AND REPORTING THE DATA, AND CONSIDERING THE IMPLICATIONS OF THE FINDINGS.....</b>	<b>18</b>
5.1. SEARCH OUTCOMES .....	18
5.1.1. <i>Outcomes of literature search in electronic bibliographic databases.....</i>	<i>18</i>
5.1.2. <i>Outcomes of literature search in internet pages of relevant key organisations ..</i>	<i>18</i>
5.2. RESULTS OF THE STUDY SELECTION PROCESS FOR ELECTRONIC BIBLIOGRAPHIC DATABASES .....	20
5.3. IMPLICATIONS OF THE RETRIEVED RELEVANT STUDIES FOR THE RISK ASSESSMENT ..	25
<b>6. CONCLUSION .....</b>	<b>26</b>
<b>REFERENCES.....</b>	<b>27</b>

## 1. INTRODUCTION

As part of the general surveillance requirements for NK603 × MON 810 genetically modified (GM) maize authorised in the European Union (EU) market under regulation (EC) No 1829/2003, Bayer Agriculture BVBA<sup>1</sup> has actively monitored scientific literature related to NK603 × MON 810 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 NK603 × MON 810 maize derived food/feed products and the introduced herbicide tolerance and insect protection 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), NK603 × MON 810 maize, derived food/feed products and the introduced herbicide tolerance and insect protection 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**.

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<sup>1</sup> 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 NK603 × MON 810 maize are addressed as general protection goals.
Intervention/exposure	NK603 × MON 810 maize, derived food/feed products and the introduced herbicide tolerance and insect protection 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).
<b>Additional key elements</b>	
Stacked events/sub-combinations	The single event(s) addressed in the study is/are the single event(s) in NK603 × MON 810 maize. NK603 × MON 810 maize is addressed in the study
Information/ data requirements, including source of studies data	The study potentially contributes to the knowledge of the risk assessment of NK603 × MON 810 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 NK603 × MON 810 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 Science™ 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 NK603 × MON 810 related publications**

Set	Field	Search string	Key elements (Intervention/Exposure)
<b>Web of Science™ platform</b>			
#11	Combination	#10 OR #9 OR #7 <i>DocType=All document types; Language=All languages;</i>	
#10	Topic	(TS=((MON810 OR "MON 810") AND (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=(Cry1Ab OR "CryI Ab" OR "Cry 1 Ab" OR "Cry 1Ab" OR CryIAb OR "CryI Ab" OR "Cry I A b" OR "Cry IAb" 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 herbicide tolerance and insect protection 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 herbicide tolerance and insect protection traits
#4	Topic	(TS=("Yield Gard Corn Borer Roundup Ready 2" OR "Yieldg* Corn Borer Roundup Ready 2" OR "Yield Gard Corn Borer RR2" OR "Yieldg* Corn Borer RR2" OR "Yield Gard Corn Borer RR 2" OR "Yieldg* Corn Borer RR 2" OR RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2" OR Yield Gard OR Yieldg* OR "Bt maize" OR "Bt corn")) <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 herbicide tolerance and insect protection traits

Set	Field	Search string	Key elements (Intervention/Exposure)
#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
<b>EBSCOhost platform</b> ( <i>All document types and all languages</i> )			
S14	Combination	S10 OR S12 OR S13	
S13	All Text	TX ((NK603 OR "NK 603") AND (MON810 OR "MON 810"))	Events
S12	Combination	S11 AND (S2 OR S1)	The newly expressed proteins in GM organisms, including maize
S11	All Text	TX (cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P" OR Cry1Ab OR "Cry1 Ab" OR "Cry 1 Ab" OR "Cry 1Ab" OR CryIAb OR "CryI Ab" OR "Cry I Ab" OR "Cry IAb")	Newly expressed proteins
S10	Combination	S8 OR S9	GM maize displaying the introduced herbicide tolerance and insect protection 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 herbicide tolerance and insect protection traits
S7	All Text	TX (RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2" OR Yield Gard OR Yieldg* OR "Bt maize" OR "Bt corn" OR "Yield Gard Corn Borer Roundup Ready 2" OR "Yieldg* Corn Borer Roundup Ready 2" OR "Yield Gard Corn Borer RR2" OR "Yieldg* Corn Borer RR2" OR "Yield Gard Corn Borer RR 2" OR "Yieldg* Corn Borer RR 2")	Trade name
S6	Combination	S3 AND (S4 OR S5)	
S5	Descriptor	DE "glyphosate"	Controlled vocabularies (subject indexes) offered by the database for introduced herbicide tolerance and insect protection 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'.

Appendix 3\_NK603 × MON 810. Annual monitoring report on the general surveillance in the EU

Bayer Agriculture BVBA, December 2019

Set	Field	Search string	Key elements (Intervention/Exposure)
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™ platform<sup>2</sup> and in the CAB Abstracts® database<sup>3</sup> using the EBSCOhost platform<sup>4</sup> (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<sup>5,6</sup>.

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<sup>7,6</sup> (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 search<sup>8</sup>. 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*”<sup>6</sup>.

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 terms<sup>9</sup>. 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.

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<sup>2</sup>[http://apps.webofknowledge.com/UA\\_GeneralSearch\\_input.do?product=UA&SID=X1sK9uHnF5WXHkLGpbw&search\\_mode=GeneralSearch](http://apps.webofknowledge.com/UA_GeneralSearch_input.do?product=UA&SID=X1sK9uHnF5WXHkLGpbw&search_mode=GeneralSearch) - Accessed on 02 October 2019

<sup>3</sup>[http://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](http://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 02 October 2019

<sup>4</sup><https://help.ebsco.com/interfaces/EBSCOhost> - Accessed on 02 October 2019

<sup>5</sup>[http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hp\\_advanced\\_examples.html](http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hp_advanced_examples.html) - Accessed on 02 October 2019

<sup>6</sup>[https://help.ebsco.com/interfaces/EBSCOhost/training\\_promotion/Advanced\\_Searching\\_EBSCOhost\\_Tutorial](https://help.ebsco.com/interfaces/EBSCOhost/training_promotion/Advanced_Searching_EBSCOhost_Tutorial) - Accessed on 02 October 2019

<sup>7</sup>[http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hs\\_advanced\\_fieldtags.html](http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hs_advanced_fieldtags.html) - Accessed on 02 October 2019

<sup>8</sup><http://clarivate.libguides.com/woscc/searchtips> - Accessed on 02 October 2019

<sup>9</sup><https://www.cabi.org/Uploads/CABI/publishing/training-materials/resources-by-interface/cab-direct-user-guides/advanced-searching-cab-abstracts.pdf> - Accessed on 02 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 NK603 × MON 810 literature search in the Web of Science™ Core Collection and CAB Abstracts® databases**

Key elements		Search terms	Comments
<b>GMO general</b>			
<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			
Reference publications		Not applicable.	This step is to focus the search on maize related papers.  The search terms, free-text terms, controlled vocabularies and the search strings are updated upon identification of a new search term.
Search terms		Maize, corn, <i>Zea mays</i> , <i>Z mays</i>	
Web of science™ platform	Search string based on free-text terms using the Topic (TS) field	(TS=(maize* OR corn* OR "zea mays" OR "z mays"))	
	Truncations and spelling variants used and their meanings	Maize* = maize, maizes, maize's Corn* = corn, corns, corn's	
EBSCOhost platform	Search string based on controlled vocabularies using the Descriptors (DE) field	DE "Zea mays" OR DE "maize"	
Intended trait			
Reference publications		Taylor, ML; Hartnell, GF; Riordan, SG; Nemeth, MA; Karunanandaa, K; George, B; Astwood, JD. (2003). Comparison of broiler performance when fed diets containing grain from Roundup Ready (NK603), YieldGard x Roundup Ready (MON810 x NK603), non-transgenic control, or commercial corn. POULTRY SCIENCE. Volume: 82, Issue: 3, Pages: 443-453, DOI: 10.1093/ps/82.3.443  Ridley, William P.; Harrigan, George G.; Breeze, Matthew L.; Nemeth, Margaret A.; Sidhu, Ravinder S.; Glenn, Kevin C. (2011). Evaluation of compositional equivalence for multitrait biotechnology crops. JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. Volume: 59, Issue: 11, Pages: 5865-5876, DOI: 10.1021/jf103874t	
Search terms		Glyphosate/ Roundup tolerance, Protection against <i>Ostrinia spp./ Sesamia spp./</i> corn borer/ lepidopteran insect pests	

Key elements		Search terms	Comments
<i>Web of science<sup>TM</sup> 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	
<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>		Taylor, ML; Hartnell, GF; Riordan, SG; Nemeth, MA; Karunanandaa, K; George, B; Astwood, JD. (2003). Comparison of broiler performance when fed diets containing grain from Roundup Ready (NK603), YieldGard x Roundup Ready (MON810 x NK603), non-transgenic control, or commercial corn. POULTRY SCIENCE. Volume: 82, Issue: 3, Pages: 443-453, DOI: 10.1093/ps/82.3.443	
<i>Search terms</i>		YieldGard Corn Borer Roundup Ready 2, YieldGard Corn Borer RR2, Roundup Ready2, RR2, YieldGard, <i>Bt</i> maize, <i>Bt</i> corn	
<i>Web of science<sup>TM</sup> platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=("Yield Gard Corn Borer Roundup Ready 2" OR "Yieldg* Corn Borer Roundup Ready 2" OR "Yield Gard Corn Borer RR2" OR "Yieldg* Corn Borer RR2" OR "Yield Gard Corn Borer RR 2" OR "Yieldg* Corn Borer RR 2" OR RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2" OR Yield Gard OR Yieldg* OR "Bt maize" OR "Bt corn"))	
	<i>Truncations and spelling variants used and their meanings</i>	“Yieldg* Corn Borer Roundup Ready 2” = YieldGard Corn Borer Roundup Ready 2 "Yieldg* Corn Borer RR 2" = YieldGard Corn Borer RR2 RoundupReady* = Roundup Ready2 Yieldg* = YieldGard	
<i>EBSCOhost platform</i>	<i>Search string based on free-text terms using the All Text (TX) field</i>	TX (RoundupReady* OR "Roundup Ready 2" OR RR OR RR2 OR "RR 2" OR Yield Gard OR Yieldg* OR "Bt maize" OR "Bt corn" OR "Yield Gard Corn Borer Roundup Ready 2" OR "Yieldg* Corn Borer Roundup Ready 2"	

Key elements		Search terms	Comments
		OR "Yield Gard Corn Borer RR2" OR "Yieldg* Corn Borer RR2" OR "Yield Gard Corn Borer RR 2" OR "Yieldg* Corn Borer RR 2")	
	<i>Truncations and spelling variants used and their meanings</i>	“Yieldg* Corn Borer Roundup Ready 2” = YieldGard Corn Borer Roundup Ready 2 "Yieldg* Corn Borer RR 2" = YieldGard Corn Borer RR2 RoundupReady* = Roundup Ready2 Yieldg* = YieldGard	
Newly expressed protein			
<i>Reference publications</i>		Taylor, ML; Hartnell, GF; Riordan, SG; Nemeth, MA; Karunanandaa, K; George, B; Astwood, JD. (2003). Comparison of broiler performance when fed diets containing grain from Roundup Ready (NK603), YieldGard x Roundup Ready (MON810 x NK603), non-transgenic control, or commercial corn. POULTRY SCIENCE. Volume: 82, Issue: 3, Pages: 443-453, DOI: 10.1093/ps/82.3.443	
<i>Search terms</i>		CP4 EPSPS L214P, Cry1Ab	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=(Cry1Ab OR "Cry1 Ab" OR "Cry 1 Ab" OR "Cry 1Ab" OR CryIAb OR "CryI Ab" OR "Cry I A b" OR "Cry IAb" OR cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P"))	
	<i>Truncations and spelling variants used and their meanings</i>	"CP4?EPSPS?L214P" = CP4-EPSPS-L214P	
<i>EBSCOhost platform</i>	<i>Search string based on free-text terms using the All Text (TX) field</i>	TX (cp4epsps OR "cp4 epsps" OR "CP4?EPSPS?L214P" OR Cry1Ab OR "Cry1 Ab" OR "Cry 1 Ab" OR "Cry 1Ab" OR CryIAb OR "CryI Ab" OR "Cry I Ab" OR "Cry IAb")	

Key elements		Search terms	Comments
	<i>Truncations and spelling variants used and their meanings</i>	"CP4?EPSPS?L214P" = CP4-EPSPS-L214P	
<b>Event</b>			
	<i>Reference publications</i>	<p>Taylor, ML; Hartnell, GF; Riordan, SG; Nemeth, MA; Karunanandaa, K; George, B; Astwood, JD. (2003). Comparison of broiler performance when fed diets containing grain from Roundup Ready (NK603), YieldGard x Roundup Ready (MON810 x NK603), non-transgenic control, or commercial corn. POULTRY SCIENCE. Volume: 82, Issue: 3, Pages: 443-453, DOI: 10.1093/ps/82.3.443</p> <p>Ridley, William P.; Harrigan, George G.; Breeze, Matthew L.; Nemeth, Margaret A.; Sidhu, Ravinder S.; Glenn, Kevin C. (2011). Evaluation of compositional equivalence for multitrait biotechnology crops. JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY. Volume: 59, Issue: 11, Pages: 5865-5876, DOI: 10.1021/jf103874t</p>	
	<i>Search terms</i>	NK603, MON 810	
<i>Web of science™ platform</i>	<i>Search string based on free-text terms using the Topic (TS) field</i>	(TS=((MON810 OR "MON 810") AND (NK603 OR "NK 603")))	
	<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 ((NK603 OR "NK 603") AND (MON810 OR "MON 810"))	
	<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 database<sup>10</sup> and the CAB Abstracts® database<sup>11</sup> for performing the literature searches. The advanced literature search was conducted using the Web of Science™ platform<sup>4</sup> for the Web of Science™ Core collection database and using the EBSCOhost platform<sup>6</sup> for the CAB Abstracts® database<sup>3</sup>.

The Web of Science™ Core Collection database<sup>10</sup> 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.*”<sup>10</sup>. 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 search<sup>10</sup>.

The CAB Abstracts® database<sup>11</sup> 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 science<sup>12</sup>. 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.

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<sup>10</sup> Web of Science Core Collection; <https://clarivate.com/products/web-of-science/web-science-form/web-science-core-collection/> - Accessed on 2 October 2019.

<sup>11</sup> CABI CAB Abstracts® database; <http://www.cabi.org/cab-direct/> - Accessed on 2 October 2019.

<sup>12</sup> Web of Science™; <http://wokinfo.com/essays/journal-selection-process/> - Accessed on 2 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) don't regulate stack products. Two (OGTR and GEAC), for the time being, only assess cotton and oilseed rape. From the remaining three, EPA regulates only stacks with Plant-Incorporated Protectant (PIP) combinations while CTNBio and CONABIA regulate stack products. Therefore, the internet search focused on the last three organisations (EPA, CTNBio and CONABIA)<sup>13</sup> relevant for NK603 × MON 810.

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 NK603 × MON 810 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.

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<sup>13</sup> Internet pages of the relevant key organisations for NK603 × MON 810 maize:

US EPA (<https://www.epa.gov/environmental-topics/science-topics>) - Accessed on 02 October 2019;

CTNBio (<http://ctnbio.mcti.gov.br/>) - Accessed on 02 October 2019;

CONABIA(<https://www.argentina.gob.ar/>) - Accessed on 02 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**

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 NK603 × MON 810 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 Science™ Core Collection and the CAB Abstracts® databases on a monthly basis, covering the time span June 2018–May 2019. As a result, 117 hits were identified using Web of Science™ Core Collection database and 147 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 2 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 NK603 × MON 810 maize**

Relevant key organisations	Link to the relevant information and summary of the retrieved data
US EPA	<p><a href="https://www.epa.gov/ingredients-used-pesticide-products/current-and-previously-registered-section-3-plant-incorporated">https://www.epa.gov/ingredients-used-pesticide-products/current-and-previously-registered-section-3-plant-incorporated</a> – Accessed on 02 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 NK603 × MON 810.</p>
CTNBio	<p><a href="http://ctnbio.mcti.gov.br/liberacao-comercial#/liberacao-comercial/consultar-processo">http://ctnbio.mcti.gov.br/liberacao-comercial#/liberacao-comercial/consultar-processo</a> – Accessed on 02 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 NK603 × MON 810</p>
CONABIA	<p><a href="https://www.argentina.gob.ar/agroindustria/alimentos-y-bioeconomia/ogm-comerciales">https://www.argentina.gob.ar/agroindustria/alimentos-y-bioeconomia/ogm-comerciales</a> – Accessed on 02 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 NK603 × MON 810</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**. No relevant studies were identified. Excluded studies after detailed assessment of the full text documents for relevance are listed in **Table 6**.

**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)	117	147
Number of <i>studies</i> excluded from the search results after rapid assessment for relevance	100	129
Total number of <i>full-text documents</i> assessed in detail (excluding duplicates)	35	
Number of <i>studies</i> excluded from further consideration after detailed assessment for relevance	35	
Total number of unobtainable/unclear studies	0	
Total number of relevant studies	0	

**Table 6. Report of studies excluded from the risk assessment after detailed assessment of full-text documents (classified by authors)**

<b>Study Author(s)</b>	<b>Year</b>	<b>Title</b>	<b>Source</b>	<b>Reason(s) for exclusion</b>
Walker, E <i>et al.</i>	2017	A spatio-temporal exposure-hazard model for assessing biological risk and impact	Risk analysis	It is not a safety study on NK603 × MON 810
Fatoretto, JC <i>et al.</i>	2017	Adaptive potential of fall armyworm (Lepidoptera: Noctuidae) limits <i>Bt</i> trait durability in Brazil	Journal of Integrated Pest Management	It is not a food/feed safety study on NK603 × MON 810
Mesnage, R	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 NK603 × MON 810
Agapito-Tenfen, SZ	2018	Bio-safety of Helicoverpa-resistant transgenic chickpea with <i>Bacillus thuringiensis</i> genes in the environment	Indian Journal of Agricultural Sciences	It is not a food/feed safety study on NK603 × MON 810
De Sousa, MF <i>et al.</i>	2017	Biology of <i>Trichogramma pretiosum</i> (Hymenoptera: Trichogrammatidae) fed transgenic maize pollen	Florida Entomologist	It is not a food/feed safety study on NK603 × MON 810
Glenn, KC <i>et al.</i>	2017	Bringing new plant varieties to market: plant breeding and selection practices advance beneficial characteristics while minimizing unintended changes	Crop Science	It is not a food/feed safety study on NK603 × MON 810
Suassuna, ND <i>et al.</i>	2018	BRS 430 B2RF and BRS 432 B2RF: Insect-resistant and glyphosate-tolerant high-yielding cotton cultivars	Crop Breeding and Applied Biotechnology	The hybrid used to conduct the study is not NK603 × MON 810
de Santis, B <i>et al.</i>	2017	Case studies on genetically modified organisms (GMOs): Potential risk scenarios and associated health indicators	Food and Chemical Toxicology	It is not a food/feed safety study on NK603 × MON 810

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
Alves, LRA <i>et al.</i>	2018	Differences in production costs' structures of conventional and genetically modified corn in Brazil, on the second crop: 2010/2011, 2013/2014 and 2014/2015	Custos e @gronegocio	It is not a food/feed safety study on NK603 × MON 810
Zhang, S <i>et al.</i>	2019	Effects of non-genetically and genetically modified organism (maize-soybean) diet on growth performance, nutrient digestibility, carcass weight, and meat quality of broiler chicken	Asian-Australasian Journal of Animal Sciences	The hybrid used to conduct the study is not NK603 × MON 810
Li Z <i>et al.</i>	2018	Enhancing auxin accumulation in maize root tips improves root growth and dwarfs plant height	Plant Biotechnology Journal	The hybrid used to conduct the study is not NK603 × MON 810
van der Voet, H <i>et al.</i>	2019	Equivalence limit scaled differences for untargeted safety assessments: comparative analyses to guard against unintended effects on the environment or human health of genetically modified maize	Food and Chemical Toxicology	It is not a safety study on NK603 × MON 810
Strobbe, S <i>et al.</i>	2018	From <i>in planta</i> function to vitamin-rich food crops: the ACE of biofortification	Frontiers in Plant Science	It is not a food/feed safety study on NK603 × MON 810
Smith, JL <i>et al.</i>	2018	<i>Fusarium graminearum</i> mycotoxins in maize associated with <i>Striacosta albicosta</i> (Lepidoptera: Noctuidae) injury	Journal of Economic Entomology	The hybrid used to conduct the study is not NK603 × MON 810
Abbas, MST	2018	Genetically engineered (modified) crops ( <i>Bacillus thuringiensis</i> crops) and the world controversy on their safety	Egyptian Journal of Biological Pest Control	It is not a food/feed safety study on NK603 × MON 810

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
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 NK603 × MON 810
Zdziarski, IM <i>et al.</i>	2018	Histopathological investigation of the stomach of rats fed a 60% genetically modified corn diet	Food and Nutrition Sciences	The hybrid used to conduct the study is not NK603 × MON 810
El-Esawi, MA	2018	Introductory chapter: introduction to biotechnological approaches for maize improvement	Maize germplasm; IntechOpen Limited, 2019	It is not a food/feed safety study on NK603 × MON 810
Costa, FR <i>et al.</i>	2018	Lack of effects of glyphosate and glufosinate on growth, mineral content, and yield of glyphosate- and glufosinate-resistant maize	GM Crops and Food: Biotechnology in Agriculture and the Food Chain	The study did not use a non-GM comparator
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 safety study on NK603 × MON 810
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 NK603 × MON 810
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 NK603 × MON 810
Farinós, GP <i>et al.</i>	2018	Monitoring of <i>Sesamia nonagrioides</i> resistance to MON 810 maize in the European Union: lessons from a long-term harmonized plan	Pest Management Science	It is not a food/feed safety study on NK603 × MON 810

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
Oliveira, MR <i>et al.</i>	2018	Nutritional composition and aerobic stability of wheat and corn silages stored under different environmental conditions	Semina: Ciências Agrárias (Londrina)	The hybrid used to conduct the study is not NK603 × MON 810
Hilbeck, A <i>et al.</i>	2017	Procedure to select test organisms for environmental risk assessment of genetically modified crops in aquatic systems	Integrated Environmental Assessment and Management (IEAM)	It is not a food/feed safety study on NK603 × MON 810
Strydom, E <i>et al.</i>	2019	Resistance status of <i>Busseola fusca</i> (Lepidoptera: Noctuidae) 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 NK603 × MON 810
Urechean, V and Bonea, D	2018	The comparative study of Bt corn and conventional corn regarding the <i>Ostrinia nubilalis</i> attack and the <i>Fusarium</i> spp. infestation in the central part of Oltenia	Romanian Biotechnological Letters	It is not a food/feed safety study on NK603 × MON 810
Latham, JR <i>et al.</i>	2017	The distinct properties of natural and GM cry insecticidal proteins.	Biotechnol Genet Eng Rev.	It is not a food/feed safety study on NK603 × MON 810
Brester, G <i>et al.</i>	2019	The influence of genetic modification technologies on U.S. and EU crop yields	Journal of Agricultural and Resource Economics	It is not a food/feed safety study on NK603 × MON 810
Baudron, F <i>et al.</i>	2019	Understanding the factors influencing fall armyworm ( <i>Spodoptera frugiperda</i> JE Smith) damage in African smallholder maize fields and quantifying its impact on yield. A case study in Eastern Zimbabwe	Crop Protection	It is not a safety study on NK603 × MON 810
Buso, WHD <i>et al.</i>	2017	Use of technology to increase the productivity of corn in Brazil	Maize germplasm; IntechOpen Limited, 2018	It is not a food/feed safety study on NK603 × MON 810



<b>Study Author(s)</b>	<b>Year</b>	<b>Title</b>	<b>Source</b>	<b>Reason(s) for exclusion</b>
Brown, ZS	2018	Voluntary programs to encourage refuges for pesticide resistance management: lessons from a quasi-experiment.	American Journal of Agricultural Economics	It is not a food/feed safety study on NK603 × MON 810

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

No relevant publications were identified in this literature search. 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 NK603 × MON 810. Therefore, a systematic review would not add value to the risk assessment of this product.

## 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 NK603 × MON 810 in the EU, identified no relevant publications that would invalidate the initial conclusions of the NK603 × MON 810 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 NK603 × MON 810 in the EU.

## REFERENCES

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

- 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.