APPENDIX 3

LITERATURE SEARCH FOR ANNUAL MONITORING ON THE GENERAL SURVEILLANCE OF 40-3-2 SOYBEAN IN THE EU

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1. INTRODUCTION

As part of the general surveillance requirements for 40-3-2 genetically modified (GM) soybean authorised in the European Union (EU) market under regulation (EC) No 1829/2003, Bayer Agriculture BVBA [1] has actively monitored scientific literature related to 40-3-2 soybean, 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 to for the risk assessment of this product.

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 40-3-2 soybean derived food/feed products and the introduced herbicide tolerance trait 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 soybean 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), 40-3-2 soybean derived food/feed products and the introduced herbicide tolerance trait (= intervention/exposure), conventional counterpart or non-GM soybean (= 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.e.* authorisation for all uses as any other soybean, but excluding the cultivation of 40-3-2 soybean are addressed as general protection goals.
Intervention/exposure	40-3-2 soybean derived food/feed products and the introduced herbicide tolerance trait 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 soybean 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 40-3-2 soybean intended for all uses as any other soybean, 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 40-3-2 soybean.

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 40-3-2 related publications

Set	Field	Search string	Key elements (Intervention/Exposure)
Web of Science™ platform			
#11	Combination	#10 OR #9 OR #7 *DocType=All document types;* *Language=All languages;*	
#10	Topic	(TS=(GTS* OR "40 3 2" OR "GTS 40 3 2")) *DocType=All document types;* *Language=All languages;*	Events
#9	Combination	#8 AND (#2 OR #1) *DocType=All document types;* *Language=All languages;*	The newly expressed proteins in GM organisms, including soybean
#8	Topic	(TS=(cp4epsps OR "cp4 epsps")) *DocType=All document types;* *Language=All languages;*	Newly expressed proteins
#7	Combination	#6 OR #5 *DocType=All document types;* *Language=All languages;*	GM soybean displaying the introduced herbicide tolerance trait OR GM soybean with the indicated trade names
#6	Combination	#4 AND #2 AND #1 *DocType=All document types;* *Language=All languages;*	GM soybean with the indicated trade names
#5	Combination	#3 AND #2 AND #1 *DocType=All document types;* *Language=All languages;*	GM soybean displaying the introduced herbicide tolerance trait
#4	Topic	(TS=(RoundupReady* OR "Roundup Ready" OR RR OR "first generation")) *DocType=All document types;* *Language=All languages;*	Trade names
#3	Topic	(TS=((TOLERAN* OR RESISTAN* OR PROTEC*) NEAR/5 (GLYPHOSATE OR ROUNDUP))) *DocType=All document types;* *Language=All languages;*	Introduced herbicide tolerance trait
#2	Topic	(TS=(soybean* OR soy* OR "*Glycine max*" OR "G max" OR "soy bean")) *DocType=All document types;* *Language=All languages;*	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 manipulat* OR improv* OR engineer* OR deriv*)))) *DocType=All document types;* *Language=All languages;*	GMO general

Set	Field	Search string	Key elements (Intervention/Exposure)
EBSCOhost platform *(All document types and all languages)*			
S13	Combination	S9 OR S11 OR S12	
S12	All Text	TX (GTS* OR "40 3 2" OR "GTS 40 3 2")	Events
S11	Combination	S10 AND (S2 OR S1)	The newly expressed proteins in GM organisms, including soybean
S10	All Text	TX (cp4epsps OR "cp4 epsps")	Newly expressed proteins
S9	Combination	S7 OR S8	GM soybean displaying the introduced herbicide tolerance trait OR GM soybean with the indicated trade name
S8	Combination	S1 AND S2 AND S6	GM soybean with the indicated trade name
S7	Combination	S1 AND S2 AND S5	GM soybean displaying the introduced herbicide tolerance trait
S6	All Text	TX (RoundupReady* OR "Roundup Ready" OR RR OR "first generation")	Trade name
S5	Combination	S3 AND S4	
S4	Descriptor	DE "glyphosate"	Controlled vocabularies (subject indexes) offered by the database for introduced herbicide tolerance trait
S3	Descriptor	DE "weed control"	
S2	Descriptor	DE "soyabeans"	Controlled vocabularies (subject indexes) offered by the database for plant species. Note that the term '*Glycine max*' is covered by the term 'soyabeans'.
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[2] and in the CAB Abstracts® database[3] using the EBSCOhost platform[4] (*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 search[8]. 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 terms[9]. 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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[2] http://apps.webofknowledge.com/UA_GeneralSearch_input.do?product=UA&SID=X1sK9uHnF5WXHkLGpbw&search_mode=GeneralSearch - Accessed on 09 October 2019

[3] 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&dbs=,lah - Accessed on 09 October 2019

[4] https://help.ebsco.com/interfaces/EBSCOhost - Accessed on 09 October 2019

[5] http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hp_advanced_examples.html - Accessed on 09 October 2019

[6] https://help.ebsco.com/interfaces/EBSCOhost/training_promotion/Advanced_Searching_EBSCOhost_Tutorial - Accessed on 09 October 2019

[7] http://images.webofknowledge.com/WOKRS5251R3/help/WOS/hs_advanced_fieldtags.html - Accessed on 09 October 2019

[8] http://clarivate.libguides.com/woscc/searchtips - Accessed on 09 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 09 October 2019

3.5. Reference study searches

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 40-3-2 literature search in the Web of Science™ Core Collection and CAB Abstracts® databases

Key elements		Search terms	Comments
GMO general			
	Reference publications	Not applicable.	This step is to focus the search on GM 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	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.	
Web of science™ platform	*Search string based on free-text terms using the Topic (TS) field*	(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*))))	
	Truncations and spelling variants used and their meanings	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	
EBSCOhost platform	*Search string based on controlled vocabularies using the Descriptors (DE) field*	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 soybean 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	Soybean, *Glycine max*, soy, soya	
Web of science™ platform	*Search string based on free-text terms using the Topic (TS) field*	(TS=(soybean* OR soy* OR "*Glycine max*" OR "G max" OR "soy bean"))	
	Truncations and spelling variants used and their meanings	soybean* = soybean, soybeans, soybean's G max = *Glycine max*	
EBSCOhost platform	*Search string based on controlled vocabularies using the Descriptors (DE) field*	DE "soyabeans"	
Intended trait			
	Reference publications	1) Taylor *et al.* (1999). Compositional analysis of glyphosate-tolerant soybeans treated with glyphosate. Journal of Agricultural and Food Chemistry, 47, 4469-4473. 2) McCann *et al.* (2005). Glyphosate-tolerant soybeans remain compositionally equivalent to conventional soybeans (*Glycine max* L.) during three years of field testing. Journal of Agricultural and Food Chemistry, 53, 5331-5335. 3) Harrigan *et al.* (2007). Chemical composition of glyphosate-tolerant soybean 40-3-2 grown in Europe remains equivalent with that of conventional soybean (*Glycine max* L.). Journal of Agricultural and Food Chemistry, 55, 6160-6168. 4) Zhou *et al.* (2011). Stability in the composition equivalence of grain from insect-protected maize and seed from glyphosate-tolerant soybean to conventional counterparts over multiple seasons, locations, and breeding germplasms. Journal of Agricultural and Food Chemistry, 59, 8822-8828.	
	Search terms	Glyphosate/ Roundup tolerance	

Key elements		Search terms	Comments
Web of science™ platform	*Search string based on free-text terms using the Topic (TS) field*	(TS=((TOLERAN* OR RESISTAN* OR PROTEC*) NEAR/5 (GLYPHOSATE OR ROUNDUP)))	
	Truncations and spelling variants used and their meanings	Toleran* = tolerance, tolerant Resistan* = resistance, resistant Protect* = protection, protected	
EBSCOhost platform	*Search string based on controlled vocabularies using the Descriptors (DE) field*	DE "glyphosate" DE "weed control"	
Trade names			
	Reference publications	1) Taylor *et al.* (1999). Compositional analysis of glyphosate-tolerant soybeans treated with glyphosate. Journal of Agricultural and Food Chemistry, 47, 4469-4473. 2) McCann *et al.* (2005). Glyphosate-tolerant soybeans remain compositionally equivalent to conventional soybeans (*Glycine max* L.) during three years of field testing. Journal of Agricultural and Food Chemistry, 53, 5331-5335. 3) Harrigan *et al.* (2007). Chemical composition of glyphosate-tolerant sobyean 40-3-2 grown in Europe remains equivalent with that of conventional soybean (*Glycine max* L.). Journal of Agricultural and Food Chemistry, 55, 6160-6168. 4) Zhou *et al.* (2011). Stability in the composition equivalence of grain from insect-protected maize and seed from glyphosate-tolerant soybean to conventional counterparts over multiple seasons, locations, and breeding germplasms. Journal of Agricultural and Food Chemistry, 59, 8822-8828.	
	Search terms	Roundup Ready®	
Web of science™ platform	*Search string based on free-text terms using the Topic (TS) field*	(TS=(RoundupReady* OR "Roundup Ready" OR RR OR "first generation"))	

Key elements		Search terms	Comments
	Truncations and spelling variants used and their meanings	RoundupReady* = RoundupReady®	
EBSCOhost platform	*Search string based on free-text terms using the All Text (TX) field*	TX (RoundupReady* OR "Roundup Ready" OR RR OR "first generation")	
	Truncations and spelling variants used and their meanings	RoundupReady* = RoundupReady®	
Newly expressed protein			
	Reference publications	1) Taylor *et al.* (1999). Compositional analysis of glyphosate-tolerant soybeans treated with glyphosate. Journal of Agricultural and Food Chemistry, 47, 4469-4473. 2) McCann *et al.* (2005). Glyphosate-tolerant soybeans remain compositionally equivalent to conventional soybeans (*Glycine max* L.) during three years of field testing. Journal of Agricultural and Food Chemistry, 53, 5331-5335. 3) Harrigan *et al.* (2007). Chemical composition of glyphosate-tolerant soybean 40-3-2 grown in Europe remains equivalent with that of conventional soybean (*Glycine max* L.). Journal of Agricultural and Food Chemistry, 55, 6160-6168. 4) Zhou *et al.* (2011). Stability in the composition equivalence of grain from insect-protected maize and seed from glyphosate-tolerant soybean to conventional counterparts over multiple seasons, locations, and breeding germplasms. Journal of Agricultural and Food Chemistry, 59, 8822-8828.	
	Search terms	CP4 EPSPS	
Web of science™ platform	*Search string based on free-text terms using the Topic (TS) field*	(TS=(cp4epsps OR "cp4 epsps"))	

Key elements		Search terms	Comments
	Truncations and spelling variants used and their meanings	The options shown in the search string above are spelling variants. Truncations are not applicable.	
EBSCOhost platform	*Search string based on free-text terms using the All Text (TX) field*	TX (cp4epsps OR "cp4 epsps")	
	Truncations and spelling variants used and their meanings	The options shown in the search string above are spelling variants. Truncations are not applicable.	
Event			
	Reference publications	1) Taylor *et al.* (1999). Compositional analysis of glyphosate-tolerant soybeans treated with glyphosate. Journal of Agricultural and Food Chemistry, 47, 4469-4473. 2) McCann *et al.* (2005). Glyphosate-tolerant soybeans remain compositionally equivalent to conventional soybeans (*Glycine max* L.) during three years of field testing. Journal of Agricultural and Food Chemistry, 53, 5331-5335. 3) Harrigan *et al.* (2007). Chemical composition of glyphosate-tolerant soybean 40-3-2 grown in Europe remains equivalent with that of conventional soybean (*Glycine max* L.). Journal of Agricultural and Food Chemistry, 55, 6160-6168. 4) Zhou *et al.* (2011). Stability in the composition equivalence of grain from insect-protected maize and seed from glyphosate-tolerant soybean to conventional counterparts over multiple seasons, locations, and breeding germplasms. Journal of Agricultural and Food Chemistry, 59, 8822-8828.	
	Search terms	40-3-2, GTS	
Web of science™ platform	*Search string based on free-text terms using the Topic (TS) field*	(TS=(GTS* OR "40 3 2" OR "GTS 40 3 2"))	

Key elements		Search terms	Comments
	Truncations and spelling variants used and their meanings	GTS* = GTS, GTSs	
EBSCOhost platform	*Search string based on free-text terms using the All Text (TX) field*	TX (GTS* OR "40 3 2" OR "GTS 40 3 2")	
	Truncations and spelling variants used and their meanings	GTS* = GTS, GTSs	

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[10] and the CAB Abstracts® database[11] for performing the literature searches. The advanced literature search was conducted using the Web of Science™ platform[4] for the Web of Science™ Core collection database and using the EBSCOhost platform[6] for the CAB Abstracts® database[3].

The Web of Science™ Core Collection database[10] 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 search[10].

The CAB Abstracts® database[11] 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[12]. 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 09 October 2019
[11] CABI CAB Abstracts® database; http://www.cabi.org/cab-direct/ - Accessed on 09 October 2019
[12] Web of Science™; http://wokinfo.com/essays/journal-selection-process/ - Accessed on 09 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), eight[13] are involved in risk assessment of single GM soybean products while two of the remaining five (CIBIOGEM and Environment and Climate Change Canada) are not involved in GM risk assessment. Two (OGTR and GEAC), for the time being, only assess in GM cotton and oilseed rape. The US EPA is only involved in the assessment of events containing Plant-Incorporated Protectants (PIP). Therefore, the internet search focused on the eight key organisations relevant for 40-3-2.

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 40-3-2 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 40-3-2 soybean:
USDA (https://www.usda.gov/media) - Accessed on 09 October 2019;
US FDA (https://www.fda.gov/) - Accessed on 09 October 2019;
CFIA (http://www.inspection.gc.ca/eng/1297964599443/1297965645317) - Accessed on 09 October 2019;
Health Canada (https://www.canada.ca/en/health-canada.html) - Accessed on 09 October 2019;
FSANZ (http://www.foodstandards.gov.au/Pages/default.aspx) - Accessed on 09 October 2019,
CTNBio (http://ctnbio.mcti.gov.br/) - Accessed on 09 October 2019;
CONABIA(https://www.argentina.gob.ar/) - Accessed on 09 October 2019;
Japan MAFF (http://www.maff.go.jp/e/) - Accessed on 09 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 40-3-2 soybean for all uses as any other soybean 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, 326 hits were identified using Web of Science™ Core Collection database while 92 hits were retrieved from the search conducted 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 09 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 40-3-2 soybean

Relevant key organisations	Link to relevant information and summary of the retrieved data
USDA	https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/permits-notifications-petitions/petitions/petition-status - Accessed on 09 October 2019. The webpage dedicated to petitions for determination of nonregulated status was checked. *Date of the most recent website update at the time of the search*: 26/09/2019 *Date span of the search*: 2018-2019 *Limits applied*: The list of the petitions was sorted by 'Effective Date' and those completed/ released starting from 01/01/2018 were assessed. *Number of records retrieved matching the abovementioned criteria*: "5". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2.
US FDA	https://www.accessdata.fda.gov/scripts/fdcc/?set=Biocon – Accessed on 09 October 2019. The webpage dedicated to biotechnology consultations on food from GE plant varieties was checked. *Date of the most recent website update at the time of the search*: 05/09/2019 *Date span of the search*: 2018-2019 *Limits applied*: The list of the consultations starting from the 'FDA Letter Date' of Jan 1, 2018 was assessed. *Number of records retrieved matching the abovementioned criteria*: "7". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2.

Relevant key organisations	Link to relevant information and summary of the retrieved data
CFIA	http://www.inspection.gc.ca/plants/plants-with-novel-traits/approved-under-review/decision-documents/eng/1303704378026/1303704484236 - Accessed on 09 October 2019. The webpage dedicated to decision documents – determination of environmental and livestock feed safety was checked. *Date of the most recent website update at the time of the search*: 28/05/2019 *Date span of the search*: 2018 – 2019 *Limits applied*: The list of decision documents starting from the DD No. = DD2018 was assessed. *Number of records retrieved matching the abovementioned criteria*: "2". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2.
Health Canada	https://www.canada.ca/en/health-canada/services/food-nutrition/genetically-modified-foods-other-novel-foods/approved-products.html - Accessed on 09 October 2019. The webpage dedicated to approved products of genetically modified (GM) foods and other novel foods was checked. *Date of the most recent website update at the time of the search*: 26/06/2019 *Date span of the search*: 2018-2019 *Limits applied*: The list of novel food decisions starting from the 'Decision Date' of 01/01/2018 was assessed. *Number of records retrieved matching the abovementioned criteria*: "7". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2.
FSANZ	http://www.foodstandards.gov.au/consumer/gmfood/applications/Pages/default.aspx - Accessed on 09 October 2019. The webpage dedicated to current GM applications and approvals was checked. *Date of the most recent website update at the time of the search*: August 2019 *Date span of the search*: 2018-2019 *Limits applied*: The list for GM applications and approvals with 'Status' approved or under assessment starting from 2018 was assessed. *Number of records retrieved matching the abovementioned criteria*: "5". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2.

Relevant key organisations	Link to relevant information and summary of the retrieved data
CTNBio	http://ctnbio.mcti.gov.br/liberacao-comercial#/liberacao-comercial/consultar-processo – Accessed on 09 October 2019. The webpage dedicated to commercial releases (= Liberações Comerciais) was checked. *Date of the most recent website update at the time of the search*: Not clear (several dates mentioned) *Date span of the search*: 2018-2019 *Limits applied*: The list of commercial releases for plants (= plantas) starting from 2018 was assessed. *Number of records retrieved matching the abovementioned criteria*: "11". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2
CONABIA	https://www.argentina.gob.ar/agroindustria/alimentos-y-bioeconomia/ogm-comerciales – Accessed on 09 October 2019. The webpage of the national advisory commission on agricultural biotechnology (= Comisión Nacional Asesora de Biotecnología Agropecuaria) was checked. *Date of the most recent website update at the time of the search*: Not available *Date span of the search*: 2018-2019 *Limits applied*: 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. *Number of records retrieved matching the abovementioned criteria*: "17". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2
MAFF	http://www.maff.go.jp/j/syouan/nouan/carta/torikumi/attach/pdf/index-189.pdf- Accessed on 09 October 2019. The weblink dedicated to list of approved genetically modified agricultural crops was checked. *Date of the most recent website update at the time of the search*: 30/05/2019 *Date span of the search*: 2018 – 2019 *Limits applied*: The list of GM agricultural crops with approval date ('承認日') starting from January 01, 2018 was assessed. *Number of records retrieved matching the abovementioned criteria*: "17". *Number of relevant records or full-text documents retrieved*: The retrieved records are not relevant to 40-3-2.

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 four 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 *studies* retrieved after all searches of the scientific literature (excluding duplicates)	326	92
Number of *studies* excluded from the search results after rapid assessment for relevance	319	86
Total number of *full-text documents* assessed in detail (excluding duplicates)	10	
Number of *studies* excluded from further consideration after detailed assessment for relevance	6	
Total number of unobtainable/unclear studies	0	
Total number of relevant studies	4	

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		
Crop composition		
Li *et al.* (2019)	Effects of glyphosate on soybean metabolism in strains bred for glyphosate-resistance	Physiology and Molecular Biology of Plants
Pavlovskaya *et al.* (2018)	Comparative biochemical analysis of soybean varieties including genetically modified	Agrarnaya Rossiya
Agronomic and phenotypic characteristics		
Galazzi *et al.* (2019)	Evaluation of some effects on plant metabolism through proteins and enzymes in transgenic and non-transgenic soybeans after cultivation with silver nanoparticles	Journal of Proteomics
Nutrition		
Liu *et al.* (2018)	Effects of genetically modified and non-genetically modified soybeans with different heat treatments on growth and health of *Cyprinidae* species with different feeding habits	Aquaculture Research
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
Pruekprasert, N *et al.*	2018	Activation of Alpha7 nicotinic acetylcholine receptor by GTS21 regulates nuclear factor kappa-light-chain-enhancer of activated B cells inflammatory pathway in hepatocytes	Journal of the American College of Surgeons	It is not a safety study on 40-3-2
Suassuna, ND *et al.*	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 40-3-2

Study Author(s)	Year	Title	Source	Reason(s) for exclusion
de Vos, CJ *et al.*	2018	Health effects of feeding genetically modified (GM) crops to livestock animals: A review	Food and Chemical Toxicology	The hybrid used to conduct the study is not 40-3-2
Chen, H *et al.*	2018	Molecular mechanisms of tannin accumulation in *Rhus* galls and genes involved in plant-insect interactions	Scientific Reports	It is not a safety study on 40-3-2
Sbruzzi, FA *et al.*	2013	Transgenic and conventional Brazilian soybeans don't cause or prevent preneoplastic colon lesions or oxidative stress in a 90-day *in vivo* study	Revista de Nutrição	Article already reported in 2013-2014 season
Ye, Z *et al.*	2018	Triglyceride structure modulates gastrointestinal digestion fates of lipids: a comparative study between typical edible oils and triglycerides using fully designed *in vitro* digestion model	Journal of Agricultural and Food Chemistry	It is not a safety study on 40-3-2

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 40-3-2 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 40-3-2. 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]
Crop composition		
Li *et al.* (2019)	Not reliable	None, because no new hazards, modified exposure, or new scientific uncertainties are reported
Pavlovskaya *et al.* (2018)	Not reliable	None, because no new hazards, modified exposure, or new scientific uncertainties are reported
Nutrition		
Liu *et al.* (2018)	Not reliable	None, because no new hazards, modified exposure, or new scientific uncertainties are reported
Agronomic and phenotypic characteristics		
Galazzi *et al.* (2019)	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 40-3-2 in the EU, identified no relevant publications that would invalidate the initial conclusions of the 40-3-2 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 40-3-2 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.

Galazzi RM, Lopes Júnior CA, De Lima TB, Gozzo FC and Zezzi Arruda MA, 2019. Evaluation of some effects on plant metabolism through proteins and enzymes in transgenic and non-transgenic soybeans after cultivation with silver nanoparticles. Journal of Proteomics, 191, 88-106.

Li W, Lu P, Xie H, Li G, Wang J, Guo D and Liang X, 2019. Effects of glyphosate on soybean metabolism in strains bred for glyphosate-resistance. Physiol Mol Biol Plants, 25(2), 523-532.

Liu H, Liui X, Han D, Jin J, Zhu X, Yang Y and Xie S, 2018. Effects of genetically modified and non-genetically modified soybeans with different heat treatments on growth and health of Cyprinidae species with different feeding habits. Aquaculture Research, 50, 599-610.

Pavlovskaya NE, Gagarina IN, Solokhina IY, Lushnikov AV, Kostromicheva EV and Gneusheva IA, 2018. Comparative Biochemical Analysis Of Soybean Varieties Including Genetically Modified. Agrarian Russia, 10, 1-6.