Title

Summary of the Literature Review for FG72 Soybean
October 1, 2018 – September 30, 2019

Final Report

Data or Guideline Requirement

Explanatory note on literature searching
conducted in the context of GMO applications for (renewed) market authorization
and annual post-market environmental monitoring reports on GMOs authorised in the EU market.
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SIGNATURE PAGE

Principal author: [redacted] Date 2019-12-02

(YYYY-MM-DD)

BASF Belgium Coordination Center CommV

STUDY PERSONNEL

Electronic database search	[redacted]
Manual search	[redacted]
Stage 1 assessment	[redacted]
Stage 2 assessment	Food and Feed safety [redacted] Molecular characterization [redacted] Environmental safety [redacted]
Report	[redacted]

TABLE OF CONTENTS

TABLES

APPENDICES

SUMMARY

FG72 (OECD unique identifier: MST-FGØ72-2) is a genetically modified (GM) soybean designed to provide new options for weed control in the crop. FG72 soybean expresses the 5-enolpyruvyl-shikimate-3-phosphate synthase protein (2mEPSPS) and the 4-hydroxyphenylpyruvate dioxygenase protein (HPPD W336), which confer tolerance to glyphosate and HPPD inhibiting herbicides, respectively.

A scoping review was performed for FG72 soybean and its newly expressed proteins, 2mEPSPS and HPPD W336. The objective was to determine if there were studies about the molecular characterization of FG72 soybean, its effect on food and feed safety, or on environmental safety, that might require in-depth examination. A set of broad literature searches was performed using several bibliographic databases covering scientific literature from October 1, 2018 to September 30, 2019. Additional sources of information, such as web pages of regulatory authorities for food and feed safety, agriculture, and biotechnology were searched for the same time window, along with the bibliographies of relevant reviews. The references identified were evaluated for potential relevance to the scoping review questions according to pre-defined criteria.

The literature searches identified a total of 131 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. A total of 22 publications were progressed for further assessment. After a detailed review, all but three of the 22 publications were determined to be not relevant. The three relevant publications did not constitute new data on molecular characterization of FG72 soybean, or the 2mEPSPS and HPPD W336 proteins, nor did they suggest any potential adverse effects on human and animal health or on the environment. No evidence was identified that would warrant conducting a systematic review.

In summary, these literature searches and the review of the retrieved publications identified three relevant publications that support the existing safety assessment of FG72 soybean.

1. INTRODUCTION

FG72 (OECD unique identifier: MST-FGØ72-2) is a genetically modified (GM) soybean designed to provide new options for weed control in the crop. FG72 soybean expresses the 5-enolpyruvyl-shikimate-3-phosphate synthase protein (2mEPSPS) and the 4-hydroxyphenylpyruvate dioxygenase protein (HPPD W336), which confer tolerance to glyphosate and HPPD inhibiting herbicides, respectively.

The objective of the literature searches described here was to determine if there were publications published between October 1, 2018 and September 30, 2019 that mention the molecular characterization of FG72 soybean, and/or any adverse effects of FG72 soybean in food, feed or the environment. In that context, broad and inclusive literature searches were performed and the articles retrieved were reviewed in a comprehensive and transparent manner. The literature review was performed as recommended in the European Food Safety Authority (EFSA) explanatory note on literature searching conducted in the context of Genetically Modified Organisms (GMO)[1] applications and post-market environmental monitoring activities (2019).

The literature searches were performed for FG72 soybean and its newly expressed proteins 2mEPSPS and HPPD W336. The search terms also included relevant synonyms, intended trait, plant species and general GMO terms.

2. OVERALL METHODS

2.1. Objective of the scoping review

The objective of the scoping review was to survey the evidence base for FG72 soybean and the newly expressed proteins 2mEPSPS and HPPD W336, in order to identify any issues related to the molecular characterization of FG72 soybean, food or feed safety or environmental safety that may require a more detailed examination.

2.2. Review questions

Review questions were formulated to conform to PECO structure (Population, Exposure, Comparators, Outcome) if possible, and to meet data requirements. They were modeled after the review question examples provided in the EFSA 2019 explanatory note[1].

Question 1: Were any studies published during the reporting period that describe adverse effects on human or animal health or the environment of FG72 soybean and the 2mEPSPS and HPPD W336 proteins?

Key elements:

Population: Human health; animal health; environmental safety

Exposure: FG72 soybean, derived food/feed products, newly expressed proteins in FG72 soybean

Comparators: When applicable, comparable populations or subjects exposed to appropriate controls (e.g., vehicle only, innocuous control protein, non-GM comparator) or conventional counterpart used for comparative analysis of plant material

Outcome: Adverse effects

Question 2: Were any studies published during the reporting period that focus on the molecular characterization of FG72 soybean and the 2mEPSPS and HPPD W336 proteins?

Key elements:

Population: FG72 soybean and newly expressed proteins in FG72 soybean

Outcome: Molecular characterization (which would indicate the information/data requirement for molecular characteristics)

2.3. Criteria for relevance

Criteria for establishing the relevance of retrieved publications were defined prior to conduct of the search. These criteria were modeled after those given in the EFSA 2019 explanatory note[1] and are described in Table 1.

Table 1: Eligibility/inclusion criteria to establish the relevance of retrieved publications

Concepts	Criteria	Comment
Key elements of review questions with PECO structure		
Population	The publication addresses human and animal health, and/or the environment (including biodiversity, ecosystem services, service providing units, and endangered species) as general protection goals	From the publications that address the GMO under consideration, those that address protection goals relevant to the risk assessment of the GMO are eligible
Intervention/exposure	The publication addresses the GMO, derived food/feed products, and/or the intended trait(s) (e.g., newly expressed protein(s)) that are identical or like those under regulatory review	This enables the selection of publications that address the GMO, derived food/feed products, and/or the intended trait(s) under consideration
Comparator	If the publication reports a comparative study that uses plant material as test material, eligible publications must report a non-GM variety as comparator	In those cases where the publication addresses the GMO under consideration, reports a comparative analysis study and uses plant material as test material, eligible publications also need to include an appropriate non-GM line as comparator
Outcome	The publication addresses effects/impacts on human and animal health, and/or the environment	Publications that address the GMO under consideration also need to address effects/impacts on entities of concern, and potential determinants of exposure that place these entities at risk, in order to be relevant to the risk assessment of the GMO

Additional concepts		
Information/data requirements	The publication reports information pertaining to one or more information/data requirement(s) outlined in Appendix A for the GMO and derived food/feed products under consideration, including the intended trait(s)	Publications that potentially contribute to the knowledge informing the risk assessment of the GMO under consideration, and thus the risk hypotheses addressed, taking account of both hazard and exposure, can be considered relevant according to this eligibility/inclusion criterion. Publications addressing other issues such as benefits, socio-economics, ethics, crop protection, detection methods, efficacy, public perception and risk communication can be excluded, as they are not necessarily relevant to the risk assessment of GMOs
Plant species	The publication addresses the same plant species as the GMO under consideration	This eligibility/inclusion criterion permits the exclusion of publications on GMOs that contain the same intended trait(s) as the GMO under consideration, but which are introduced in another plant species
Scope of GMO application	The publication addresses pathways and levels of exposure to the GMO, derived food/feed products, and the intended trait(s) that are relevant for the intended uses of the GMO and derived food/feed products under regulatory review	From the publications that address the GMO under consideration, those that consider pathways and levels of exposure relevant to the scope of the GMO application (i.e., import and processing for food/feed uses, cultivation) are eligible
Target pests/organisms	The publication addresses target pests/organisms that are established in the EU	This permits the exclusion of publications that address interactions between the GMO and target pests/organisms that do not occur in the EU

Stacked events obtained by conventional crosses/subcombinations	The publication addresses the higher stacked event and/or a subcombination or subcombinations of the single events of the higher stacked event, independently of its/their origin	This permits the selection of publications on the higher stacked event and/or subcombinations of the single events of the higher stacked event that are in the scope of the GMO application(e), independently of their origin. This permits the exclusion of publications on the single events of the higher stacked event, because the risk assessment of GMO applications for stacked events covers only the products in the scope of the GMO application – i.e., the higher stacked event and subcombinations of the singles involved, independently of their origin
Molecular stacks	The publication addresses the molecular stack; all newly expressed proteins in the molecular stack; and/or one or several of the newly expressed proteins in the molecular stack that has/have not been previously risk assessed by EFSA and/or its GMO Panel and for which no safe use has been determined yet by EFSA and/or its GMO Panel	This permits the exclusion of publications that address one or several (not all) of the newly expressed proteins in the molecular stack that has/have been previously risk assessed by EFSA and/or its GMO Panel and for which the safe use has been determined by EFSA and/or its GMO Panel
Previously risk assessed publications	The publication has not been previously risk assessed by EFSA and/or its GMO Panel and is not cited/referenced in an EFSA/GMO Panel output	This permits the exclusion of publications that have been previously risk assessed by EFSA and/or its GMO Panel and cited/referenced in an EFSA/GMO Panel output
Access	Full-text document is accessible	If potentially relevant full-text documents cannot be obtained, they should be listed in a table with a description of the (unsuccessful) methods that have been used to try to obtain a copy

Reporting format	The publication presents original/primary data	This permits the exclusion of publications that do not present original/primary data (e.g., editorials, position papers). Reviews should only be included if they present data that are not available from a primary research study.
Reporting format	A study in a publication should only be presented once, but if it is presented in more than one publication, all publications should be listed and grouped	Duplicate publications should be excluded at the screening stage. Only one copy of a study is required even if it is reported in different publications, and identified in more than one database.

Table adapted from EFSA, 2019: 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.

2.4. Reference publication

One publication that is relevant for FG72 soybean was previously identified and was used to test and validate the search strategy:

- Dreesen R; Capt A; Oberdoerfer R; Coats I; Pallett KE (2018). Supplementary data on the characterization and safety evaluation of HPPD W336, a modified 4-hydroxyphenylpyruvate dioxygenase protein, which confers herbicide tolerance, and on the compositional assessment of field grown MST-FGO72-2 soybean expressing HPPD W336. Data in brief, Vol. 21, pp. 111-121

3. SEARCH METHODS AND OUTCOMES

The search strategies used here followed the 2019 EFSA explanatory note on literature searching conducted in the context of GMO applications and post-market environmental monitoring activities[1]. The search strategies were designed to be broad and sensitive enough to capture any relevant publications, if available.

An information specialist with background in plant biotechnology selected the databases, identified relevant search terms, developed search profiles, designed search strategies and conducted the searches.

3.1. Time window and date of the literature search

The database searches were performed on November 22, 2019. Only documents updated between October 1, 2018 and September 30, 2019, were considered in the search.

3.2. Search strategy

The search profiles were designed to cover event name, trade name, newly expressed proteins and intended traits. Since the ‘intended trait’ profile produced too many results when used on their own, it

was combined with a 'general GMO' profile as well as with a 'plant species' profile. See Table 2 for the detailed search profile.

All searches were performed in the Basic Index (BI) field, which includes the following subject headings/field names:

- **Agricola**: title (TI), controlled term (CT), supplementary term (ST), abstract (AB), named person (NA), corporate name (CO), note (NTE), geographic term, CABA and other fields (GT)

- **Biosis**: title (TI), abstract (AB), biosystematic codes (BC), chemical name (CN), controlled term (CT), gene name (GEN), geographic term (GT), organism (ORGN) and supplementary term (ST); as well as CAS Registry Numbers (RN)

- **CA-Plus**: title (TI), supplementary term (ST), index term (IT) and abstract (AB); as well as CAS Registry Numbers

- **CABA**: title (TI), controlled term (CT), supplementary term (ST), broader term (BT), abstract (AB), organism name (ORGN) and geographic term (GT); as well as CAS Registry Numbers

- **Medline**: title (TI), chemical name (CN), gene name (GEN), controlled term (excluding MeSH numbers) (CT), supplementary term (ST), named person (NA), other source (OS), and abstract (AB), as well as CAS Registry Numbers and GenBank Numbers

The search results were limited to documents updated between October 1, 2018 and September 30, 2019 (UP>=20181001 and UP<=20190930), and to non-patent documents (not P/DT). To ensure that documents with indexing errors where two DTs (one eligible and one ineligible) were attached to a single record were not missed, documents with both 'journal' and 'patent' as *document type* were also kept. These putative documents would be identified with (P/DT AND J/DT) in CABA and CAPlus.

Table 3 summarizes the number of results obtained from each of the databases searched.

See Appendix 1 for a complete search history.

Table 2: Search profile for database search

Set	Search string	Concepts
1	FG72 or FG(w)72 or MST(w)FGØ72 or MST(w)FG072 or MST(w)FGO72	Event name
2	GT27 or GT27TM	Trade name
3	(2MEPSPS or 2(w)MEPSPS or 2M(w)EPSPS or 2(w)M(w)EPSPS or EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUVOYLSHIKAMATE or ENOYLPYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC)(4W)(PHOSPHATE OR PHOSPHORIC)(2W)(SYNTHASE OR SYNTHETASE) or (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL)(W)(PHOSPHOSHIKIMATE OR PHOSPHOSHIKIMIC or ENOLPYRUVYLSHIKIMATEPHOSPHATE)(2W)(SYNTHASE OR SYNTHETASE) or (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE)(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE) or (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIKIMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(3W)PHOSPHOSYNTHASE) (s) ((DOUBL# or DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)) or (HPPDW336 or HPPD(w)W336 or HPPD(w)W(w)336 or HPPDW(w)336 or ((hydroxyphenylpyruvate or hydroxy(w)phenylpyruvate or hydroxyphenyl(w)pyruvate or hydroxy(w)phenyl(w)pyruvate)(w)(dehydrogenase or dioxygenase) or hppd)(s)(modif? or MUTANT# OR MUTAT?))	Newly expressed proteins
4	(herbicid? or HPPD(w)inhibitor# or isoxaflutole# or diketonitrile# or pyrazolone# or triketone# or GL!PHOSATE# or GL!FOSATE# OR G360 or g(w)360 or roundup? or round(w)up?)(5a)(resist? or toleran? or protect?)	Intended trait
5	soy or soya or soja or soybean# or soyabean# or sojabean# or glycine(w)max or g(w)max	Plant species
6	GMO OR GMOs OR LMO OR LMOs OR GM OR GE OR transgen? OR (genetic?(3a)(modif? OR transform? OR manipulat? OR improv? OR engineer?))	GMO general
7	4 and 5 and 6	Intended trait AND Plant species AND GMO general
8	1 or 2 or 3 or 7	Event name OR Trade name or Newly expressed proteins OR (Intended trait AND Plant species AND GMO general)

3.3. Databases used in the literature search

All searches were performed in the host STN (Scientific and Technical Information Network), an online database service operated jointly by CAS and FIZ Karlsruhe. STN provides access to a broad range of databases from the most renowned database producers worldwide.

The searches described here were performed in five databases: three multidisciplinary/large databases (Biosis, Medline and CA-Plus) and two subject-specific databases focused on agriculture-related topics (Agricola and CABA).

The dates of the most recent database updates are provided in Table 3.
See Appendix 2 for detailed database descriptions.

Table 3: Overview of the selected databases and summary of search results from each database

Database	AGRICOLA	BIOSIS	CAB Abstracts	CAPLUS	MEDLINE
Database Provider	STN International	STN International	STN International	STN International	STN International
Coverage	1970-present	1926-present	1973-present	1907-present	1946-present
Date of search	22 Nov 2019	22 Nov 2019	22 Nov 2019	22 Nov 2019	22 Nov 2019
Datespan of the search	1 Oct 2018 – 30 Sept 2019	1 Oct 2018 – 30 Sept 2019	1 Oct 2018 – 30 Sept 2019	1 Oct 2018 – 30 Sept 2019	1 Oct 2018 – 30 Sept 2019
Latest database update	5 Nov 2019	20 Nov 2019	20 Nov 2019	21 Nov 2019	21 Nov 2019
Number of records retrieved	25	43	44	48	39
Number of records after duplicate removal	17	29	25	21	39
Number of *relevant* records after rapid assessment	2	4	7	2	7

4. MANUAL SEARCHES

4.1. Manual searches of web pages of food safety, agriculture, and biotechnology-related authority webpages

A search of the web pages of regulatory authorities for food and feed safety, agriculture, and biotechnology was conducted. Search results were manually examined for relevant records that were either published during the time period of October 1, 2018 to September 30, 2019 or refer to relevant records published during this time frame. Relevance of results was determined based on the criteria listed in Table 1 and are summarized in Table 4. All web pages searched were chosen based on them being recommended as part of the EFSA 2019 explanatory note[1]. Search terms consisted of FG72 or MST-FG072-2; or HPPD W336 or modified-hydroxyphenylpyruvate dioxygenase; or 2mEPSPS or double mutant 5-enolpyruvyl shikimate-3-phosphate synthase enzyme in FG72 soybean. (All searched singly, with no search limits applied).

Table 4: Search of websites for regulatory authorities for food and feed safety, agriculture, and biotechnology

Source Site Name	Website URL	Date of Most Recent Site Update	Date of Search	No. of Relevant Records
US Environmental Protection Agency (EPA)	https://www.epa.gov/	Oct 9, 2019	Oct 9, 2019	0
US Department of Agriculture (USDA)	https://www.usda.gov/	Oct 8, 2019	Oct 9, 2019	0
US Food and Drug Administration (FDA)	https://www.fda.gov/	Oct 8, 2019	Oct 10, 2019	0
Health Canada	https://www.canada.ca/en/health-canada.html	Oct 7, 2019	Oct 10, 2019	0
Canadian Food Inspection Agency	https://www.canada.ca/en/food-inspection-agency.html	Aug 21, 2019	Oct 10, 2019	0
Environment and Climate Change Canada	https://www.canada.ca/en/services/environment/weather/climatechange.html	Jul 26, 2019	Oct 10, 2019	0
Food Standards Australia New Zealand (FSANZ)	http://www.foodstandards.gov.au/Pages/default.aspx	Oct 10, 2019	Oct 10, 2019	0
Office of the Gene Technology Regulator (OGTR)	http://www.ogtr.gov.au/	Oct 8, 2019	Oct 10, 2019	0
National Technical Commission on Biosafety (CTNBio)	http://ctnbio.mcti.gov.br/en	Sept. 2019	Oct 7-21, 2019	1
National Advisory Commission on Agricultural Biotechnology (CONABIA)	https://www.argentina.gob.ar/agroindustria/bioeconomia/biotecnologia	Oct 1, 2019	Oct 2, 2019	0
National Food Safety and Quality Service (SENASA)	https://www.argentina.gob.ar/senasa	Oct 2, 2019	Oct 2, 2019	0
Ministry of Environment, Forest, and Climate Change. Government of India	http://moef.gov.in/	Sept 30, 2019	Oct 10, 2019	0
Ministry of Agriculture, Forestry and Fisheries (MAFF)	http://www.maff.go.jp/	Oct 30, 2019	Oct 30, 2019	0
Ministry of Health, Labor and Welfare (MHLW)	http://www.mhlw.go.jp/	Oct 30, 2019	Oct 30, 2019	0

4.2. Manual searches of reference lists of recent review articles

Recent articles published between October 1, 2018 and September 30, 2019 served as sources for reference lists to search for potentially relevant studies. The review articles were identified by searching of PubMed.gov for general terms such as “GMO” or “GM crops” in the titles and abstracts. A list of review articles and resulting number of relevant studies found within the bibliographies is given in Table 5.

Table 5: Documents for which reference lists were scanned for relevant studies

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
1	Agapito-Tenfen SZ, Okoli AS, Bernstein MJ, Wikmark OG, Myhr AI. 2018	Revisiting Risk Governance of GM Plants: The Need to Consider New and Emerging Gene-Editing Techniques.	Front Plant Sci. 2018 Dec 21;9:1874. doi: 10.3389/fpls.2018.01874.	0
2	Alarcon CM, Shan G, Layton DT, Bell TA, Whipkey S, Shillito RD. 2019	Application of DNA- and Protein-Based Detection Methods in Agricultural Biotechnology.	J Agric Food Chem. 2019 Jan 30;67(4):1019-1028. doi: 10.1021/acs.jafc.8b05157.	0
3	Bogner A, Torgersen H. 2018	Precaution, Responsible Innovation and Beyond - In Search of a Sustainable Agricultural Biotechnology Policy.	Front Plant Sci. 2018 Dec 18;9:1884. doi: 10.3389/fpls.2018.01884.	0
4	Boonchaisri S, Rochfort S, Stevenson T, Dias DA. 2019	Recent developments in metabolomics-based research in understanding transgenic grass metabolism.	Metabolomics. 2019 Mar 15;15(4):47. doi: 10.1007/s11306-019-1507-4.	0
5	Collins C, Lorenzen N, Collet B. 2019	DNA vaccination for finfish aquaculture.	Fish Shellfish Immunol. 2019 Feb;85:106-125. doi: 10.1016/j.fsi.2018.07.012.	0
6	Gaffar FY, Koch A. 2019	Catch Me If You Can! RNA Silencing-Based Improvement of Antiviral Plant Immunity.	Viruses. 2019 Jul 23;11(7). pii: E673. doi: 10.3390/v11070673.	0
7	Ghosh S, Ghosh S, Sil PC. 2019	Role of nanostructures in improvising oral medicine.	Toxicol Rep. 2019 Apr 15;6:358-368. doi: 10.1016/j.toxrep.2019.04.004.	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
8	Halford NG. 2019	Legislation governing genetically modified and genome-edited crops in Europe: the need for change.	J Sci Food Agric. 2019 Jan 15;99(1):8-12. doi: 10.1002/jsfa.9227.	0
9	Hamburger DJS. 2018	Normative Criteria and Their Inclusion in a Regulatory Framework for New Plant Varieties Derived From Genome Editing.	Front Bioeng Biotechnol. 2018 Dec 19;6:176. doi: 10.3389/fbioe.2018.00176.	0
10	Hundleby PAC, Harwood WA. 2019	Impacts of the EU GMO regulatory framework for plant genome editing.	Food Energy Secur. 2019 May;8(2):e00161. doi: 10.1002/fes3.161.	0
11	Ichim MC. 2019	The Romanian experience and perspective on the commercial cultivation of genetically modified crops in Europe.	Transgenic Res. 2019 Feb;28(1):1-7. doi: 10.1007/s11248-018-0095-9.	0
12	Ishaq N, Bilal M, Iqbal HMN. 2019	Medicinal Potentialities of Plant Defensins: A Review with Applied Perspectives.	Medicines (Basel). 2019 Feb 19;6(1). pii: E29. doi: 10.3390/medicines6010029	0
13	Jyoti A, Kaushik S, Srivastava VK, Datta M, Kumar S, Yugandhar P, Kothari SL, Rai V, Jain A. 2019	The potential application of genome editing by using CRISPR/Cas9, and its engineered and ortholog variants for studying the transcription factors involved in the maintenance of phosphate homeostasis in model plants.	Semin Cell Dev Biol. 2019 Apr 6. pii: S1084-9521(18)30112-5. doi: 10.1016/j.semcdb.2019.03.010.	0
14	Kauffmann F, Van Damme P, Leroux-Roels G, Vandermeulen C, Berthels N, Beuneu C, Mali S. 2019	Clinical trials with GMO-containing vaccines in Europe: Status and regulatory framework.	Vaccine. 2019 Sep 30;37(42):6144-6153. doi: 10.1016/j.vaccine.2019.08.018.	0
15	Looi FY, Baker ML, Townson T, Richard M, Novak B, Doran TJ, Short KR. 2018	Creating Disease Resistant Chickens: A Viable Solution to Avian Influenza?	Viruses. 2018 Oct 15;10(10). pii: E561. doi: 10.3390/v10100561.	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
16	Mat Jalaluddin NS, Othman RY, Harikrishna JA. 2019	Global trends in research and commercialization of exogenous and endogenous RNAi technologies for crops.	Crit Rev Biotechnol. 2019 Feb;39(1):67-78. doi: 10.1080/07388551.2018.1496064.	0
17	Napier JA, Haslam RP, Tsalavouta M, Sayanova O. 2019	The challenges of delivering genetically modified crops with nutritional enhancement traits.	Nat Plants. 2019 Jun;5(6):563-567. doi: 10.1038/s41477-019-0430-z.	0
18	Rostoks N, GrantiÅ†a-IeviÅ†a L, IeviÅ†a B, Evelone V, ValciÅ†a O, Aleksejeva I. 2019	Genetically modified seeds and plant propagating material in Europe: potential routes of entrance and current status.	Heliyon. 2019 Feb 15;5(2):e01242. doi: 10.1016/j.heliyon.2019.e01242.	0
19	Tyczewska A, WoÅºniak E, Gracz J, KuczyÅ„ski J, Twardowski T. 2018	Towards Food Security: Current State and Future Prospects of Agrobiotechnology.	Trends Biotechnol. 2018 Dec;36(12):1219-1229. doi: 10.1016/j.tibtech.2018.07.008.	0
20	Wolt JD, Wolf C. 2018	Policy and Governance Perspectives for Regulation of Genome Edited Crops in the United States.	Front Plant Sci. 2018 Nov 8;9:1606. doi: 10.3389/fpls.2018.01606.	0
21	Wu Y, Li J, Li X, Zhai S, Gao H, Li Y, Zhang X, Wu G. 2019	Development and strategy of reference materials for the DNA-based detection of genetically modified organisms.	Anal Bioanal Chem. 2019 Mar;411(9):1729-1744. doi: 10.1007/s00216-019-01576-w.	0
22	Zimny T, Sowa S, Tyczewska A, Twardowski T. 2019	Certain new plant breeding techniques and their marketability in the context of EU GMO legislation - recent developments.	N Biotechnol. 2019 Jul 25;51:49-56. doi: 10.1016/j.nbt.2019.02.003.	0

5. RESULTS OF THE STUDY IDENTIFICATION AND SELECTION PROCESS

The database searches (Section 3) identified a total of 199 references, which were reduced to 131 after removal of duplicates (Table 3). The manual search identified one publication which had already been identified in the automated search (Section 4).

5.1. Screening of titles and abstracts to exclude obviously irrelevant references (Stage 1)

All references identified in the database searches described in Section 3 were assessed for relevance based on the information in their title and abstract by two reviewers independently. If opinions of relevance differed, the discrepancies were discussed between the reviewers and if a disagreement persisted, the publication under the discussion was transferred to Stage 2 for detailed evaluation by the experts.

Clearly irrelevant records were tagged as “Not Relevant”. These included:

- Duplicate entries
- Secondary literature (reviews), other than assessments from regulatory authorities
- Articles on non-relevant topics like detection methods, socio-economic implications of GM crops, GM policy, agronomical performance, other herbicide resistant GM crops, unrelated topics, etc.

Publications which appeared to be relevant and those of unclear relevance were tagged as “Relevant” and progressed to Stage 2 (detailed assessment; see Section 5.2).

The number of publications excluded after rapid assessment for relevance is presented in Table 6.

5.2. Detailed assessment of eligible references (Stage 2)

Publications tagged as “Relevant” in Stage 1 were assessed in detail independently by two scientific experts in each of three corresponding areas (i.e., Molecular Characterization, Food and Feed Safety, Environmental Safety), based on the full text of the publications.

If opinions of relevance differed between reviewers within each area, the initial reviewers discussed the discrepancy as necessary and consulted additional reviewers to resolve the discrepancy if needed. All eligible references were assessed in detail. This detailed assessment included evaluation of the scope of the article as well as the quality and reliability of the study. Categorization of reliability (as described in the EFSA 2019 explanatory note[1] and reported in Table 11) was dependent upon the following:

- appropriateness of methodology
- whether the description of methodology would allow independent repetition of the study
- extent of characterization of test materials
- reporting of evidence of reproducibility

Table 6 gives an overview of the reference selection process and results of the detailed assessment.

Table 6: Results of the publication selection process

Total number of publications retrieved after all searches of the scientific literature (excluding duplicates)	131
Number of publications excluded from the search results after rapid assessment for relevance (Stage 1)	109
Total number of full-text documents assessed in detail	22
Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2)	19
Total number of unobtainable/unclear publications	0
Total number of relevant publications	3

Table 7 lists the publications determined to be relevant along with their potential impact on the safety assessment after detailed evaluation. Publications that were clearly not relevant after a detailed assessment are listed in Table 8. Table 9 lists the publications for which full-text documents were unobtainable for detailed assessment or for which relevance was unclear after detailed assessment.

Table 7: Report of all relevant publications retrieved after detailed assessment of full-text documents for relevance: ordered by category of information/data requirement(s)

Main category of information/data requirement	Study (Author(s) and year)	Title	Source
Food and feed safety	Xie, Zixin Zou, Shiying Xu, Wentao Huang, Kunlun Liu, Xu He, Xiaoyun 2018	No subchronic toxicity of multiple herbicide - resistant soybean FG72 in Sprague-Dawley rats by 90-days feeding study.	Regulatory toxicology and pharmacology : RTP, (2018 Apr) Vol. 94, pp. 299-305.
Food and feed safety	Dreesen, Rozemarijn Pallett, Kenneth Edward Capt, Annabelle Oberdoerfer, Regina Coats, Isabelle 2018a	Characterization and safety evaluation of HPPD W336, a modified 4-hydroxyphenylpyruvate dioxygenase protein, and the impact of its expression on plant metabolism in herbicide-tolerant MST -FGO72 -2 soybean.	Regulatory toxicology and pharmacology : RTP, (2018 Aug) Vol. 97, pp. 170-185.
Food and feed safety	Dreesen, Rozemarijn Pallett, Kenneth Edward Capt, Annabelle Oberdoerfer, Regina Coats, Isabelle 2018b	Supplementary data on the characterization and safety evaluation of HPPD W336 ,a modified 4-hydroxyphenylpyruvate dioxygenase protein, which confers herbicide tolerance, and on the compositional assessment of field grown MST -FGO72 -2 soybean expressing HPPD W336 .	Data in brief, (2018 Dec) Vol. 21, pp. 111-121.

Table 8: Report of publications excluded from the risk assessment after detailed assessment of full-text documents

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Chinnadurai Parimala Stojsin Duska Liu Kang Frierdich Gregory E Glenn Kevin C Geng Tao Schapaugh Adam Huang Keguo Deffenbaugh Andrew E Liu Zi L Burzio Luis A 2018	Variability of CP4 EPSPS expression in genetically engineered soybean (*Glycine max L. Merrill*).	Transgenic research, (20181200) Vol. 27, No. 6, pp. 511-524.	The study examined the expression of CP4 EPSPS, which is not expressed in FG72 soybean.
Xiao Pei-ying Liu Yi Cao Yue-ping [Reprint Author] 2019	Overexpression of G10-EPSPS in soybean provides high glyphosate tolerance .	Journal of Integrative Agriculture, (AUG 2019) Vol. 18, No. 8, pp. 1851-1858.	The study examined the expression of G10-EPSPS which is not expressed in FG72.
Shi Zongyong Lu Chao Wu Boze Zou Shiying Huang Kunlun He Xiaoyun Zhao Changhui 2019	Evaluation of the effects of feeding glyphosate - tolerant soybeans (CP4 EPSPS) on the testis of male Sprague-Dawley rats.	GM crops + food, (2019) Vol. 10, No. 3, pp. 181-190.	FG72 soybean was not the subject of this study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Liu Weixiao Li Liang Dong Mei Wan Yusong Jin Wujun Xu Wentao He Xiaoyun Huang Kunlun 2018	iTRAQ-based quantitative tissue proteomic analysis of differentially expressed proteins (DEPs) in non-transgenic and transgenic soybean seeds.	Scientific reports, (20181205) Vol. 8, No. 1, pp. 17681.	FG72 soybean was used in the evaluation of an analytical method development. The results have no relevance to the safety of FG72 soybean.
Xia, Yimiao Chen, Fusheng [Reprint Author] Liu, Kunlun Zhang, Lifen Duan, Xiaojie Zhang, Xin Zhu, Zhenya 2019	Compositional differences between conventional Chinese and genetically modified Roundup Ready soybeans .	Crop + Pasture Science, (JUN 2019) Vol. 70, No. 6, pp. 526-534.	FG72 soybean was not the subject of this study.
Papineni, Sabitha Fletcher, Dale W. Cromwell, Gary L. Ekmay, Ricardo D. 2017	Comparative performance of broilers fed diets containing DAS-44406-6 and non-transgenic soybean meal.	Poultry Science, (MAY 2017) Vol. 96, No. 5, pp. 1244-1249.	FG72 soybean was not the subject of this study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Duke, Stephen O Rimando, Agnes M Reddy, Krishna N Cizdziel, James V Bellaloui, Nacer Shaw, David R Williams, Martin M, II Maul, Jude E 2018	Lack of transgene and glyphosate effects on yield, and mineral and amino acid content of glyphosate -resistant soybean.	Pest management science (2018), Volume 74, Number 5, pp. 1166-1173 ISSN: 1526-498X Published by: John Wiley + Sons, Ltd Source Note: 2018 May, v. 74, no. 5	FG72 soybean was not the subject of this study.
Papineni, Sabitha Christina M Dunville Ekmay Ricardo Jennifer A Murray Johnson Thomas Radha Krishna Sura 2017	Evaluation of the safety of a genetically modified DAS-444O6-6 soybean meal and hulls in a 90-day dietary toxicity study in rats	Food and chemical toxicology (2017), pp. 245-252 ISSN: 0278-6915 Published by: Elsevier Ltd Source Note: 2017 Nov., v. 109	FG72 soybean was not the subject of this study.
Chorna, I. 2019	Structural-functional state of kidneys of rats of two generations when using glyphosate -resistant genetically modified soy and herbicide Roundup .	ScienceRise: Biological Science (2019), Number 1, pp. 25-29, 42-43, 12 refs. ISSN: 2519-8017 Published by: PC Technology Center, Kharkiv	FG72 soybean was not the subject of this study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Naegeli, H. Bresson, J. L. Dalmay, T. Dewhurst, I. C. Epstein, M. M. Firbank, L. G. Guerche, P. Hejatko, J. Moreno, F. J. Mullins, E. Nogue, F. Rostoks, N. Juan, J. Serrano, S. Savoini, G. Veromann, E. Veronesi, F. Alvarez, F. Ardizzone, M. Paraskevopoulos, K. 2018	Assessment of genetically modified soybean MON 89788 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO -RX-011).	EFSA Journal (2018), Volume 16, Number 11, e05468 p., 6 refs. ISSN: 1831-4732 DOI: 10.2903/j.efsa.2018.5468 Published by: Wiley, Oxford	FG72 soybean was not the subject of this document.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Herman, R. A. Ekmay, R. D. Schafer, B. W. Song Ping Fast, B. J. Papineni, S. Shan GuoMin Juberg, D. R. Song, P. Shan, G. M. 2018	Food and feed safety of DAS-444O6-6 herbicide - tolerant soybean .	Regulatory Toxicology and Pharmacology (2018), Volume 94, pp. 70-74 ISSN: 0273-2300 DOI: 10.1016/j.yrtph.2018.01.016 Published by: Elsevier, New York	FG72 soybean was not the subject of this study.
Papineni, S. Passage, J. K. Ekmay, R. D. Thomas, J. 2018	Evaluation of 30% DAS-444O6-6 soybean meal in a subchronic rat toxicity study.	Regulatory Toxicology and Pharmacology (2018), Volume 94, pp. 57-69 ISSN: 0273-2300 DOI: 10.1016/j.yrtph.2018.01.005 Published by: Elsevier, New York	FG72 soybean was not the subject of this study.
Yuan JianQin Tang ZhongWei Zhao JiangHe Shi ZongYong Wang JunDong Yuan, J. Q. Tang, Z. W. Zhao, J. H. Shi, Z. Y. Wang, J. D. 2017	Toxicologic evaluation of chronic feeding of glyphosate -resistant transgenic soybean GTS40-3-2 meal to rats.	Emirates Journal of Food and Agriculture (2017), Volume 29, Number 11, pp. 856-862, 37 refs. ISSN: 2079-052X DOI: 10.9755/ejfa.2017.v29.i11.1495 Published by: United Arab Emirates University, Faculty of Food and Agriculture, Al Anin	FG72 soybean was not the subject of this study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
EFSA Panel on Genetically Modified Organisms Naegeli, Hanspeter Birch, Andrew Nicholas Casacuberta, Josep De Schrijver, Adinda Gralak, Mikolaj Antoni Jones, Huw Manachini, Barbara Messean, Antoine Nielsen, Elsa Ebbesen Nogue, Fabien Robaglia, Christophe Rostoks, Nils Sweet, Jeremy Tebbe, Christoph Visioli, Francesco Wal, Jean-Michel Alvarez, Fernando Ardizzone, Michele Liu, Yi Neri, Franco Maria Ramon, Matthew 2017	Scientific opinion on an application by Dow AgroSciences LLC (EFSA-GMO -NL-2012-106) for the placing on the market of genetically modified herbicide -tolerant soybean DAS-44406-6 for food and feed uses, import and processing under Regulation (EC) No 1829/2003	EFSA Journal (2017), 15(3), n/a CODEN: EJFOA6; ISSN: 1831-4732	FG72 soybean was not the subject of this document.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Shen Bin Hong Xin Han Cheng Zhong Wen Hui Cao Yue Ping Liu Biao 2018	Effects of glyphosate - resistant transgenic soybean on soil rhizospheric bacteria and rhizobia.	Ying yong sheng tai xue bao = The journal of applied ecology, (2018 Sep) Vol. 29, No. 9, pp. 2988-2996. Journal code: 9425159. ISSN: 1001-9332. L-ISSN: 1001-9332.	The study reports on the impact of glyphosate resistant soybean on soil rhizospheric bacteria and rhizobia. FG72 soybean is not the subject of this study.
Ricroch, Agnes Akkoyunlu, Serife Martin-Laffon, Jacqueline Kuntz, Marcel 2018	Assessing the Environmental Safety of Transgenic Plants: Honey Bees as a Case Study.	Kuntz, M [Editor]. Adv. Bot. Res., (2018) pp. 111-167. Transgenic Plants and Beyond. Publisher: ACADEMIC PRESS LTD-ELSEVIER SCIENCE LTD, 24-28 OVAL ROAD, LONDON NW1 7DX, UK. Series: Advances in Botanical Research. CODEN: ABTRAJ. ISSN: 0065-2296. ISBN: 978-0-12-809447-1(P).	Report reviewed the impact of insecticidal and herbicidal traits on the health of honey bees. FG72 soybean is not the subject of this study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Lu GuiHua Hua XiaoMei Liang Li Wen ZhongLing Du MeiHang Meng FanFan Pang YanJun Qi JinLiang Tang ChengYi Yang YongHua Lu, G. H. Hua, X. M. Liang, L. Wen, Z. L. Du, M. H. Meng, F. F. Pang, Y. J. Qi, J. L. Tang, C. Y. Yang, Y. H. 2018	Identification of major rhizobacterial taxa affected by a glyphosate -tolerant soybean line via shotgun metagenomic approach.	Genes (2018), Volume 9, Number 4, 214 p., 99 refs. ISSN: 2073-4425 DOI: 10.3390/genes9040214 Published by: MDPI Publishing, Basel	Study evaluated the impact of GM soybean NZL06-698 on soil microbial community through 15S rRNA gene sequencing. FG72 soybean is not the subject of this study.
Pereira, J. L. Lopes, M. C. Parish, J. B. Silva, A. A. Picanco, M. C. 2018	Impact of RR soybeans and glyphosate on the community of soil surface arthropods.	Planta Daninha (2018), Volume 36, e018171324 p., 16 refs. ISSN: 0100-8358 Published by: Sociedade Brasileira da Ciencia das Plantas Daninhas, Vicosa	Study evaluated the impact of BRS Favorita Roundup Ready soybean on soil surface arthropods. FG72 soybean is not the subject of this study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Lu, Gui-Hua Zhu, Yin-Ling Kong, Ling-Ru Cheng, Jing Tang, Cheng-Yi Hua, Xiao-Mei Meng, Fan-Fan Pang, Yan-Jun Yang, Rong-Wu Qi, Jin-Liang Yang, Yong-Hua 2017	Impact of a glyphosate - tolerant soybean line on the Rhizobacteria, revealed by Illumina Miseq	Journal of Microbiology and Biotechnology (2017), 27(3), 561-572 CODEN: JOMBES; ISSN: 1017-7825	The study evaluated the impact of glyphosate tolerant soybean N698 on the soil microbial community using 16S rRNA sequencing. FG72 soybean is not the subject of this study.

Table 9: Report of unobtainable/unclear publications

Study (Author(s) and year)	Title	Source	Description of (unsuccessful) methods used to try and obtain a copy of the publication
No publications in this category.			

6. NARRATIVE SYNTHESIS AND SUMMARY OF RELEVANT STUDIES

A total of 22 publications were selected during Stage 1 evaluation (rapid assessment based on title and abstract). After Stage 2 evaluation (detailed review based on full text), it was determined that three publications were relevant for the safety assessment of FG72 soybean and its newly expressed proteins, 2mEPSPS and HPPD W336.

In the references identified as relevant, Xie *et al.*, 2018 reported the safety of the soybean expressing 2mEPSPS and HPPD W336 through 90-day subchronic rat studies. Dreesen *et al.* (2018a) reported no amino acid sequence homology of the HPPD W336 protein to known allergens or toxins. Dreesen *et al.* (2018b) demonstrated *in vitro* the absence of hemolytic activity from the HPPD W336 protein as a follow up to detected sequence similarities to toxins annotated as hemolysins. Dreesen *et al.* (2018b) showed that the surrogate protein produced in bacteria and used for the studies was substantially similar to the plant-expressed protein. The HPPD W336 protein was rapidly digested in simulated gastric fluid assay. These studies fall into the main category of toxicological assessment of the HPPD W336 protein and the findings support the safety assessment of FG72 soybean and its newly expressed proteins, 2mEPSPS and HPPD W336.

Table 10 and Table 11 list the relevant publications along with a summary of any adverse effects reported and the reliability of the publications.

Table 10: Summary of all relevant publications retrieved after detailed assessment of full-text documents for relevance (Stage 2): ordered by category of information/data requirement(s)

Main category of information/data requirement	Study (Author(s) and year)	Intervention/ test materials used	Adverse effects reported	Which adverse effect reported
Food and feed safety	Xie, Zixin Zou, Shiying Xu, Wentao Huang, Kunlun Liu, Xu He, Xiaoyun 2018	Herbicide-tolerant FG72 soybean	No adverse effects reported	Not applicable
Food and feed safety	Dreesen, Rozemarijn Pallett, Kenneth Edward Capt, Annabelle Oberdoerfer, Regina Coats, Isabelle 2018a	HPPD W336, a modified 4-hydroxyphenylpyruvate dioxygenase protein Herbicide -tolerant FG72 soybean	No adverse effects reported	Not applicable
Food and feed safety	Dreesen, Rozemarijn Pallett, Kenneth Edward Capt, Annabelle Oberdoerfer, Regina Coats, Isabelle 2018b	Herbicide-tolerant FG72 soybean expressing HPPD W336	No adverse effects reported	Not applicable

Table 11: Report of the reliability and implications for the risk assessment of all relevant publications retrieved after detailed assessment of full-text documents for relevance (Stage 2): ordered by category of information/data requirement(s)

Main category of information/data requirement	Study (Author(s) and year)	Summary of reliability appraisal	Implications for risk assessment
Food and feed safety	Xie, Zixin Zou, Shiying Xu, Wentao Huang, Kunlun Liu, Xu He, Xiaoyun 2018	The study presented reliable methods and findings.	**No negative impact on risk assessment.**
Food and feed safety	Dreesen, Rozemarijn Pallett, Kenneth Edward Capt, Annabelle Oberdoerfer, Regina Coats, Isabelle 2018a	The study presented reliable methods and findings.	**No negative impact on risk assessment.**
Food and feed safety	Dreesen, Rozemarijn Pallett, Kenneth Edward Capt, Annabelle Oberdoerfer, Regina Coats, Isabelle 2018b	The study presented reliable methods and findings.	**No negative impact on risk assessment.**

7. CONCLUSION

The literature searches performed for FG72 soybean, 2mEPSPS and HPPD W336 for the period from October 1, 2018 to September 30, 2019, identified a total of 131 unique publications. A total of 22 publications were progressed for detailed assessment after excluding 109 obviously irrelevant publications during Stage 1 evaluation (rapid assessment based on title and abstract).
These 22 publications were evaluated in detail based on their full text for potential relevance, following the pre-established criteria. Three relevant references with no adverse effects on human and animal safety were identified. These references support the food and feed safety assessment of FG72 soybean. No relevant publications with bearing on molecular characterization or environmental safety were identified. No issues or topics were identified that would trigger or warrant a more specific question formulation.

8. REFERENCES

No.	Author(s), title, source, edition, year, pages
1.	Devos Y, Guajardo IM, Alvarez F and Glanville J. 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 supporting publications 2019:EN-1614. 62 pages. doi:10.2903/sp.efsa.2019.EN-1614.

9. APPENDICES

Appendix 1 Search history

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     FILE 'MEDLINE' ENTERED AT 13:10:58 ON 22 NOV 2019
L1             6 SEA FG72 OR FG(W)72 OR MST(W)FGØ72 OR MST(W)FG072 OR MST(W)FGO7
                  2
L2             4 SEA GT27 OR GT27TM
L3             9 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L4          4080 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
                  ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
                  OYLSHIKAMATE OR ENOYLPYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC)(
                  4W)(PHOSPHATE OR PHOSPHORIC)(2W)(SYNTHASE OR SYNTHETASE)
L5             0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL)(W)(PHOSPHOSHIKI
                  MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE)(2W)(S
                  YNTHASE OR SYNTHETASE)
L6           344 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                  ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                  )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L7           443 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
                  IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                  3W)PHOSPHOSYNTHASE)
L8         22859 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L9            14 SEA L3 OR (((L4 OR L5 OR L6 OR L7))(S)L8)
L10            3 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L11           32 SEA ((HYDROXYPHENYLPYRUVATE OR HYDROXY(W)PHENYLPYRUVATE OR
                  HYDROXYPHENYL(W)PYRUVATE OR HYDROXY(W)PHENYL(W)PYRUVATE)(W)(DEH
                  YDROGENASE OR DIOXYGENASE) OR HPPD)(S)(MODIF? OR MUTANT# OR
                  MUTAT?)
L12           32 SEA (L10 OR L11)
L13           45 SEA L9 OR L12
L14         2973 SEA (HERBICID? OR HPPD(W)INHIBITOR# OR ISOXAFLUTOLE# OR
                  DIKETONITRILE# OR PYRAZOLONE# OR TRIKETONE# OR GL!PHOSATE# OR
                  GL!FOSATE# OR G360 OR G(W)360 OR ROUNDUP? OR ROUND(W)UP?)(5A)(R
                  ESIST? OR TOLERAN? OR PROTECT?)
L15        60500 SEA SOY OR SOYA OR SOJA OR SOYBEAN# OR SOYABEAN# OR SOJABEAN#
                  OR GLYCINE(W)MAX OR G(W)MAX
L16      3455516 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                  (GENETIC?(3A)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                  ENGINEER?))
L17          272 SEA L14 AND L15 AND L16
L18          313 SEA L1 OR L2 OR L13 OR L17
L19           68 SEA L18 AND PY>=2017
L20           39 SEA L19 AND UP>=20181001 AND UP<=20190930

     FILE 'BIOSIS' ENTERED AT 13:11:38 ON 22 NOV 2019
L21            8 SEA FG72 OR FG(W)72 OR MST(W)FGØ72 OR MST(W)FG072 OR MST(W)FGO7
                  2
L22            4 SEA GT27 OR GT27TM
L23           12 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L24         4866 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
                  ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
                  OYLSHIKAMATE OR ENOYLPYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC)(
                  4W)(PHOSPHATE OR PHOSPHORIC)(2W)(SYNTHASE OR SYNTHETASE)
L25            0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL)(W)(PHOSPHOSHIKI
                  MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE)(2W)(S
                  YNTHASE OR SYNTHETASE)
L26          651 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                  ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                  )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L27           27 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
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                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L28        25482 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L29           17 SEA L23 OR (((L24 OR L25 OR L26 OR L27))(S)L28)
L30            3 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L31           46 SEA ((HYDROXYPHENYLPYRUVATE OR HYDROXY(W)PHENYLPYRUVATE OR
                HYDROXYPHENYL(W)PYRUVATE OR HYDROXY(W)PHENYL(W)PYRUVATE)(W)(DEH
                YDROGENASE OR DIOXYGENASE) OR HPPD)(S)(MODIF? OR MUTANT# OR
                MUTAT?)
L32           46 SEA (L30 OR L31)
L33           62 SEA L29 OR L32
L34        10078 SEA (HERBICID? OR HPPD(W)INHIBITOR# OR ISOXAFLUTOLE# OR
                DIKETONITRILE# OR PYRAZOLONE# OR TRIKETONE# OR GL!PHOSATE# OR
                GL!FOSATE# OR G360 OR G(W)360 OR ROUNDUP? OR ROUND(W)UP?)(5A)(R
                ESIST? OR TOLERAN? OR PROTECT?)
L35       156956 SEA SOY OR SOYA OR SOJA OR SOYBEAN# OR SOYABEAN# OR SOJABEAN#
                OR GLYCINE(W)MAX OR G(W)MAX
L36       430468 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                (GENETIC?(3A)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                ENGINEER?))
L37         505 SEA L34 AND L35 AND L36
L38         567 SEA L21 OR L22 OR L33 OR L37
L39          94 SEA L38 AND PY>=2017
L40          43 SEA L39 AND UP>=20181001 AND UP<=20190930

     FILE 'AGRICOLA' ENTERED AT 13:12:13 ON 22 NOV 2019
L41           3 SEA FG72 OR FG(W)72 OR MST(W)FGØ72 OR MST(W)FG072 OR MST(W)FGO7
                2
L42           1 SEA GT27 OR GT27TM
L43           2 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L44         560 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
                ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
                OYLSHIKAMATE OR ENOYLPYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC)(
                4W)(PHOSPHATE OR PHOSPHORIC)(2W)(SYNTHASE OR SYNTHETASE)
L45           0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL)(W)(PHOSPHOSHIKI
                MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE)(2W)(S
                YNTHASE OR SYNTHETASE)
L46         270 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L47         180 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L48        5879 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L49           6 SEA L43 OR (((L44 OR L45 OR L46 OR L47))(S)L48)
L50           0 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L51          26 SEA ((HYDROXYPHENYLPYRUVATE OR HYDROXY(W)PHENYLPYRUVATE OR
                HYDROXYPHENYL(W)PYRUVATE OR HYDROXY(W)PHENYL(W)PYRUVATE)(W)(DEH
                YDROGENASE OR DIOXYGENASE) OR HPPD)(S)(MODIF? OR MUTANT# OR
                MUTAT?)
L52          26 SEA (L50 OR L51)
L53          32 SEA L49 OR L52
L54        7723 SEA (HERBICID? OR HPPD(W)INHIBITOR# OR ISOXAFLUTOLE# OR
                DIKETONITRILE# OR PYRAZOLONE# OR TRIKETONE# OR GL!PHOSATE# OR
                GL!FOSATE# OR G360 OR G(W)360 OR ROUNDUP? OR ROUND(W)UP?)(5A)(R
                ESIST? OR TOLERAN? OR PROTECT?)
L55       82172 SEA SOY OR SOYA OR SOJA OR SOYBEAN# OR SOYABEAN# OR SOJABEAN#
                OR GLYCINE(W)MAX OR G(W)MAX
L56       90652 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                (GENETIC?(3A)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                ENGINEER?))
L57         391 SEA L54 AND L55 AND L56
L58         424 SEA L41 OR L42 OR L53 OR L57
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L59          44 SEA L58 AND PY>=2017
L60          25 SEA L59 AND UP>=20181001 AND UP<=20190930

     FILE 'CABA' ENTERED AT 13:13:04 ON 22 NOV 2019
L61           8 SEA FG72 OR FG(W)72 OR MST(W)FGØ72 OR MST(W)FG072 OR MST(W)FGO7
                  2
L62           1 SEA GT27 OR GT27TM
L63          12 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L64         948 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
                  ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
                  OYLSHIKAMATE OR ENOYLPYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC)(
                  4W)(PHOSPHATE OR PHOSPHORIC)(2W)(SYNTHASE OR SYNTHETASE)
L65           0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL)(W)(PHOSPHOSHIKI
                  MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE)(2W)(S
                  YNTHASE OR SYNTHETASE)
L66         373 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                  ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                  )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L67         142 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
                  IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                  3W)PHOSPHOSYNTHASE)
L68        6659 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L69          16 SEA L63 OR (((L64 OR L65 OR L66 OR L67))(S)L68)
L70           2 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L71          46 SEA ((HYDROXYPHENYLPYRUVATE OR HYDROXY(W)PHENYLPYRUVATE OR
                  HYDROXYPHENYL(W)PYRUVATE OR HYDROXY(W)PHENYL(W)PYRUVATE)(W)(DEH
                  YDROGENASE OR DIOXYGENASE) OR HPPD)(S)(MODIF? OR MUTANT# OR
                  MUTAT?)
L72          46 SEA (L70 OR L71)
L73          60 SEA L69 OR L72
L74       17344 SEA (HERBICID? OR HPPD(W)INHIBITOR# OR ISOXAFLUTOLE# OR
                  DIKETONITRILE# OR PYRAZOLONE# OR TRIKETONE# OR GL!PHOSATE# OR
                  GL!FOSATE# OR G360 OR G(W)360 OR ROUNDUP? OR ROUND(W)UP?)(5A)(R
                  ESIST? OR TOLERAN? OR PROTECT?)
L75      178283 SEA SOY OR SOYA OR SOJA OR SOYBEAN# OR SOYABEAN# OR SOJABEAN#
                  OR GLYCINE(W)MAX OR G(W)MAX
L76      166876 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                  (GENETIC?(3A)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                  ENGINEER?))
L77         833 SEA L74 AND L75 AND L76
L78         888 SEA L61 OR L62 OR L73 OR L77
L79         105 SEA L78 AND PY>=2017
L80          44 SEA L79 AND UP>=20181001 AND UP<=20190930
L81          44 SEA L80 NOT P/DT
L82           0 SEA L80 AND (P/DT AND J/DT)
L83          44 SEA L81 OR L82

     FILE 'HCAPLUS' ENTERED AT 13:13:48 ON 22 NOV 2019
L84          13 SEA FG72 OR FG(W)72 OR MST(W)FGØ72 OR MST(W)FG072 OR MST(W)FGO7
                  2
L85           6 SEA GT27 OR GT27TM
L86          29 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L87        4131 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
                  ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
                  OYLSHIKAMATE OR ENOYLPYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC)(
                  4W)(PHOSPHATE OR PHOSPHORIC)(2W)(SYNTHASE OR SYNTHETASE)
L88           9 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL)(W)(PHOSPHOSHIKI
                  MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE)(2W)(S
                  YNTHASE OR SYNTHETASE)
L89        1009 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                  ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                  )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L90          79 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
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                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L91         71960 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L92            39 SEA L86 OR (((L87 OR L88 OR L89 OR L90))(S)L91)
L93             4 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L94           130 SEA ((HYDROXYPHENYLPYRUVATE OR HYDROXY(W)PHENYLPYRUVATE OR
                HYDROXYPHENYL(W)PYRUVATE OR HYDROXY(W)PHENYL(W)PYRUVATE)(W)(DEH
                YDROGENASE OR DIOXYGENASE) OR HPPD)(S)(MODIF? OR MUTANT# OR
                MUTAT?)
L95           130 SEA (L93 OR L94)
L96           166 SEA L92 OR L95
L97         26076 SEA (HERBICID? OR HPPD(W)INHIBITOR# OR ISOXAFLUTOLE# OR
                DIKETONITRILE# OR PYRAZOLONE# OR TRIKETONE# OR GL!PHOSATE# OR
                GL!FOSATE# OR G360 OR G(W)360 OR ROUNDUP? OR ROUND(W)UP?)(5A)(R
                ESIST? OR TOLERAN? OR PROTECT?)
L98        372772 SEA SOY OR SOYA OR SOJA OR SOYBEAN# OR SOYABEAN# OR SOJABEAN#
                OR GLYCINE(W)MAX OR G(W)MAX
L99        638496 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                (GENETIC?(3A)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                ENGINEER?))
L100         5495 SEA L97 AND L98 AND L99
L101         5624 SEA L84 OR L85 OR L96 OR L100
L102         1480 SEA L101 AND PY>=2017
L103          356 SEA L102 AND UP>=20181001 AND UP<=20190930
L104           48 SEA L103 NOT P/DT
L105            0 SEA L103 AND (P/DT AND J/DT)
L106           48 SEA L104 OR L105

     FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 13:14:44 ON 22
     NOV 2019
L107          131 DUP REM L20 L40 L60 L83 L106 (68 DUPLICATES REMOVED)
                  ANSWERS '1-39' FROM FILE MEDLINE
                  ANSWERS '40-68' FROM FILE BIOSIS
                  ANSWERS '69-85' FROM FILE AGRICOLA
                  ANSWERS '86-110' FROM FILE CABA
                  ANSWERS '111-131' FROM FILE HCAPLUS
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Appendix 2 Database descriptions

Host	File	Description
STN	AGRICOLA	Agriculture Online Access is a bibliographic database containing selected worldwide literature of agriculture and related fields. AGRICOLA is the locator and bibliographic access and control system of the National Agricultural Library (NAL) collections and also includes records from other cooperating institutions. Coverage of the database includes agricultural economics and rural sociology, agricultural production, animal sciences, chemistry, entomology, food and human nutrition, forestry, natural resources, pesticides, plant science, soils and fertilizers, and water resources. Also covered are related areas such as biology and biotechnology, botany, ecology, and natural history. The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. Bibliographic information, abstracts, geographic terms, controlled terms, and supplementary terms are searchable.
STN	BIOSIS	BIOSIS Previews® is the largest and most comprehensive life science database in the world. Amongst others subject coverage includes Agriculture, Biochemistry, Biophysics, Botany, Environmental Biology, Physiology, Toxicology. Sources include periodicals, journals, conference proceedings, reviews, reports, patents, and short communications. Nearly 6,000 life source journals, 1,500 international meetings as well as review articles, books, and monographs are reviewed for inclusion. Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are all searchable.
STN	CABA/CAB	The CAB Abstracts database covers worldwide literature from all areas of agriculture and related sciences including Agriculture, Agricultural chemicals, Animal sciences and production, Crop protection, Crop sciences and production, Environment, Soils and fertilizers. Sources for CABA include journals, books, reports, published theses, conference proceedings, and patents. Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are searchable.
STN	CAS-CA/CAPLUS	The Chemical Abstracts (CA) database covers all areas of Biochemistry, Chemistry and Chemical engineering, and related sciences. Sources include over 8,000 journals, patents from 38 national patent offices and two international patent organizations, technical reports, books, conference proceedings, and dissertations. Electronic only journals and Web preprints are also covered. Bibliographic terms, indexing terms, roles, CAS Registry Numbers, International Patent Classification, and abstracts are searchable.

Host	File	Description
STN	MEDLINE	MEDLINE contains information on every area of medicine. The MEDLINE database corresponds to Index Medicus, Index to Dental Literature, and International Nursing Index; OLDMEDLINE, with data from NLM's from the Cumulated Index Medicus (1960-1965) and Current List of Medical Literature (1958-1959); and, since August 2001, IN-PROCESS records, the latest documents before they have been completely indexed for inclusion on MEDLINE. Sources include journals and chapters in books or symposia. Bibliographic information, indexing terms, abstracts, chemical names, and CAS Registry Numbers are all searchable. Online thesauri are available for the Medical Subject Headings (/MN), Controlled Terms (/CT) and Chemical Name (/CN) fields.