

Title

**Summary of the Literature Review for GHB811 Cotton
July 1, 2022 – June 30, 2023**

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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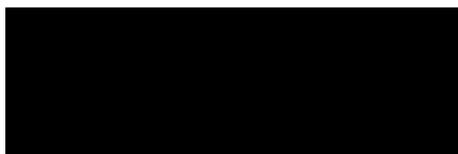
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SUMMARY

GHB811 cotton was developed through *Agrobacterium*-mediated transformation using the vector pTSIH09 containing hppdPfw336-1Pa and 2mepsps expression cassettes. GHB811 cotton produces the 4-hydroxyphenylpyruvate dioxygenase protein (HPPD W336) and the 5-enolpyruvylshikimate 3-phosphate synthase protein (2mEPSPS), which confer tolerance to HPPD inhibitors, such as isoxaflutole, and glyphosate herbicides, respectively. The OECD identifier is BCS-GH811-4.

A scoping review was performed for the GHB811 cotton and its newly expressed proteins, HPPD W336 and 2mEPSPS. The objective of this scoping review was to determine if there were studies about the molecular characterization of GHB811 cotton, its effect on food and feed safety or environmental safety, that might require in-depth examination. A set of broad literature searches was performed using several bibliographic databases covering scientific literature from July 1, 2022 to June 30, 2023. Additional sources of information, such as web pages of food safety, agriculture, and biotechnology-related authorities 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.

These literature searches identified a total of 53 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. Four publications were progressed for detailed assessment, and one of the four publications was determined to be relevant after detailed review.

The relevant article did not constitute new data on molecular characterization of GHB811 cotton or the HPPD W336 and 2mEPSPS proteins, nor did it 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 review of the retrieved articles identified one relevant publication that supports the existing safety assessment of GHB811 cotton.

1. INTRODUCTION

GHB811 cotton was developed through *Agrobacterium*-mediated transformation using the vector pTSIH09 containing hppdPFW336-1Pa and 2mepsps expression cassettes. GHB811 cotton produces the 4-hydroxyphenylpyruvate dioxygenase protein (HPPD W336) and the 5-enolpyruvylshikimate 3-phosphate synthase protein (2mEPSPS), which confer tolerance to HPPD inhibitors, such as isoxaflutole, and glyphosate herbicides, respectively. The OECD identifier is BCS-GH811-4.

The objective of the literature searches described here was to determine if there were publications published between July 1, 2022 and June 30, 2023 that mention the molecular characterization of the GHB811 cotton, and/or any adverse effect of GHB811 cotton in food, feed or the environment. In that context, a broad and inclusive literature search was performed, and the articles retrieved were reviewed in a comprehensive and transparent manner. This was intended as a scoping review. 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) applications and post-market environmental monitoring activities (2019; (1)).

The literature searches were performed for the GHB811 cotton and its newly expressed proteins, HPPD W336 and 2mEPSPS. The search terms also included relevant synonyms, the trade name and intended trait. When needed, plant species and general GMO terms were used to limit the search results (described in [Section 3.3](#)).

2. OVERALL METHODS

2.1. Objective of the scoping review

The objective of the scoping review was to survey the evidence base for the GHB811 cotton and its newly expressed proteins, HPPD W336 and 2mEPSPS, in order to identify any specific issues related to food or feed safety, molecular characterization or environmental safety that might require in-depth examination.

2.2. Review questions

Review questions were formulated to conform to PE(I)CO structure (Population, Exposure (Intervention), Comparators, Outcome) if possible, and to address 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 the GHB811 cotton and its newly expressed proteins HPPD W336 and 2mEPSPS?

Key elements:

Population: Human health; animal health; environmental safety

Exposure: GHB811 cotton, derived food/feed products, newly expressed proteins in GHB811 cotton

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 molecular characterization of the GHB811 cotton and its newly expressed proteins HPPD W336 and 2mEPSPS in cotton?

Key elements:

Population: GHB811 cotton and newly expressed proteins in GHB811 cotton

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
Exposure (Intervention)	The publication addresses the GMO, derived food/feed products, and/or the intended trait(s) (e.g., newly expressed proteins(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

Concepts	Criteria	Comment
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>i.e.</i> , 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

Concepts	Criteria	Comment
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(s), 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>i.e.</i> , 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

Concepts	Criteria	Comment
Reporting format	The publication presents original/primary data, or it is a risk assessment from a relevant key organisation (such as regulatory agencies and risk assessment bodies involved in the risk assessment of GMOs)	This permits the exclusion of publications that do not present original/primary data (e.g., editorials, position papers), and the inclusion of relevant risk assessments performed and reported by relevant key organisations. 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 (1).

2.4. Reference publication

Two studies were used to test and validate the search profiles:

- Schafer, Barry W.; Embrey, Shawna K.; Herman, Rod A. (2016) Rapid simulated gastric fluid digestion of in-seed/grain proteins expressed in genetically engineered crops. *Regulatory Toxicology and Pharmacology* **81**: 106 - 112.
- Gottula, John; Chapman, Kelly; Gao, Yutuan; Gillikin, Nancy; Beale, John; Dharmasri, Cecil; Privalle, Laura. *Molecular biology and physiology*. (2018) Agronomic performance and crop composition of genetically engineered cotton tolerant to HPPD inhibiting herbicides. *Journal of Cotton Science* **22(1)**: 75-85

The first study (Schafer *et al.*, 2016) is not directly relevant to GHB811 cotton but it was selected as reference study because it mentions the 2mEPSPS protein. The second study (Gottula *et al.*, 2018) is directly relevant to GHB811 cotton and it mentions both newly expressed proteins (HPPD W336 and 2mEPSPS), the crop (cotton), and the intended trait (herbicide tolerance). Since these two articles were published before the search period of this literature review, the profile elements were tested without applying the time limit used in the final profile (UP>=20220701 and UP<=20230630).

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 July 13, 2023. Only documents updated between July 1, 2022 and June 30, 2023, were considered in the search. The dates of most recent database updates are provided in [Table 4](#).

3.2. 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).

See [Appendix 1](#) for detailed database descriptions.

3.3. Search strategy

The search profiles were designed to cover event name, trade name, newly expressed proteins and intended traits. Since the 'newly expressed proteins' profile identified too many documents when used on its own, it was combined with a 'plant species' profile. For the same reason the 'intended trait' profile was combined with two additional profiles: a 'general GMO' profile and the 'plant species' profile. The reference publications ([Section 2.4](#)) were identified by the search profile, confirming the validity of the applied search strategy. See Table 2 for a detailed search profile.

Table 2: Search profile for database search

Set	Search string	Concepts
1	GHB811 OR GHB(W)811 OR BCS-GH811-4 OR BCSGH811-4 OR BCS(w)GH811(w)4 OR BCSGH811(w)4 or GH811-4 or GH811(w)4	Event name
2	Axant?	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	Newly expressed proteins

Set	Search string	Concepts
	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?))	
4	(herbicide? or GL!PHOSATE# or GL!FOSATE# OR G360 or g(w)360 or roundup? or round(w)up? or HPPD(w)inhibitor# or diketonitrile# or pyrazolone# or triketone# or isoxaflutol## or IFT) (5a) (resist? or toleran? or protect?)	Intended traits
5	cotton# or gossypium or G(w)hirsutum or G(w)barbadense	Plant species
6	GMO OR GMOs OR LMO OR LMOs OR GM OR GE OR transgen? OR (genetic?(3a) (modif? OR transform? OR manipulatur? OR improv? OR engineer?))	GMO general
6	3 and 5	Newly expressed proteins AND Plant species
7	4 and 5 and 6	Intended traits AND Plant species AND GMO general
8	1 or 2 or 6 or 7	Event name OR Trade name OR (Newly expressed proteins AND Plant species) OR (Intended traits AND Plant species AND GMO general)

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

Relevant controlled terms (Table 3) were not searched separately because they are included in the Basic Index and were captured by the free-text searches.

Table 3: Relevant controlled terms (CT) and index terms (IT) in each database

Database	Event	New proteins	Intended traits	Plant species	GM plants
Agricola	None	None	"HERBICIDE RESISTANCE"	Cotton Gossypium hirsutum Gossypium barbadense	"TRANSGENIC PLANTS"
Biosis	None	None	No terms for herbicide resistance	Cotton	None
CABA	None	None	"HERBICIDE RESISTANCE"	Cotton	"TRANSGENIC PLANTS"
CAS	None	None	"HERBICIDE RESISTANCE"	Cotton Gossypium hirsutum Gossypium barbadense	"GENETICALLY MODIFIED PLANTS"
Medline	None	None	"HERBICIDE RESISTANCE"	None	"PLANTS, GENETICALLY MODIFIED"

The search results were limited to documents updated between July 1, 2022 and June 30, 2023 (UP>=20220701 and UP<=20230630), and to non-patent documents (not P/DT). To ensure that documents with indexing errors where two document types (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 4 summarizes the number of results obtained from each of the databases searched.

See [Appendix 2](#) for a complete search history.

Table 4: Overview of the selected databases and summary of search results from each database

Database	AGRICOLA	BIOSIS	CABA	CA-Plus	Medline
Database Provider	STN International				
Coverage	1970-present	1926-present	1973-present	1907-present	1946-present
Date of search	13 Jul 2023				
Datespan of the search	1 Jul 2022 – 30 Jun 2023				

Database	AGRICOLA	BIOSIS	CABA	CA-Plus	Medline
Latest database update	10 Jul 2023	12 Jul 2023	27 Jun 2023	12 Jul 2023	12 Jul 2023
Number of records retrieved	4	17	25	11	5
Number of records after duplicate removal	4	16	21	7	5
Number of relevant records after rapid assessment	0	0	4	0	0

4. INTERNET and MANUAL SEARCHES

4.1. Internet Searches of food safety, agriculture, and biotechnology-related authority webpages

A search of the web pages of food safety, agriculture, and biotechnology-related authorities was conducted. Search results were manually examined for relevant records that were either published during the time period under consideration (date span of search: July 1, 2022 to June 30, 2023) or refer to relevant records published during this time frame. Relevance of results were determined based on the criteria listed in [Table 1](#) and they were summarized in [Table 5](#). All web pages searched were justified by their recommendation in the EFSA 2019 explanatory note (1). Of the 13 key organisations cited in the EFSA 2019 explanatory note (1), Environment and Climate Change Canada and Intersecretarial Commission on Biosafety of GMOs (CIBIOGEM) were excluded, since they are not involved in the risk assessment of GM plants. The US-EPA website was excluded, since GHB811 cotton does not contain an insect-resistant trait. Therefore, the internet search was limited to 10 key organisations relevant for GHB811 cotton. Search terms consisted of GHB811 or BCS-GH811-4, HPPD W336 or modified-hydroxyphenylpyruvate dioxygenase, and 2mEPSPS or double mutant 5-enolpyruvyl shikimate-3-phosphate synthase enzyme (all searched singly, with no search limits applied).

Table 5: Results of search of food safety, agriculture, and biotechnology-related authority websites

Source Site Name	Website URL	Date of Most Recent Site Update (dd.mm.yyyy)	Date of Search (dd.mm.yyyy)	No. of Relevant Records
US Department of Agriculture (USDA)	https://www.usda.gov/	25.07.2023	25.07.2023	0
US Food and Drug Administration (FDA)	https://www.fda.gov/	25.07.2023	28.07.2023	0

Source Site Name	Website URL	Date of Most Recent Site Update (dd.mm.yyyy)	Date of Search (dd.mm.yyyy)	No. of Relevant Records
Health Canada	https://www.canada.ca/en/health-canada.html	26.06.2023	10.07.2023	0
Canadian Food Inspection Agency (CFIA)	https://www.canada.ca/en/food-inspection-agency.html	26.06.2023	20.07.2023	0
Food Standards Australia New Zealand (FSANZ)	http://www.foodstandards.gov.au/Pages/default.aspx	30.06.2023	10.07.2023	0
Office of the Gene Technology Regulator (OGTR) Australia	http://www.ogtr.gov.au/	06.04.2023	10.07.2023	0
National Technical Commission on Biosafety (CTNBio) Brazil	http://ctnbio.mcti.gov.br/en	24.07.2023	17-24.07.2023	0
National Advisory Commission on Agricultural Biotechnology (CONABIA) Argentina	https://www.argentina.gob.ar/agroindustria/bioeconomia/biotechnologia	17.07.2023	17.07.2023	0
Genetic Engineering Approval Committee (GEAC) India	http://moef.gov.in/	19.07.2023	19.07.2023	0
Ministry of Agriculture, Forestry and Fisheries (MAFF) Japan	http://www.maff.go.jp/	27.07.2023	27.07.2023	0

4.2. Manual searches of reference lists of recent review articles

Recent review articles as sources of reference lists to search for potentially relevant studies were identified via searches of PubMed.gov for general terms such as “GMO” or “GM crops” in the titles and abstracts. The search of PubMed.gov was also restricted to recent reviews published between July 1, 2022 and June 30, 2023. The resulting number of relevant studies found within the bibliographies of these review articles is given in Table 6.

Table 6: Documents for which reference lists were scanned for relevant studies

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
1	Bhattacharjee S, Bhowmick R, Kant L, Paul K. 2023	Strategic transgene-free approaches of CRISPR-based genome editing in plants.	Mol Genet Genomics. 2023 May;298(3):507-520	0
2	Cermakova E, Lencova S, Mukherjee S, Horka P, Vobruba S, Demnerova K, Zdenkova K. 2023	Identification of Fish Species and Targeted Genetic Modifications Based on DNA Analysis: State of the Art.	Foods. 2023 Jan 3;12(1):228.	0
3	Connolly JB, Romeis J, Devos Y, Glandorf DCM, Turner G, Coulibaly MB. 2023	Gene drive in species complexes: defining target organisms.	Trends Biotechnol. 2023 Feb;41(2):154-164.	0
4	Eckerstorfer MF, Dolezel M, Engelhard M, Giovannelli V, Grabowski M, Heissenberger A, Lener M, Reichenbecher W, Simon S, Staiano G, Wüst Saucy AG, Zünd J, Lüthi C. 2023	Recommendations for the Assessment of Potential Environmental Effects of Genome-Editing Applications in Plants in the EU.	Plants (Basel). 2023 Apr 25;12(9):1764.	0
5	Ghidoli M, Ponzoni E, Araniti F, Miglio D, Pilu R. 2023	Genetic Improvement of <i>Camelina sativa</i> (L.) Crantz: Opportunities and Challenges.	Plants (Basel). 2023 Jan 27;12(3):570.	0
6	Krasnodębski C, Sawuła A, Kaźmierczak U, Żuk M. 2023	Oligo-Not Only for Silencing: Overlooked Potential for Multidirectional Action in Plants.	Int J Mol Sci. 2023 Feb 24;24(5):4466.	0
7	Křížkovská B, Viktorová J, Lipov J. 2022	Approved Genetically Modified Potatoes (<i>Solanum tuberosum</i>) for Improved Stress Resistance and Food Safety.	J Agric Food Chem. 2022 Sep 28;70(38):11833-11843.	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
8	Liang J, Yang X, Jiao Y, Wang D, Zhao Q, Sun Y, Li Y, Wu K. 2022	The evolution of China's regulation of agricultural biotechnology.	aBIOTECH. 2022 Dec 5;3(4):237-249.	0
9	Platani M, Sokefun O, Bassil E, Apidianakis Y. 2023	Genetic engineering and genome editing in plants, animals, and humans: Facts and myths. Gene.	2023 Mar 10; 856:147141.	0
10	Pott A, Bundschuh M, Otto M, Schulz R. 2023	Assessing Effects of Genetically Modified Plant Material on the Aquatic Environment Using higher-tier Studies.	Bull Environ Contam Toxicol. 2023 Jan 2;110(1):35.	0
11	Rai GK, Kumar P, Choudhary SM, Kossler R, Khanday DM, Choudhary S, Kumar B, Magotra I, Kumar RR, Ram C, Roupheal Y, Corrado G, Behera TK. 2022	Biomimetic Strategies for Developing Abiotic Stress-Tolerant Tomato Cultivars:	An Overview. Plants (Basel). 2022 Dec 23;12(1):86	0
12	Rozas P, Kessi-Pérez EI, Martínez C. 2022	Genetically modified organisms: adapting regulatory frameworks for evolving genome editing technologies.	Biol Res. 2022 Oct 20;55(1):31.	0
13	Spök A, Sprink T, Allan AC, Yamaguchi T, Dayé C. 2022	Towards social acceptability of genome-edited plants in industrialised countries? Emerging evidence from Europe, United States, Canada, Australia, New Zealand, and Japan.	Front Genome Ed. 2022 Aug 31;4:899331.	0
14	Tatineni S, Hein GL. 2023	Plant Viruses of Agricultural Importance: Current and Future Perspectives of Virus Disease Management Strategies.	Phytopathology. 2023 Feb;113(2):117-141.	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
15	Tripathi S, Purchase D, Chandra R, Nadda AK, Bhargava PC. 2022	Mitigation of hazards and risks of emerging pollutants through innovative treatment techniques of post methanated distillery effluent - A review.	Chemosphere. 2022 Aug;300:134586 . doi: 10.1016/j.chemosphere.2022.134586.	0
16	Wang M, Wang H, Li K, Li X, Wang X, Wang Z. 2023	Review of CRISPR/Cas Systems on Detection of Nucleotide Sequences.	Foods. 2023 Jan 19;12(3):477.	0
17	Zimny T. 2023	Regulation of GMO field trials in the EU and new genomic techniques: will the planned reform facilitate experimenting with gene-edited plants?	BioTechnologia (Pozn). 2023 Mar 27;104(1):75-83.	0

5. RESULTS OF THE STUDY IDENTIFICATION AND SELECTION PROCESS

The database searches ([Section 3](#)) identified a total of 62 references, which were reduced to 53 after duplicate removal ([Table 4](#)). No additional studies were identified in the manual searches ([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 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 discussion was transferred to Stage 2 for detailed evaluation by the experts. In this search, both evaluators were in 100% agreement.

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

- Duplicated entries
- Secondary literature (reviews), other than assessments from regulatory agencies
- Articles on non-relevant topics like detection methods, socio-economic implications of GM crops, GM policy, agronomical performance, other herbicide tolerant GM crops, other insect 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 0](#)).

The number of publications excluded after rapid assessment for relevance is presented in [Table 7](#) documenting the selection process.

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 Biology, 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.

In the relevance assessment of the literature review for the GHB811 cotton, reviewers agreed in 100% of the Stage 2 evaluations.

Table 7 gives an overview of the reference selection process and results of the detailed assessment.

Table 7: Results of the publication selection process

Total number of publications retrieved after all searches of the scientific literature (excluding duplicates)	53
Number of publications excluded from the search results after rapid assessment for relevance (Stage 1)	49
Total number of full-text documents assessed in detail	4
Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2)	3
Total number of unobtainable/unclear publications	0
Total number of relevant publications	1

Table 8 lists the publications determined to be relevant based on the detailed evaluation. Publications that were clearly not relevant after a detailed assessment are listed in Table 9. Table 10 lists the publications for which full-text documents were unobtainable for detailed assessment or for which relevance was unclear after detailed assessment.

Table 8: 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	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. Serrano, J. J. S. Savoini, G. Veromann, E. Veronesi, F. Ardizzone, M. Sanctis, G. de Fernandez, A. Federici, S. Gennaro, A. Ruiz, J. A. G. Lanzoni, A. Neri, F. M. Paraskevopoulos, K. Raffaello, T. de Sanctis, G. 2021	Assessment of genetically modified cotton GHB811 for food and feed uses, under Regulation (EC) No 1829/2003 (application EFSA-GMO -ES-2018-154).	EFSA Journal (2021), Volume 19, Number 8, 44 refs. ISSN: 1831-4732 DOI: https://doi.org/10.2903/j.efsa.2021.6781 Published by: Wiley, Oxford

Table 9: 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
<p>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. Serrano, J. J. S. Savoini, G. Veromann, E. Veronesi, F. Alvarez, F. Ardizzone, M. Raffaello, T.</p> <p>2021</p>	<p>Assessment of genetically modified cotton GHB614 for renewal authorisation under regulation (EC) No 1829/2003 (application EFSA-GMO -RX-018).</p>	<p>EFSA Journal (2021), Volume 19, Number 7, 10 refs. ISSN: 1831-4732 DOI: https://doi.org/10.2903/j.efs.a.2021.6671 Published by: Wiley, Oxford</p>	<p>The GHB811 event is not considered in this publication.</p>
<p>Rodrigues, N. R. Ferreira Souza, A. P. de Moraes, P. P. P. Braga, D. P. V. Crivellari, A. C. Favoretto, L. R. G. Berger, G. U. de Ferreira Souza, A. P.</p> <p>2021</p>	<p>Residues of glyphosate and aminomethyl phosphonic acid (AMPA) in genetically modified glyphosate tolerant soybean, corn and cotton crops.</p>	<p>Ciencia Rural (2021), Volume 51, Number 1, 23 refs. ISSN: 0103-8478; 1678-4596 DOI: https://doi.org/10.1590/0103-8478cr20190244. Published by: Centro de Ciencias Rurais, Universidade Federal de Santa Maria, Santa Maria</p>	<p>The authors monitor glyphosate residues levels and its metabolite AMPA. Soybean and corn grains and cotton seeds were within the Maximum Residue Limits (MRLs) established by ANVISA and Codex Alimentarius. The publication is not related to the safety assessment of GHB811 cotton.</p>

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Sharkey, S. M. Williams, B. J. Parker, K. M. 2021	Herbicide drift from genetically engineered herbicide -tolerant crops.	Environmental Science + Technology (2021), Volume 55, Number 23, pp. 15559-15568, 107 refs. ISSN: 0013-936X; 1520-5851 DOI: https://doi.org/10.1021/acs.est.1c01906 Published by: American Chemical Society, Washington	The authors present concepts surrounding the physiochemical phenomena of herbicide drift from GM HT crops to support the development of effective approaches to reduce it. The publication does not contain original data. The environmental safety assessment is not related to GHB811 cotton.

Table 10: 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/SUMMARY OF RELEVANT STUDIES

A total of four 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 one publication was relevant for the safety assessment of the GHB811 cotton and its newly expressed proteins, HPPD W336 and 2mEPSPS.

The publication identified as relevant, Naegeli *et al.*, 2021, provides a scientific risk assessment performed by the EFSA GMO Panel on data submitted in the context of the GHB811 cotton application for food and feed uses, under Regulation (EC) No 1829/2003. The GMO Panel concluded that the molecular characterisation data and bioinformatic analyses do not identify issues requiring food/feed safety assessment and that GHB811 cotton is as safe as its conventional counterpart and the tested non-GM cotton reference varieties with respect to potential effects on human and animal health and the environment.

Table 11 lists the relevant publication along with a summary of any reported adverse effects.

Table 11: Summary report for all relevant publications retrieved after detailed assessment of full-text documents for relevance and implications for the risk assessment: 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	Implications for risk assessment
Food and Feed Safety	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. Serrano, J. J. S. Savoini, G. Veromann, E. Veronesi, F. Ardizzone, M. Sanctis, G. de Fernandez, A. Federici, S. Gennaro, A. Ruiz, J. A. G. Lanzoni, A. Neri, F. M. Paraskevopoulos, K. Raffaello, T. de Sanctis, G. 2021	GHB811	None	Not applicable	None, GHB811 cotton is as safe as its conventional counterpart

7. CONCLUSION

The literature searches performed for the GHB811 cotton and its newly expressed proteins, HPPD W336 and 2mEPSPS, for the period from July 1, 2022 to June 30, 2023, identified a total of 53 unique publications (after duplicate removal). A total of four publications were progressed for detailed assessment after excluding 49 obviously irrelevant publications during Stage 1 evaluation (rapid assessment based on title and abstract). The four publications that progressed to Stage 2 were evaluated in detail, based on full text, for potential relevance, following the pre-established criteria listed in [Table 1](#).

One relevant publication(s) with bearing on molecular characterization and food and feed safety was identified. The data and knowledge generated from this study does not impact the safety assessment of GHB811 cotton. No issues or topics were identified that would trigger or warrant 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: Database descriptions

Host	File	Description
STN	AGRICOLA	<p>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.</p> <p>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.</p>
STN	BIOSIS	<p>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.</p> <p>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.</p> <p>Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are all searchable.</p>
STN	CABA/CAB	<p>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.</p> <p>Sources for CABA include journals, books, reports, published theses, conference proceedings, and patents.</p> <p>Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are searchable.</p>
STN	CAS/CAPLUS	<p>The Chemical Abstracts (CA) database covers all areas of Biochemistry, Chemistry and Chemical engineering, and related sciences.</p> <p>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.</p> <p>Bibliographic terms, indexing terms, roles, CAS Registry Numbers, International Patent Classification, and abstracts are searchable.</p>

Host	File	Description
STN	MEDLINE	<p>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.</p> <p>Sources include journals and chapters in books or symposia. Bibliographic information, indexing terms, abstracts, chemical names, and CAS Registry Numbers are all searchable.</p> <p>Online thesauri are available for the Medical Subject Headings (/MN), Controlled Terms (/CT) and Chemical Name (/CN) fields.</p>

Appendix 2: Search history

```
FILE 'MEDLINE' ENTERED AT 07:16:47 ON 13 JUL 2023
L1      1 SEA GHB811 OR GHB(W)811 OR BCS-GH811-4 OR BCSGH811-4 OR
        BCS(W)GH811(W)4 OR BCSGH811(W)4 OR GH811-4 OR GH811(W)4
L2      69 SEA AXANT?
L3      14 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L4      4349 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      421 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
        ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W)SHIKIMATE
        ) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)
L7      514 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
        IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (
        3W) PHOSPHOSYNTHASE)
L8      25882 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L9      21 SEA L3 OR ((L4 OR L5 OR L6 OR L7)) (S)L8)
L10     5 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L11     47 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     48 SEA (L10 OR L11)
L13     66 SEA L9 OR L12
L14     4052 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360
        OR ROUNDUP? OR ROUND(W)UP? OR HPPD(W)INHIBITOR# OR DIKETONITRIL
        E# OR PYRAZOLONE# OR TRIKETONE# OR ISOXAFLUTOL## OR IFT) (5A) (RE
        SIST? OR TOLERAN? OR PROTECT?)
L15     30476 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L16     4178353 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     5 SEA L13 AND L15
L18     134 SEA L14 AND L15 AND L16
L19     206 SEA L1 OR L2 OR L17 OR L18
L20     16 SEA L19 AND PY>=2021
L21     5 SEA L20 AND UP>=20220701 AND UP<=20230630

FILE 'BIOSIS' ENTERED AT 07:16:54 ON 13 JUL 2023
L22     0 SEA GHB811 OR GHB(W)811 OR BCS-GH811-4 OR BCSGH811-4 OR
        BCS(W)GH811(W)4 OR BCSGH811(W)4 OR GH811-4 OR GH811(W)4
L23     164 SEA AXANT?
L24     12 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L25     5178 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)
L26     0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKI
        MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S
        YNTHASE OR SYNTHETASE)
L27     761 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
        ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W)SHIKIMATE
        ) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)
L28     29 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
        IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (
        3W) PHOSPHOSYNTHASE)
L29     28113 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L30     21 SEA L24 OR ((L25 OR L26 OR L27 OR L28)) (S)L29)
```

L31 3 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L32 69 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?)
L33 69 SEA (L31 OR L32)
L34 89 SEA L30 OR L33
L35 11905 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360
OR ROUNDUP? OR ROUND(W)UP? OR HPPD(W)INHIBITOR# OR DIKETONITRIL
E# OR PYRAZOLONE# OR TRIKETONE# OR ISOXAFLUTOL## OR IFT) (5A) (RE
SIST? OR TOLERAN? OR PROTECT?)
L36 79416 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L37 495499 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?))
L38 3 SEA L34 AND L36
L39 308 SEA L35 AND L36 AND L37
L40 474 SEA L22 OR L23 OR L38 OR L39
L41 30 SEA L40 AND PY>=2021
L42 17 SEA L41 AND UP>=20220701 AND UP<=20230630

FILE 'AGRICOLA' ENTERED AT 07:17:01 ON 13 JUL 2023

L43 0 SEA GHB811 OR GHB(W)811 OR BCS-GH811-4 OR BCSGH811-4 OR
BCS(W)GH811(W)4 OR BCSGH811(W)4 OR GH811-4 OR GH811(W)4
L44 15 SEA AXANT?
L45 4 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L46 741 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)
L47 0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKI
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S
YNTHASE OR SYNTHETASE)
L48 337 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W)SHIKIMATE
) (3W)PHOSPHATE(W) (SYNTHASE OR SYNTHETASE)
L49 271 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
3W)PHOSPHOSYNTHASE)
L50 7060 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L51 10 SEA L45 OR ((L46 OR L47 OR L48 OR L49)) (S) L50
L52 1 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L53 45 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?)
L54 45 SEA (L52 OR L53)
L55 55 SEA L51 OR L54
L56 9430 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360
OR ROUNDUP? OR ROUND(W)UP? OR HPPD(W)INHIBITOR# OR DIKETONITRIL
E# OR PYRAZOLONE# OR TRIKETONE# OR ISOXAFLUTOL## OR IFT) (5A) (RE
SIST? OR TOLERAN? OR PROTECT?)
L57 68097 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L58 113690 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?))
L59 2 SEA L55 AND L57
L60 250 SEA L56 AND L57 AND L58
L61 266 SEA L43 OR L44 OR L59 OR L60
L62 12 SEA L61 AND PY>=2021
L63 4 SEA L62 AND UP>=20220701 AND UP<=20230630

FILE 'CABA' ENTERED AT 07:17:08 ON 13 JUL 2023

L64 1 SEA GHB811 OR GHB(W)811 OR BCS-GH811-4 OR BCSGH811-4 OR
BCS(W)GH811(W)4 OR BCSGH811(W)4 OR GH811-4 OR GH811(W)4

L65 70 SEA AXANT?

L66 14 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS

L67 1268 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) (4
W) (PHOSPHATE OR PHOSPHORIC) (2W) (SYNTHASE OR SYNTHETASE)

L68 0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKI
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S
YNTHASE OR SYNTHETASE)

L69 477 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE
) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)

L70 202 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (3
W) PHOSPHOSYNTHASE)

L71 7766 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)

L72 24 SEA L66 OR ((L67 OR L68 OR L69 OR L70)) (S) L71)

L73 4 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336

L74 75 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?)

L75 75 SEA (L73 OR L74)

L76 96 SEA L72 OR L75

L77 20582 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360
OR ROUNDUP? OR ROUND(W)UP? OR HPPD(W)INHIBITOR# OR DIKETONITRIL
E# OR PYRAZOLONE# OR TRIKETONE# OR ISOXAFLUTOL## OR IFT) (5A) (RE
SIST? OR TOLERAN? OR PROTECT?)

L78 112536 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE

L79 204631 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?))

L80 8 SEA L76 AND L78

L81 561 SEA L77 AND L78 AND L79

L82 635 SEA L64 OR L65 OR L80 OR L81

L83 635 SEA L82 NOT P/DT

L84 0 SEA L82 AND (P/DT AND J/DT)

L85 635 SEA L83 OR L84

L86 37 SEA L85 AND PY>=2021

L87 25 SEA L86 AND UP>=20220701 AND UP<=20230630

FILE 'HCAPLUS' ENTERED AT 07:17:20 ON 13 JUL 2023

L88 0 SEA GHB811 OR GHB(W)811 OR BCS-GH811-4 OR BCSGH811-4 OR
BCS(W)GH811(W)4 OR BCSGH811(W)4 OR GH811-4 OR GH811(W)4

L89 69 SEA AXANT?

L90 31 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS

L91 4631 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) (4
W) (PHOSPHATE OR PHOSPHORIC) (2W) (SYNTHASE OR SYNTHETASE)

L92 9 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKI
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S
YNTHASE OR SYNTHETASE)

L93 1133 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE
) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)

L94 90 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (3
W) PHOSPHOSYNTHASE)

L95 77228 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)

L96 46 SEA L90 OR ((L91 OR L92 OR L93 OR L94)) (S) L95)

L97 4 SEA HPPDW336 OR HPPD(W)W336 OR HPPD(W)W(W)336 OR HPPDW(W)336
L98 232 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?)
L99 232 SEA (L97 OR L98)
L100 275 SEA L96 OR L99
L101 32318 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360
OR ROUNDUP? OR ROUND(W)UP? OR HPPD(W)INHIBITOR# OR DIKETONITRIL
E# OR PYRAZOLONE# OR TRIKETONE# OR ISOXAFLUTOL## OR IFT) (5A) (RE
SIST? OR TOLERAN? OR PROTECT?)
L102 293538 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L103 747559 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?))
L104 48 SEA L100 AND L102
L105 1487 SEA L101 AND L102 AND L103
L106 1566 SEA L88 OR L89 OR L104 OR L105
L107 361 SEA L106 NOT P/DT
L108 0 SEA L106 AND (P/DT AND J/DT)
L109 361 SEA L107 OR L108
L110 32 SEA L109 AND PY>=2021
L111 11 SEA L110 AND UP>=20220701 AND UP<=20230630

FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 01:17:30 ON 13
JUL 2023

L112 53 DUP REM L21 L42 L63 L87 L111 (9 DUPLICATES REMOVED)
ANSWERS '1-5' FROM FILE MEDLINE
ANSWERS '6-21' FROM FILE BIOSIS
ANSWERS '22-25' FROM FILE AGRICOLA
ANSWERS '26-46' FROM FILE CABA
ANSWERS '47-53' FROM FILE HCAPLUS