

Title

**Summary of the Literature Review for GHB614 cotton  
October 1, 2020 – September 30, 2021**

**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.  
EFSA supporting publications 2019:EN-1614

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November 9, 2021

Principal author

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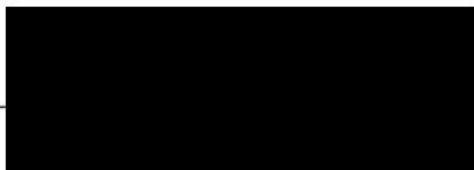
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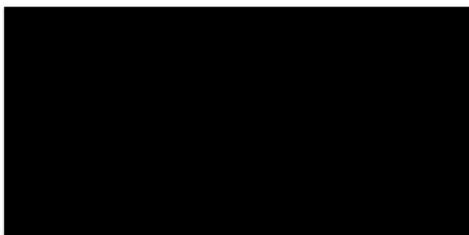
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**SIGNATURE PAGE**

Principal author:



Date

2021-11-09

**STUDY PERSONNEL**

<b>Electronic database search</b>	[REDACTED]
<b>Agency website search</b>	Global Regulatory Manager
<b>Manual search (reference list from review articles)</b>	[REDACTED]
<b>Stage 1 assessment</b>	[REDACTED] [REDACTED]
<b>Stage 2 assessment</b>	<u>Food and Feed safety</u> [REDACTED] [REDACTED] <u>Molecular characterization</u> [REDACTED] [REDACTED] <u>Environmental safety</u> [REDACTED] [REDACTED]
<b>Report</b>	[REDACTED] [REDACTED] [REDACTED]

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## SUMMARY

The GHB614 cotton event was developed through *Agrobacterium*-mediated transformation using the vector pTEM2 containing the *2mepsps* gene. GHB614 produces the *Zea mays* L. 5-enolpyruvylshikimate 3-phosphate synthase (2mEPSPS) protein which confers tolerance to glyphosate herbicides. The OECD identifier is BCS-GHØØ2-5.

A scoping review was performed for the GHB614 cotton and its newly expressed protein, 2mEPSPS. The objective of this scoping review was to determine if there were studies about the molecular characterization of GHB614 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 October 1, 2020 to September 30, 2021. 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 64 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. A total of 10 publications were progressed for detailed assessment.

One of the 10 publications was determined to be relevant after detailed review. The relevant article did not constitute new data on molecular characterization of GHB614 cotton or the 2mEPSPS protein, 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. No issues or topics were identified that would trigger or warrant more specific question formulation.

In summary, these literature searches and review of the retrieved publications identified one relevant publication that supports the existing safety assessment of GHB614 cotton.

## 1. INTRODUCTION

The GHB614 cotton event was developed through *Agrobacterium*-mediated transformation using the vector pTEM2 containing the *2mepsps* gene. GHB614 produces the *Zea mays* L. 5-enolpyruvylshikimate 3-phosphate synthase (2mEPSPS) protein which confers tolerance to glyphosate herbicides. The OECD identifier is BCS-GHØØ2-5.

The objective of the literature searches described here was to determine if there were studies published between October 1, 2020 and September 30, 2021 that mention the molecular characterization of the GHB614 cotton, and/or any adverse effect of GHB614 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)<sup>1</sup> applications and post-market environmental monitoring activities (2019).

The literature searches were performed for the GHB614 cotton and its newly expressed protein, 2mEPSPS. The search terms also included relevant synonyms, trade name and 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 the GHB614 cotton and its newly expressed protein, 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<sup>1</sup>.

**Question 1:** Were any studies published during the reporting period that describe adverse effects on human or animal health or the environment of the GHB614 cotton and its newly expressed protein 2mEPSPS?

**Key elements:**

**Population:** Human health; animal health; environmental safety

**Exposure (Intervention):** GHB614 cotton, derived food/feed products, newly expressed protein in GHB614 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 GHB614 cotton and its newly expressed protein 2mEPSPS in cotton?

**Key elements:**

Population: GHB614 cotton and newly expressed protein in GHB614 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<sup>1</sup> 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
Additional concepts		

Concepts	Criteria	Comment
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

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.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

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.

#### 2.4. Reference publication

Two previously identified publications related to GHB614 cotton were used to test and validate the search strategy:

- Wu A-J; Chapman K; Sathischandra S; Massengill J; Araujo R; Soria M; Bugas M; Bishop Z; Haas C; Holliday B; Cisneros K; Lor J; Canez C; New S; Mackie S; Ghoshal D; Privalle L; Hunst P; Pallett K (2019). GHB614 x T304-40 x GHB119 x COT102 Cotton: Protein Expression Analyses of Field-Grown Samples. *Journal of Agricultural and Food Chemistry* 67:275-281
- Naegeli H; Birch AN; Casacuberta J; De Schrijver A; Galak MA; Guerche P; Jones H; Manachini B; Messean A; Nielsen EE; Nogue F; Robaglia C; Rostoks N; Sweet J; Tebbe C; Visioli F; Wal J-M; Broll H; Gennaro A; Neri Franco M; Paraskevopoulos K (2018). Assessment of genetically modified cotton GHB614 x LLCotton25 x MON 15985 for food and feed uses, under Regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2011-94). *EFSA Journal* 16(4):e05213

These two publications are not directly relevant to the GHB614 event. Nevertheless they were selected as reference publications because they include in the searchable fields the event name (GHB614), newly expressed protein (2mEPSPS), intended trait (herbicide tolerance) and/or target crop (cotton). Since these documents were published before the search period described in this report, the profile elements were tested without applying the time limit used in the final profile (UP>=20201001 and UP<=20210930).

### 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<sup>1</sup>.

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 October 8, 2021. Only documents updated between October 1, 2020 and September 30, 2021, were considered in the search. The dates of most recent database updates are provided in [Table 3](#).

### 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 profile was designed to cover event name, trade name, newly expressed protein, and intended trait. Since the 'newly expressed protein' profile and the 'intended trait' profile produced too many results when used on their own, they were combined with additional profiles: the 'newly expressed proteins' profiles were combined with a 'plant species' profile while the 'intended trait' profiles were combined with a 'general GMO' profile as well as with 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	GHB614 OR GHB(W)614 OR BCS-GH002-5 OR BCSGH002-5 OR BCS(W)GH002(W)5 OR BCSGH002(W)5 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR BCSGH002(W)5 or BCS-GH002-5 or BCS(w)GH002(w)5 or BCSGH002-5	Event name
2	GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(w)TOL OR GLY(w)TOLTM OR GLY(w)TOLRTM	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	Newly expressed protein

	SYNTHETASE) or (ENOL(W)PYRUVOYL SHIKIMATE OR ENOLPYRUVYL SHIKIMATE OR ENOLPYRUVYL SHIKIMIC 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))	
4	(herbicid? 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	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 manipulat? OR improv? OR engineer?))	GMO general
7	4 or 5 or 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 protein OR (Intended trait 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"	"GOSSYPIUM BARBADENSE" "GOSSYPIUM HIRSUTUM"	"TRANSGENIC PLANTS"
Biosis	None	None	No terms for herbicide resistance	"GOSSYPIUM BARBADENSE" "GOSSYPIUM HIRSUTUM"	None
CABA	None	None	"HERBICIDE RESISTANCE"	"GOSSYPIUM BARBADENSE"/CT "GOSSYPIUM HIRSUTUM"/CT	"TRANSGENIC PLANTS"
CAS	None	None	"HERBICIDE RESISTANCE"	GOSSYPIUM/CT	"GENETICALLY MODIFIED PLANTS"
Medline	None	None	"HERBICIDE RESISTANCE"	"GOSSYPIUM BARBADENSE" "GOSSYPIUM HIRSUTUM"	"PLANTS, GENETICALLY MODIFIED"

The search results were limited to documents updated between October 1, 2020 and September 30, 2021 (UP>=20201001 and UP<=20210930), 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	CAB Abstracts	CAPLUS	MEDLINE
Database Provider	STN International				
Coverage	1970-present	1926-present	1973-present	1907-present	1946-present
Date of search	8 Oct 2021				

Database	AGRICOLA	BIOSIS	CAB Abstracts	CAPLUS	MEDLINE
Datespan of the search	1 Oct 2020 – 30 Sept 2021				
Latest database update	14 Sept 2021	6 Oct 2021	5 Oct 2021	6 Oct 2021	7 Oct 2021
Number of records retrieved	8	18	29	14	8
Number of records after duplicate removal	8	15	24	9	8
Number of relevant records after rapid assessment	0	1	4	4	1

#### 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: October 1, 2020 to September 30, 2021) 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<sup>1</sup>. Of the 13 key organisations cited in the EFSA 2019 explanatory note<sup>1</sup>, 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 the GHB614 cotton does not contain an insect-resistant trait. Therefore, the internet search was limited to 10 key organisations relevant for GHB614 cotton. Search terms consisted of GHB614 cotton, BCS-GHØØ2-5, or 2mEPSPS protein (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	Date of Search	No. of Relevant Records
US Department of Agriculture (USDA)	<a href="https://www.usda.gov/">https://www.usda.gov/</a>	Oct 22, 2021	Oct 22, 2021	0
US Food and Drug Administration (FDA)	<a href="https://www.fda.gov/">https://www.fda.gov/</a>	Oct 22, 2021	Oct 22, 2021	0

Source Site Name	Website URL	Date of Most Recent Site Update	Date of Search	No. of Relevant Records
Health Canada	<a href="https://www.canada.ca/en/health-canada.html">https://www.canada.ca/en/health-canada.html</a>	Sep 2021	Oct 21, 2021	0
Canadian Food Inspection Agency (CFIA)	<a href="https://www.canada.ca/en/food-inspection-agency.html">https://www.canada.ca/en/food-inspection-agency.html</a>	Sep 2021	Oct 21, 2021	0
Food Standards Australia New Zealand (FSANZ)	<a href="http://www.foodstandards.gov.au/Pages/default.aspx">http://www.foodstandards.gov.au/Pages/default.aspx</a>	Oct 10, 2021	Oct 10, 2021	0
Office of the Gene Technology Regulator (OGTR) Australia	<a href="http://www.ogtr.gov.au/">http://www.ogtr.gov.au/</a>	Oct 10, 2021	Oct 10, 2021	0
National Technical Commission on Biosafety (CTNBio) Brazil	<a href="http://ctnbio.mcti.gov.br/en">http://ctnbio.mcti.gov.br/en</a>	Oct 2021	Oct 13-15, 2021	0
National Advisory Commission on Agricultural Biotechnology (CONABIA) Argentina	<a href="https://www.argentina.gob.ar/agroindustria/bioeconomia/biotechnologia">https://www.argentina.gob.ar/agroindustria/bioeconomia/biotechnologia</a>	Oct 1, 2021	Oct 15-28 2021	0
Genetic Engineering Approval Committee (GEAC) India	<a href="http://moef.gov.in/">http://moef.gov.in/</a>	Oct 2021	Oct 14, 2021	0
Ministry of Agriculture, Forestry and Fisheries (MAFF) Japan	<a href="http://www.maff.go.jp/">http://www.maff.go.jp/</a>	Oct 14, 2021	Oct 14, 2021	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 October 1, 2020 and September 30, 2021. 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	Golnar AJ, Ruell E, Lloyd AL, Pepin KM. 2021	Embracing Dynamic Models for Gene Drive Management.	Trends Biotechnol. 2021 Mar;39(3):211-214. doi: 10.1016/j.tibtech.2020.08.011. Epub 2020 Sep 30. PMID: 33010965.	0
2	Gupta S, Kumar A, Patel R, Kumar V. 2021	Genetically modified crop regulations: scope and opportunity using the CRISPR-Cas9 genome editing approach.	Mol Biol Rep. 2021 May;48(5):4851-4863. doi: 10.1007/s11033-021-06477-9. Epub 2021 Jun 10. PMID: 34114124.	0
3	Hadrup N, Frederiksen M, Wedebye EB, Nikolov NG, Carøe TK, Sørlø JB, Frydendall KB, Liguori B, Sejbaek CS, Wolkoff P, Flachs EM, Schlünssen V, Meyer HW, Clausen PA, Hougaard KS. 2021	Asthma-inducing potential of 28 substances in spray cleaning products-Assessed by quantitative structure activity relationship (QSAR) testing and literature review.	J Appl Toxicol. 2021 Jul 11. doi:10.1002/jat.4215. Epub ahead of print. PMID: 34247391.	0
4	Kumar V, Guleria P. 2020	Application of DNA-Nanosensor for Environmental Monitoring: Recent Advances and Perspectives.	Curr Pollut Rep. 2020 Dec 12:1-21. doi: 10.1007/s40726-020-00165-1. Epub ahead of print. PMID: 33344145; PMCID: PMC7732738.	0
5	Hameed A, Mehmood MA, Shahid M, Fatma S, Khan A, Ali S. 2020	Prospects for potato genome editing to engineer resistance against viruses and cold-induced sweetening.	GM Crops Food. 2020 Oct 1;11(4):185-205. doi: 10.1080/21645698.2019.1631115. Epub 2019 Jul 6. PMID: 31280681; PMCID: PMC7518746.	0
6	Leska A, Nowak A, Nowak I, Górczyńska A. 2021	Effects of Insecticides and Microbiological Contaminants on <i>Apis mellifera</i> .	Health. Molecules. 2021 Aug 22;26(16):5080. doi: 10.3390/molecules26165080. PMID: 34443668; PMCID: PMC8398688	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
7	Madzak C. 2021	<i>Yarrowia lipolytica</i> Strains and Their Biotechnological Applications: How Natural Biodiversity and Metabolic Engineering Could Contribute to Cell Factories Improvement.	J Fungi (Basel). 2021 Jul 10;7(7):548. doi: 10.3390/jof7070548. PMID: 34356927; PMCID: PMC8307478.	0
8	Menz J, Modrzejewski D, Hartung F, Wilhelm R, Sprink T. 2020	Genome Edited Crops Touch the Market: A View on the Global Development and Regulatory Environment.	Front Plant Sci. 2020 Oct 9;11:586027. doi: 10.3389/fpls.2020.586027. PMID:33163013; PMCID: PMC7581933.	0
9	Mushtaq M, Ahmad Dar A, Skalicky M, Tyagi A, Bhagat N, Basu U, Bhat BA, Zaid A, Ali S, Dar TU, Rai GK, Wani SH, Habib-Ur-Rahman M, Hejnak V, Vachova P, Brestic M, Çığ A, Çığ F, Erman M, El Sabagh A. 2021	CRISPR-Based Genome Editing Tools: Insights into Technological Breakthroughs and Future Challenges.	Genes (Basel). 2021 May 24;12(6):797. doi: 10.3390/genes12060797. PMID: 34073848; PMCID: PMC8225059.	0
10	Okoli AS, Blix T, Myhr AI, Xu W, Xu X. 2021	Sustainable use of CRISPR/Cas in fish aquaculture: the biosafety perspective.	Transgenic Res. 2021 Jul 25. doi:10.1007/s11248-021-00274-7. Epub ahead of print. PMID: 34304349.	0
11	Teferra TF. 2021	Should we still worry about the safety of GMO foods? Why and why not? A review.	Food Sci Nutr. 2021 Jul 27;9(9):5324-5331. doi: 10.1002/fsn3.2499. PMID: 34532037; PMCID: PMC8441473.	0
12	Turnbull C, Lillemo M, Hvoslef-Eide TAK. 2021	Global Regulation of Genetically Modified Crops Amid the Gene Edited Crop Boom - A Review.	Front Plant Sci. 2021 Feb 24;12:630396. doi: 10.3389/fpls.2021.630396. PMID: 33719302; PMCID: PMC7943453	0
13	Woźniak E, Tyczewska A, Twardowski T.	A Shift Towards Biotechnology: Social Opinion in the EU.	Trends Biotechnol. 2021 Mar;39(3):214-218. doi: 10.1016/j.tibtech.2020.08.0	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
	2021		01. Epub 2020 Sep 4. PMID: 32896439.	
14	Zhang Y, Restall J, Crisp P, Godwin I, Liu G. 2021	Current status and prospects of plant genome editing in Australia.	In Vitro Cell Dev Biol Plant. 2021 May 24:1-10. doi: 10.1007/s11627-021-10188-y. Epub ahead of print. PMID: 34054265; PMCID: PMC8143062.	0

## 5. RESULTS OF THE STUDY IDENTIFICATION AND SELECTION PROCESS

The database searches ([Section 3](#)) identified a total of 77 references, which were reduced to 64 after removal of duplicates ([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 the 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 resistant 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 5.2](#)).

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 GHB614 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)	64
Number of publications excluded from the search results after rapid assessment for relevance (Stage 1)	54
Total number of full-text documents assessed in detail	10
Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2)	9
Total number of unobtainable/unclear publications	0
Total number of relevant publications	1

[Table 8](#) lists the publications determined to be relevant along with their potential impact on the safety assessment based on 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. Alvarez, F. Ardizzone, M. Raffaello, T. 2021	Assessment of genetically modified cotton GHB614 for renewal authorisation under regulation (EC) No 1829/2003 (application EFSA-GMO -RX-018).	EFSA Journal (2021), Volume 19, Number 7, 10 refs. ISSN: 1831-4732 DOI: <a href="https://doi.org/10.2903/j.efsa.2021.6671">https://doi.org/10.2903/j.efsa.2021.6671</a> 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 <a href="#">Table 1</a>
Eum, Soon-Jae. Kim, Il Ryong Lim, Hye Song. Lee, Jung Ro Choi, Wonkyun. 2019	Event-specific multiplex PCR method for four genetically modified cotton varieties, and its application	Applied Biological Chemistry (2019 ), 62(1), 1-7 CODEN: ABCPCW; ISSN: 2468-0842	The authors aimed to develop a method to simultaneously detect four GM cotton varieties (COT102, T304-40, MON88701, and DAS-81910-7) in order to establish a screening system for cotton volunteers in South Korea. To validate the developed method, they applied the limit of detection, randomly mixed reference materials (RMs), and living modified organism (LMO) monitoring sample analysis.  The GHB614 cotton was not included in the study. The study is not related to the ERA of GHB614 cotton.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in <a href="#">Table 1</a>
Fast Brandon J. Shan Guomin Herman Rod A. Gampala Satyalinga Srinivas. 2019	Transgene expression in sprayed and non-sprayed herbicide - tolerant genetically engineered crops is equivalent.	Regulatory toxicology and pharmacology : RTP, (2020 Mar) Vol. 111, pp. 104572. Electronic Publication Date: 26 Dec 2019 Journal code: 8214983. E-ISSN: 1096-0295. L-ISSN: 0273-2300.	The GHB614 cotton event was not included in this study.
Hernandez-Teran, Alejandra Wegier, Ana Benitez, Mariana Lira, Rafael Sosa Fuentes, Tania Gabriela Escalante, Ana E. 2019	In vitro performance in cotton plants with different genetic backgrounds: the case of <i>Gossypium hirsutum</i> in Mexico, and its implications for germplasm conservation.	PeerJ, (JUN 10 2019 ) Vol. 7, pp. Article No.: e7017. <a href="https://peerj.com/">https://peerj.com/</a> . ISSN: 2167-8359. E-ISSN: 2167-8359.	The authors evaluated and compared <i>in vitro</i> performance of wild and domesticated cotton populations in Mexico and its relationship with transgenes (Cry1Ab/Ac, Cry2Ab and CP4EPSPS).  The study is not related to the ERA of GHB614 cotton.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in <a href="#">Table 1</a>
<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. 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</p>	<p>Assessment of genetically modified cotton GHB811 for food and feed uses, under Regulation (EC) No 1829/2003 (application EFSA-GMO -ES-2018-154).</p>	<p>EFSA Journal (2021), Volume 19, Number 8, 44 refs. ISSN: 1831-4732 DOI: <a href="https://doi.org/10.2903/j.efs.a.2021.6781">https://doi.org/10.2903/j.efs.a.2021.6781</a> Published by: Wiley, Oxford</p>	<p>The GMO Panel concluded that GHB811 cotton is as safe as its conventional counterpart and the tested non-GM cotton.</p> <p>The GHB614 cotton event is not considered in this publication.</p>
<p>Pan, Xiaoping 2019</p>	<p>Determining pollen-mediated gene flow in transgenic cotton</p>	<p>Methods in Molecular Biology (New York, NY, United States) (2019 ), 1902(Transgenic Cotton), 309-321 CODEN: MMBIED; ISSN: 1940-6029</p>	<p>The authors used transgenic IR and HT cotton as two examples to present a field practice method for determining transgene flow in cotton.</p> <p>The study does not present primary data and it is not related to the ERA of GHB614 cotton.</p>

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in <a href="#">Table 1</a>
Rodrigues, N. R. Ferreira Souza, A. P. de Morais, P. P. P. Braga, D. P. V. Crivellari, A. C. Favoretto, L. R. G. Berger, G. U. de Ferreira Souza, A. P. 2021	Residues of glyphosate and aminomethyl phosphonic acid (AMPA) in genetically modified soybean, corn and cotton crops.	Ciencia Rural (2021), Volume 51, Number 1, 23 refs. ISSN: 0103-8478 DOI: 10.1590/0103-8478cr20190244. Published by: Centro de Ciencias Rurais, Universidade Federal de Santa Maria, Santa Maria	The aim of the paper is to monitor glyphosate and its metabolite (AMPA) residues in crops and compare with ANVISA MRLs and Codex. Pesticide residues were analysed in FG72 soybean.  The GHB614 cotton event was not included in this study.
Singh, M. Randhawa, G. Singh, S. Kak, A. Sangwan, O. 2020	Monitoring adventitious presence of transgenes in cotton collections from Genebank and experimental plots: ensuring GM -free conservation and cultivation of genetic resources.	Agricultural Research (2020), Volume 9, Number 4, pp. 469-476, 25 refs. ISSN: 2249-720X DOI: 10.1007/s40003-019-00449-z Published by: Springer (India) Private Limited, New Delhi	The authors used PCR for checking adventitious presence of transgenes in a set of 100 accessions of <i>ex situ</i> cotton collection being conserved in the National Genebank of India. Adventitious presence of transgenes was also monitored in 50 samples collected from experimental plots, growing adjacent to Bt cotton, using molecular markers for specific GM cotton (MON15985).  The study is not related to the ERA of GHB614 cotton.
Torres, Amada Reyes-Perez, Juan Jose Marquez-Hernandez, Cando Estrada-Arellano, Josue Esparza-Rivera, Juan Ramon Preciado-Rangel, Pablo Murillo-Amador, Bernardo. 2019	Potential transference of CP4 5-enolpiruvil shikimato-3-phosphate synthase to weed species from genetically modified <i>Gossypium hirsutum</i> in Northern Mexico	Notulae Botanicae Horti Agrobotanici Cluj-Napoca (2019 ), 47(2), 294-299 CODEN: NBHABI; ISSN: 0255-965X URL: <a href="http://www.notulaebotanicae.ro/index.php/nbha/index">http://www.notulaebotanicae.ro/index.php/nbha/index</a>	The objective of the study was to quantify and identify weed species associated to genetically modified cotton (Bollgard II) fields and to detect the presence of glyphosate-insensitive EPSP synthases (CP4 EPSPS) in these species.  The study is not related to the ERA of GHB614 cotton.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in <a href="#">Table 1</a>
Verkest, Aurine Bourout, Stephane Debaveye, Jurgen Reynaert, Kristine Saey, Bernadette den Brande, Ilse Van D'Halluin, Kathleen. 2019	Impact of differential DNA methylation on transgene expression in cotton ( <i>Gossypium hirsutum</i> L.) events generated by targeted sequence insertion	Plant Biotechnology Journal (2019 ), 17(7), 1236-1247 CODEN: PBJLAE; ISSN: 1467-7652	The study was about transgene expression in the Targeted Sequence Insertion events generated by targeted genome optimization technology.  The study was not related to safety assessment of GHB614 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 10 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 GHB614 cotton and its newly expressed protein 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 renewal application for the GHB614 cotton. The GMO Panel concluded that there is no evidence in the renewal application for new hazards, modified exposure, or scientific uncertainties that would change the conclusions of the original risk assessment on GHB614 cotton.

[Table 11](#) lists the relevant publication along with a summary of any adverse effects reported and the reliability of the publications.

**Table 11: Summary report for all relevant publications retrieved after detailed assessment of full-text documents for relevance and report of the reliability 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	Summary of reliability appraisal	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. Alvarez, F. Ardizzone, M. Raffaello, T. 2021	GHB614	None	Not applicable	High	None, because no new hazards, modified exposure, or scientific uncertainties are reported.

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## 7. CONCLUSION

The literature searches performed for the GHB614 cotton and its newly expressed protein, 2mEPSPS, for the period from October 1, 2020 to September 30, 2021, identified a total of 64 unique publications (after duplicate removal). A total of 10 publications were progressed for detailed assessment after excluding 54 obviously irrelevant publications during Stage 1 evaluation (rapid assessment based on title and abstract).

The 10 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 reference with bearing on food and feed safety was identified. The data and knowledge generated from this study does not impact the safety assessment of GHB614 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
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- |    |   |
|----|---|
| 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-CA/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>

<b>Host</b>	<b>File</b>	<b>Description</b>
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 10:49:31 ON 08 OCT 2021

L1 4 SEA GHB614 OR GHB(W)614 OR BCS-GH002-5 OR BCSGH002-5 OR  
BCS(W)GH002(W)5 OR BCSGH002(W)5 OR BCS-GH002-5 OR BCS(W)GH002(W)  
)5 OR BCSGH002(W)5

L2 0 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM  
OR GLY(W)TOLRTM

L3 14 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS

L4 4216 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 382 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR  
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W)SHIKIMATE  
) (3W)PHOSPHATE(W) (SYNTHASE OR SYNTHETASE)

L7 481 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK  
IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(  
3W)PHOSPHOSYNTHASE)

L8 24411 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)

L9 20 SEA L3 OR ((L4 OR L5 OR L6 OR L7)) (S)L8)

L10 3521 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360  
OR ROUNDUP? OR ROUND(W)UP?) (5A) (RESIST? OR TOLERAN? OR  
PROTECT?)

L11 26877 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE

L12 3820466 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?))

L13 123 SEA L10 AND L11 AND L12

L14 142 SEA L1 OR L2 OR L9 OR L13

L15 19 SEA L14 AND PY>=2019

L16 8 SEA L15 AND UP>=20201001 AND UP<=20210930

FILE 'BIOSIS' ENTERED AT 10:50:05 ON 08 OCT 2021

L17 4 SEA GHB614 OR GHB(W)614 OR BCS-GH002-5 OR BCSGH002-5 OR  
BCS(W)GH002(W)5 OR BCSGH002(W)5 OR BCS-GH002-5 OR BCS(W)GH002(W)  
)5 OR BCSGH002(W)5

L18 2 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM  
OR GLY(W)TOLRTM

L19 12 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS

L20 5035 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)

L21 0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKI  
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S  
YNTHASE OR SYNTHETASE)

L22 719 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR  
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W)SHIKIMATE  
) (3W)PHOSPHATE(W) (SYNTHASE OR SYNTHETASE)

L23 27 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK  
IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(  
3W)PHOSPHOSYNTHASE)

L24 26878 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)

L25 19 SEA L19 OR ((L20 OR L21 OR L22 OR L23)) (S)L24)

L26 11054 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360  
OR ROUNDUP? OR ROUND(W)UP?) (5A) (RESIST? OR TOLERAN? OR  
PROTECT?)

L27 75275 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM

L28 465984 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?))  
L29 285 SEA L26 AND L27 AND L28  
L30 307 SEA L17 OR L18 OR L25 OR L29  
L31 30 SEA L30 AND PY>=2019  
L32 18 SEA L31 AND UP>=20201001 AND UP<=20210930

FILE 'AGRICOLA' ENTERED AT 10:50:34 ON 08 OCT 2021

L33 2 SEA GHB614 OR GHB(W)614 OR BCS-GH002-5 OR BCSGH002-5 OR BCS(W)GH002(W)5 OR BCSGH002(W)5 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR BCSGH002(W)5  
L34 2 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM OR GLY(W)TOLRTM  
L35 4 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS  
L36 651 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)  
L37 0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKIMATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (SYNTHASE OR SYNTHETASE)  
L38 306 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)  
L39 237 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIKIMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (3W) PHOSPHOSYNTHASE)  
L40 6578 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)  
L41 9 SEA L35 OR ((L36 OR L37 OR L38 OR L39)) (S)L40)  
L42 8628 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360 OR ROUNDUP? OR ROUND(W)UP?) (5A) (RESIST? OR TOLERAN? OR PROTECT?)  
L43 64210 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM  
L44 103176 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?))  
L45 238 SEA L42 AND L43 AND L44  
L46 248 SEA L33 OR L34 OR L41 OR L45  
L47 13 SEA L46 AND PY>=2019  
L48 8 SEA L47 AND UP>=20201001 AND UP<=20210930

FILE 'CABA' ENTERED AT 10:51:09 ON 08 OCT 2021

L49 7 SEA GHB614 OR GHB(W)614 OR BCS-GH002-5 OR BCSGH002-5 OR BCS(W)GH002(W)5 OR BCSGH002(W)5 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR BCSGH002(W)5  
L50 4 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM OR GLY(W)TOLRTM  
L51 14 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS  
L52 1117 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)  
L53 0 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKIMATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (SYNTHASE OR SYNTHETASE)  
L54 429 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)  
L55 172 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIKIMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (3W) PHOSPHOSYNTHASE)  
L56 7304 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)  
L57 21 SEA L51 OR ((L52 OR L53 OR L54 OR L55)) (S)L56)

L58 19059 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360  
OR ROUNDUP? OR ROUND(W)UP?) (5A) (RESIST? OR TOLERAN? OR  
PROTECT?)  
L59 96175 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM  
L60 184643 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?))  
L61 531 SEA L58 AND L59 AND L60  
L62 552 SEA L49 OR L50 OR L57 OR L61  
L63 41 SEA L62 AND PY>=2019  
L64 29 SEA L63 AND UP>=20201001 AND UP<=20210930  
L65 29 SEA L64 NOT P/DT  
L66 0 SEA L64 AND (P/DT AND J/DT)  
L67 29 SEA L65 OR L66

FILE 'HCAPLUS' ENTERED AT 10:51:47 ON 08 OCT 2021

L68 7 SEA GHB614 OR GHB(W)614 OR BCS-GH002-5 OR BCSGH002-5 OR  
BCS(W)GH002(W)5 OR BCSGH002(W)5 OR BCS-GH002-5 OR BCS(W)GH002(W)  
)5 OR BCSGH002(W)5  
L69 5 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM  
OR GLY(W)TOLRTM  
L70 28 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS  
L71 4390 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)  
L72 9 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKI  
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S  
YNTHASE OR SYNTHETASE)  
L73 1076 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR  
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE  
) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)  
L74 83 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK  
IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (  
3W) PHOSPHOSYNTHASE)  
L75 74626 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)  
L76 40 SEA L70 OR ((L71 OR L72 OR L73 OR L74)) (S) L75)  
L77 29034 SEA (HERBICID? OR GL!PHOSATE# OR GL!FOSATE# OR G360 OR G(W)360  
OR ROUNDUP? OR ROUND(W)UP?) (5A) (RESIST? OR TOLERAN? OR  
PROTECT?)  
L78 266018 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM  
L79 692486 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 1381 SEA L77 AND L78 AND L79  
L81 1421 SEA L68 OR L69 OR L76 OR L80  
L82 451 SEA L81 AND PY>=2019  
L83 56 SEA L82 AND UP>=20201001 AND UP<=20210930  
L84 14 SEA L83 NOT P/DT  
L85 0 SEA L83 AND (P/DT AND J/DT)  
L86 14 SEA L84 OR L85

FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 10:52:24 ON 08  
OCT 2021

L87 64 DUP REM L16 L32 L48 L67 L86 (13 DUPLICATES REMOVED)  
ANSWERS '1-8' FROM FILE MEDLINE  
ANSWERS '9-23' FROM FILE BIOSIS  
ANSWERS '24-31' FROM FILE AGRICOLA  
ANSWERS '32-55' FROM FILE CABA  
ANSWERS '56-64' FROM FILE HCAPLUS