

Title

**Summary of the Literature Review for GHB614 Cotton
October 1, 2019 – September 30, 2020**

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

Completion date

November 30, 2020

Principal Author



The following statement is only intended and valid for submissions which are subject to the United States – Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that the information not designated as within the scope of FIFRA, section 10 (d)(1)(A),(B), or (C) in the USA and which pertains to a registered or previously registered pesticide is not entitled to confidential treatment and may be released to the public, subject to provisions regarding disclosure to multinational entities under FIFRA 10(g) in the USA.

However, these data are the property of BASF Agricultural Solutions Seed GmbH or one of its affiliates and, as such, are considered to be a trade secret and confidential for all purposes other than compliance with FIFRA 10 in USA.

Submission of these data in compliance with FIFRA does not constitute a waiver of any right to confidentiality which may exist under any other statute or in any country other than the USA.

Submitter
signature: _____



Date: _____

2020-11-30
(YYYY-MM-DD)

Typed name of submitter: _____



Typed name of company: _____

BASF Agricultural Solutions GmbH

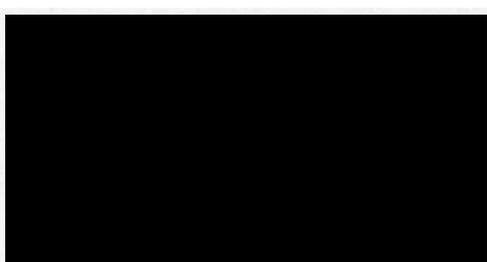
The above statement supersedes all other statements of confidentiality that may occur elsewhere in this report.



We create chemistry

Report No: 20-RSCT0209
Summary of the Literature Review for GHB614 cotton
October 1, 2019 – September 30, 2020
Page 3 of 35

SIGNATURE PAGE

Principal author:		Date <u>2020-11-30</u> (YYYY-MM-DD)
-------------------	---	--

STUDY PERSONNEL

Electronic database search	[REDACTED]
Manual search	[REDACTED] [REDACTED] [REDACTED] [REDACTED]
Stage 1 assessment	[REDACTED] [REDACTED]
Stage 2 assessment	<u>Food and Feed safety</u> [REDACTED] [REDACTED] <u>Molecular characterization</u> [REDACTED] [REDACTED] <u>Environmental safety</u> [REDACTED] [REDACTED]
Report	[REDACTED] [REDACTED] [REDACTED]

TABLE OF CONTENTS

STATEMENT OF NO DATA CONFIDENTIALITY CLAIMS	2
SIGNATURE PAGE	3
STUDY PERSONNEL.....	4
TABLE OF CONTENTS	5
SUMMARY.....	7
1. INTRODUCTION.....	8
2. OVERALL METHODS	8
2.1. Objective of the scoping review.....	8
2.2. Review questions	8
2.3. Criteria for relevance	9
2.4. Reference study searches.....	12
3. SEARCH METHODS AND OUTCOMES	12
3.1. Time window and date of the literature search.....	13
3.2. Databases used in the literature search.....	13
3.3. Search strategy.....	13
4. MANUAL SEARCHES.....	15
4.1. Manual searches of web pages of food safety, agriculture, and biotechnology-related authority webpages	15
4.2. Manual searches of reference lists of recent review articles.....	16
5. RESULTS OF THE STUDY IDENTIFICATION AND SELECTION PROCESS.....	20
5.1. Screening of titles and abstracts to exclude obviously irrelevant references (Stage 1)...	20
5.2. Detailed assessment of eligible references (Stage 2).....	20
6. NARRATIVE SYNTHESIS/SUMMARY OF RELEVANT STUDIES.....	29
7. CONCLUSION	29
8. REFERENCES.....	29
9. APPENDICES	30

TABLES

Table 1:	Eligibility/inclusion criteria to establish the relevance of retrieved publications	9
Table 2:	Search profile for database search.....	14
Table 3:	Overview of the selected databases and summary of search results from each database	15
Table 4:	Results of search of food safety, agriculture, and biotechnology-related authority websites.....	15
Table 5:	Documents for which reference lists were scanned for relevant studies	17
Table 6:	Results of the publication selection process	21
Table 7:	Report of all relevant publications retrieved after detailed assessment of full-text documents for relevance: ordered by category of information/data requirement(s)	22
Table 8:	Report of publications excluded from the risk assessment after detailed assessment of full-text documents.....	22
Table 9:	Report of unobtainable/unclear publications	28

APPENDICES

Appendix 1	Database descriptions	30
Appendix 2	Search history	32

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 effects on food and feed safety, or on environmental safety, that might require in-depth examination. A set of broad literature searches was performed using several bibliographic databases covering scientific literature from October 1, 2019 to September 30, 2020. 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 48 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. A total of 11 publications were progressed for detailed assessment and were determined to be not relevant after detailed review.

No new publications were found that contained new data on the molecular characterization of the GHB614 cotton and its newly expressed protein, 2mEPSPS. Similarly, no new publications were found that suggested any potential adverse effects of GHB614 cotton on human health, animal health, or the environment. No issues or topics were identified that would trigger or warrant more specific question formulation or indicate that a systematic review would be of value.

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-enolpyruvyl-shikimate 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 publications published between October 1, 2019 and September 30, 2020 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)¹ 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, 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 PECO structure (Population, Exposure, Comparators, Outcome) if possible, and to address data requirements. They were modeled after the review question examples provided in the EFSA 2019 explanatory note¹.

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: 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 note¹ 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		
Intervention/exposure	The publication addresses the GMO, derived food/feed products, and/or the intended trait(s) (e.g., newly expressed protein(s)) that are identical or like those under regulatory review	This enables the selection of publications that address the GMO, derived food/feed products, and/or the intended trait(s) under consideration
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
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
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

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

<p>Stacked events obtained by conventional crosses/subcombinations</p>	<p>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</p>	<p>This permits the selection of publications on the higher stacked event and/or subcombinations of the single events of the higher stacked event that are in the scope of the GMO application(e), independently of their origin. This permits the exclusion of publications on the single events of the higher stacked event, because the risk assessment of GMO applications for stacked events covers only the products in the scope of the GMO application – i.e., the higher stacked event and subcombinations of the singles involved, independently of their origin</p>
<p>Molecular stacks</p>	<p>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</p>	<p>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</p>
<p>Previously risk assessed publications</p>	<p>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</p>	<p>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</p>
<p>Access</p>	<p>Full-text document is accessible</p>	<p>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</p>

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

Table adapted from EFSA, 2019: Explanatory note on literature searching conducted in the context of GMO applications for (renewed) market authorisation and annual post-market environmental monitoring reports on GMOs authorised in the EU market.

2.4. Reference publication

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; Gralak 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

The Naegeli *et al.* 2018 publication is not directly relevant to the GHB614 event. Nevertheless it was selected as reference publications because it includes in the searched fields the event name (GHB614), newly expressed protein (2mEPSPS), intended trait (herbicide tolerance) and/or target crop (cotton). Since both 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>=20191001 and UP<=20200930).

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 activities¹. 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, 2020. Only documents updated between October 1, 2019 and September 30, 2020, 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 profiles were designed to cover event name, trade name, newly expressed protein and intended traits. Since the 'intended trait' profile retrieved a very large number of publications when used on its own, it was combined with additional profiles: a 'general GMO' profile as well as with the 'plant species' profile. See [Table 2](#) for a detailed search profile.

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

- **Agricola:** title (TI), controlled term (CT), supplementary term (ST), abstract (AB), named person (NA), corporate name (CO), note (NTE), geographic term, CABA and other fields (GT)
- **Biosis:** title (TI), abstract (AB), biosystematic codes (BC), chemical name (CN), controlled term (CT), gene name (GEN), geographic term (GT), organism (ORGN) and supplementary term (ST); as well as CAS Registry Numbers (RN)
- **CA-Plus:** title (TI), supplementary term (ST), index term (IT) and abstract (AB); as well as CAS Registry Numbers
- **CABA:** title (TI), controlled term (CT), supplementary term (ST), broader term (BT), abstract (AB), organism name (ORGN) and geographic term (GT); as well as CAS Registry Numbers
- **Medline:** title (TI), chemical name (CN), gene name (GEN), controlled term (excluding MeSH numbers) (CT), supplementary term (ST), named person (NA), other source (OS), and abstract (AB), as well as CAS Registry Numbers and GenBank Numbers

The search results were limited to documents updated between October 1, 2019 and September 30, 2020 (UP>=20191001 and UP<=20200930), and to non-patent documents (not P/DT). To ensure that documents with indexing errors where two DTs (one eligible and one ineligible) were attached to a single record were not missed, documents with both 'journal' and 'patent' as *document type* were also kept. These putative documents would be identified with (P/DT AND J/DT) in CABA and CAPlus.

[Table 3](#) summarizes the number of results obtained from each of the databases searched.

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

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 SYNTHETASE) or (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE) or (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIKIMATE (2W) CARBOXYVINYL(W) TRANSFERASE OR ENOLPYRUVOYL(W) SHIKIMIC (3W) PHOSPHOSYNTHASE) (s) ((DOUBL# or DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M))	Newly expressed protein
4	(herbicide? 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)

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

Database	AGRICOLA	BIOSIS	CAB Abstracts	CAPLUS	MEDLINE
Database Provider	STN International				
Coverage	1970-present	1926-present	1973-present	1907-present	1946-present
Date of search	8 Oct 2020				
Datespan of the search	1 Oct 2019 – 30 Sept 2020				
Latest database update	24 Aug 2020	7 Oct 2020	7 Oct 2020	7 Oct 2020	7 Oct 2020
Number of records retrieved	4	14	13	20	12
Number of records after duplicate removal	3	11	11	11	12
Number of relevant records after rapid assessment	0	1	2	4	4

4. MANUAL SEARCHES

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

In accordance with the EFSA 2019 explanatory note¹, the search in electronic bibliographic databases has been complemented with an internet search in webpages of relevant key organisations involved in the risk assessment of GM plants. Of the 13 key organisations cited in the EFSA 2019 explanatory note¹, two (Environment and Climate Change Canada and CIBIOGEM) are not involved in the risk assessment of GM plants, and the US Environmental Protection Agency (EPA) is only involved in the regulation of GM crops with plant-incorporated protectants (PIPs). Therefore, the internet search was limited to ten key organisations relevant for GHB614 cotton.

Search terms consisted of GlyTol or GHB614 or BCS-GH002-5; or 2mEPSPS OR Double mutant 5-enolpyruvyl shikimate-3-phosphate synthase enzyme in GHB614 cotton (all searched singly, with no search limits applied). Search results were manually examined for relevant records that were either published during the time period under consideration (date span of search: October 1, 2019 to September 30, 2020) 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 4](#).

Table 4: 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)	https://www.usda.gov/	Oct 29 2020	Oct 28-30 2020	0
US Food and Drug Administration (FDA)	https://www.fda.gov/	Oct 30 2020	Oct 28-30 2020	0
Health Canada	https://www.canada.ca/en/health-canada.html	Oct 26 2020	Oct 28-30 2020	0
Food Inspection Agency Canada	https://www.canada.ca/en/food-inspection-agency.html	Oct 30 2020	Oct 28-30 2020	0
Food Standards Australia New Zealand (FSANZ)	http://www.foodstandards.gov.au/Pages/default.aspx	Oct 28 2020	Oct 28-30 2020	0
Office of the Gene Technology Regulator (OGTR) Australia	http://www.ogtr.gov.au/	Oct 15 2020	Oct 28-30 2020	0
National Technical Commission on Biosafety (CTNBio) Brazil	http://ctnbio.mcti.gov.br/en	Oct 2020	Oct 22-28 2020	0
National Advisory Commission on Agricultural Biotechnology (CONABIA) Argentina	https://www.argentina.gob.ar/agroindustria/bioeconomia/biotechnologia	later than Aug 21 2020	Oct 21-22 2020	0
Genetic Engineering Approval Committee (GEAC) India	http://moef.gov.in/ *	Oct 27 2020	Nov 3 2020	0
Ministry of Agriculture, Forestry and Fisheries (MAFF) Japan	http://www.maff.go.jp/	Oct 26 2020	Oct 26 2020	0

* As the GEAC website does not have a search function the moef.gov.in website was searched instead.

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, 2019 and September 30, 2020. The resulting number of relevant studies found within the bibliographies of these review articles is given in [Table 5](#).

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

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
1	Ansari WA, Chandanshive SU, Bhatt V, Nadaf AB, Vats S, Katara JL, Sonah H, Deshmukh R. 2020	Genome Editing in Cereals: Approaches, Applications and Challenges	Int J Mol Sci. 2020 Jun 5;21(11):4040. doi: 10.3390/ijms21114040	0
2	Arpaia S, Christiaens O, Giddings K, Jones H, Mezzetti B, Moronta-Barrios F, Perry JN, Sweet JB, Taning CNT, Smagghe G, Dietz-Pfeilstetter A. 2020	Biosafety of GM Crop Plants Expressing dsRNA: Data Requirements and EU Regulatory Considerations	Front Plant Sci. 2020 Jun 24;11:940. doi: 10.3389/fpls.2020.00940. eCollection 2020.	0
3	Babar U, Nawaz MA, Arshad U, Azhar MT, Atif RM, Golokhvast KS, Tsatsakis AM, Shcerbakova K, Chung G, Rana IA. 2020	Transgenic crops for the agricultural improvement in Pakistan: a perspective of environmental stresses and the current status of genetically modified crops	GM Crops Food. 2020;11(1):1-29. doi: 10.1080/21645698.2019.1680078. Epub 2019 Nov 3.	0
4	Bachtarzi H, Farries T. 2019	The Genetically Modified Organism Medicinal Framework in Europe, United States, and Japan: Underlying Scientific Principles and Considerations Toward the Development of Gene Therapy and Genetically Modified Cell-Based Products	Hum Gene Ther Clin Dev. 2019 Sep;30(3):114-128. doi: 10.1089/humc.2019.042. Epub 2019 Jun 21.	0

5	Bedair M, Glenn KC. 2020	Evaluation of the use of untargeted metabolomics in the safety assessment of genetically modified crops	Metabolomics. 2020 Oct 9;16(10):111. doi: 10.1007/s11306-020-01733-8.	0
6	Feng XJ, Yi HM, Ren XX, Ren JL, Ge JR, Wang FG. 2020	[Digital PCR and its application in biological detection]	Yi Chuan. 2020 Apr 20;42(4):363-373. doi: 10.16288/j.ycz.19-351.	0
7	Giraldo PA, Shinozuka H, Spangenberg GC, Cogan NOI, Smith KF. 2019	Safety Assessment of Genetically Modified Feed: Is There Any Difference From Food?	Front Plant Sci. 2019 Dec 11;10:1592. doi: 10.3389/fpls.2019.01592. eCollection 2019.	0
8	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.	0
9	Holme IB, Gregersen PL, Brinch-Pedersen H. 2019	Induced Genetic Variation in Crop Plants by Random or Targeted Mutagenesis: Convergence and Differences	Front Plant Sci. 2019 Nov 14;10:1468. doi: 10.3389/fpls.2019.01468. eCollection 2019.	0
10	Jyoti A, Kaushik S, Srivastava VK, Datta M, Kumar S, Yugandhar P, Kothari SL, Rai V, Jain A. 2019	The potential application of genome editing by using CRISPR/Cas9, and its engineered and ortholog variants for studying the transcription factors involved in the maintenance of phosphate homeostasis in model plants	Semin Cell Dev Biol. 2019 Dec;96:77-90. doi: 10.1016/j.semcdb.2019.03.010. Epub 2019 Apr 7.	0

11	Kadoić Balaško M, Mikac KM, Bažok R, Lemic D. 2020	Modern Techniques in Colorado Potato Beetle (<i>Leptinotarsa decemlineata</i> Say) Control and Resistance Management: History Review and Future Perspectives	Insects. 2020 Sep 1;11(9):581. doi: 10.3390/insects11090581.	0
12	Kamle M, Mahato DK, Devi S, Soni R, Tripathi V, Mishra AK, Kumar P. 2020	Nanotechnological interventions for plant health improvement and sustainable agriculture	3 Biotech. 2020 Apr;10(4):168. doi: 10.1007/s13205-020-2152-3. Epub 2020 Mar 14.	0
13	Kauffmann F, Van Damme P, Leroux-Roels G, Vandermeulen C, Berthels N, Beuneu C, Mali S. 2019	Clinical trials with GMO-containing vaccines in Europe: Status and regulatory framework	Vaccine. 2019 Sep 30;37(42):6144-6153. doi: 10.1016/j.vaccine.2019.08.018. Epub 2019 Sep 4.	0
14	Kenter MJH, Clevers JC, Cornelissen J, Medema RH. 2019	[Environmental regulations impede cancer research and treatment]	Ned Tijdschr Geneeskd. 2019 Dec 5;163:D4267.	0
15	Keshani P, Sharifi MH, Heydari MR, Joulaei H. 2020	The Effect of Genetically Modified Food on Infertility Indices: A Systematic Review Study	ScientificWorldJournal. 2020 Aug 13;2020:1424789. doi: 10.1155/2020/1424789. eCollection 2020.	0
16	Kumar K, Gambhir G, Dass A, Tripathi AK, Singh A, Jha AK, Yadava P, Choudhary M, Rakshit S. 2020	Genetically modified crops: current status and future prospects	Planta. 2020 Mar 31;251(4):91. doi: 10.1007/s00425-020-03372-8.	0
17	Papadopoulou N, Devos Y, Álvarez-Alfageme F, Lanzoni A, Waigmann E. 2020	Risk Assessment Considerations for Genetically Modified RNAi Plants: EFSA's Activities and Perspective	Front Plant Sci. 2020 Apr 21;11:445. doi: 10.3389/fpls.2020.00445. eCollection 2020.	0

18	Pottinger SE, Innes RW. 2020	RPS5-Mediated Disease Resistance: Fundamental Insights and Translational Applications	Annu Rev Phytopathol. 2020 Aug 25;58:139-160. doi: 10.1146/annurev-phyto-010820-012733. Epub 2020 Apr 13.	0
19	Rumin J, Nicolau E, Junior RGO, Fuentes-Grünwald C, Picot L. 2020	Analysis of Scientific Research Driving Microalgae Market Opportunities in Europe	Mar Drugs. 2020 May 18;18(5):264. doi: 10.3390/md18050264.	0
20	Woźniak E, Waszkowska E, Zimny T, Sowa S, Twardowski T. 2019	The Rapeseed Potential in Poland and Germany in the Context of Production, Legislation, and Intellectual Property Rights	Front Plant Sci. 2019 Nov 5;10:1423. doi: 10.3389/fpls.2019.01423. eCollection 2019.	0

5. RESULTS OF THE STUDY IDENTIFICATION AND SELECTION PROCESS

The database searches (Section 3) identified a total of 63 references, which were reduced to 48 after removal of duplicates (Table 3). 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 case, there were no disagreements between the two stage 1 evaluators

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, unrelated topics, etc.

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

The number of publications excluded after rapid assessment for relevance is presented in Table 6 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. All eligible references were assessed in detail. This detailed assessment included evaluation of the scope of the article and the study quality and reliability. Categorization of reliability (as described in the EFSA 2019 explanatory note¹) was dependent upon the following:

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

[Table 6](#) gives an overview of the reference selection process and results of the detailed assessment.

Table 6: Results of the publication selection process

Total number of publications retrieved after all searches of the scientific literature (excluding duplicates)	48
Number of publications excluded from the search results after rapid assessment for relevance (Stage 1)	37
Total number of full-text documents assessed in detail	11
Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2)	11
Total number of unobtainable/unclear publications	0
Total number of relevant publications	0

[Table 7](#) 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 8](#). [Table 9](#) lists the publications for which full-text documents were unobtainable for detailed assessment or for which relevance was unclear after detailed assessment.

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

Main category of information/data requirement	Study Author(s). Year	Title	Source
Molecular Characterization	No studies in this category		
Food & Feed Safety	No studies in this category		
Environmental Safety	No studies in this category		

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

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Fast Brandon J Shan Guomin Herman Rod A Gampala Satyalinga Srinivas. 2020	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.	GHB614 was not included in the study

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Garcia-Ruiz, Esteban Loureiro, Inigo [Reprint Author] Farinos, Gema P. Gomez, Pablo Gutierrez, Elena Javier Sanchez, Francisco Concepcion Escorial, Maria Ortego, Felix Cristina Chueca, Maria Castanera, Pedro. 2018	Weeds and ground-dwelling predators+apos; response to two different weed management systems in glyphosate - tolerant cotton : A farm-scale study.	PLoS One, (JAN 19 2018) Vol. 13, No. 1, pp. Article No.: e0191408. http://journals.plos.org/plosone/ . ISSN: 1932-6203. E-ISSN: 1932-6203.	Two weed management regimes by application of glyphosate at different timings (application of glyphosate at pre and post emergence vs. application of glyphosate at post-emergence only) on GHB614 cotton crop were compared for its effects on weed abundance , diversity and ground-dwelling predators. No ERA related to GHB614 cotton.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
<p>Naegeli Hanspeter Birch Andrew Nicholas Casacuberta Josep De Schrijver Adinda Gralak Mikolaj Antoni Guerche Philippe Jones Huw Manachini Barbara Messean Antoine Nielsen Elsa Ebbesen Nogue Fabien Robaglia Christophe Rostoks Nils Sweet Jeremy Tebbe Christoph Visioli Francesco Wal Jean-Michel Broll Hermann Gennaro Andrea Neri Franco Maria Paraskevopoulos Konstantinos. 2018</p>	<p>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).</p>	<p>EFSA journal. European Food Safety Authority, (2018 Apr) Vol. 16, No. 4, pp. e05213. Electronic Publication Date: 20 Apr 2018 Journal code: 101642076. E-ISSN: 1831-4732. L-ISSN: 1831-4732. Report No.: PMC-PMC7009700.</p>	<p>The report is not specific to GHB614 cotton. The report focuses on GHB614 x LLCotton25 x MON 15985 cotton.</p>

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
<p>Naegeli Hanspeter Birch Andrew Nicholas Casacuberta Josep De Schrijver Adinda Gralak Mikolaj Antoni Guerche Philippe Jones Huw Manachini Barbara Messean Antoine Nielsen Elsa Ebbesen Nogue Fabien Robaglia Christophe Rostoks Nils Sweet Jeremy Tebbe Christoph Visioli Francesco Wal Jean-Michel Ardizzone Michele Fernandez-Dumont Antonio Gennaro Andrea Gomez Ruiz Jose Angel Lanzoni Anna Neri Franco Maria Papadopoulou Nikoletta Paraskevopoulos Konstantinos. 2018</p>	<p>Assessment of genetically modified cotton GHB614 x T304-40 x GHB119 for food and feed uses, import and processing under Regulation (EC) No 1829/2003 (application EFSA-GMO-NL-2014-122).</p>	<p>EFSA journal. European Food Safety Authority, (2018 Jul) Vol. 16, No. 7, pp. e05349. Electronic Publication Date: 25 Jul 2018 Journal code: 101642076. E-ISSN: 1831-4732. L-ISSN: 1831-4732. Report No.: PMC-PMC7009458.</p>	<p>The report is not specific to GHB614 cotton. The report focuses on GHB614 x T304-40 x GHB119 cotton.</p>

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Pan, Xiaoping 2019	Determining pollen-mediated gene flow in transgenic cotton	Methods in Molecular Biology (New York, NY, United States) (2019), 1902(Transgenic Cotton), 309-321 CODEN: MMBIED; ISSN: 1940-6029	The paper evaluated the extent of gene flow of NewCott 33B and TFD cotton in the field. No ERA related to GHB614 cotton.
Ricroch, A. Akkoyunlu, S. Martin-Laffon, J. Kuntz, M. Editor(s): Kuntz, M. 2018	Assessing the environmental safety of transgenic plants: honey bees as a case study. Special Issue: Transgenic plants and beyond.	Advances in Botanical Research (2018), Volume 86, pp. 111-167, 34 refs. ISSN: 0065-2296 Published by: Elsevier Ltd, Oxford	Review of 64 peer-reviewed papers (from 1994 to 2017) and 18 US EPA studies (from 1993 to 2002) related to the effect of GM crops (protease inhibitors, Cry, Vip, RNAi-producing and HT) such as cotton, soybean and maize on honey bees. No original/primary data related to ERA of GHB614.
Salisu, Ibrahim Bala Shahid, Ahmad Ali Yaqoob, Amina Rao, Abdul Qayyum Husnain, Tayyab. 2019	Effect of dietary supplementation of recombinant Cry and Cp4 epsps proteins on haematological indices of growing rabbits	Journal of Animal Physiology and Animal Nutrition (2019), 103(1), 305-316 CODEN: JAPNEF; ISSN: 0931-2439	GHB614 cotton not included in the study.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Shahid, A. A., Haider, T. Samiullah, T. R., Ali, M. A. Bajwa, K. S., Rao, A. Q. Salisu, I. B., Husnain, T. 2019	Risk assessment of transgenic cotton harboring Bt and glyphosate resistance gene on fish (Labeo rohita).	JAPS, Journal of Animal and Plant Sciences (2019), Volume 29, Number 6, pp. 1761-1769, 31 refs. ISSN: 1018-7081 Published by: Pakistan Agricultural Scientists Forum, Lahore	The authors assessed morphological, histological, biochemical and molecular characteristics of Rohu fish (Labeo rohita) treated with a diet composed with GM cotton fuzzy seeds (1- Cry1Ac+Cry2A ; 2- Cp4EPSPS). The biochemical and molecular analysis confirmed that there was no negative effect of Cry and Cp4EPSPS protein on fish. The varieties and their technologies are not described in the paper. No ERA related to GHB614.
Singh, Monika Randhawa, Gurinderjit Bhoge, Rajesh K. Singh, Sushmita Kak, Anjali Sangwan, Omender. 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) Ahead of Print CODEN: ARGEFW; ISSN: 2249-7218	The authors tested adventitious presence of transgenes in 100 ex situ accessions of cotton being conserved in the National Genebank of India using Pentaplex PCR assay. No ERA related to 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 EPSPS to weed species from genetically modified Gossypium hirsutum in Northern Mexico	Notulae Botanicae Horti Agrobotanici Cluj-Napoca (2019), 47(2), 294-299 CODEN: NBHABI; ISSN: 0255-965X URL: http://www.notulaeobotanicae.ro/index.php/nbha/index	The objective of this study was to quantify and identify weed species associated to genetically modified cotton (BGII) fields and to detect the presence of glyphosate-insensitive EPSP synthases (CP4 EPSPS) in these species. No ERA related to GHB614 cotton.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
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, (20190700) Vol. 17, No. 7, pp. 1236-1247. Electronic Publication Date: 19 Jan 2019 Journal code: 101201889. E-ISSN: 1467-7652. L-ISSN: 1467-7644. Report No.: PMC-PMC6576080.	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 9: Report of unobtainable/unclear publications

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

6. NARRATIVE SYNTHESIS/SUMMARY OF RELEVANT STUDIES

A total of 11 publications were selected during Stage 1 evaluation (rapid assessment based on title and abstract). After Stage 2 evaluation (detailed review based on full text), no relevant references were found in the searches on GHB614 cotton and its newly expressed protein, 2mEPSPS, covering October 1, 2019 to September 30, 2020 to provide additional information.

7. CONCLUSION

The literature searches performed for the GHB614 cotton and its newly expressed protein 2mEPSPS for the period from October 1, 2019 to September 30, 2020, identified a total of 48 unique publications (after duplicate removal). A total of 11 publications were progressed for detailed assessment after excluding 37 obviously irrelevant publications during Stage 1 evaluation (rapid assessment based on title and abstract).

The 11 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](#). No relevant publications with bearing on molecular characterization, human or animal safety assessment, or environmental safety assessment were identified. 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-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>

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 09:06:08 ON 08 OCT 2020
L1      3 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 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR
        BCSGH002-5
L2      0 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM
        OR GLY(W)TOLRTM
L3      12 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L4      4134 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
        ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
        OYLSHIKAMATE OR ENOYLPYRUVYOYLSHIKIMATE 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      357 SEA (ENOL(W)PYRUVYOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
        ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE
        ) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)
L7      458 SEA (PHOSPHOSHIKIMATE(2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
        IMATE(2W) CARBOXYVINYL(W) TRANSFERASE OR ENOLPYRUVOYL(W) SHIKIMIC (
        3W) PHOSPHOSYNTHASE)
L8      23569 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L9      18 SEA L3 OR ((L4 OR L5 OR L6 OR L7)) (S)L8)
L10     3225 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     25098 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L12     3600878 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     119 SEA L10 AND L11 AND L12
L14     137 SEA L1 OR L2 OR L9 OR L13
L15     29 SEA L14 AND PY>=2018
L16     12 SEA L15 AND UP>=20191001 AND UP<=20200930

FILE 'BIOSIS' ENTERED AT 09:06:33 ON 08 OCT 2020
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 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR
        BCSGH002-5
L18     1 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     4941 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYLSHIKIMATE OR
        ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR ENOLPYRUV
        OYLSHIKAMATE OR ENOYLPYRUVYOYLSHIKIMATE 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     681 SEA (ENOL(W)PYRUVYOYLSHIKIMATE 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     26115 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L25     18 SEA L19 OR ((L20 OR L21 OR L22 OR L23)) (S)L24)
L26     10474 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 72395 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L28 446752 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 272 SEA L26 AND L27 AND L28
L30 292 SEA L17 OR L18 OR L25 OR L29
L31 36 SEA L30 AND PY>=2018
L32 14 SEA L31 AND UP>=20191001 AND UP<=20200930

FILE 'AGRICOLA' ENTERED AT 09:06:56 ON 08 OCT 2020

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 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR
BCSGH002-5
L34 2 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM
OR GLY(W)TOLRTM
L35 2 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L36 593 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) (PHOSPHOSHIKI
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S
YNTHASE OR SYNTHETASE)
L38 286 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE
) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)
L39 209 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVOYL (W) SHIKIMIC (
3W) PHOSPHOSYNTHASE)
L40 6092 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L41 7 SEA L35 OR ((L36 OR L37 OR L38 OR L39)) (S) L40
L42 7984 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 61052 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L44 93951 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 221 SEA L42 AND L43 AND L44
L46 229 SEA L33 OR L34 OR L41 OR L45
L47 12 SEA L46 AND PY>=2018
L48 4 SEA L47 AND UP>=20191001 AND UP<=20200930

FILE 'CABA' ENTERED AT 09:07:28 ON 08 OCT 2020

L49 6 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 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR
BCSGH002-5
L50 4 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM
OR GLY(W)TOLRTM
L51 12 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L52 1020 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) (PHOSPHOSHIKI
MATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYLSHIKIMATEPHOSPHATE) (2W) (S
YNTHASE OR SYNTHETASE)
L54 400 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
ENOLPYRUVYLSHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE
) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)
L55 151 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK

IMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVYL (W) SHIKIMIC (3W) PHOSPHOSYNTHASE)
L56 6857 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L57 17 SEA L51 OR ((L52 OR L53 OR L54 OR L55)) (S) L56)
L58 18020 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 91934 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L60 173769 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 501 SEA L58 AND L59 AND L60
L62 520 SEA L49 OR L50 OR L57 OR L61
L63 45 SEA L62 AND PY>=2018
L64 13 SEA L63 AND UP>=20191001 AND UP<=20200930
L65 13 SEA L64 NOT P/DT
L66 0 SEA L64 AND (P/DT AND J/DT)
L67 13 SEA L65 OR L66

FILE 'HCAPLUS' ENTERED AT 09:08:07 ON 08 OCT 2020
L68 8 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 OR BCS-GH002-5 OR BCS(W)GH002(W)5 OR BCSGH002-5
L69 5 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM OR GLY(W)TOLRTM
L70 29 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L71 4244 SEA EPSPS OR EPSP(W)SYNTHASE OR (ENOL(W)PYRUVYL)SHIKIMATE OR ENOL(W)PYRUVYL(W)SHIKIMATE OR ENOLPYRUVYL(W)SHIKIMATE OR ENOLPYRUVYL(W)SHIKIMATE OR ENOYL(PYRUVYL)SHIKIMATE OR ENOLPYRUVYL(W)SHIKIMIC (4W) (PHOSPHATE OR PHOSPHORIC) (2W) (SYNTHASE OR SYNTHETASE)
L72 9 SEA (ENOLPYRUVYL OR ENOLPYRUYL OR ENOLPYRUVOYL) (W) (PHOSPHOSHIKIMATE OR PHOSPHOSHIKIMIC OR ENOLPYRUVYL(W)SHIKIMATEPHOSPHATE) (2W) (SYNTHASE OR SYNTHETASE)
L73 1039 SEA (ENOL(W)PYRUVOYL)SHIKIMATE OR ENOLPYRUVYL(W)SHIKIMATE OR ENOLPYRUVYL(W)SHIKIMIC OR ENOL(W) (PYRUVYL OR PYRUVOYL) (W) SHIKIMATE) (3W) PHOSPHATE (W) (SYNTHASE OR SYNTHETASE)
L74 87 SEA (PHOSPHOSHIKIMATE (2W) CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIKIMATE (2W) CARBOXYVINYL (W) TRANSFERASE OR ENOLPYRUVYL (W) SHIKIMIC (3W) PHOSPHOSYNTHASE)
L75 73346 SEA ((DOUBL# OR DOBL#) (W) (MUTANT# OR MUTAT?) OR 2M)
L76 41 SEA L70 OR ((L71 OR L72 OR L73 OR L74)) (S) L75)
L77 27396 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 250415 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L79 663632 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 1334 SEA L77 AND L78 AND L79
L81 1376 SEA L68 OR L69 OR L76 OR L80
L82 474 SEA L81 AND PY>=2018
L83 86 SEA L82 AND UP>=20191001 AND UP<=20200930
L84 20 SEA L83 NOT P/DT
L85 0 SEA L83 AND (P/DT AND J/DT)
L86 20 SEA L84 OR L85

FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 09:08:43 ON 08 OCT 2020
L87 48 DUP REM L16 L32 L48 L67 L86 (15 DUPLICATES REMOVED)
ANSWERS '1-12' FROM FILE MEDLINE
ANSWERS '13-23' FROM FILE BIOSIS
ANSWERS '24-26' FROM FILE AGRICOLA



We create chemistry

Report No: 20-RSCT0209
Summary of the Literature Review for GHB614 cotton
October 1, 2019 – September 30, 2020
Page 35 of 35

ANSWERS '27-37' FROM FILE CABA
ANSWERS '38-48' FROM FILE HCAPLUS