Title

**Summary of the Literature Review for GHB614 Cotton**
**October 1, 2018 – September 30, 2019**

**Final Report**

Data or Guideline Requirement

Explanatory note on literature searching
conducted in the context of GMO applications for (renewed) market authorization
and annual post-market environmental monitoring reports on GMOs authorised in the EU market.
EFSA supporting publications 2019:EN-1614

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**SIGNATURE PAGE**

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BASF Agricultural Solutions GmbH

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| **Electronic database search** | [redacted] |
| **Manual search** | [redacted] |
| **Stage 1 assessment** | [redacted] |
| **Stage 2 assessment** | Food and Feed safety<br>[redacted]<br>Molecular characterization<br>[redacted]<br>Environmental safety<br>[redacted] |
| **Report** | [redacted] |

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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.

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, 2018 to September 30, 2019. 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 67 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. A total of 15 publications were progressed for detailed assessment.

One of the 15 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.

In summary, these literature searches and review of the retrieved publications identified only one relevant publication that supports the existing safety assessment of the 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-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, 2018 and September 30, 2019 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 note[1].

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

**Key elements:**

**P**opulation: Human health; animal health; environmental safety
**E**xposure: GHB614 cotton, derived food/feed products, newly expressed protein in GHB614 cotton
**C**omparators: 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
**O**utcome: Adverse effects

**Question 2:** Were any studies published during the reporting period that focus on molecular characterization the of GHB614 cotton and its newly expressed protein 2mEPSPS in cotton?

**Key elements:**

**P**opulation: GHB614 cotton and newly expressed protein in GHB614 cotton
**O**utcome: Molecular characterization (which would indicate the information/data requirement for molecular characteristics)

### 2.3. Criteria for relevance

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

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

| Concepts | Criteria | Comment |
|---|---|---|
| Key elements of review questions with PECO structure | | |
| 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 |

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

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

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

### 2.4. Reference publication

One publication related to GHB614 cotton was previously identified and was 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

## 3. SEARCH METHODS AND OUTCOMES

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

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

### 3.1. Time window and date of the literature search

The database searches were performed on October 17, 2019. Only documents updated between October 1, 2018 and September 30, 2019, 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 additonal 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, 2018 and September 30, 2019 (UP>=20181001 and UP<=20190930), and to non-patent documents (not P/DT). To ensure that documents with indexing errors where two DTs (one eligible and one ineligible) were attached to a single record were not missed, documents with both 'journal' and 'patent' as *document type* were also kept. These putative documents would be identified with (P/DT AND J/DT) in CABA and CAPlus.

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

See Appendix 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-GHOO2-5 OR BCS(W)GHOO2(W)5 OR BCSGHOO2(W)5 or BCS-GHØØ2-5 or BCS(w)GHØØ2(w)5 or BCSGHØØ2-5 | 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 | (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) |

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

| Database | AGRICOLA | BIOSIS | CAB Abstracts | CAPLUS | MEDLINE |
|---|---|---|---|---|---|
| **Database Provider** | STN International | STN International | STN International | STN International | STN International |
| **Coverage** | 1970-present | 1926-present | 1973-present | 1907-present | 1946-present |
| **Date of search** | 17 Oct 2019 | 17 Oct 2019 | 17 Oct 2019 | 17 Oct 2019 | 17 Oct 2019 |
| **Datespan of the search** | 1 Oct 2018 – 30 Sept 2019 | 1 Oct 2018 – 30 Sept 2019 | 1 Oct 2018 – 30 Sept 2019 | 1 Oct 2018 – 30 Sept 2019 | 1 Oct 2018 – 30 Sept 2019 |
| **Latest database update** | 4 Oct 2019 | 16 Oct 2019 | 16 Oct 2019 | 16 Oct 2019 | 16 Oct 2019 |
| **Number of records retrieved** | 10 | 24 | 23 | 27 | 13 |
| **Number of records after duplicate removal** | 6 | 21 | 13 | 14 | 13 |
| **Number of *relevant* records after rapid assessment** | 1 | 3 | 2 | 4 | 5 |

## 4. MANUAL SEARCHES

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

A search of the web pages of 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, 2018 to September 30, 2019) 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. All web pages searched were justified by their recommendation in the EFSA 2019 explanatory note[1]. Search terms consisted of GlyTol or GHB614 or BCS-GH002-5 or 2mEPSPS or Double mutant 5-enolpyruvyl shikimate-3-phosphate synthase enzyme (all searched singly, with no search limits applied).

**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 Environmental Protection Agency (EPA) | https://www.epa.gov/ | Oct 4 2019 | Oct 8 2019 | 0 |
| US Department of Agriculture (USDA) | https://www.usda.gov/ | Oct 8 2019 | Oct 9 2019 | 0 |
| US Food and Drug Administration (FDA) | https://www.fda.gov/ | Oct 9 2019 | Oct 9 2019 | 0 |
| Health Canada | https://www.canada.ca/en/health-canada.html | Oct 7 2019 | Oct 9 2019 | 0 |
| Food Inspection Agency Canada | https://www.canada.ca/en/food-inspection-agency.html | Aug 23 2019 | Oct 9 2019 | 0 |
| Environment and Climate Change Canada | https://www.canada.ca/en/services/environment/weather/climatechange.html | Jul 26 2019 | Oct 9 2019 | 0 |
| Food Standards Australia New Zealand (FSANZ) | http://www.foodstandards.gov.au/Pages/default.aspx | Oct 9 2019 | Oct 9 2019 | 0 |
| Office of the Gene Technology Regulator (OGTR) Australia | http://www.ogtr.gov.au/ | Oct 8 2019 | Oct 9 2019 | 0 |
| National Technical Commission on Biosafety (CTNBio) Brazil | http://ctnbio.mcti.gov.br/en | Sep 19 | Oct 7-21 2019 | 0 |
| National Advisory Commission on Agricultural Biotechnology (CONABIA) Argentina | https://www.argentina.gob.ar/agroindustria/bioeconomia/biotecnologia | Oct 1 2019 | Oct 2 2019 | 0 |
| National Food Safety and Quality Service (SENASA) Argentina | https://www.argentina.gob.ar/senasa | Oct 2 2019 | Oct 2 2019 | 0 |
| Genetic Engineering Approval Committee (GEAC) India | http://moef.gov.in/ | Sep 30 2019 | Oct 9 2019 | 0 |
| Ministry of Agriculture, Forestry and Fisheries (MAFF) Japan | http://www.maff.go.jp/ | Oct 30 2019 | Oct 30 2019 | 0 |

| Source Site Name | Website URL | Date of Most Recent Site Update | Date of Search | No. of Relevant Records |
|---|---|---|---|---|
| Ministry of Health, Labour and Welfare (MHLW) Japan | http://www.mhlw.go.jp/ | Oct 30 2019 | Oct 30 2019 | 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, 2018 and September 30, 2019. 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 | Agapito-Tenfen SZ, Okoli AS, Bernstein MJ, Wikmark OG, Myhr AI. 2018 | Revisiting Risk Governance of GM Plants: The Need to Consider New and Emerging Gene-Editing Techniques. | Front Plant Sci. 2018 Dec 21;9:1874. doi: 10.3389/fpls.2018.01874. | 0 |
| 2 | Alarcon CM, Shan G, Layton DT, Bell TA, Whipkey S, Shillito RD. 2019 | Application of DNA- and Protein-Based Detection Methods in Agricultural Biotechnology. | J Agric Food Chem. 2019 Jan 30;67(4):1019-1028. doi: 10.1021/acs.jafc.8b05157. | 0 |
| 3 | Bogner A, Torgersen H. 2018 | Precaution, Responsible Innovation and Beyond - In Search of a Sustainable Agricultural Biotechnology Policy. | Front Plant Sci. 2018 Dec 18;9:1884. doi: 10.3389/fpls.2018.01884. | 0 |
| 4 | Boonchaisri S, Rochfort S, Stevenson T, Dias DA. 2019 | Recent developments in metabolomics-based research in understanding transgenic grass metabolism. | Metabolomics. 2019 Mar 15;15(4):47. doi: 10.1007/s11306-019-1507-4. | 0 |
| 5 | Collins C, Lorenzen N, Collet B. 2019 | DNA vaccination for finfish aquaculture. | Fish Shellfish Immunol. 2019 Feb;85:106-125. doi: 10.1016/j.fsi.2018.07.012. | 0 |

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|---|---|---|---|---|
| 6 | Gaffar FY, Koch A.<br>2019 | Catch Me If You Can! RNA Silencing-Based Improvement of Antiviral Plant Immunity. | Viruses. 2019 Jul 23;11(7). pii: E673. doi: 10.3390/v11070673. | 0 |
| 7 | Ghosh S, Ghosh S, Sil PC.<br>2019 | Role of nanostructures in improvising oral medicine. | Toxicol Rep. 2019 Apr 15;6:358-368. doi: 10.1016/j.toxrep.2019.04.004. | 0 |
| 8 | Halford NG.<br>2019 | Legislation governing genetically modified and genome-edited crops in Europe: the need for change. | J Sci Food Agric. 2019 Jan 15;99(1):8-12. doi: 10.1002/jsfa.9227. | 0 |
| 9 | Hamburger DJS.<br>2018 | Normative Criteria and Their Inclusion in a Regulatory Framework for New Plant Varieties Derived From Genome Editing. | Front Bioeng Biotechnol. 2018 Dec 19;6:176. doi: 10.3389/fbioe.2018.00176. | 0 |
| 10 | Hundleby PAC, Harwood WA.<br>2019 | Impacts of the EU GMO regulatory framework for plant genome editing. | Food Energy Secur. 2019 May;8(2):e00161. doi: 10.1002/fes3.161. | 0 |
| 11 | Ichim MC.<br>2019 | The Romanian experience and perspective on the commercial cultivation of genetically modified crops in Europe. | Transgenic Res. 2019 Feb;28(1):1-7. doi: 10.1007/s11248-018-0095-9. | 0 |
| 12 | Ishaq N, Bilal M, Iqbal HMN.<br>2019 | Medicinal Potentialities of Plant Defensins: A Review with Applied Perspectives. | Medicines (Basel). 2019 Feb 19;6(1). pii: E29. doi: 10.3390/medicines6010029. | 0 |
| 13 | Jyoti A, Kaushik S, Srivastava VK, Datta M, Kumar S, Yugandhar P, Kothari SL, Rai V, Jain A.<br>2019 | The potential application of genome editing by using CRISPR/Cas9, and its engineered and ortholog variants for studying the transcription factors involved in the maintenance of phosphate homeostasis in model plants. | Semin Cell Dev Biol. 2019 Apr 6. pii: S1084-9521(18)30112-5. doi: 10.1016/j.semcdb.2019.03.010. | 0 |
| 14 | Kauffmann F, Van Damme P, Leroux-Roels G, Vandermeulen C, Berthels N, Beuneu C, Mali S.<br>2019 | Clinical trials with GMO-containing vaccines in Europe: Status and regulatory framework. | Vaccine. 2019 Sep 30;37(42):6144-6153. doi: 10.1016/j.vaccine.2019.08.018. | 0 |

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|---|---|---|---|---|
| 15 | Looi FY, Baker ML, Townson T, Richard M, Novak B, Doran TJ, Short KR. 2018 | Creating Disease Resistant Chickens: A Viable Solution to Avian Influenza? | Viruses. 2018 Oct 15;10(10). pii: E561. doi: 10.3390/v10100561. | 0 |
| 16 | Mat Jalaluddin NS, Othman RY, Harikrishna JA. 2019 | Global trends in research and commercialization of exogenous and endogenous RNAi technologies for crops. | Crit Rev Biotechnol. 2019 Feb;39(1):67-78. doi: 10.1080/07388551.2018.1496064. | 0 |
| 17 | Napier JA, Haslam RP, Tsalavouta M, Sayanova O. 2019 | The challenges of delivering genetically modified crops with nutritional enhancement traits. | Nat Plants. 2019 Jun;5(6):563-567. doi: 10.1038/s41477-019-0430-z. | 0 |
| 18 | Rostoks N, Grantiņa-Ieviņa L, Ieviņa B, Evelone V, Valciņa O, Aleksejeva I. 2019 | Genetically modified seeds and plant propagating material in Europe: potential routes of entrance and current status. | Heliyon. 2019 Feb 15;5(2):e01242. doi: 10.1016/j.heliyon.2019.e01242. | 0 |
| 19 | Tyczewska A, Wozniak E, Gracz J, Kuczynski J, Twardowski T. 2018 | Towards Food Security: Current State and Future Prospects of Agrobiotechnology. | Trends Biotechnol. 2018 Dec;36(12):1219-1229. doi: 10.1016/j.tibtech.2018.07.008. | 0 |
| 20 | Wolt JD, Wolf C. 2018 | Policy and Governance Perspectives for Regulation of Genome Edited Crops in the United States. | Front Plant Sci. 2018 Nov 8;9:1606. doi: 10.3389/fpls.2018.01606. | 0 |
| 21 | Wu Y, Li J, Li X, Zhai S, Gao H, Li Y, Zhang X, Wu G. 2019 | Development and strategy of reference materials for the DNA-based detection of genetically modified organisms. | Anal Bioanal Chem. 2019 Mar;411(9):1729-1744. doi: 10.1007/s00216-019-01576-w. | 0 |
| 22 | Zimny T, Sowa S, Tyczewska A, Twardowski T. 2019 | Certain new plant breeding techniques and their marketability in the context of EU GMO legislation - recent developments. | N Biotechnol. 2019 Jul 25;51:49-56. doi: 10.1016/j.nbt.2019.02.003. | 0 |

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

The database searches (Section 3) identified a total of 97 references, which were reduced to 67 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.

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 note[1] and reported in Table 11) was dependent upon the following:

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

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

**Table 6: Results of the publication selection process**

| | |
|---|---|
| Total number of publications retrieved after all searches of the scientific literature (excluding duplicates) | 67 |
| Number of publications excluded from the search results after rapid assessment for relevance (Stage 1) | 52 |
| Total number of full-text documents assessed in detail | 15 |
| Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2) | 14 |
| Total number of unobtainable/unclear publications | 0 |
| Total number of relevant publications | 1 |

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) and year) | Title | Source |
|---|---|---|---|
| Molecular Charaterization | Wu A-J, Sathischandra S, Massengill J, Araujo R, Soria M, Bugas M, Bishop Z, Haas C, Cisneros K, Lor J, Canez C, New S, Mackie S, Ghoshal D, Privalle L, Hunst P, Chapman K, Holliday B, Pallett. 2019 | GHB614 x T304-40 x GHB119 x COT102 Cotton: Protein Expression Analyses of Field-Grown Samples. | Journal of agricultural and food chemistry, (2019 Jan 09) Vol. 67, No. 1, pp. 275-281. Electronic Publication Date: 19 Dec 2018 Journal code: 0374755. E-ISSN: 1520-5118. L-ISSN: 0021-8561. |

**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 |
|---|---|---|---|
| Barroso PAV, Suassuna ND, Pedrosa MB, Morello CdL, Filho JLDS, Lamas FM, Bogiani JC.<br>2017 | BRS 368RF: a glyphosate tolerant , midseason upland cotton cultivar for Northeast and North Brazilian cerrado | CBAB, Crop Breeding and Applied Biotechnology (2017 ), 17(4), 399-402 CODEN: CCBAA9; ISSN: 1984-7033 | The study is related to MON88913 cotton and not about GHB614 cotton. |

| Study (Author(s) and year) | Title | Source | Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1 |
|---|---|---|---|
| Garcia-Ruiz E, Loureiro I, Farinos GP, Gomez P, Gutierrez E, Sanchez FJ, Escorial MC, Ortego F, Chueca MC, Castanera P.<br>2018 | Weeds and ground-dwelling predators' response to two different weed management systems in glyphosate - tolerant cotton : A farmscale study | PLoS One (2018 ), 13(1), e0191408/1-e0191408/18 CODEN: POLNCL; ISSN: 1932-6203 | Assessed two regimes of weed control with herbicides in a 3-year farm-scale study with the GHB614 cotton. No significant differences were obtained between conventional and glyphosate herbicide regimes.<br>The publication can be excluded since it does not include a non-GM line as comparator and is related to crop protection. |
| Gottula J, Chapman K, Gao Y, Gillikin N, Beale J, Dharmasri C, Privalle L.<br>2018 | Molecular biology and physiology. Agronomic performance and crop composition of genetically engineered cotton tolerant to HPPD inhibiting herbicides | Journal of Cotton Science (2018 ), 22(1), 75-85 CODEN: JCOSF6; ISSN: 1524-3303 URL: http://www.cotton.org/journal/index.cfm | The study is related to a different product (not about GHB614 cotton). The cotton studied contains an additional gene, HPPD. |
| Hernandez-Teran A, Wegier A, Benitez M, Lira R, Sosa Fuentes TG, Escalante AE [Reprint Author].<br>2019 | In vitro performance in cotton plants with different genetic backgrounds: the case of Gossypium hirsutum in Mexico, and its implications for germplasm conservation. | PeerJ, (JUN 10 2019 ) Vol. 7, pp. Article No.: e7017. https://peerj.com/. ISSN: 2167-8359. E-ISSN: 2167-8359. | Evaluated and compared in vitro performance of wild and domesticated cotton populations in Mexico. No Environmental Risk Assessment (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 |
|---|---|---|---|
| Liang, Chengzhen; Sun, Bao; Meng, Zhigang; Meng, Zhaohong; Wang, Yuan; Sun, Guoqing; Zhu, Tao; Lu, Wei; Zhang, Wei; Malik, Waqas; Lin, Min [Reprint Author]; Zhang, Rui [Reprint Author]; Guo, Sandui [Reprint Author].<br>2017 | Co-expression of GR79 EPSPS and GAT yields herbicide -resistant cotton with low glyphosate residues. | Plant Biotechnology Journal, (DEC 2017 ) Vol. 15, No. 12, pp. 1622-1629. http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1467-7652. ISSN: 1467-7644. E-ISSN: 1467-7652. | The study is related to a different cotton product (not about GHB614 cotton). The product studied contains an additional gene, GAT. |
| Mei, Lei; Feng, Chao; Zhao, Tianlun; Li, Cheng; Yan, Shufeng; Li, Cong; Feng, Jiyu; Zhang, Fan; Zhang, Yi; Xiao, Qinzhi; He, Qiuling; Chen, Jinhong; Zhu, Shuijin.<br>2019 | Characterizations of male sterility in a glyphosate -tolerant upland cotton (Gossypium hirsutum L.) induced by glyphosate and its assessments on safety utilization | Industrial crops and products (2019), Volume 134, pp. 318-327 ISSN: 0926-6690 Published by: Elsevier B.V. Source Note: 2019 Aug., v. 134 | Assessed the effect of glyphosate on the male sterility in a glyphosate tolerant cotton GRR (GRR8321 or G6-1) line (expressing G6-EPSPS mRNA) by evaluating morphological phenotype, microsporogenesis, expressing pattern of exogenous G6-EPSPS mRNA, and antioxidant enzymes response. It can be excluded since it adresses a benefit of using glyphosate tolerant cotton to obtain hybrid seeds also being related to crop protection (not relevant to the GMO risk assessment). |

| Study (Author(s) and year) | Title | Source | Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1 |
|---|---|---|---|
| Naegeli H, Birch AN, Casacuberta J, de Schrijver A, Gralak M A, Guerche P, Jones H, Manachini B, Messean A, Nielsen EE, Nogue F, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal JM, Ardizzone M, Fernandez-Dumont A, Gennaro A, Ruiz J A G, Lanzoni A, Neri F M, Papadopoulou N, Paraskevopoulos K.<br>2018 | 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). | EFSA Journal (2018), Volume 16, Number 7, e05349 p., 35 refs. ISSN: 1831-4732 DOI: 10.2903/j.efsa.2018.5349 Published by: Wiley, Oxford | The publication was excluded since it does not present original/primary data. In addition, report is on a stacked product involving GHB614 cotton and not on GHB614 cotton itself. |
| Naegeli H, Birch AN, Casacuberta J, de Schrijver A, Gralak M A, Guerche P, Jones H, Manachini B, Messean A, Nielsen EE, Nogue F, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal JM, Broll H, Gennaro A, Neri F M, Paraskevopoulos K.<br>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 (2018), Volume 16, Number 4, e05213 p., many ref. ISSN: 1831-4732 DOI: 10.2903/j.efsa.2018.5213 Published by: Wiley, Oxford | The publication was excluded since it does not present original/primary data. In addition, report is on a stacked product involving GHB614 cotton and not on GHB614 cotton itself. |

| Study (Author(s) and year) | Title | Source | Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1 |
|---|---|---|---|
| Ricroch A [Reprint Author], Akkoyunlu S, Martin-Laffon J, Kuntz M.<br>2018 | Assessing the Environmental Safety of Transgenic Plants: Honey Bees as a Case Study. | Kuntz, M [Editor]. Adv. Bot. Res., (2018 ) pp. 111-167. Transgenic Plants and Beyond. Publisher: ACADEMIC PRESS LTD-ELSEVIER SCIENCE LTD, 24-28 OVAL ROAD, LONDON NW1 7DX, UK. Series: Advances in Botanical Research. CODEN: ABTRAJ. ISSN: 0065-2296. ISBN: 978-0-12-809447-1(P). | Review on the impact of insecticidal and herbicidal trait on the health of honey bees. Not original research and no ERA related to GHB614 cotton. |
| Salisu Ibrahim Bala; Shahid Ahmad Ali; Yaqoob Amina; Rao Abdul Qayyum; Husnain Tayyab.<br>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 Jan) Vol. 103, No. 1, pp. 305-316. Electronic Publication Date: 29 Oct 2018 Journal code: 101126979. E-ISSN: 1439-0396. L-ISSN: 0931-2439. | Study is not specific to the GHB614 cotton. It involves expression of other proteins. |
| Thornby D, Werth J, Keenan M, Hereward J, Chauhan Bhagirath S.<br>2018 | Herbicide resistance evolution can be tamed by diversity in irrigated Australian cotton : a multi-species, multi-herbicide modelling approach. | Pest management science, (2018 Oct) Vol. 74, No. 10, pp. 2363-2375. Electronic Publication Date: 6 Apr 2018 Journal code: 100898744. E-ISSN: 1526-4998. L-ISSN: 1526-498X. | It presents prediction models for some weeds evolution resistance to herbicides in AU considering the adoption of different HT GM cotton stacks. Can be excluded, since it is not necessarily relevant to the risk assessment of GMOs. |

| Study (Author(s) and year) | Title | Source | Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1 |
|---|---|---|---|
| Torres A, Reyes-Perez JJ, Marquez-Hernandez C, Estrada-Arellano J, Esparza-Rivera JR, Preciado-Rangel P, Murillo-Amador B.<br>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.notulaebotanicae.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. The study is not related to cotton event GHB614 and its expressed protein 2mEPSPS. |
| Verkest A, Bourout S, Debaveye J, Reynaert K, Saey B, den Brande I, Van D'Halluin K.<br>2019 | Impact of differential DNA methylation on transgene expression in cotton (Gossypium hirsutum L.) events generated by targeted sequence insertion. | Plant biotechnology journal, (2019 Jul) 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 is about different events that are molecularly stacked to combine multiple genes by insertion of additional trait gene(s) at a pre-existing trangenic locus. The study is not related to GHB614 cotton. |
| Xiaoping P.<br>2019 | Determining Pollen-Mediated Gene Flow in Transgenic Cotton . | Methods in molecular biology (Clifton, N.J.), (2019) Vol. 1902, pp. 309-321. Journal code: 9214969. E-ISSN: 1940-6029. L-ISSN: 1064-3745. | Evaluated the extent of gene flow for GM cotton (NewCott 33B and TFD) in field. No ERA related to 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 15 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 molecular charaterization of the GHB614 cotton and its newly expressed protein 2mEPSPS.

In the publication identified as relevant, Wu *et al.* 2018, protein expression level and pattern were compared between the single parent events including GHB614 and the stack events created by conventional breeding. The data and knowledge generated from this study does not impact on safety assessment of GHB614.

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

**Table 10: Report of the summary 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) | Intervention/ test materials used | Adverse effects reported | Which adverse effect reported |
|---|---|---|---|---|
| Molecular Charaterization | Wu A-J, Sathischandra S, Massengill J, Araujo R, Soria M, Bugas M, Bishop Z, Haas C, Cisneros K, Lor J, Canez C, New S, Mackie S, Ghoshal D, Privalle L, Hunst P, Chapman K, Holliday B, Pallett. 2019 | 2mEPSPS | None | Not applicable |

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

| Main category of information/data requirement | Study (Author(s) and year) | Summary of reliability appraisal | Implications for risk assessment |
|---|---|---|---|
| Molecular Charaterization | Wu A-J, Sathischandra S, Massengill J, Araujo R, Soria M, Bugas M, Bishop Z, Haas C, Cisneros K, Lor J, Canez C, New S, Mackie S, Ghoshal D, Privalle L, Hunst P, Chapman K, Holliday B, Pallett. 2019 | Moderate | None, because no new hazards, modified exposure, or scientific uncertainties are reported. |

## 7. CONCLUSION

The literature searches performed for the GHB614 cotton and its newly expressed protein 2mEPSPS for the period from October 1, 2018 to September 30, 2019, identified a total of 67 unique publications (after duplicate removal). A total of 15 publications were progressed for detailed assessment after excluding 52 obviously irrelevant publications during Stage 1 evaluation (rapid assessment based on title and abstract).

The 15 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 molecular characterization was identified. The data and knowledge generated from this study does not impact the safety assessment of GHB614. 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 | 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.<br><br>The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. Bibliographic information, abstracts, geographic terms, controlled terms, and supplementary terms are searchable. |
| STN | BIOSIS | BIOSIS Previews® is the largest and most comprehensive life science database in the world. Amongst others subject coverage includes Agriculture, Biochemistry, Biophysics, Botany, Environmental Biology, Physiology, Toxicology.<br><br>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.<br><br>Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are all searchable. |
| STN | CABA/CAB | The CAB Abstracts database covers worldwide literature from all areas of agriculture and related sciences including Agriculture, Agricultural chemicals, Animal sciences and production, Crop protection, Crop sciences and production, Environment, Soils and fertilizers.<br><br>Sources for CABA include journals, books, reports, published theses, conference proceedings, and patents.<br><br>Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are searchable. |
| STN | CAS-CA/CAPLUS | The Chemical Abstracts (CA) database covers all areas of Biochemistry, Chemistry and Chemical engineering, and related sciences.<br><br>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.<br><br>Bibliographic terms, indexing terms, roles, CAS Registry Numbers, International Patent Classification, and abstracts are searchable. |

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

## Appendix 2 Search history

```
     FILE 'MEDLINE' ENTERED AT 13:43:22 ON 17 OCT 2019
L1            1 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-GHOO2-5 OR BCS(W)GHOO2(W
                )5 OR BCSGHOO2(W)5 OR BCS-GHØØ2-5 OR BCS(W)GHØØ2(W)5 OR
                BCSGHØØ2-5
L2            0 SEA GLYTOL OR GLYTOLTM OR GLYTOLRTM OR GLY(W)TOL OR GLY(W)TOLTM
                 OR GLY(W)TOLRTM
L3            9 SEA 2MEPSPS OR 2(W)MEPSPS OR 2M(W)EPSPS OR 2(W)M(W)EPSPS
L4         4071 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          341 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L7          441 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L8        22765 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L9           14 SEA L3 OR (((L4 OR L5 OR L6 OR L7))(S)L8)
L10        2934 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       23545 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L12     3440689 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         110 SEA L10 AND L11 AND L12
L14         123 SEA L1 OR L2 OR L9 OR L13
L15          29 SEA L14 AND PY>=2017
L16          13 SEA L15 AND UP>=20181001 AND UP<=20190930

     FILE 'BIOSIS' ENTERED AT 13:43:54 ON 17 OCT 2019
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-GHOO2-5 OR BCS(W)GHOO2(W
                )5 OR BCSGHOO2(W)5 OR BCS-GHØØ2-5 OR BCS(W)GHØØ2(W)5 OR
                BCSGHØØ2-5
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        4862 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         649 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       25423 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L25          17 SEA L19 OR (((L20 OR L21 OR L22 OR L23))(S)L24)
L26       10026 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       70275 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L28      428965 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         264 SEA L26 AND L27 AND L28
L30         283 SEA L17 OR L18 OR L25 OR L29
L31          40 SEA L30 AND PY>=2017
L32          24 SEA L31 AND UP>=20181001 AND UP<=20190930

     FILE 'AGRICOLA' ENTERED AT 13:44:23 ON 17 OCT 2019
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-GHOO2-5 OR BCS(W)GHOO2(W
                )5 OR BCSGHOO2(W)5 OR BCS-GHØØ2-5 OR BCS(W)GHØØ2(W)5 OR
                BCSGHØØ2-5
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         559 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         270 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L39         179 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L40        5858 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L41           6 SEA L35 OR (((L36 OR L37 OR L38 OR L39))(S)L40)
L42        7709 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       59357 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L44       90274 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         218 SEA L42 AND L43 AND L44
L46         225 SEA L33 OR L34 OR L41 OR L45
L47          18 SEA L46 AND PY>=2017
L48          10 SEA L47 AND UP>=20181001 AND UP<=20190930

     FILE 'CABA' ENTERED AT 13:44:54 ON 17 OCT 2019
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-GHOO2-5 OR BCS(W)GHOO2(W
                )5 OR BCSGHOO2(W)5 OR BCS-GHØØ2-5 OR BCS(W)GHØØ2(W)5 OR
                BCSGHØØ2-5
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         943 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         372 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L55         141 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
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                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L56          6636 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L57            16 SEA L51 OR (((L52 OR L53 OR L54 OR L55))(S)L56)
L58         17269 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         89132 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L60        166048 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          493 SEA L58 AND L59 AND L60
L62          511 SEA L49 OR L50 OR L57 OR L61
L63           55 SEA L62 AND PY>=2017
L64           23 SEA L63 AND UP>=20181001 AND UP<=20190930
L65           23 SEA L64 NOT P/DT
L66            0 SEA L64 AND (P/DT AND J/DT)
L67           23 SEA L65 OR L66

     FILE 'HCAPLUS' ENTERED AT 13:45:30 ON 17 OCT 2019
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-GHOO2-5 OR BCS(W)GHOO2(W
                )5 OR BCSGHOO2(W)5 OR BCS-GHØØ2-5 OR BCS(W)GHØØ2(W)5 OR
                BCSGHØØ2-5
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         4121 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         1005 SEA (ENOL(W)PYRUVOYLSHIKIMATE OR ENOLPYRUVYLSHIKIMATE OR
                ENOLPYRUVYLSHIKIMIC OR ENOL(W)(PYRUVYL OR PYRUVOYL)(W)SHIKIMATE
                )(3W)PHOSPHATE(W)(SYNTHASE OR SYNTHETASE)
L74           79 SEA (PHOSPHOSHIKIMATE(2W)CARBOXYVINYLTRANSFERASE OR PHOSPHOSHIK
                IMATE(2W)CARBOXYVINYL(W)TRANSFERASE OR ENOLPYRUVOYL(W)SHIKIMIC(
                3W)PHOSPHOSYNTHASE)
L75         71804 SEA ((DOUBL# OR DOBL#)(W)(MUTANT# OR MUTAT?) OR 2M)
L76           39 SEA L70 OR (((L71 OR L72 OR L73 OR L74))(S)L75)
L77         25803 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        236178 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM
L79        636059 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         1274 SEA L77 AND L78 AND L79
L81         1313 SEA L68 OR L69 OR L76 OR L80
L82          509 SEA L81 AND PY>=2017
L83           92 SEA L82 AND UP>=20181001 AND UP<=20190930
L84           27 SEA L83 NOT P/DT
L85            0 SEA L83 AND (P/DT AND J/DT)
L86           27 SEA L84 OR L85

     FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 13:46:10 ON 17
     OCT 2019
L87           67 DUP REM L16 L32 L48 L67 L86 (30 DUPLICATES REMOVED)
                     ANSWERS '1-13' FROM FILE MEDLINE
                     ANSWERS '14-34' FROM FILE BIOSIS
                     ANSWERS '35-40' FROM FILE AGRICOLA
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ANSWERS '41-53' FROM FILE CABA
ANSWERS '54-67' FROM FILE HCAPLUS
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