Title

Summary of the Literature Review for T304-40 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.
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Stage 2 assessment	Food and Feed safety [redacted] Molecular characterization [redacted] Environmental safety [redacted]
Report	[redacted]

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The T304-40 cotton event produces the *Bacillus thuringiensis* subsp. *berliner* Cry1Ab protein that is effective in controlling lepidopteran larvae such as cotton bollworm and tobacco budworm. T304-40 cotton also expresses the herbicide tolerant inert ingredient phosphinothricin acetyl transferase (PAT/*bar*) as a selectable marker which confers tolerance to glufosinate-ammonium herbicides. The OECD identifier is BCS-GHØØ4-7.

A scoping review was performed for the T304-40 cotton and its newly expressed proteins, Cry1Ab and PAT/*bar*. The objective of this scoping review was to determine if there were studies about the molecular characterization of T304-40 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 219 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. A total of 11 publications were progressed for detailed assessment.

One of the 11 publications was determined to be relevant after detailed review. The relevant article did not constitute new data on molecular characterization of T304-40 cotton, or the Cry1Ab and PAT/*bar* proteins, nor did it suggest any potential adverse effects on human and animal health or on the environment. No evidence was identified that would warrant conducting a systematic review.

In summary, these literature searches and review of the retrieved articles identified only one relevant publication that supports the existing safety assessment of T304-40 cotton.

1. INTRODUCTION

The T304-40 cotton event produces the *Bacillus thuringiensis* subsp. *berliner* Cry1Ab protein that is effective in controlling lepidopteran larvae such as cotton bollworm and tobacco budworm. T304-40 cotton also expresses the herbicide tolerant inert ingredient phosphinothricin acetyl transferase (PAT/*bar*) as a selectable marker which confers tolerance to glufosinate-ammonium herbicides. The OECD identifier is BCS-GHØØ4-7.

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 T304-40 cotton, and/or any adverse effect of T304-40 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 T304-40 cotton and its newly expressed proteins Cry1Ab and PAT/*bar*. 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 T304-40 cotton and its newly expressed proteins Cry1Ab and PAT/*bar*, 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 T304-40 cotton and its newly expressed proteins Cry1Ab and PAT/*bar*?

Key elements:

Population: Human health; animal health; environmental safety
Exposure: T304-40 cotton, derived food/feed products, newly expressed proteins in T304-40 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 T304-40 cotton and its newly expressed proteins Cry1Ab and PAT/*bar*?

Key elements:

Population: T304-40 cotton and newly expressed proteins in T304-40 cotton
Outcome: Molecular characterization (which would indicate the information/data requirement for molecular characteristics)

2.3. Criteria for relevance

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

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

Concepts	Criteria	Comment
Key elements of review questions with PECO structure		
Intervention/exposure	The publication addresses the GMO, derived food/feed products, and/or the intended trait(s) (e.g., newly expressed proteins(s)) that are identical or like those under regulatory review	This enables the selection of publications that address the GMO, derived food/feed products, and/or the intended trait(s) under consideration
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 T304-40 cotton was previously identified and 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 Agriculture and Food Chemistry 67(1):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 22, 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, newly expressed proteins and intended traits. The search profile for T304-40 cotton did not include “Trade name”, because there is no trade name available for this product. Since the two ‘newly expressed proteins’ profiles and the two ‘intended trait’ profiles produced too many results when used on their own, they were combined with additonal profiles: the two ‘newly expressed proteins’ profiles were combined with a ‘plant species’ profile while the two ‘intended trait’ profiles were combined with 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	T304-40 or T304(w)40 or T(w)304(w)40 or BCS-GHØØ4-7 or BCS-GH004-7 or BCS-GHOO4-7 or BCS(w)GHØØ4(w)7 or BCS(w)GH004(w)7 or BCS(w)GHOO4(w)7 or BCSGHØØ4(w)7 or BCSGH004(w)7 or BCSGHOO4(w)7	Event name
	none	Trade name
2	(((bar or pat)(2a)(gene# or protein# or enzyme#)) or ppt(2w)acetyltransferase or ppt(2w)acetyl(w)transferase or pt(w)n(2w)acetyltransferase or pt(w)n(2w)acetyl(w)transferase or phosphinothricin(w)n(w)acetyltransferase or phosphinothricin(2w)acetyltransferase or phosphinothricin(2w)acetyl(w)transferase or phosphinothricinacetyl(w)transferase) or (cry1ab# or cry(w)1(w)ab# or cry(w)1ab# or cry1(w)ab# or cry1(w)a(w)b# or cry(w)1(w)a(w)b# or cry1a(w)b# or cryIab# or cry(w)I(w)ab# or cry(w)Iab# or cryI(w)ab# or cryI(w)a(w)b# or cry(w)I(w)a(w)b# or cryIa(w)b# or crylab# or cry(w)l(w)ab# or cry(w)lab# or cryl(w)ab# or cryl(w)a(w)b# or cry(w)l(w)a(w)b# or cryla(w)b#)	Newly expressed proteins
3	(herbicid? or bialaphos or basta or glufosinate or gluphosinate or phosphinothricin or liberty? or Insect# OR pest# OR Lepidoptera# OR Noctuidae OR Crambidae OR borer# OR cornborer# OR stalkborer# OR earworm# OR ear(w)worm# OR armyworm# OR army(w)worm# OR cutworm# OR cut(w)worm# OR Ostrinia OR O(w)nubilalis OR Sesamia OR S(w)nonagrioides or Diatraea OR D(w)grandiosella OR D(w)crambidoides OR Helicoverpa OR H(w)zea OR Spodoptera OR S(w)frugiperda OR Papaipema OR P(w)nebris OR Elasmopalpus OR E(w)lignosellus OR D(w)saccharalis OR Striacosta OR S(w)albicosta or Agrotis OR A(w)ipsilon OR S(w)cretica OR Mythimna OR M(w)unipuncta OR ECB OR MCB OR SWCB OR SCSB OR CEW OR FAW OR SCB OR WBC (5a) (resist? OR protect? OR toleran?)	Intended traits
4	cotton# or gossypium or G(w)hirsutum or g(w)barbadense	Plant species
5	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
6	2 and 4	Newly expressed proteins AND Plant species
7	3 and 4 and 5	Intended traits AND Plant species AND GMO general
8	1 or 6 or 7	Event name OR (Newly expressed proteins AND Plant species) OR (Intended traits 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	22 Oct 2019	22 Oct 2019	22Oct 2019	22 Oct 2019	22 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	21 Oct 2019	21 Oct 2019
Number of records retrieved	39	71	86	64	75
Number of records after duplicate removal	19	41	53	31	75
Number of *relevant* records after rapid assessment	0	1	5	1	4

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 T304-40 or BCS-GH004-7 or Cry1Ab or PAT/*bar*, Phosphinothricin in T304-40 cotton (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

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

15	Looi FY, Baker ML, Townson T, Richard M, Novak B, Doran TJ, Short KR. 2018	Creating Disease Resistant Chickens: A Viable Solution to Avian Influenza?	Viruses. 2018 Oct 15;10(10). pii: E561. doi: 10.3390/v10100561.	0
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 335 references, which were reduced to 219 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, other insect 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)	219
Number of publications excluded from the search results after rapid assessment for relevance (Stage 1)	208
Total number of full-text documents assessed in detail	11
Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2)	10
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
Guan ZhengJun; Lu ShunBao; Huo YanLin; Hao HaoYong; Cao JianBin; Wei Wei; Liu Biao; Guan Z J; Lu SB; Huo Y L; Hao HY; Cao JB; Wei W; Liu B. 2018	Effects of Bt crops on non-target insect pests.	Biodiversity Science (2018), Volume 26, Number 6, pp. 636-644, 85 refs. ISSN: 1005-0094 DOI: 10.17520/biods.2017315 Published by: Biodiversity Science, Beijing	Reviewed the characteristics and status of non-target insect pest outbreaks and analyzed the main causes. Also discussed the effects of GM crops on non-target pests over long term. Contained no primary data.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Haller S, Romeis J, Meissle M. 2017	Effects of purified or plant-produced Cry proteins on Drosophila melanogaster (Diptera: Drosophilidae) larvae.	Scientific reports, (20170911) Vol. 7, No. 1, pp. 11172. Electronic Publication Date: 11 Sep 2017 Journal code: 101563288. E-ISSN: 2045-2322. L-ISSN: 2045-2322. Report No.: PMC-PMC5593937.	Evaluated effect of purified or plant-produced Cry proteins from Bollgard II cotton and SmartStax maize on *Drosophila melanogaster* as a surrogate for decomposing *Diptera*. No environmental risk assessment (ERA) related to T304-40 cotton.
Mirzaei S, Dezhsetan S, Tohidfar M. 2018	Stacking of cry1Ab and Chitinase genes in commercial cotton varieties through crossing.	Journal of Agricultural Science and Technology (2018), Volume 20, Number 6, pp. 1259-1268, 33 refs. ISSN: 1680-7073 Published by: Tarbiat Modares University, Tehran	The study was not related to T304-40 cotton.
EFSA Panel on GMOs Naegeli H, Birch AN, Casacuberta J, de Schrijver A, Gralak M A, Jones H, Manachini B, Messean A, Nielsen EE, Nogue F, Robaglia C, Rostoks N, Sweet J, Tebbe C, Visioli F, Wal JM, Poeting A, Alvarez F, Broll H, Ramon M. 2017	Scientific opinion on an application by Monsanto (EFSA-GMO -NL-2013-114) for the placing on the market of a herbicide -tolerant genetically modified cotton MON 88701 for food and feed uses, import and processing under Regulation (EC) No 1829/2003	EFSA Journal (2017), 15(3), n/a CODEN: EJFOA6; ISSN: 1831-4732	This publication was excluded since it does not contain original/primary data. In addition, it is not related to T304-40 cotton.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Naegeli H, Bresson J L, Dalmay T, Dewhurst I C, Epstein M M, Firbank L G, Guerche P, Hejatko J, Moreno F J, Mullins E, Nogue F, Rostoks N, Serrano J J S, Savoini G, Veromann E, Veronesi F, Alvarez F, Ardizzone M, Paraskevopoulos K. 2018	Assessment of genetically modified LLCotton25 for renewal of authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO -RX-010).	EFSA Journal (2018), Volume 16, Number 11, e05473 p., 7 refs. ISSN: 1831-4732 DOI: 10.2903/j.efsa.2018.5473 Published by: Wiley, Oxford	This publication was excluded since it does not contain original/primary data. In addition, report is on LLCotton25 and not related to T304-40 cotton.
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. 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	This publication was excluded since it does not contain original/primary data. In addition, it is on a stacked product involving T304-40 cotton but not on T304-40 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. 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. It does not contain original/primary data.
Xiaoping P. 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 T304-40 cotton.
Xie Ming; Zhang YanJun; Peng DeLiang; Li Qian; Hu XinPing; Zhang ZhaoRong; Xie M; Zhang Y J; Peng D L; Li Q; Hu XP; Zhang Z R. 2017	No significant impact of transgenic Cry1Ab /1Ac cotton on rhizosphere-soil enzyme activities and bacterial communities.	Agronomy Journal (2017), Volume 109, Number 4, pp. 1271-1279 ISSN: 0002-1962 DOI: 10.2134/agronj2016.10.0618 Published by: American Society of Agronomy, Madison	Evaluated the impact of GK12 cotton on soil bacterial communities. No impact was observed.

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Zhang Baolong; Guo Wangzhen; Zhang Tianzhen. 2019	Inheritance of Transgenes in Transgenic Bt Lines Resistance to Helicoverpa armigera in Upland Cotton .	Methods in molecular biology (Clifton, N.J.), (2019) Vol. 1902, pp. 199-210. Journal code: 9214969. E-ISSN: 1940-6029. L-ISSN: 1064-3745.	The study was not related to T304-40 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), it was determined that one publication was relevant for the safety assessment of the T304-40 cotton and its newly expressed proteins Cry1Ab and PAT/*bar*.

In the publication identified as relevant, Wu *et al.* 2018, protein expression level and pattern were compared between the single parent events including T304-40 and the stack events created by conventional breeding. The data and knowledge generated from this study does not impact on safety assessment of T304-40.

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	Cry1Ab, Pat/*bar*	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 T304-40 cotton and its newly expressed proteins, Cry1Ab and PAT/*bar*, for the period from October 1, 2018 to September 30, 2019, identified a total of 219 unique publications (after duplicate removal). A total of 11 publications were progressed for detailed assessment after excluding 208 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. 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 T304-40. 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. The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. Bibliographic information, abstracts, geographic terms, controlled terms, and supplementary terms are searchable.
STN	BIOSIS	BIOSIS Previews® is the largest and most comprehensive life science database in the world. Amongst others subject coverage includes Agriculture, Biochemistry, Biophysics, Botany, Environmental Biology, Physiology, Toxicology. Sources include periodicals, journals, conference proceedings, reviews, reports, patents, and short communications. Nearly 6,000 life source journals, 1,500 international meetings as well as review articles, books, and monographs are reviewed for inclusion. Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are all searchable.
STN	CABA/CAB	The CAB Abstracts database covers worldwide literature from all areas of agriculture and related sciences including Agriculture, Agricultural chemicals, Animal sciences and production, Crop protection, Crop sciences and production, Environment, Soils and fertilizers. Sources for CABA include journals, books, reports, published theses, conference proceedings, and patents. Bibliographic information, indexing terms, abstracts, and CAS Registry Numbers are searchable.
STN	CAS-CA/CAPLUS	The Chemical Abstracts (CA) database covers all areas of Biochemistry, Chemistry and Chemical engineering, and related sciences. Sources include over 8,000 journals, patents from 38 national patent offices and two international patent organizations, technical reports, books, conference proceedings, and dissertations. Electronic only journals and Web preprints are also covered. Bibliographic terms, indexing terms, roles, CAS Registry Numbers, International Patent Classification, and abstracts are searchable.

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

Appendix 2 Search history

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     FILE 'MEDLINE' ENTERED AT 09:57:46 ON 22 OCT 2019
L1             3 SEA T304-40 OR T304(W)40 OR T(W)304(W)40 OR BCS-GHØØ4-7 OR
                  BCS-GH004-7 OR BCS-GHOO4-7 OR BCS(W)GHØØ4(W)7 OR BCS(W)GH004(W)
                  7 OR BCS(W)GHOO4(W)7 OR BCSGHØØ4(W)7 OR BCSGH004(W)7 OR
                  BCSGHOO4(W)7
L2          1321 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
                  PPT(2W)ACETYLTRANSFERASE OR PPT(2W)ACETYL(W)TRANSFERASE OR
                  PT(W)N(2W)ACETYLTRANSFERASE OR PT(W)N(2W)ACETYL(W)TRANSFERASE
L3           194 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                  N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                  ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L4           829 SEA CRY1AB# OR CRY(W)1(W)AB# OR CRY(W)1AB# OR CRY1(W)AB# OR
                  CRY1(W)A(W)B# OR CRY(W)1(W)A(W)B# OR CRY1A(W)B#
L5           114 SEA CRYIAB# OR CRY(W)I(W)AB# OR CRY(W)IAB# OR CRYI(W)AB# OR
                  CRYI(W)A(W)B# OR CRY(W)I(W)A(W)B# OR CRYIA(W)B#
L6            35 SEA CRYLAB# OR CRY(W)L(W)AB# OR CRY(W)LAB# OR CRYL(W)AB# OR
                  CRYL(W)A(W)B# OR CRY(W)L(W)A(W)B# OR CRYLA(W)B#
L7          2344 SEA (L2 OR L3 OR L4 OR L5 OR L6)
L8         27039 SEA HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR GLUPHOSIN
                  ATE OR PHOSPHINOTHRICIN OR LIBERTY?
L9        185565 SEA INSECT# OR PEST# OR LEPIDOPTERA# OR NOCTUIDAE OR CRAMBIDAE
                  OR BORER# OR CORNBORER# OR STALKBORER# OR EARWORM# OR EAR(W)WOR
                  M# OR ARMYWORM# OR ARMY(W)WORM# OR CUTWORM# OR CUT(W)WORM# OR
                  OSTRINIA OR O(W)NUBILALIS OR SESAMIA OR S(W)NONAGRIOIDES
L10        12855 SEA DIATRAEA OR D(W)GRANDIOSELLA OR D(W)CRAMBIDOIDES OR
                  HELICOVERPA OR H(W)ZEA OR SPODOPTERA OR S(W)FRUGIPERDA OR
                  PAPAIPEMA OR P(W)NEBRIS OR ELASMOPALPUS OR E(W)LIGNOSELLUS OR
                  D(W)SACCHARALIS OR STRIACOSTA OR S(W)ALBICOSTA
L11        19429 SEA AGROTIS OR A(W)IPSILON OR S(W)CRETICA OR MYTHIMNA OR
                  M(W)UNIPUNCTA OR ECB OR MCB OR SWCB OR SCSB OR CEW OR FAW OR
                  SCB OR WBC
L12      2107045 SEA (RESIST? OR PROTECT? OR TOLERAN?)
L13         9628 SEA ((L8 OR L9 OR L10 OR L11))(5A)L12
L14        23570 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L15      3442202 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?))
L16           62 SEA L7 AND L14
L17          570 SEA L13 AND L14 AND L15
L18          601 SEA L1 OR L16 OR L17
L19          118 SEA L18 AND PY>=2017
L20           75 SEA L19 AND UP>=20180901 AND UP<=20190930

     FILE 'BIOSIS' ENTERED AT 09:58:40 ON 22 OCT 2019
L21            2 SEA T304-40 OR T304(W)40 OR T(W)304(W)40 OR BCS-GHØØ4-7 OR
                  BCS-GH004-7 OR BCS-GHOO4-7 OR BCS(W)GHØØ4(W)7 OR BCS(W)GH004(W)
                  7 OR BCS(W)GHOO4(W)7 OR BCSGHØØ4(W)7 OR BCSGH004(W)7 OR
                  BCSGHOO4(W)7
L22         2643 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
                  PPT(2W)ACETYLTRANSFERASE OR PPT(2W)ACETYL(W)TRANSFERASE OR
                  PT(W)N(2W)ACETYLTRANSFERASE OR PT(W)N(2W)ACETYL(W)TRANSFERASE
L23          321 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                  N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                  ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L24         1443 SEA CRY1AB# OR CRY(W)1(W)AB# OR CRY(W)1AB# OR CRY1(W)AB# OR
                  CRY1(W)A(W)B# OR CRY(W)1(W)A(W)B# OR CRY1A(W)B#
L25          226 SEA CRYIAB# OR CRY(W)I(W)AB# OR CRY(W)IAB# OR CRYI(W)AB# OR
                  CRYI(W)A(W)B# OR CRY(W)I(W)A(W)B# OR CRYIA(W)B#
L26          259 SEA CRYLAB# OR CRY(W)L(W)AB# OR CRY(W)LAB# OR CRYL(W)AB# OR
                  CRYL(W)A(W)B# OR CRY(W)L(W)A(W)B# OR CRYLA(W)B#
L27         4399 SEA (L22 OR L23 OR L24 OR L25 OR L26)
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L28       83353 SEA HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR GLUPHOSIN
                ATE OR PHOSPHINOTHRICIN OR LIBERTY?
L29     1347934 SEA INSECT# OR PEST# OR LEPIDOPTERA# OR NOCTUIDAE OR CRAMBIDAE
                OR BORER# OR CORNBORER# OR STALKBORER# OR EARWORM# OR EAR(W)WOR
                M# OR ARMYWORM# OR ARMY(W)WORM# OR CUTWORM# OR CUT(W)WORM# OR
                OSTRINIA OR O(W)NUBILALIS OR SESAMIA OR S(W)NONAGRIOIDES
L30       25023 SEA DIATRAEA OR D(W)GRANDIOSELLA OR D(W)CRAMBIDOIDES OR
                HELICOVERPA OR H(W)ZEA OR SPODOPTERA OR S(W)FRUGIPERDA OR
                PAPAIPEMA OR P(W)NEBRIS OR ELASMOPALPUS OR E(W)LIGNOSELLUS OR
                D(W)SACCHARALIS OR STRIACOSTA OR S(W)ALBICOSTA
L31       27576 SEA AGROTIS OR A(W)IPSILON OR S(W)CRETICA OR MYTHIMNA OR
                M(W)UNIPUNCTA OR ECB OR MCB OR SWCB OR SCSB OR CEW OR FAW OR
                SCB OR WBC
L32     2165880 SEA (RESIST? OR PROTECT? OR TOLERAN?)
L33       30787 SEA ((L28 OR L29 OR L30 OR L31))(5A)L32
L34       70275 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L35      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?))
L36         180 SEA L27 AND L34
L37         864 SEA L33 AND L34 AND L35
L38         972 SEA L21 OR L36 OR L37
L39         117 SEA L38 AND PY>=2017
L40          71 SEA L39 AND UP>=20180901 AND UP<=20190930

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L41           1 SEA T304-40 OR T304(W)40 OR T(W)304(W)40 OR BCS-GHØØ4-7 OR
                BCS-GH004-7 OR BCS-GHOO4-7 OR BCS(W)GHØØ4(W)7 OR BCS(W)GH004(W)
                7 OR BCS(W)GHOO4(W)7 OR BCSGHØØ4(W)7 OR BCSGH004(W)7 OR
                BCSGHOO4(W)7
L42         710 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
                PPT(2W)ACETYLTRANSFERASE OR PPT(2W)ACETYL(W)TRANSFERASE OR
                PT(W)N(2W)ACETYLTRANSFERASE OR PT(W)N(2W)ACETYL(W)TRANSFERASE
L43         238 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L44         839 SEA CRY1AB# OR CRY(W)1(W)AB# OR CRY(W)1AB# OR CRY1(W)AB# OR
                CRY1(W)A(W)B# OR CRY(W)1(W)A(W)B# OR CRY1A(W)B#
L45         153 SEA CRYIAB# OR CRY(W)I(W)AB# OR CRY(W)IAB# OR CRYI(W)AB# OR
                CRYI(W)A(W)B# OR CRY(W)I(W)A(W)B# OR CRYIA(W)B#
L46           9 SEA CRYLAB# OR CRY(W)L(W)AB# OR CRY(W)LAB# OR CRYL(W)AB# OR
                CRYL(W)A(W)B# OR CRY(W)L(W)A(W)B# OR CRYLA(W)B#
L47        1762 SEA (L42 OR L43 OR L44 OR L45 OR L46)
L48       52816 SEA HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR GLUPHOSIN
                ATE OR PHOSPHINOTHRICIN OR LIBERTY?
L49      312001 SEA INSECT# OR PEST# OR LEPIDOPTERA# OR NOCTUIDAE OR CRAMBIDAE
                OR BORER# OR CORNBORER# OR STALKBORER# OR EARWORM# OR EAR(W)WOR
                M# OR ARMYWORM# OR ARMY(W)WORM# OR CUTWORM# OR CUT(W)WORM# OR
                OSTRINIA OR O(W)NUBILALIS OR SESAMIA OR S(W)NONAGRIOIDES
L50       12767 SEA DIATRAEA OR D(W)GRANDIOSELLA OR D(W)CRAMBIDOIDES OR
                HELICOVERPA OR H(W)ZEA OR SPODOPTERA OR S(W)FRUGIPERDA OR
                PAPAIPEMA OR P(W)NEBRIS OR ELASMOPALPUS OR E(W)LIGNOSELLUS OR
                D(W)SACCHARALIS OR STRIACOSTA OR S(W)ALBICOSTA
L51        3900 SEA AGROTIS OR A(W)IPSILON OR S(W)CRETICA OR MYTHIMNA OR
                M(W)UNIPUNCTA OR ECB OR MCB OR SWCB OR SCSB OR CEW OR FAW OR
                SCB OR WBC
L52      520326 SEA (RESIST? OR PROTECT? OR TOLERAN?)
L53       27011 SEA ((L48 OR L49 OR L50 OR L51))(5A)L52
L54       59357 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L55       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?))
L56          89 SEA L47 AND L54
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L57          673 SEA L53 AND L54 AND L55
L58          723 SEA L41 OR L56 OR L57
L59           61 SEA L58 AND PY>=2017
L60           39 SEA L59 AND UP>=20180901 AND UP<=20190930

     FILE 'CABA' ENTERED AT 10:01:02 ON 22 OCT 2019
L61            6 SEA T304-40 OR T304(W)40 OR T(W)304(W)40 OR BCS-GHØØ4-7 OR
                   BCS-GH004-7 OR BCS-GHOO4-7 OR BCS(W)GHØØ4(W)7 OR BCS(W)GH004(W)
                   7 OR BCS(W)GHOO4(W)7 OR BCSGHØØ4(W)7 OR BCSGH004(W)7 OR
                   BCSGHOO4(W)7
L62         1437 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
                   PPT(2W)ACETYLTRANSFERASE OR PPT(2W)ACETYL(W)TRANSFERASE OR
                   PT(W)N(2W)ACETYLTRANSFERASE OR PT(W)N(2W)ACETYL(W)TRANSFERASE
L63          364 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                   N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                   ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L64         1573 SEA CRY1AB# OR CRY(W)1(W)AB# OR CRY(W)1AB# OR CRY1(W)AB# OR
                   CRY1(W)A(W)B# OR CRY(W)1(W)A(W)B# OR CRY1A(W)B#
L65          215 SEA CRYIAB# OR CRY(W)I(W)AB# OR CRY(W)IAB# OR CRYI(W)AB# OR
                   CRYI(W)A(W)B# OR CRY(W)I(W)A(W)B# OR CRYIA(W)B#
L66           26 SEA CRYLAB# OR CRY(W)L(W)AB# OR CRY(W)LAB# OR CRYL(W)AB# OR
                   CRYL(W)A(W)B# OR CRY(W)L(W)A(W)B# OR CRYLA(W)B#
L67         3307 SEA (L62 OR L63 OR L64 OR L65 OR L66)
L68       144093 SEA HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR GLUPHOSIN
                   ATE OR PHOSPHINOTHRICIN OR LIBERTY?
L69       851638 SEA INSECT# OR PEST# OR LEPIDOPTERA# OR NOCTUIDAE OR CRAMBIDAE
                   OR BORER# OR CORNBORER# OR STALKBORER# OR EARWORM# OR EAR(W)WOR
                   M# OR ARMYWORM# OR ARMY(W)WORM# OR CUTWORM# OR CUT(W)WORM# OR
                   OSTRINIA OR O(W)NUBILALIS OR SESAMIA OR S(W)NONAGRIOIDES
L70        30278 SEA DIATRAEA OR D(W)GRANDIOSELLA OR D(W)CRAMBIDOIDES OR
                   HELICOVERPA OR H(W)ZEA OR SPODOPTERA OR S(W)FRUGIPERDA OR
                   PAPAIPEMA OR P(W)NEBRIS OR ELASMOPALPUS OR E(W)LIGNOSELLUS OR
                   D(W)SACCHARALIS OR STRIACOSTA OR S(W)ALBICOSTA
L71        11435 SEA AGROTIS OR A(W)IPSILON OR S(W)CRETICA OR MYTHIMNA OR
                   M(W)UNIPUNCTA OR ECB OR MCB OR SWCB OR SCSB OR CEW OR FAW OR
                   SCB OR WBC
L72      1152527 SEA (RESIST? OR PROTECT? OR TOLERAN?)
L73        79815 SEA ((L68 OR L69 OR L70 OR L71))(5A)L72
L74        89132 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L75       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?))
L76          209 SEA L67 AND L74
L77         2048 SEA L73 AND L74 AND L75
L78         2160 SEA L61 OR L76 OR L77
L79          197 SEA L78 AND PY>=2017
L80           86 SEA L79 AND UP>=20180901 AND UP<=20190930
L81           86 SEA L80 NOT P/DT
L82            0 SEA L80 AND (P/DT AND J/DT)
L83           86 SEA L81 OR L82

     FILE 'HCAPLUS' ENTERED AT 10:01:50 ON 22 OCT 2019
L84            5 SEA T304-40 OR T304(W)40 OR T(W)304(W)40 OR BCS-GHØØ4-7 OR
                   BCS-GH004-7 OR BCS-GHOO4-7 OR BCS(W)GHØØ4(W)7 OR BCS(W)GH004(W)
                   7 OR BCS(W)GHOO4(W)7 OR BCSGHØØ4(W)7 OR BCSGH004(W)7 OR
                   BCSGHOO4(W)7
L85         6272 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
                   PPT(2W)ACETYLTRANSFERASE OR PPT(2W)ACETYL(W)TRANSFERASE OR
                   PT(W)N(2W)ACETYLTRANSFERASE OR PT(W)N(2W)ACETYL(W)TRANSFERASE
L86          744 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                   N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                   ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L87         1673 SEA CRY1AB# OR CRY(W)1(W)AB# OR CRY(W)1AB# OR CRY1(W)AB# OR
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                CRY1(W)A(W)B# OR CRY(W)1(W)A(W)B# OR CRY1A(W)B#
L88         1234 SEA CRYIAB# OR CRY(W)I(W)AB# OR CRY(W)IAB# OR CRYI(W)AB# OR
                CRYI(W)A(W)B# OR CRY(W)I(W)A(W)B# OR CRYIA(W)B#
L89           55 SEA CRYLAB# OR CRY(W)L(W)AB# OR CRY(W)LAB# OR CRYL(W)AB# OR
                CRYL(W)A(W)B# OR CRY(W)L(W)A(W)B# OR CRYLA(W)B#
L90         8640 SEA (L85 OR L86 OR L87 OR L88 OR L89)
L91       144807 SEA HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR GLUPHOSIN
                ATE OR PHOSPHINOTHRICIN OR LIBERTY?
L92       275153 SEA INSECT# OR PEST# OR LEPIDOPTERA# OR NOCTUIDAE OR CRAMBIDAE
                OR BORER# OR CORNBORER# OR STALKBORER# OR EARWORM# OR EAR(W)WOR
                M# OR ARMYWORM# OR ARMY(W)WORM# OR CUTWORM# OR CUT(W)WORM# OR
                OSTRINIA OR O(W)NUBILALIS OR SESAMIA OR S(W)NONAGRIOIDES
L93        20729 SEA DIATRAEA OR D(W)GRANDIOSELLA OR D(W)CRAMBIDOIDES OR
                HELICOVERPA OR H(W)ZEA OR SPODOPTERA OR S(W)FRUGIPERDA OR
                PAPAIPEMA OR P(W)NEBRIS OR ELASMOPALPUS OR E(W)LIGNOSELLUS OR
                D(W)SACCHARALIS OR STRIACOSTA OR S(W)ALBICOSTA
L94        19875 SEA AGROTIS OR A(W)IPSILON OR S(W)CRETICA OR MYTHIMNA OR
                M(W)UNIPUNCTA OR ECB OR MCB OR SWCB OR SCSB OR CEW OR FAW OR
                SCB OR WBC
L95      5167344 SEA (RESIST? OR PROTECT? OR TOLERAN?)
L96        49484 SEA ((L91 OR L92 OR L93 OR L94))(5A)L95
L97       236296 SEA COTTON# OR GOSSYPIUM OR G(W)HIRSUTUM OR G(W)BARBADENSE
L98       636311 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?))
L99          454 SEA L90 AND L97
L100        2229 SEA L96 AND L97 AND L98
L101        2449 SEA L84 OR L99 OR L100
L102         742 SEA L101 AND PY>=2017
L103         155 SEA L102 AND UP>=20180901 AND UP<=20190930
L104          64 SEA L103 NOT P/DT
L105           0 SEA L103 AND (P/DT AND J/DT)
L106          64 SEA L104 OR L105

     FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 10:02:36 ON 22
     OCT 2019
L107         219 DUP REM L20 L40 L60 L83 L106 (116 DUPLICATES REMOVED)
                    ANSWERS '1-75' FROM FILE MEDLINE
                    ANSWERS '76-116' FROM FILE BIOSIS
                    ANSWERS '117-135' FROM FILE AGRICOLA
                    ANSWERS '136-188' FROM FILE CABA
                    ANSWERS '189-219' FROM FILE HCAPLUS
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