Title

Summary of the Literature Review for MS8, RF3 and MS8 x RF3 *Brassica napus*
July 1, 2022 – June 30, 2023

Final Report

Data or guideline requirement

Explanatory note on literature searching
conducted in the context of GMO applications for (renewed) market authorization
and annual post-market environmental monitoring reports on GMOs authorised in the EU market.
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MS8 x RF3 *Brassica napus* (*B. napus*) is a stacked trait product generated through conventional breeding of MS8 *B. napus* (OECD identifier ACS-BNØØ5-8) and RF3 *B. napus* (OECD identifier ACS-BNØØ3-6). MS8 *B. napus* (male sterile line) was produced by means of *Agrobacterium*-mediated transformation using vector pTHW107. MS8 *B. napus* contains the *barnase* gene (origin *Bacillus amyloliquefaciens*), coding for the Barnase protein. The *barnase* gene is driven by the Pta29 promoter that restricts gene expression to the tapetal cells during anther development. Expression of Barnase in the tapetal cells of MS8 *B. napus* results in lack of viable pollen and male sterility. MS8 *B. napus* also contains the *bar* gene (origin *Streptomyces hygroscopicus*) coding for phosphinothricin acetyltransferase (PAT/*bar*) conferring tolerance to glufosinate-ammonium. The *bar* gene is driven by the PssuAt plant promoter that is active in all green tissues of the plant. RF3 *B. napus* (fertility restorer line) was produced by means of *Agrobacterium*-mediated transformation using vector pTHW118. RF3 *B. napus* contains the *barstar* gene (origin *Bacillus amyloliquefaciens*), coding for the Barstar protein, which is an inhibitor of the Barnase protein. The *barstar* gene is driven by the Pta29 promoter that restricts gene expression to the tapetal cells during anther development. Expression of the Barstar protein in the tapetal cells leads to restoration of fertility after crossing to a male sterile (MS) *B. napus* line. RF3 *B. napus* also contains the *bar* gene (origin *Streptomyces hygroscopicus*) coding for PAT/*bar* conferring tolerance to glufosinate-ammonium. The *bar* gene is driven by the PssuAt plant promoter that is active in all green tissues of the plant. MS8 x RF3 *B. napus* plants are fully fertile hybrids and express the PAT/*bar* protein which confers tolerance to glufosinate-ammonium. The OECD identifier of MS8 x RF3 *B. napus* is ACS-BNØØ5-8 x ACS-BNØØ3-6.

A scoping review was performed for MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins, PAT/*bar*, Barnase and Barstar. The objective of this scoping review was to determine if there were studies about the molecular characterization of MS8, RF3 and MS8 *x* RF3 *B. napus*, their effect on food and feed or environmental safety, that might require in-depth examination. A set of broad literature searches was performed using several bibliographic databases covering scientific literature from July 1, 2022 until June 30, 2023. Additional sources of information, such as web pages of food safety, agriculture, and biotechnology-related authorities were searched for the same time window, along with the bibliographies of relevant reviews. The references identified were evaluated for potential relevance to the scoping review questions according to pre-defined criteria.

These literature searches identified a total of 782 unique publications, which were subject to rapid assessment to exclude obviously irrelevant publications. A total of three publications were progressed for detailed assessment.

Two of the three publications were determined to be relevant after detailed review. The relevant articles did not constitute new data on molecular characterization of MS8, RF3 and MS8 *x* RF3 *B. napus*, or the PAT/*bar*, Barnase and Barstar proteins, nor did they 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 two relevant publications that support the previous safety assessment of MS8, RF3 and MS8 *x* RF3 *B. napus*.

1. INTRODUCTION

MS8 x RF3 *Brassica napus* (*B. napus*) is a stacked trait product generated through conventional breeding of MS8 *B. napus* (OECD identifier ACS-BNØØ5-8) and RF3 *B. napus* (OECD identifier ACS-BNØØ3-6). MS8 *B. napus* (male sterile line) was produced by means of *Agrobacterium*-mediated transformation using vector pTHW107. MS8 *B. napus* contains the *barnase* gene (origin *Bacillus amyloliquefaciens*), coding for the Barnase protein. The *barnase* gene is driven by the Pta29 promoter that restricts gene expression to the tapetal cells during anther development. Expression of Barnase in the tapetal cells of MS8 *B. napus* results in lack of viable pollen and male sterility. MS8 *B. napus* also contains the *bar* gene (origin *Streptomyces hygroscopicus*) coding for phosphinothricin acetyltransferase (PAT/*bar*) conferring tolerance to glufosinate-ammonium. The *bar* gene is driven by the PssuAt plant promoter that is active in all green tissues of the plant. RF3 *B. napus* (fertility restorer line) was produced by means of *Agrobacterium*-mediated transformation using vector pTHW118. RF3 *B. napus* contains the *barstar* gene (origin *Bacillus amyloliquefaciens*), coding for the Barstar protein, which is an inhibitor of the Barnase protein. The *barstar* gene is driven by the Pta29 promoter that restricts gene expression to the tapetal cells during anther development. Expression of the Barstar protein in the tapetal cells leads to restoration of fertility after crossing to a male sterile (MS) *B. napus* line. RF3 *B. napus* also contains the *bar* gene (origin *Streptomyces hygroscopicus*) coding for PAT/*bar* conferring tolerance to glufosinate-ammonium. The *bar* gene is driven by the PssuAt plant promoter that is active in all green tissues of the plant. MS8 x RF3 *B. napus* plants are fully fertile hybrids and express the PAT/*bar* protein which confers tolerance to glufosinate-ammonium. The OECD identifier of MS8 x RF3 *B. napus* is ACS-BNØØ5-8 x ACS-BNØØ3-6.

The objective of the literature searches described here was to determine if there were publications published between July 1, 2022 and June 30, 2023 that mention the molecular characterization of the MS8, RF3 and MS8 *x* RF3 *B. napus*, and/or any adverse effect of MS8, RF3 and MS8 *x* RF3 *B. napus* related to food and feed safety or the environment. In that context, a broad and inclusive literature search was performed, and the articles retrieved were reviewed in a comprehensive and transparent manner. This was intended as a scoping review. The literature review was performed as recommended in the European Food Safety Authority (EFSA) explanatory note on literature searching conducted in the context of Genetically Modified Organisms (GMO) applications and post-market environmental monitoring activities (2019; (1)).

The literature searches were performed for the MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins, PAT/*bar*, Barnase and Barstar. The search terms also included relevant synonyms, the trade name and intended traits. When needed, plant species and general GMO terms were used to limit the search results (described in section 3.3).

2. OVERALL METHODS

2.1. Objective of the scoping review

The objective of the scoping review was to survey the evidence base for the MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins, PAT/*bar*, Barnase and Barstar, in order to identify any specific issues related to food or feed safety, molecular characterization or environmental safety that might require in-depth examination.

2.2. Review questions

Review questions were formulated to conform to PE(I)CO structure (Population, Exposure (Intervention), Comparators, Outcome) if possible, and to address data requirements. They were modeled after the review question examples provided in the EFSA 2019 explanatory note[1].

Question 1: Were any studies published during the reporting period that describe adverse effects on human or animal health or the environment of the MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins PAT/*bar*, Barnase and Barstar?

Key elements:

Population: Human health; animal health; environmental safety
Exposure: MS8, RF3 and MS8 *x* RF3 *B. napus*, derived food/feed products, newly expressed proteins in MS8, RF3 and MS8 *x* RF3 *B. napus*
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 MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins PAT/*bar*, Barnase and Barstar in *B. napus*?

Key elements:

Population: MS8, RF3 and MS8 *x* RF3 *B. napus* and newly expressed proteins in MS8, RF3 and MS8 *x* RF3 *B. napus*
Outcome: Molecular characterization (which would indicate the information/data requirement for molecular characteristics)

2.3. Criteria for relevance

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

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

Concepts	Criteria	Comment
Key elements of review questions with PECO structure		
Population	The publication addresses human and animal health, and/or the environment (including biodiversity, ecosystem services, service providing units, and endangered species) as general protection goals	From the publications that address the GMO under consideration, those that address protection goals relevant to the risk assessment of the GMO are eligible
Exposure (Intervention)	The publication addresses the GMO, derived food/feed products, and/or the intended trait(s) (e.g., newly expressed proteins(s)) that are identical or like those under regulatory review	This enables the selection of publications that address the GMO, derived food/feed products, and/or the intended trait(s) under consideration

Concepts	**Criteria**	**Comment**
Comparator	If the publication reports a comparative study that uses plant material as test material, eligible publications must report a non-GM variety as comparator	In those cases where the publication addresses the GMO under consideration, reports a comparative analysis study and uses plant material as test material, eligible publications also need to include an appropriate non-GM line as comparator
Outcome	The publication addresses effects/impacts on human and animal health, and/or the environment	Publications that address the GMO under consideration also need to address effects/impacts on entities of concern, and potential determinants of exposure that place these entities at risk, in order to be relevant to the risk assessment of the GMO
Additional concepts		
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

Concepts	Criteria	Comment
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(s), independently of their origin. This permits the exclusion of publications on the single events of the higher stacked event, because the risk assessment of GMO applications for stacked events covers only the products in the scope of the GMO application – i.e., the higher stacked event and subcombinations of the singles involved, independently of their origin
Molecular stacks	The publication addresses: the molecular stack; all newly expressed proteins in the molecular stack; and/or one or several of the newly expressed proteins in the molecular stack that has/have not been previously risk assessed by EFSA and/or its GMO Panel and for which no safe use has been determined yet by EFSA and/or its GMO Panel	This permits the exclusion of publications that address one or several (not all) of the newly expressed proteins in the molecular stack that has/have been previously risk assessed by EFSA and/or its GMO Panel and for which the safe use has been determined by EFSA and/or its GMO Panel

Concepts	Criteria	Comment
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, or it is a risk assessment from a relevant key organisation (such as regulatory agencies and risk assessment bodies involved in the risk assessment of GMOs)	This permits the exclusion of publications that do not present original/primary data (e.g., editorials, position papers), and the inclusion of relevant risk assessments performed and reported by relevant key organisations. Reviews should only be included if they present data that are not available from a primary research study
Reporting format	A study in a publication should only be presented once, but if it is presented in more than one publication, all publications should be listed and grouped	Duplicate publications should be excluded at the screening stage. Only one copy of a study is required even if it is reported in different publications, and identified in more than one database

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

2.4. Reference publication

Two publications were used to validate the search profile:

- Naegeli, H.; Birch, A. N.; Casacuberta, J.; Schrijver, A. de; Gralak, M. A.; Guerche, P.; Jones, H.; Manachini, B.; Messean, A.; Nielsen, E. E.; Nogue, F.; Robaglia, C.; Rostoks, N.; Sweet, J.; Tebbe, C.; Visioli, F.; Wal, J. M.; Ardizzone, M.; Devos, Y.; Paraskevopoulos, K.; de Schrijver, A. (2017) Assessment of genetically modified oilseed rape MS8, RF3 and MS8 x RF3 for renewal of authorisation under regulation (EC) No 1829/2003 (application EFSA-GMO-RX-004). *EFSA Journal* **15(11):**e05067

- Zhang CJ; Yook MJ; Park HR; Lim SH; Kim JW; Nah G; Song HR; Jo BH; Roh KH; Park S; Kim DS (2018). Assessment of potential environmental risks of transgene flow in smallholder farming systems in Asia: *Brassica napus* as a case study in Korea. The Science of the total environment Vol 640-641, pp 688-695

Naegeli *et al* (2017) was selected because it mentions the event names (MS8 x RF3, MS8 and RF3), the crop (oilseed rape) and one of the intended traits (herbicide tolerance). Zhang *et al* (2018) was selected because even though it is not directly relevant for MS8 x RF3 *B. napus* or the single events, it refers to the plant species (*B. napus*) and the specific herbicide tolerance (glufosinate). Since both these articles were published before the current search period, the search profile was tested without applying the time limit used in the final search profile (UP>=20220701 and UP<=20230630).

3. SEARCH METHODS AND OUTCOMES

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

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

3.1. Time window and date of the literature search

The database searches were performed on July 10, 2023. Only documents updated between July 1, 2022 and June 30, 2023, were considered in the search. The dates of the 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. Since the ‘newly expressed proteins’ profiles and the ‘intended trait’ profiles produced too many results when used on their own, they were combined with additonal profiles: the ‘newly expressed proteins’ profiles were combined with a ‘plant species’ profile while the ‘intended trait’ profiles were combined with a ‘general GMO’ profile as well as with the ‘plant species’ profile. The reference publication (Section 2.4) was identified by the search profiles confirming the validity of the applied search strategy. See Table 2 for a detailed search profile.

Table 2: Search profile for database search

Set	Search string	Concepts
1	MS8 or MS8x or MS-8 or MS-8x or ACS(w)BNØØ5-8 or ACS(w)BN005-8 or ACS(w)BNOO5-8 or ACSBNØØ5-8 or ACSBN005-8 or ACSBNOO5-8 or ACS(w)BNØØ5-8x or	Event name MS8

Set	Search string	Concepts
	ACS(w)BN005-8x or ACS(w)BNOO5-8x or ACSBNØØ5-8x or ACSBN005-8x or ACSBNOO5-8x	
2	RF3 or xRF3 or RF-3 or xRF-3 or ACS(w)BNØØ3-6 or ACS(w)BN003-6 or ACS(w)BNOO3-6 or ACSBNØØ3-6 or ACSBN003-6 or ACSBNOO3-6 or xACS(w)BNØØ3-6 or xACS(w)BN003-6 or xACS(w)BNOO3-6 or xACSBNØØ3-6 or xACSBN003-6 or xACSBNOO3-6	Event name RF3
3	MS8XRF3 or MS(w)8XRF-3 or MS8.time#.RF3 or ACS(w)BNØØ5(w)8xACS(w)BNØØ3-6 or ACS(w)BN005(w)8xACS-BN003-6 or ACS(w)BNOO5(w)8xACS(w)BNOO3-6	Event name MS8 x RF3
4	1 or 2 or 3	Event name MS8, RF3, MS8 x RF3
5	invigor or invigorr or invigortm or in(w)vigor or in(w)vigorr or in(w)vigortm or in(w)vigorrtm	Trade name MS8, RF3, MS8 x RF3
6	barnase or RNase(w)Ba or (bacterial(w)RiboNuclease and ((Bacillus or b)(w)amyloliquefaciens)) or P00648 or IPR001887 or barstar or barnase(w)inhibitor or IPR000468 or ((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	Newly expressed proteins MS8, RF3, MS8 x RF3
7	(herbicid? or bialaphos or basta or glufosinate or phosphinothricin or liberty)(5a)(resist? or toleran? or protect?) or male(3a)steril? or (fertil?(3a)restor?) or restor?(w)line or pollination(w)control	Intended traits MS8, RF3, MS8 x RF3
8	((*BRASSICA* or B)(w)(*napus* or juncea)) OR RAPE? or CANOLA# OR OILSEED(w)RAPE OR oil(w)seed(w)rape or colza	Plant species
9	GMO OR GMOs OR LMO OR LMOs OR GM OR GE OR transgen? OR (genetic?(3w)(modif? OR transform? OR manipulat? OR improv? OR engineer?)) or (stacked(w)(gene# or trait# or event#))	GMO general
10	7 and 8 and 9	Intended traits MS8, RF3, MS8 x RF3 AND Plant species AND GMO general
11	4 or 5 or 6 or 10	Event name MS8, RF3, MS8 x RF3 OR Trade name MS8, RF3, MS8 x RF3 OR Newly expressed proteins MS8, RF3, MS8 x RF3 OR (Intended traits MS8, RF3, MS8 x RF3 AND Plant species AND GMO general)

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

- **Agricola**: title (TI), controlled term (CT), supplementary term (ST), abstract (AB), named person (NA), corporate name (CO), note (NTE), geographic term, CABA and other fields (GT)

- **Biosis**: title (TI), abstract (AB), biosystematic codes (BC), chemical name (CN), controlled term (CT), gene name (GEN), geographic term (GT), organism (ORGN) and supplementary term (ST); as well as CAS Registry Numbers (RN)

- **CA-Plus**: title (TI), supplementary term (ST), index term (IT) and abstract (AB); as well as CAS Registry Numbers

- **CABA**: title (TI), controlled term (CT), supplementary term (ST), broader term (BT), abstract (AB), organism name (ORGN) and geographic term (GT); as well as CAS Registry Numbers

- **Medline**: title (TI), chemical name (CN), gene name (GEN), controlled term (excluding MeSH numbers) (CT), supplementary term (ST), named person (NA), other source (OS), and abstract (AB), as well as CAS Registry Numbers and GenBank Numbers

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

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

Database	Events	New proteins	Intended traits	Plant species	GM plants
Agricola	None	None	"HERBICIDE RESISTANCE" "MALE STERILITY"	"*BRASSICA NAPUS*" CANOLA	"TRANSGENIC PLANTS"
Biosis	None	None	No terms for herbicide resistance "MALE STERILITY"	None	None
CABA	None	None	"HERBICIDE RESISTANCE" "MALE STERILITY"	RAPE	"TRANSGENIC PLANTS"
CAS	None	None	"HERBICIDE RESISTANCE" No terms for male sterility	CANOLA "*BRASSICA NAPUS*"	"GENETICALLY MODIFIED PLANTS"
Medline	None	None	"HERBICIDE RESISTANCE" No terms for male sterility	*BRASSICA NAPUS*	"PLANTS, GENETICALLY MODIFIED"

The search results were limited to documents updated between July 1, 2022 and June 30, 2023 (UP>=20220701 and UP<=20230630), and to non-patent documents (not P/DT). To ensure that documents with indexing errors where two document types (DTs) (one eligible and one ineligible) were

attached to a single record were not missed, documents with both 'journal' and 'patent' as document type were also kept. These putative documents would be identified with (P/DT AND J/DT) in CABA and CAPlus.

Table 4 summarizes the number of results obtained from each of the databases searched.

See Appendix 2 for a complete search history.

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

Database	AGRICOLA	BIOSIS	CABA	CA-Plus	Medline
Database Provider	STN International	STN International	STN International	STN International	STN International
Coverage	1970-present	1926-present	1973-present	1907-present	1946-present
Date of search	10 Jul 2023	10 Jul 2023	10 Jul 2023	10 Jul 2023	10 Jul 2023
Datespan of the search	1 Jul 2022 – 30 Jun 2023	1 Jul 2022 – 30 Jun 2023	1 Jul 2022 – 30 Jun 2023	1 Jul 2022 – 30 Jun 2023	1 Jul 2022 – 30 Jun 2023
Latest database update	7 Jun 2023	5 Jul 2023	27 Jun 2023	9 Jul 2023	9 Jul 2023
Number of records retrieved	31	160	207	407	153
Number of records after duplicate removal	25	122	172	311	152
Number of *relevant* records after rapid assessment	0	0	1	0	2

4. INTERNET and MANUAL SEARCHES

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

A search of the web pages of food safety, agriculture, and biotechnology-related authorities was conducted. Search results were manually examined for relevant records that were either published during the time period under consideration (date span of search: July 1, 2022 until June 30, 2023) or refer to relevant records published during this time frame. Relevance of results were determined based on the criteria listed in Table 1 and they were summarized in Table 5. All web pages searched were justified by their recommendation in the EFSA 2019 explanatory note[1]. Of the 13 key organisations

cited in the EFSA 2019 explanatory note[1], Environment and Climate Change Canada and Intersecretarial Commission on Biosafety of GMOs (CIBIOGEM) were excluded, since they are not involved in the risk assessment of GM plants. The US-EPA website was excluded, since MS8, RF3 and MS8 x RF3 *B. napus* do not contain an insect-resistant trait. The GEAC website was excluded, since this agency has only regulated GM cotton products. The CTNBio and CONABIA websites were excluded, since these agencies have not regulated any GM products for canola. Therefore, the internet search was limited to 7 key organisations relevant for MS8, RF3 and MS8 *x* RF3 *B. napus*.

Search terms consisted of MS8 Canola, MS8 Oilseed, MS8 *Brassica*, RF3 Canola, RF3 Oilseed, RF3 *Brassica*, ACS-BN005-8, ACS-BN003-6, Barstar, Barnase, PAT/*bar and* phosphinothricin (all searched singly, with no search limits applied).

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

Source Site Name	Website URL	Date of Most Recent Site Update	Date of Search	No. of Relevant Records
US Department of Agriculture (USDA)	https://www.usda.gov/	25/07/2023	25/07/2023	0
US Food and Drug Administration (FDA)	https://www.fda.gov/	25/07/2023	28/07/2023	0
Health Canada	https://www.canada.ca/en/health-canada.html	26/06/2023	10/07/2023	0
Canadian Food Inspection Agency (CFIA)	https://www.canada.ca/en/food-inspection-agency.html	26/06/2023	20/07/2023	0
Food Standards Australia New Zealand (FSANZ)	http://www.foodstandards.gov.au/Pages/default.aspx	30/06/2023	10/07/2023	0
Office of the Gene Technology Regulator (OGTR) Australia	http://www.ogtr.gov.au/	06/04/2023	10/07/2023	0
Ministry of Agriculture, Forestry and Fisheries (MAFF) Japan	http://www.maff.go.jp/	27/07/2023	27/07/2023	0

4.2. Manual searches of reference lists of recent review articles

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

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

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
1	Bhattacharjee S, Bhowmick R, Kant L, Paul K. 2023	Strategic transgene-free approaches of CRISPR-based genome editing in plants.	Mol Genet Genomics. 2023 May;298(3):507-520	0
2	Cermakova E, Lencova S, Mukherjee S, Horka P, Vobruba S, Demnerova K, Zdenkova K. 2023	Identification of Fish Species and Targeted Genetic Modifications Based on DNA Analysis: State of the Art.	Foods. 2023 Jan 3;12(1):228.	0
3	Connolly JB, Romeis J, Devos Y, Glandorf DCM, Turner G, Coulibaly MB. 2023	Gene drive in species complexes: defining target organisms.	Trends Biotechnol. 2023 Feb;41(2):154-164.	0
4	Eckerstorfer MF, Dolezel M, Engelhard M, Giovannelli V, Grabowski M, Heissenberger A, Lener M, Reichenbecher W, Simon S, Staiano G, Wüst Saucy AG, Zünd J, Lüthi C. 2023	Recommendations for the Assessment of Potential Environmental Effects of Genome-Editing Applications in Plants in the EU.	Plants (Basel). 2023 Apr 25;12(9):1764.	0
5	Ghidoli M, Ponzoni E, Araniti F, Miglio D, Pilu R. 2023	Genetic Improvement of *Camelina sativa* (L.) Crantz: Opportunities and Challenges.	Plants (Basel). 2023 Jan 27;12(3):570.	0
6	Krasnodębski C, Sawuła A, Kaźmierczak U, Żuk M. 2023	Oligo-Not Only for Silencing: Overlooked Potential for Multidirectional Action in Plants.	Int J Mol Sci. 2023 Feb 24;24(5):4466.	0
7	Křížkovská B, Viktorová J, Lipov J. 2022	Approved Genetically Modified Potatoes (*Solanum tuberosum*) for Improved Stress Resistance and Food Safety.	J Agric Food Chem. 2022 Sep 28;70(38):11833-11843.	0
8	Liang J, Yang X, Jiao Y, Wang D,	The evolution of China's regulation of agricultural biotechnology.	aBIOTECH. 2022 Dec 5;3(4):237-249.	0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
	Zhao Q, Sun Y, Li Y, Wu K. 2022			
9	Platani M, Sokefun O, Bassil E, Apidianakis Y. 2023	Genetic engineering and genome editing in plants, animals, and humans: Facts and myths. Gene.	2023 Mar 10; 856:147141.	0
10	Pott A, Bundschuh M, Otto M, Schulz R. 2023	Assessing Effects of Genetically Modified Plant Material on the Aquatic Environment Using higher-tier Studies.	Bull Environ Contam Toxicol. 2023 Jan 2;110(1):35.	0
11	Rai GK, Kumar P, Choudhary SM, Kosser R, Khanday DM, Choudhary S, Kumar B, Magotra I, Kumar RR, Ram C, Rouphael Y, Corrado G, Behera TK. 2022	Biomimetic Strategies for Developing Abiotic Stress-Tolerant Tomato Cultivars:	An Overview. Plants (Basel). 2022 Dec 23;12(1):86	0
12	Rozas P, Kessi-Pérez EI, Martínez C. 2022	Genetically modified organisms: adapting regulatory frameworks for evolving genome editing technologies.	Biol Res. 2022 Oct 20;55(1):31.	0
13	Spök A, Sprink T, Allan AC, Yamaguchi T, Dayé C. 2022	Towards social acceptability of genome-edited plants in industrialised countries? Emerging evidence from Europe, United States, Canada, Australia, New Zealand, and Japan.	Front Genome Ed. 2022 Aug 31;4:899331.	0
14	Tatineni S, Hein GL. 2023	Plant Viruses of Agricultural Importance: Current and Future Perspectives of Virus Disease Management Strategies.	Phytopathology. 2023 Feb;113(2):117-141.	0
15	Tripathi S, Purchase D, Chandra R, Nadda AK, Bhargava PC. 2022	Mitigation of hazards and risks of emerging pollutants through innovative treatment techniques of post methanated distillery effluent - A review.	Chemosphere. 2022 Aug;300:134586. doi: 10.1016/j.chemosphere.2022.134586.	0
16	Wang M, Wang H, Li K, Li X, Wang X, Wang Z. 2023	Review of CRISPR/Cas Systems on Detection of Nucleotide Sequences.	Foods. 2023 Jan 19;12(3):477.	0
17	Zimny T.			0

No	Author(s) and Year	Title	Source	Number of relevant bibliographic references retrieved
	2023	Regulation of GMO field trials in the EU and new genomic techniques: will the planned reform facilitate experimenting with gene-edited plants?	BioTechnologia (Pozn). 2023 Mar 27;104(1):75-83.	

5. RESULTS OF THE STUDY IDENTIFICATION AND SELECTION PROCESS

The database searches (Section 3) identified a total of 958 references, which were reduced to 782 references after removal of duplicates (Table 4). No additional studies were identified in the manual searches (Section 4).

5.1. Screening of titles and abstracts to exclude obviously irrelevant references (Stage 1)

All references identified in the database searches described in Section 3 were assessed for relevance based on information in their title and abstract by two reviewers independently. If opinions of relevance differed, the discrepancies were discussed between the reviewers and if a disagreement persisted, the publication under discussion was transferred to Stage 2 for detailed evaluation by the experts. In this search, both evaluators were in 100 % agreement.

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

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

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

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

5.2. Detailed assessment of eligible references (Stage 2)

Publications tagged as “Relevant” in Stage 1 were assessed in detail independently by two scientific experts in each of three corresponding areas (*i.e.*, Molecular Biology, Food and Feed Safety, Environmental Safety), based on the full text of the publications. If opinions of relevance differed between reviewers within each area, the initial reviewers discussed the discrepancy as necessary and consulted additional reviewers to resolve the discrepancy if needed.

In the relevance assessment of the literature review for the MS8, RF3 and MS8 *x* RF3 *B. napus*, reviewers agreed in 100% of the Stage 2 evaluations.

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

Table 7: Results of the publication selection process

Total number of publications retrieved after all searches of the scientific literature (excluding duplicates)	782
Number of publications excluded from the search results after rapid assessment for relevance (Stage 1)	779
Total number of full-text documents assessed in detail	3
Number of publications excluded from further consideration after detailed assessment for relevance (Stage 2)	1
Total number of unobtainable/unclear publications	0
Total number of relevant publications	2

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

6. NARRATIVE SYNTHESIS/SUMMARY OF RELEVANT STUDIES

A total of 3 publications were selected during Stage 1 evaluation (rapid assessment based on title and abstract). After Stage 2 evaluation (detailed review of full text), it was determined that 2 publications were relevant for the safety assessment of the MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins, PAT/*bar*, Barnase and Barstar.

The publication of Mackie (2021) reviews scientific data generated during the development of RF3 *B. napus* and of RF3 *B. juncea*. The data and knowledge generated from this publication do not have an impact on the previous safety assessment of MS8, RF3 or MS8 *x* RF3 *B. napus* and do not give evidence that could change the conclusions therein.

Mullins *et al.* (2023) provides a scientific risk assessment performed by the EFSA GMO Panel on data submitted in the context of the renewal application for MS8, RF3 and MS8 *x* RF3 *B. napus*. The GMO Panel concluded that there is no evidence in the renewal application for new hazards, modified exposure, or scientific uncertainties that would change the conclusions of the previous risk assessment on MS8, RF3 and MS8 *x* RF3 *B. napus*.

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

Table 8: Report of all relevant publications retrieved after detailed assessment of full-text documents for relevance: ordered by category of information/data requirement(s)

Main category of information/data requirement	Study (Author(s) and year)	Title	Source
Molecular characterization	Mackie, S. J. W. (2021)	Comparison of RF3 *B. juncea* to RF3 *B. napus*.	Food and Nutrition Sciences (2021), Volume 12, Number 11, pp. 1041-1061, 40 refs. ISSN: 2157-944X; 2157-9458 DOI: https://doi.org/10.4236/fns.2021.121107 7 Published by: Scientific Research Publishing, Irvine
Food and feed safety	Mullins Ewen, Bresson Jean Louis, Dalmay Tamas, Dewhurst Ian Crawford, Epstein Michelle M, Firbank Leslie George, Guerche Philippe, Hejatko Jan, Moreno Francisco Javier, Naegeli Hanspeter, Nogue Fabien, Rostoks Nils, Sanchez Serrano Jose Juan, Savoini Giovanni, Veromann Eve, Veronesi Fabio, Ardizzone Michele, Camargo Ana M, Fernandez Antonio, Goumperis Tilemachos, Lenzi Paolo, Lewandowska Aleksandra, Raffaello Tommaso, Streissl Franz (2023)	Assessment of genetically modified oilseed rape MS8 , RF3 and MS8 × RF3 for renewal authorisation under Regulation (EC) No 1829/2003 (application EFSA-GMO -RX-024).	EFSA journal. European Food Safety Authority, (2023 Apr) Vol. 21, No. 4, pp. e07934. Electronic Publication Date: 26 Apr 2023 Journal code: 101642076. E-ISSN: 1831-4732. L-ISSN: 1831-4732. Report No.: PMC-PMC10131089.

Table 9: Report of publications excluded from the risk assessment after detailed assessment of full-text documents

Study (Author(s) and year)	Title	Source	Reason(s) for exclusion based on eligibility/inclusion criteria listed in Table 1
Shao Zicheng, Huang Lei, Zhang Yuchi, Qiang Sheng, Song Xiaoling (2022)	Transgene Was Silenced in Hybrids between Transgenic Herbicide -Resistant Crops and Their Wild Relatives Utilizing Alien Chromosomes.	Plants (Basel, Switzerland), (2022 Nov 22) Vol. 11, No. 23. Electronic Publication Date: 22 Nov 2022 Journal code: 101596181. ISSN: 2223-7747. L-ISSN: 2223-7747. Report No.: PMC-PMC9741405.	The publication is not related to MS8, RF3 or MS8 x RF3 *B. napus.*

Table 10: Report of unobtainable/unclear publications

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

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

Main category of information/data requirement	Study (Author(s) and year)	Intervention/ test materials used	Adverse effects reported	Which adverse effect reported	Implications for risk assessment
Molecular Characterization - Food and Feed Safety	Mackie, S. J. W. (2021)	RF3 canola	None	Not applicable	The paper summarizes and compares scientific data generated during the safety assessments of RF3 *B.napus* and RF3 *B. juncea*, showing close comparability of both.
Food and Feed Safety	Mullins Ewen, Bresson Jean Louis, Dalmay Tamas, Dewhurst Ian Crawford, Epstein Michelle M, Firbank Leslie George, Guerche Philippe, Hejatko Jan, Moreno Francisco Javier, Naegeli Hanspeter, Nogue Fabien, Rostoks Nils, Sanchez Serrano Jose Juan, Savoini Giovanni, Veromann Eve, Veronesi Fabio, Ardizzone Michele, Camargo Ana M, Fernandez Antonio, Goumperis Tilemachos, Lenzi Paolo, Lewandowska Aleksandra, Raffaello Tommaso, Streissl Franz (2023)	MS8, RF3 and MS8 x RF3 canola	None	Not applicable	None, because no new hazards, modified exposure, or scientific uncertainties are reported.

7. CONCLUSION

The literature searches performed for the MS8, RF3 and MS8 *x* RF3 *B. napus* and their newly expressed proteins, PAT/*bar*, Barnase and Barstar, for the period from July 1, 2022 until June 30, 2023, identified a total of 782 unique publications (after duplicate removal). A total of 3 publication(s) were progressed for detailed assessment after excluding 779 obviously irrelevant publications during Stage 1 evaluation (rapid assessment based on title and abstract).

The 3 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. Two relevant publications with bearing on molecular characterization and food and feed safety were identified. The data and knowledge generated from these studies does not impact the previous safety assessment of MS8, RF3 and MS8 *x* RF3 *B. napus*. 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/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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L1          338 SEA MS8 OR MS8X OR MS-8 OR MS-8X OR ACS(W)BN005-8 OR ACS(W)BNOO
                5-8 OR ACSBN005-8 OR ACSBNOO5-8 OR ACS(W)BN005-8X OR ACS(W)BNOO
                5-8X OR ACSBN005-8X OR ACSBNOO5-8X
L2          303 SEA RF3 OR XRF3 OR RF-3 OR XRF-3 OR ACS(W)BN003-6 OR ACS(W)BNOO
                3-6 OR ACSBN003-6 OR ACSBNOO3-6 OR XACS(W)BN003-6 OR XACS(W)BNO
                O3-6 OR XACSBNÃ□Ã□3-6 OR XACSBN003-6 OR XACSBNOO3-6
L3            8 SEA MS8XRF3 OR MS(W)8XRF-3 OR MS8(W)TIME#(W)RF3 OR ACS(W)BN005(
                W)8XACS-BN003-6 OR ACS(W)BNOO5(W)8XACS(W)BNOO3-6
L4          630 SEA L1 OR L2 OR L3
L5          172 SEA INVIGOR OR INVIGORR OR INVIGORTM OR IN(W)VIGOR OR IN(W)VIGO
                RR OR IN(W)VIGORTM OR IN(W)VIGORRTM
L6          657 SEA BARNASE OR RNASE(W)BA OR (BACTERIAL(W)RIBONUCLEASE AND
                ((BACILLUS OR B)(W)AMYLOLIQUEFACIENS)) OR P00648 OR IPR001887
L7          380 SEA BARSTAR OR BARNASE(W)INHIBITOR OR IPR000468
L8         1590 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
L9          208 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L10        2466 SEA (L6 OR L7 OR L8 OR L9)
L11        3817 SEA (HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR
                PHOSPHINOTHRICIN OR LIBERTY)(5A)(RESIST? OR TOLERAN? OR
                PROTECT?)
L12       10033 SEA MALE(3A)STERIL? OR (FERTIL?(3A)RESTOR?) OR RESTOR?(W)LINE
                OR POLLINATION(W)CONTROL
L13       13801 SEA (L11 OR L12)
L14       25700 SEA ((BRASSICA OR B)(W)(NAPUS OR JUNCEA)) OR RAPE? OR CANOLA#
                OR OILSEED(W)RAPE OR OIL(W)SEED(W)RAPE OR COLZA
L15     4171999 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                (GENETIC?(3W)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                ENGINEER?)) OR (STACKED(W)(GENE# OR TRAIT# OR EVENT#))
L16         429 SEA L13 AND L14 AND L15
L17        3661 SEA L4 OR L5 OR L10 OR L16
L18         360 SEA L17 AND PY>=2021
L19         153 SEA L18 AND UP>=20220701 AND UP<=20230630

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                5-8X OR ACSBN005-8X OR ACSBNOO5-8X
L21         398 SEA RF3 OR XRF3 OR RF-3 OR XRF-3 OR ACS(W)BN003-6 OR ACS(W)BNOO
                3-6 OR ACSBN003-6 OR ACSBNOO3-6 OR XACS(W)BN003-6 OR XACS(W)BNO
                O3-6 OR XACSBNÃ□Ã□3-6 OR XACSBN003-6 OR XACSBNOO3-6
L22           7 SEA MS8XRF3 OR MS(W)8XRF-3 OR MS8(W)TIME#(W)RF3 OR ACS(W)BN005(
                W)8XACS-BN003-6 OR ACS(W)BNOO5(W)8XACS(W)BNOO3-6
L23         735 SEA L20 OR L21 OR L22
L24          61 SEA INVIGOR OR INVIGORR OR INVIGORTM OR IN(W)VIGOR OR IN(W)VIGO
                RR OR IN(W)VIGORTM OR IN(W)VIGORRTM
L25         772 SEA BARNASE OR RNASE(W)BA OR (BACTERIAL(W)RIBONUCLEASE AND
                ((BACILLUS OR B)(W)AMYLOLIQUEFACIENS)) OR P00648 OR IPR001887
L26         360 SEA BARSTAR OR BARNASE(W)INHIBITOR OR IPR000468
L27        2986 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
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                PT(W)N(2W)ACETYLTRANSFERASE OR PT(W)N(2W)ACETYL(W)TRANSFERASE
L28         337 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L29        3969 SEA (L25 OR L26 OR L27 OR L28)
L30       10574 SEA (HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR
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                PHOSPHINOTHRICIN OR LIBERTY)(5A)(RESIST? OR TOLERAN? OR
                PROTECT?)
L31        17104 SEA MALE(3A)STERIL? OR (FERTIL?(3A)RESTOR?) OR RESTOR?(W)LINE
                OR POLLINATION(W)CONTROL
L32        27558 SEA (L30 OR L31)
L33        50320 SEA ((BRASSICA OR B)(W)(NAPUS OR JUNCEA)) OR RAPE? OR CANOLA#
                OR OILSEED(W)RAPE OR OIL(W)SEED(W)RAPE OR COLZA
L34       472375 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                (GENETIC?(3W)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                ENGINEER?)) OR (STACKED(W)(GENE# OR TRAIT# OR EVENT#))
L35          470 SEA L32 AND L33 AND L34
L36         5162 SEA L23 OR L24 OR L29 OR L35
L37          307 SEA L36 AND PY>=2021
L38          160 SEA L37 AND UP>=20220701 AND UP<=20230630

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                5-8X OR ACSBN005-8X OR ACSBNOO5-8X
L40          117 SEA RF3 OR XRF3 OR RF-3 OR XRF-3 OR ACS(W)BN003-6 OR ACS(W)BNOO
                3-6 OR ACSBN003-6 OR ACSBNOO3-6 OR XACS(W)BN003-6 OR XACS(W)BNO
                O3-6 OR XACSBNÃ□Ã□3-6 OR XACSBN003-6 OR XACSBNOO3-6
L41            3 SEA MS8XRF3 OR MS(W)8XRF-3 OR MS8(W)TIME#(W)RF3 OR ACS(W)BN005(
                W)8XACS-BN003-6 OR ACS(W)BNOO5(W)8XACS(W)BNOO3-6
L42          222 SEA L39 OR L40 OR L41
L43          138 SEA INVIGOR OR INVIGORR OR INVIGORTM OR IN(W)VIGOR OR IN(W)VIGO
                RR OR IN(W)VIGORTM OR IN(W)VIGORRTM
L44          114 SEA BARNASE OR RNASE(W)BA OR (BACTERIAL(W)RIBONUCLEASE AND
                ((BACILLUS OR B)(W)AMYLOLIQUEFACIENS)) OR P00648 OR IPR001887
L45           57 SEA BARSTAR OR BARNASE(W)INHIBITOR OR IPR000468
L46          826 SEA ((BAR OR PAT)(2A)(GENE# OR PROTEIN# OR ENZYME#)) OR
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L47          257 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
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L49         8861 SEA (HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR
                PHOSPHINOTHRICIN OR LIBERTY)(5A)(RESIST? OR TOLERAN? OR
                PROTECT?)
L50         8621 SEA MALE(3A)STERIL? OR (FERTIL?(3A)RESTOR?) OR RESTOR?(W)LINE
                OR POLLINATION(W)CONTROL
L51        17409 SEA (L49 OR L50)
L52        29622 SEA ((BRASSICA OR B)(W)(NAPUS OR JUNCEA)) OR RAPE? OR CANOLA#
                OR OILSEED(W)RAPE OR OIL(W)SEED(W)RAPE OR COLZA
L53       111045 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                (GENETIC?(3W)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                ENGINEER?)) OR (STACKED(W)(GENE# OR TRAIT# OR EVENT#))
L54          307 SEA L51 AND L52 AND L53
L55         1660 SEA L42 OR L43 OR L48 OR L54
L56          106 SEA L55 AND PY>=2021
L57           31 SEA L56 AND UP>=20220701 AND UP<=20230630

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                5-8X OR ACSBN005-8X OR ACSBNOO5-8X
L59          288 SEA RF3 OR XRF3 OR RF-3 OR XRF-3 OR ACS(W)BN003-6 OR ACS(W)BNOO
                3-6 OR ACSBN003-6 OR ACSBNOO3-6 OR XACS(W)BN003-6 OR XACS(W)BNO
                O3-6 OR XACSBNÃ□Ã□3-6 OR XACSBN003-6 OR XACSBNOO3-6
L60           18 SEA MS8XRF3 OR MS(W)8XRF-3 OR MS8(W)TIME#(W)RF3 OR ACS(W)BN005(
                W)8XACS-BN003-6 OR ACS(W)BNOO5(W)8XACS(W)BNOO3-6
L61          543 SEA L58 OR L59 OR L60
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L62          292 SEA INVIGOR OR INVIGORR OR INVIGORTM OR IN(W)VIGOR OR IN(W)VIGO
                 RR OR IN(W)VIGORTM OR IN(W)VIGORRTM
L63          157 SEA BARNASE OR RNASE(W)BA OR (BACTERIAL(W)RIBONUCLEASE AND
                 ((BACILLUS OR B)(W)AMYLOLIQUEFACIENS)) OR P00648 OR IPR001887
L64           70 SEA BARSTAR OR BARNASE(W)INHIBITOR OR IPR000468
L65         1630 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
L66          387 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                 N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                 ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L67         1876 SEA (L63 OR L64 OR L65 OR L66)
L68        19754 SEA (HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR
                 PHOSPHINOTHRICIN OR LIBERTY)(5A)(RESIST? OR TOLERAN? OR
                 PROTECT?)
L69        25659 SEA MALE(3A)STERIL? OR (FERTIL?(3A)RESTOR?) OR RESTOR?(W)LINE
                 OR POLLINATION(W)CONTROL
L70        45189 SEA (L68 OR L69)
L71        76380 SEA ((BRASSICA OR B)(W)(NAPUS OR JUNCEA)) OR RAPE? OR CANOLA#
                 OR OILSEED(W)RAPE OR OIL(W)SEED(W)RAPE OR COLZA
L72       200326 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                 (GENETIC?(3W)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
                 ENGINEER?)) OR (STACKED(W)(GENE# OR TRAIT# OR EVENT#))
L73          750 SEA L70 AND L71 AND L72
L74         3360 SEA L61 OR L62 OR L67 OR L73
L75          245 SEA L74 AND PY>=2021
L76          207 SEA L75 AND UP>=20220701 AND UP<=20230630
L77          207 SEA L76 NOT P/DT
L78            0 SEA L76 AND (P/DT AND J/DT)
L79          207 SEA L77 OR L78

     FILE 'HCAPLUS' ENTERED AT 10:33:11 ON 10 JUL 2023
L80          446 SEA MS8 OR MS8X OR MS-8 OR MS-8X OR ACS(W)BN005-8 OR ACS(W)BNOO
                 5-8 OR ACSBN005-8 OR ACSBNOO5-8 OR ACS(W)BN005-8X OR ACS(W)BNOO
                 5-8X OR ACSBN005-8X OR ACSBNOO5-8X
L81         1180 SEA RF3 OR XRF3 OR RF-3 OR XRF-3 OR ACS(W)BN003-6 OR ACS(W)BNOO
                 3-6 OR ACSBN003-6 OR ACSBNOO3-6 OR XACS(W)BN003-6 OR XACS(W)BNO
                 O3-6 OR XACSBNÃ□Ã□3-6 OR XACSBN003-6 OR XACSBNOO3-6
L82           13 SEA MS8XRF3 OR MS(W)8XRF-3 OR MS8(W)TIME#(W)RF3 OR ACS(W)BN005(
                 W)8XACS-BN003-6 OR ACS(W)BNOO5(W)8XACS(W)BNOO3-6
L83         1598 SEA L80 OR L81 OR L82
L84            9 SEA INVIGOR OR INVIGORR OR INVIGORTM OR IN(W)VIGOR OR IN(W)VIGO
                 RR OR IN(W)VIGORTM OR IN(W)VIGORRTM
L85         1327 SEA BARNASE OR RNASE(W)BA OR (BACTERIAL(W)RIBONUCLEASE AND
                 ((BACILLUS OR B)(W)AMYLOLIQUEFACIENS)) OR P00648 OR IPR001887
L86          657 SEA BARSTAR OR BARNASE(W)INHIBITOR OR IPR000468
L87         5700 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
L88          809 SEA PHOSPHINOTHRICIN(W)N(W)ACETYLTRANSFERASE OR PHOSPHINOTHRICI
                 N(2W)ACETYLTRANSFERASE OR PHOSPHINOTHRICIN(2W)ACETYL(W)TRANSFER
                 ASE OR PHOSPHINOTHRICINACETYL(W)TRANSFERASE
L89         7473 SEA (L85 OR L86 OR L87 OR L88)
L90        30958 SEA (HERBICID? OR BIALAPHOS OR BASTA OR GLUFOSINATE OR
                 PHOSPHINOTHRICIN OR LIBERTY)(5A)(RESIST? OR TOLERAN? OR
                 PROTECT?)
L91        27262 SEA MALE(3A)STERIL? OR (FERTIL?(3A)RESTOR?) OR RESTOR?(W)LINE
                 OR POLLINATION(W)CONTROL
L92        45410 SEA (L90 OR L91)
L93       117410 SEA ((BRASSICA OR B)(W)(NAPUS OR JUNCEA)) OR RAPE? OR CANOLA#
                 OR OILSEED(W)RAPE OR OIL(W)SEED(W)RAPE OR COLZA
L94       671993 SEA GMO OR GMOS OR LMO OR LMOS OR GM OR GE OR TRANSGEN? OR
                 (GENETIC?(3W)(MODIF? OR TRANSFORM? OR MANIPULAT? OR IMPROV? OR
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                ENGINEER?)) OR (STACKED(W)(GENE# OR TRAIT# OR EVENT#))
L95         1370 SEA L92 AND L93 AND L94
L96        10243 SEA L83 OR L84 OR L89 OR L95
L97         1443 SEA L96 AND PY>=2021
L98          581 SEA L97 AND UP>=20220701 AND UP<=20230630
L99          406 SEA L98 NOT P/DT
L100           1 SEA L98 AND (P/DT AND J/DT)
L101         407 SEA L99 OR L100

     FILE 'MEDLINE, BIOSIS, AGRICOLA, CABA, HCAPLUS' ENTERED AT 04:33:18 ON 10
     JUL 2023
L102         782 DUP REM L19 L38 L57 L79 L101 (176 DUPLICATES REMOVED)
                     ANSWERS '1-152' FROM FILE MEDLINE
                     ANSWERS '153-274' FROM FILE BIOSIS
                     ANSWERS '275-299' FROM FILE AGRICOLA
                     ANSWERS '300-471' FROM FILE CABA
                     ANSWERS '472-782' FROM FILE HCAPLUS
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