チアメトキサム

公表文献追加調査結果について

提出日：令和 6 年 4 月 19 日

シンジェンタジャパン株式会社

1. 概要

チアメトキサムに関して、再評価資料提出期限の始期（2021 年 10 月 1 日）の 6 ヶ月前から過去 15 年間を含む期間に発行された公表文献について検索し、適合性及び信頼性の評価を行った報告書を令和 4 年 6 月 28 日に提出している。今回、令和 5 年 7 月 27 日に一部改正されたガイドラインを元に追加調査を行った。

2. 検索結果のまとめ

改正されたガイドラインを元に追加調査を行った期間（2015 年 3 月 1 日～2021 年 4 月 1 日）の検索結果のまとめを表 2-1 に示す。文献調査の絞り込みの過程は調査報告書に記載されているが、詳細な過程を別紙に示す。

表 2-1：評価目的との適合性評価（第一段階、第二段階）の結果のまとめ

各過程における文献数	ヒトに対する毒性	農作物及び畜産物への残留	生活環境動植物及び家畜に対する毒性	環境動態	その他
重複を除いた後の文献数	362				
各分野にキーワードで分類後の文献数	340	311	342	274	2
第一段階適合性なしの文献数	337	299	296	273	2
第一段階適合性ありの文献数	3	12	46	1	0
第二段階適合性なしの文献数	1	2	16	0	0
第二段階において国際機関が適合性ありとした文献との重複数	0	1	0	0	0
第二段階適合性ありの文献数	2	9	30	1	0
区分aの文献数	0	2	2	0	0
区分bの文献数	0	5	27	1	0
区分cの文献数	2	2	1	0	0

別紙

調査報告書中に記載の手順	文献数	詳細な文献検索の手順
The number of hits obtained in WoS by using search terms specific to the active substance and product names and then filtered for the document types, and languages	2535	有効成分名（文献調査報告書中 Table 3.1.4-1）及び製剤名（文献報告書中 Table 3.1.4-3）で WoS を用いて文献検索を実施。その後、文献の言語等で最低限絞り込みを掛けた後の文献数。 本段階では Flagship*を用いて検索された文献は除かれておらず、検索された文献内での重複がある。
Total number of papers extracted by the target pesticide names and all the Web of Science classification fields of the 4 target impact of assessment (Total of all databases) – new search	1779	前段階で検索された文献を WoS における 4 分野の分類フィールド（文献調査報告書中 Table 3.1.5-1）を用いて絞り込みを掛けた後の文献数（全データベースの合計)。 本段階では Flagship*を用いて検索された文献は除かれておらず、検索された文献内での重複がある。
Total number of previous searches	1209	既提出の文献調査報告書にて報告されている文献数。 なお、既提出の文献調査報告書中では 1211 文献であったが、前回文献調査を実施した際のキーワードで、再度 2023 年に文献検索を実施したところ、1209 文献に減っていたため、1209 文献を文献数としている。
Number of papers containing Flagship terms (False positive) in new search	576	今回の文献調査において Flagship*をキーワードとして検索された文献数。
Number of papers containing Flagship terms (False positive) in previous search	313	既提出の文献調査において Flagship*をキーワードとして検索された文献数。
Number of papers that do not contain Flagship terms (True positive)	2099	Flagship*をキーワードとして検索された文献を除いた後の合計の文献数： 「既提出の文献調査における文献数（1209)」+「今回の文献調査における文献数（1779)」-「今回及び前回の文献調査において Flagship*を用いて検索された文献数（889)」 = 2099 文献 本段階で、 Flagship*を用いて検索された文献は除かれているが、検索された文献内での重複がある。
Number of duplicate papers between previous and new searches	1683	2099 文献の中で、既提出の文献調査と今回の文献調査内で重複があった文献数。
Number of papers to be assessed (excluding papers contain Flagship terms, excluding papers from the previous search and excluding duplicates)	362	今回調査分の文献中の重複を除いた後、最終的に調査対象となった文献数： 「Flagship*を除いた合計の文献数（2099)」-「2099 文献の中で、既提出の文献調査報告書と今回の文献調査内で重複があった文献数 （1683)」 –「今回調査分の検索された文献中での重複数（54)」= 362 文献

*Flagship は、海外において販売されている、チアメトキサムを含有している製品の一つ。但し、ボートの意味を持つため、当該有効成分に無関係の文献が多くヒットする。

別紙

調査報告書中に記載の手順						詳細な文献検索の手順
Study selection process	**Toxicity to humans**	**Residues in crops and livestock products**	**Toxicity to flora and fauna in the human living environment**	**Environmen-tal Fate**	**Others**	
Total number of documents retrieved after removal of duplicates and false-positive Flagship® (global search results related to the active substance, its metabolites and plant protection products containing the active substance and web of science classification fields specific to the target impact for assessment)	362					重複と Flaghip による誤検出を除いた後の最終的に調査対象となった文献数。
Number of publications potentially relevant per target impact area (according to specific search terms relevant to each section)	340	311	342	274	2	各分野のキーワードを用いた、分野ごとに関連する可能性がある文献数。 調査対象の 362 文献を各分野のキーワード（文献調査報告書中 Table 3.1.7-1、Table 3.1.7-2、Table 3.1.7-3 及び Table 3.1.7-4）で各分野に分類。 なお、各分野間でキーワードには同じ文言があるため、分類後の文献においては重複が存在する。 どのキーワードにも属さない文献は Others に分類されている。 分類後の文献に対して、第一段階の適合性評価が行われた。

以上

Thiamethoxam

Scientific peer-review literature search on thiamethoxam

Date:

April 19th 2024

Syngenta Japan

The report is an addendum to the literature search named: “Report on published literature -Active ingredient: Thiamethoxam”, submitted on 2022-06-28 (final amendment on 2022-11-01).

This document was therefore prepared to present the results of this review, taking into account the following guidance:

- J-MAFF (2023): Guideline for collecting and selecting published literature, 27 July 2023
- FSC (2021): Handling of published documents in food health impact assessment of residual pesticides, decision by the first special investigation committee for agricultural chemicals on March 18, 2021, R30913
- EFSA (2011): Guidance of EFSA, Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009, EFSA Journal 2011;9(2):2092.
- Klimisch H-J, Andreae M and Tillmann U (1997): A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology 25, 1-5

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CHAPTER 1 SUMMARY

The literature search was done and submitted on 2022-06-28 (final amendment on 2022-11-01) to answer requirements set by Japanese Regulation regarding the renewal of active substances. The report submitted was named: “Report on published literature - Active ingredient: Thiamethoxam”

The aim of this new literature search was to complete the previous literature search by finding scientific peer-reviewed open publication, on active substance thiamethoxam and its relevant formulated products, dealing with side effects on human health and the environment.

The initial search strategy is used in line with Section IV of the “Guideline for collection and selection of published literature”. The basic procedures used include:

(1) Selection of appropriate database to search without omission.

(2) Identification of literatures that match the purpose using keywords

a. The search terms were defined, initially using terms related to the active substance, its metabolites and plant protection products containing the active substance, including synonyms.

b. The resulting publications were then filtered by selecting Web of science fields related to the specific data requirement for each target impact area in question (i.e., for toxicity to humans, residues in crops and livestock products, Toxicity of plants and animals in the environment and livestock and Environmental Fate) to refine the search.

c. After using the two-stage approach outlined above, a list of titles, authors and dates were extracted. Any duplicate summary records were removed, before proceeding.

d. The non duplicate records were then filtered with topic specific keywords relating to the specific data requirements in question (i.e., for toxicity to humans, residues in crops and livestock products, Toxicity of plants and animals in the environment and livestock and Environmental Fate) to further refine the search.

(3) Exclusion of literatures that are not compatible with the purpose of assessment:

a. Firstly, a rapid assessment for relevance was conducted based on the titles and abstracts, to exclude summary records which were obviously irrelevant to the specific data requirements in question.

b. Secondly, a detailed assessment of full-text documents was conducted to identify relevant publications.

(4) Classification of relevance and assessment of reliability for the literatures selected:

a. The full text publications found relevant were classified in categories of relevance “a”, “b” and “c”. Relevant records classified as “a”, where then classified for their reliability based on the Klimisch H-J (1997).

The results of this search were as follows:

Table 1: Summary of the selection process of relevant and reliable studies per target impact area

Study selection process	**Active substance thiamethoxam (2015-03-01 and 2021-04-01)**				
	Toxicity to humans	**Residues in crops and livestock products**	**Toxicity to flora and fauna in the human living environment**	**Environmental Fate**	**Others**
Total number of documents retrieved (with duplicates) (global search results related to the active substance, its metabolites and plant protection products containing the active substance and web of science fields specific to the target impact for assessment- Keywords type A and B)	1779				
Total number of documents retrieved after removal of duplicates and false-positive Flagship® (global search results related to the active substance, its metabolites and plant protection products containing the active substance and web of science fields specific to the target impact for assessment)	362				
Number of publications potentially relevant per target impact area (according to specific search terms relevant to each section- Keywords type A and B and C)	340	311	342	274	2
Number of publications excluded after rapid assessment for relevance by title/abstract (non-relevant to specific search terms, excluded literature)	337	299	296	273	2
Number of publications for which detailed assessment of full text are required (considered relevant after rapid assessment)	3	12	46	1	0
Number of publications excluded from further consideration after detailed assessment for relevance (non-relevant, excluded literature)	1	2	16	0	0
Number of papers from international organisation considered relevant at the full text assessment step	0	1	0	0	0
Number of publications considered relevant following the two-step process (i.e., after detailed assessment of full text)	2	9	30	1	0
Number of papers considered as relevant classified as category “a” (Literatures that may be used to set or reconsider risk assessment parameters)	0	2	2	0	0

Study selection process	Active substance thiamethoxam (2015-03-01 and 2021-04-01)				
	Toxicity to humans	**Residues in crops and livestock products**	**Toxicity to flora and fauna in the human living environment**	**Environmental Fate**	**Others**
Number of papers considered as relevant classified as category "b" (Literatures that may be used as supplementary data when setting risk assessment parameters.)	0	5	27	1	0
Number of papers considered as relevant classified as category "c" (Literatures that are not classified as a or b)	2	2	1	0	0
Number of publications considered as reliable (Klimisch score if category "a")	0	2 (all were given Klimisch score 2)	2 (all were given Klimisch score 2)	0	0

Keywords type:
Type A: keywords relevant to the active ingredient, metabolites and formulated product name
Type B: keywords relevant to the Classification field regarding the target impact for assessment in the search using Web of Science
Type C: keywords relevant to the target impact area, species and compartment for each section

In conclusion, for the period (2015-03-01 and 2021-04-01), 1779 articles were extracted. After removal of duplicates and of false positive (Flagship), 362 articles were considered and filtered according to keywords of target impact areas (340 for toxicity, 311 for residues, 342 for toxicity to flora and fauna and 274 for environmental fate and 2 for others). After the two-step process (i.e., after detailed assessment for relevance and reliability of these articles) the results are:

- 2 studies were found relevant to the section "Toxicity to humans" but were classified as category "c" and therefore not further assessed for reliability.
- 9 studies were found relevant to the section "Residues in crops and livestock products". Among them, 2 studies were classified category "a" and all were given Klimisch score 2 (reliable with restriction).
- 30 studies were found relevant to the section "Toxicity to flora and fauna in the human living environment". Among these 30 studies, only 2 studies were classified as category "a" and all of them were given Klimisch score 2 (reliable with restriction).
- 1 study was found relevant to the section "Environmental Fate" but was classified as category "b" and therefore not further assessed for reliability.
- 1 EFSA study was obtained at the full text assessment step in the section "Residues in crops and livestock products". This publication was sorted out in a separate table of results as part of the assessment reports emitted by an international authority.

CHAPTER 2 OBJECTIVE

This report will summarise the search for scientific peer-reviewed open literature on thiamethoxam and its relevant formulated products, dealing with side effects on human health and the environment. This literature search review is a second literature search and is complementary to the literature search named “Report on published literature -Active ingredient: Thiamethoxam”, submitted on 2022-06-28 (final amendment on 2022-11-01).

CHAPTER 3 SEARCH STRATEGY

The initial search strategy described in **Figure 1: Systematic review strategy** is used during this search. It is in line with Section IV of the Guideline for collecting and selecting published literature. The basic procedures used include:

I. Collection of literature

II. Confirmation of relevance from title and abstract

III. Classification of relevance and reliability in full text.

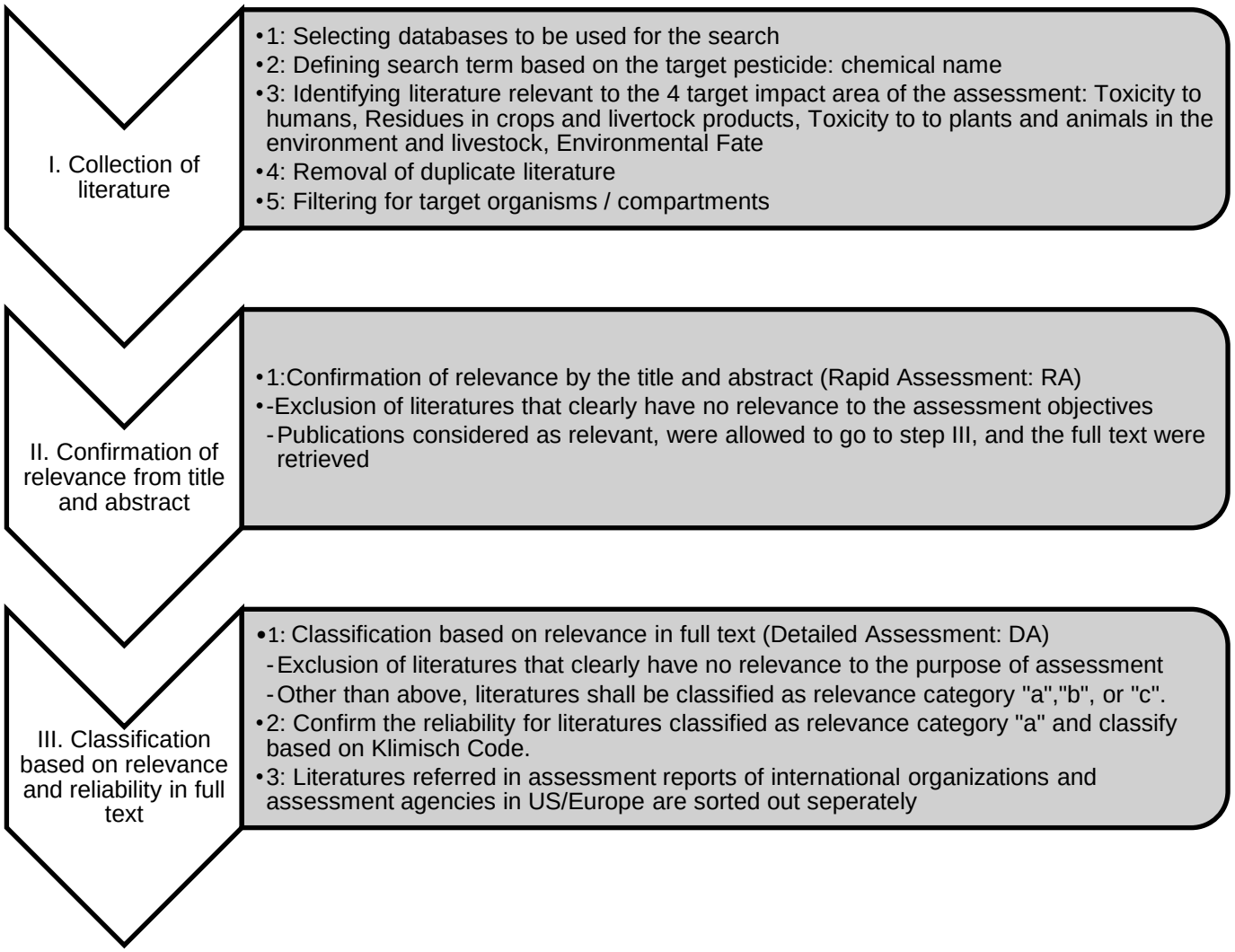

Figure 1: Systematic review strategy

3.1 Step I: Collection of literature

3.1.1 Selection of database

The bibliographic databases of the Web of Science Core Collection (company Clarivate™) are considered relevant by the Japanese Ministry of Forestry and Fisheries (MAFF) and the Food

Safety Commission (FSC). They cover adequately the sections of interest and are used to search for scientific peer-reviewed open literature published within the last 15 years prior to the date of dossier submission in Japan. They are also updated on a daily basis.

For the purpose of the literature review, the Web of science core collection used encompasses, Science citation index expanded (SCIE), Book Citation Index – Social Sciences and Humanities (BKCI-SSK), Book Citation Index (BKCI).

Table 3.1.1-1 below, provides descriptions of the databases selected, the scope of coverage and the date of search.

Table 3.1.1-1: Description of the Web of Science core collection features and search

Database	Description/Rationale for Inclusion
Web of Science Core Collection: Science Citation Index Expanded (SCI-ExPANDED), Book Citation Index Science (BKCI-S), Book Citation Index – Social Sciences and Humanities (BKCI-SSH)	This includes scholarly journals, books, and proceedings in the sciences, social sciences, and arts and humanities and includes a full citation network: 1: SCI-ExPANDED: one of the largest multidisciplinary scientific databases, is an international index to the literature covering virtually every subject area within the broad fields of science, technology, and biomedicine. More than 47.7 million records (08/2019). 1974-present 2: BKCI-S/ BKCI-SSH: Book Citation Index in Web of Science™Core collection connects a library's book collection to a powerful new discovery tool. It allows users to search seamlessly across books, journals and conference proceedings to find the information most relevant to sciences, social sciences and humanities. It indexes over 60000 editorially selected books with 10000 new books added each year.

Compared to the literature search described in the report "Report on published literature -Active ingredient: Thiamethoxam", submitted on 2022-06-28 (final amendment on 2022-11-01), the databases Social Sciences Citation Index (SSCI), Arts & Humanities Citation Index (AHCI), Emerging Sources Citation Index (ESCI) and Conference Proceedings Citation Index (CPCI) are not used for the following reasons:

- The databases SSCI and AHCI deal with social science and art and humanities and do not cover the expertise related to human and animal health as well as the environment.

- ESCI's aim is to ensure that important research is visible in the Web of Science Core Collection even if it is not yet internationally recognized. It does not provide additional value since it aims at increasing the visibility of publications even if they are not yet internationally recognised.

- Conference proceedings depict the leading edge of research — revealing emerging trends and new ideas before they appear in journals. It does not provide additional value since they provide proceedings and conferences that are not considered as peer-review literature.

3.1.2 Date of the literature search

The literature search was conducted on the 2023-08-17. Web of science is updated on a daily basis, the last update of the database being 2023-08-17.

3.1.3 Time period covered in the literature search

The period covered is the same as the “Report on published literature - Active ingredient: Thiamethoxam”, submitted on 2022-06-28 (final amendment on 2022-11-01), that is, 2015-03-01 to 2021-04-01.

3.1.4 Identification of search terms for the target pesticide

For the purpose of this amended literature search, the same chemical search terms, defined for the target pesticide during the previous submitted literature search are used.

The table below presents the general search terms used to find all literature related to the active substance, its metabolites and plant protection products containing the active substance.

The literature search is conducted for the following synonym names of the active substance, its relevant metabolites, and the formulated products. The various terms included in the search strategy are provided in Table 3.1.4-1, Table 3.1.4-2 and Table 3.1.4-3.

Table 3.1.4-1: Active ingredient (keywords used for the search)

Chemical Name	Thiamethoxam
IUPAC/Chemical name(s)	(EZ)-3-(2-chloro-1,3-thiazol-5-ylmethyl)-5-methyl-1,3,5-oxadiazinan-4-ylidene(nitro)amine
CAS number	153719-23-4
EEC number	428-650-4
Company’s development code(s)	CGA293343

Table 3.1.4-2: Metabolites (keywords used for the search)

Chemical name(s)	--
CAS number	--
Company's code(s)	--

The trade product Actara® is a granule formulation (GR) for soil and foliar application to control soil and foliar insects in multiple crops, Cruiser® is a seed treatment, Flagship® is a water-soluble granule formulation (WG) to control chewing and sucking insects in lawn and gardens, Adage® is a mixture product to control insects and seedborne and seedling diseases on soybeans.

Table 3.1.4-3: Formulated product name (keywords used for the search)

Product Names	Actara®, Cruiser®, Flagship®, Adage®
Synonym	-

These keywords defined for the active substances and the formulated product name are linked with the "OR" Boolean operators to obtain broad search results. The search string applied to the general search terms entered in each of the database is therefore:

thiamethoxam OR (EZ)-3-(2-chloro-1,3-thiazol-5-ylmethyl)-5-methyl-1,3,5-oxadiazinan-4-ylidene(nitro)amine OR 153719-23-4 OR 428-650-4 OR CGA293343 OR Actara OR Cruiser OR Flagship OR Adage

These keywords are searched in the topic section of Web of science, which covers the title/abstract of Web of Science. Only Japanese (if any) or English articles are retrieved.

Further filters are applied to exclude news items, data papers that clearly do not fit the purpose of the assessment. Only peer-reviewed publications referenced as articles, review articles, proceeding paper and correction are included.

3.1.5 Identification of literature relevant to the four target impact areas for assessment: Toxicity, Residues, Ecotoxicity, Environmental Fate

The Japanese literature search guideline has defined 4 target impact for assessment:

1. Toxicity to humans
2. Residue in crops and livestock products (Residues)
3. Toxicity to flora and fauna in the human living environment (Ecotoxicity)
4. Environmental fate

In order to identify literature relevant to the 4-target impact areas for assessment, further filters are applied by selecting the Web of science expertise fields to the results of the search obtained

in point 3.1.4. As per the recommendation of the Japanese guidelines, all the web of science fields are selected for all the target impact for assessment described in Table 3.1.5-1.

Table 3.1.5-1: Classification fields regarding the target impact areas for assessment in the search using Web of Science

Target impact areas for assessment	Classification fields (corresponds to the term "categories" in WoS)
Toxicity to humans	Toxicology* Public environmental occupational health* Agriculture Multidisciplinary Allergy Biochemistry Molecular Biology Cell Biology Clinical Neurology Critical Care Medicine Developmental Biology Emergency Medicine Endocrinology Metabolism Genetic Heredity Immunology Medicine General Internal Medicine Research Experimental Multidisciplinary Sciences Neurosciences Oncology Pediatrics Pharmacology Pharmacy Physiology Reproductive Biology Veterinary Science
Residue in crops and livestock products	Plant Sciences* Environmental Sciences* Agriculture Multidisciplinary Agriculture Dairy Animal Science Food Science Technology Multidisciplinary Sciences Pharmacology Pharmacy Veterinary Sciences Zoology
Toxicity to flora and fauna in the human living environment	Toxicology* Environmental Sciences* Entomology* Ecology* Agriculture Multidisciplinary Biochemistry Molecular Biology Biodiversity Conservation Biology Cell Biology

	Developmental Biology Endocrinology Metabolism Environmental Studies Fisheries Marine Freshwater Biology Microbiology Multidisciplinary Sciences Neurosciences Ornithology Pharmacology Pharmacy Plant Sciences Reproductive Biology Veterinary Sciences Zoology
Environmental fate	Environmental Sciences* Agriculture Multidisciplinary Ecology Environmental Studies Fisheries Limnology Marine Freshwater Biology Multidisciplinary Sciences Soil Science Water Resources

Note: This literature search included all the classification field requested in the J-MAFF (2023): Guideline for collecting and selecting published literature, 27 July 2023

The classification field regarding the target impact for assessment in the search using WoS used in the report "Report on published literature - Active ingredient: Thiamethoxam", submitted on 2022-06-28 (final amendment on 2022-11-01), are indicated by asterisk "*".

As a result of the search terms relevant to the targeted pesticide and the targeted impact areas, the publications extracted from the Web of Science core Collection are the intersection (AND) of:

1: Papers about targeted pesticides

2: Papers about four targeted impact areas:

- toxicity to humans (including studies on animal metabolism and epidemiology)
- residues in crops and livestock products,
- toxicity to flora and fauna in the human living environment, and
- environmental fate.

The first step of the Collection corresponds therefore to the extraction of publications from the web of science core collection according to:

TS=(153719-23-4 Or 428-650-4 Or thiamethoxam or (EZ)-3-(2-chloro-1,3-thiazol-5-ylmethyl)-5-methyl-1,3,5-oxadiazinan-4-ylidene(nitro)amine or CGA293343 or Actara or Cruiser or Flagship or Adage) and Article or Review Article or Proceeding Paper or Correction (Document Types) and Toxicology or Public Environmental Occupational Health or Agriculture Multidisciplinary or Biochemistry Molecular Biology or Cell Biology or Clinical Neurology or Critical Care Medicine or Emergency Medicine or Endocrinology Metabolism or Medicine General Internal or Medicine Research Experimental or Multidisciplinary Sciences or Neurosciences or Oncology or Pediatrics or Pharmacology Pharmacy or Physiology or Reproductive Biology or Veterinary Sciences or Plant Sciences or Environmental Sciences or Agriculture Dairy Animal Science or Food Science Technology or Zoology or Entomology or Ecology or Biodiversity Conservation or Biology or Environmental Studies or Fisheries or Marine Freshwater Biology or Microbiology or Ornithology or Limnology or Soil Science or Water Resources (Web of Science Categories) and Japanese or English (Languages)

3.1.6 Removal of duplicates and false positives

The publications obtained as described in section 3.1.5 are then imported in EndNote where they are processed to remove false positives and duplicates as described below.

False positive Flagship

The previous literature search reported that some false positive results occurred. The false positive papers are those containing “Flagship” terms. Flagship is one of the commercial names of the product but also a term flagship ‘boat’. Papers are considered as false positives when they are not related to the thiamethoxam plant protection product but referring to the common term “Flagship”. They are removed from the set of potentially relevant articles by filtering all articles with ‘flagship’ but without thiamethoxam.

Duplicates within the new literature search

Publications are extracted from the Web of science core collection, which includes 3 databases: Science Citation Index Expanded (SCI-ExPANDED), Book Citation Index Science (BKCI-S), Book Citation Index – Social Sciences and Humanities (BKCI-SSH). Within the scope of this new literature search, all duplicate literature publications between the 3 databases are removed by using the duplicate tool search of EndNote within all the imported publications.

Duplicates between the previous and new literature search

Since this new literature search is produced for the same period as the one of the previous literature search, duplicates between the two periods can co-exist. The previous list of publications is imported into EndNote. Then the duplicate publications between the previous and new literature searches are removed by using the duplicate tool search of EndNote between the two sets of publications. As a result, only non-duplicate publications dealing with Web of Science classification field not assessed during the previous search are kept.

At the end of these three steps only non-duplicate literatures deprived of false positive “Flagship articles” are sent to the 4 specific target impact area Endnote templates.

3.1.7 Identification of literature relevant to the target organisms and compartments

The literature obtained is further refined by the scientific fields, the organisms and the compartments related of the target impact areas for assessment:

1: Toxicity to humans,

2: Residues in crops and livestock products,

3: Toxicity to flora and fauna in the human living environment,

4: Environmental fate,

as recommended by the Japanese Ministry of Forestry and Fisheries (MAFF) and the Food Safety Commission (FSC). The keywords specific to the scientific fields, the species and the compartments required by the Japanese authorities and the selected search terms are summarised below. The search strategy defined for each target impact area is then integrated into four Endnote templates.

3.1.7.1 Toxicity to humans

Table 3.1.7-1: Search terms specific to "toxicity in humans"

Search terms specific to the scientific field	
Keywords related to the scientific field	mortality OR skin irritation OR eye irritation OR sensitization OR allergy OR hypersensitivity OR metabolism OR distribution OR absorption OR excretion OR kinetic OR PK OR TK OR cytochrome OR enzyme OR mutagen OR DNA OR genotoxicity OR carcinogen OR cancer OR tumor OR oncology OR immune OR neurotoxicity OR endocrine disruption/disruptors OR hormone OR development OR developmental toxicity OR reproduction OR malformation OR maternal toxicity OR pregnancy OR embryo OR fetus OR offspring OR dermal OR epidermal OR exposure OR operator OR worker OR occupant OR biomonitoring OR medical OR poison OR apoptosis OR necrosis OR cytotoxic OR cohort OR epidemiology OR adverse effect OR case control
Search strategy for the scientific field (Integrated to Endnote)	tox* OR hazard OR in vivo OR in vitro OR mortality OR oral OR gavage OR inhal* OR skin* OR eye* OR irrit* OR sensi* OR allerg* OR hypersensitiv* OR metabol* OR distribution OR absorption OR adsorption OR excretion OR kinetic OR PK OR TK OR cytochrome OR enzym* OR muta* OR chromos* OR clastogen* OR DNA OR gen* OR carcino* OR cancer* OR tumor OR oncolog* OR immun* OR genotox* OR neurotox* OR endocrin* OR hormon* OR development* OR reproduct* OR fertil* OR malformation* OR matern* OR pregnan* OR embryo* OR foet* OR fet* OR offspring OR dermal OR epiderm* OR exposure OR operator* OR worker* OR bystander* OR resident* OR occupant* OR biomonitoring OR medical* OR poison* OR apoptosis OR necro* OR cytotox* OR behav* OR cohort OR epidemi* OR public OR adverse OR control
Search terms specific to the species/compartments	

Keywords related to the species/compartments to be evaluated	rat OR mouse OR dog OR rabbit OR monkey OR pig OR human OR hen OR S. typhimurium OR E. coli OR public environmental occupational health OR epidemic/epidemiological
Search strategy for species/compartments to be evaluated	rat* OR mouse OR mice OR dog* OR rabbit* OR monkey* OR pig* OR human* OR hen OR typhimurium OR coli OR somatic OR gen* OR public OR health OR epidemi*

3.1.7.2 Residues in crops and livestock products

Table 3.1.7-2: Search terms specific to "Residues in crops and livestock products"

Search terms specific to the scientific field	
Keywords related to the scientific field	Uptake OR metabolism OR metabolic OR breakdown OR translocation OR degradation OR storage OR stability OR residue OR process OR preharvest OR postharvest OR preplant OR pre-/post-emergence OR processing factor OR conversion factor OR hydroxylation OR photolysis OR rotation OR succeed OR supervised trial OR field trial OR dietary exposure OR MRL OR maximum residue level/limit
Search strategy used in Endnote	uptake OR metabol* OR breakdown OR translocate* OR degrada* OR storage OR stability OR residue* OR process* OR *harvest OR *plant OR *emergence OR conversion OR hydroxylation OR hydroly* OR photoly* OR rotation* OR succeed* OR trial OR diet* OR exposure OR MRL OR consume*
Search terms specific to the species/compartments	
Keywords related to the species/compartments to be evaluated	crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry
Search strategy for species/compartments used in Endnote	crop* OR plant* OR commodity OR food OR feed* OR livestock OR hen OR cattle* OR cow* OR goat* OR pig* OR ruminant* OR poultry OR honey OR milk OR process*

3.1.7.3 Toxicity to flora and fauna in the human living environment (Ecotoxicity)

Table 3.1.7-3: Search terms specific to "Toxicity to flora and fauna in the human living environment"

Search terms specific to the scientific field	
Keywords related to the scientific field	bioaccumulation OR bioconcentration OR biomagnification OR effect OR biodiversity OR protection goals OR eco OR impact OR population OR pest OR endocrine disruptive OR acute OR chronic OR long-term OR ecotoxicology OR colony OR hive OR aquatic OR freshwater OR macro-organism OR microorganism OR microbial OR biodegradation

Search strategy used in Endnote	*tox OR tox* OR adverse OR hazard* OR poison* OR *accumulation OR accumulate* OR *concentration OR concentration* OR *magnification OR *effect OR effect* OR *diversity OR protection OR eco* OR impact OR population OR endocrin* OR acute OR chronic OR long-term OR colony OR hive* OR aquatic OR freshwater OR *organism OR organism* OR microbial OR biodegradation
Search terms specific to the species/compartments	
Keywords related to the species/compartments to be evaluated	avian OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR fish OR crustacean OR aquatic OR chironomus OR bumble/honey/solitary bee OR pollinator OR apis
Search strategy for species/compartments used in endnote	plant* OR avian OR wild OR bird* OR mallard OR duck OR quail OR bobwhite OR vertebrat* or mammal* OR rat OR mouse OR mice OR rabbit* OR hare OR lemna OR alga* OR fish OR amphib* OR reptil* OR daphni* OR crustace* OR aquatic OR marin* OR estuarine* OR chiron* OR sediment dwell* OR gastropod* OR mollusc* OR bumble OR honey OR solitary OR bee* OR pollinator OR api* OR arthropod* OR beneficial* OR insect* OR collembol* OR earthworm* OR silkworm*

3.1.7.4 Environmental fate

Table 3.1.7-4: Search terms specific to "Environmental fate"

Search terms specific to the scientific field	
Keywords related to the scientific field	degradation OR photo OR hydrolysis OR accumulate OR dissipation OR vapor pressure OR mobility OR adsorption OR desorption OR persistent OR pollution OR contamination OR aged residue OR column leaching OR leach OR lysimeter OR drift OR run-off OR atmosphere OR transport OR long-range transport OR short-range transport OR monitoring OR surveillance OR environmental OR exposure OR fate OR residue
Search strategy for the scientific field used in Endnote	degrada* OR metabol* OR breakdown OR hydroly* OR photoly* OR accumulat* OR dissipat* OR mobility OR concentration* OR vapor OR vapour OR volatil* OR mobility OR adsorption OR desorption OR persisten* OR pollution OR contaminat* OR residue* OR leach* OR lysimeter OR *drift OR run-off OR drain* OR atmospher* OR transport OR monitor* OR surveillance OR environmental* OR exposure OR fate OR residue*
Search terms specific to the species/compartments	
Keywords related to the species/compartments to be evaluated	soil OR water OR sediment
Search strategy for species/compartments used in Endnote	soil* OR water* OR sediment* OR air

As a result of these filters, 4 Endnote libraries containing references relevant to each of the expert areas are produced.

This is the end of the Collection of literature data step.

3.2 Step II: Rapid assessment (title and abstract)

All publications collected and sorted out during the collection step are then are evaluated based on title and abstract in the Rapid assessment step. They are sorted out in two groups: publications which are considered as irrelevant and publications which are potentially relevant and which will further evaluated.

Publications are considered as clearly irrelevant if they met the exclusion criteria described below:

- Papers that are not related to the pesticide (alternative formulation for the pesticide, etc.)
- Papers regarding policies, society, and economic analysis
- Papers regarding production and distribution of crops, etc.
- Papers regarding beneficial or harmful effects, and physical and chemical properties
- Papers regarding analytical method and development
- Papers written from the standpoint of new synthetic method or basic chemistry
- Literatures regarding patents
- Summaries, reviews, or books presented at academic conferences that do not contain adequate data or information for risk assessment
- Written opinions that do not provide new data which can be used for risk assessment
- Secondary information, including scientific papers and reviews on regulations, for which the primary source (original work) to which the literature refers cannot be verified.
- Papers regarding exposure to common pesticides (not limited to the pesticide but describe about wide range of pesticides)*
- Papers regarding toxicity of mixed formulation derived from different active substances
- Papers that are not related to the four target impact areas: Toxicity to humans, Residues in crops and livestock products, Toxicity to flora and fauna in the human living environment, Environmental fate.
- Papers written only in a dry lab using computer simulation, etc.
- Papers regarding formulations with recipes that are not registered in Japan**

Publications that do not meet the exclusion criteria or for which the relevance are unclear based on title and abstract are further assessed for relevance based on their full text publication.

*Publications that dealt about thiamethoxam, neonicotinoids or mixtures containing thiamethoxam were assessed.

**In order to have an exhaustive assessment, all the formulations and not only the one's registered in Japan have been taken into account.

3.3 Step III: Detailed assessment (full text)

The purpose of the detailed assessment is to detect relevant and reliable studies for the purpose of the evaluation of the active substance and to exclude non relevant articles. This is achieved through the following steps:

1. Exclusion based on the full text

- Exclusion of literatures that clearly have no relevance to the purpose of assessment based on the review of the full text. The reasons of exclusion are the same as in section 3.2.

- Additional reasons of exclusion also include study designs, system, species, or exposure routes are not appropriate from the perspective of the use in assessment, but also includes the following criteria:

  a) Studies whose methods have not been described

  b) Studies that have not been conducted with the test species that allow adequate assessment

  c) Studies that have not been administered/processed via appropriate routes

  d) Studies for which the amount of the test substance administered or processed has not been specified

  e) Studies for which the media used for addition to test substance cannot be confirmed

  f) Studies for which the analytical methods have not been described

2. Inclusion of literatures that meet the relevance criteria based on full text

   General classification criteria used are as defined in the Japanese guideline requirement:

   a) The test environment in place meets the conditions specified in the Test Guideline (TG)

   b) Purity of the test substance applied or processed is specified

   c) Number of animals/examples that allows statistical analysis has been secured

   d) Conducted in multiple doses (at least in 3 doses)

   e) Untreated plot (control plot) has been established and the result is appropriate in view of the TG.

   f) Analytical method and the result have been reported

3. Classification of included papers according to relevance category “a”, “b”, or “c” as described in section 3.3.1.

4. Confirmation of the reliability of literatures classified as relevance category “a” and classification based on Klimisch score as described in section 3.3.1.1.

5. Sorting out of assessment reports of international organizations and assessment agencies in US/Europe. They are made as the subject of assessment.

3.3.1 Classification of literatures that are relevant

The full text assessed publications which do not meet the exclusion criteria are considered as relevant and are classified into 3 categories of relevance. These categories are described in the table below.

Table 3.3.1-1: Classification of literatures that are relevant with the purpose of assessment

Category	Applicable literatures
a	Literatures that may be used to set or reconsider risk assessment parameters (ADI, ARfD, AOEL, residue standards, registration standards for flora and fauna in the human living environment, PEC for aquatic organisms, etc.)
b	Literatures that may be used as supplementary data when setting risk assessment parameters.
c	Literatures that are not classified as a or b

3.3.1.1 Reliability assessment of literatures classified as relevance category “a”

For those literatures classified as “Category a” in the relevance assessment against the purpose of assessment, appropriate reliability is then set according to the classification of Klimisch score.

Table 3.3.1-2: Summary of Klimisch score

Classification	Reliability	Evaluation criteria
1	Reliable (no restriction)	If applicable to any of the following study/data: - It is conducted with a method whose efficacy has been confirmed, or based on internationally recognized test guideline (preferably, GLP-compliant) - Test items (assessment parameter) are based on certain (country level) test guideline - All test items are highly relevant/equivalent with the method described in the test guideline
2	Reliable (with restriction)	If applicable to any of the following study/data (most of the time, non-GLP test): - Test items do not completely comply with the test guideline, but the content is acceptable. - Although the test method deviates from the test guideline, scientifically acceptable results are shown based on detailed report.
3	Not reliable	Studies/data that are unacceptable for expert judgement from the perspectives of the validity of test system, test substance or exposure route, or inadequate information
4	Unevaluable	Studies/data with only summaries or secondary information (books, reviews, etc.) are given and details are unknown

CHAPTER 4 SEARCH RESULTS

4.1 Publications extracted from the WoS databases

The number of hits obtained in WoS by using search terms specific to the active substance and product names and then filtered for the document types, and languages is 2535.

The number of hits extracted from WoS after filtering with the classification fields in relation to the target impact areas for assessment in Web of Science is 1779.

The number of hits obtained after removal of false positives Flagship publications, after removal of publications already assessed during the previous search and after removal of duplicates is 362. These papers are papers that need to be assessed. Table 4.1-1 below describes the numbers of extraction obtained from the previous search and the new search.

Table 4.1-1: Summary of the number of references processed (extracted and processed)

Step	Number of papers
Previous search	
Total number of papers	1209
Flagship (False positive)	313
New search	
Total number of papers extracted by the target pesticide names and all the Web of Science classification fields of the 4 target impact of assessment (Total of all databases)	1779
Number of papers containing Flagship terms (False positive)	576
Number of papers that do not contain Flagship terms (True positive)	2099
Number of duplicate papers between previous and new searches	1683
Number of papers to be assessed (excluding papers contain Flagship terms, excluding papers from the previous search and excluding duplicates)	362

The number of papers to be assessed are further categorized and filtered to keep only papers containing keywords relevant to each target impact areas as defined in Table 3.1.7-1, Table 3.1.7-2, Table 3.1.7-3 and Table 3.1.7-4. The only 2 papers are not categorized by the keywords. Therefore, the number of publications to be assessed for each of the target impact areas of assessment are:

- Toxicity to humans: 340
- Residues in crops and livestock products: 311
- Toxicity to flora and fauna in the human living environment: 342
- Environmental fate: 274
- Others: 2

Table 4.1-2: Summary and results of the study selection process on WoS platform and Endnote

Study selection process	Active substance thiamethoxam (2015-03-01 and 2021-04-01)				
	Toxicity to humans	Residues in crops and livestock products	Toxicity to flora and fauna in the human living environment	Environ-mental Fate	Others
Total number of documents retrieved after removal of duplicates and false-positive Flagship® (global search results related to the active substance, its metabolites and plant protection products containing the active substance and web of science classification fields specific to the target impact for assessment)	362				
Number of publications potentially relevant per target impact area (according to specific search terms relevant to each section)	340	311	342	274	2

4.2 Evaluation

4.2.1 Rapid assessment

During the rapid assessment step, the publications were evaluated based on title and abstract. Publications were considered as clearly irrelevant if they met the exclusion criteria described in section 3.2.

The results of the conformity assessment are summarised in Table 4.2-1. A summary of the number of results obtained is described below.

Table 4.2-1: Summary of the number of references after the conformity assessment with the evaluation objectives (Step 1)

Study selection process	Active substance thiamethoxam (2015-03-01 and 2021-04-01)				
	Toxicity to humans	Residues in crops and livestock products	Toxicity to flora and fauna in the human living environment	Environ-mental Fate	Others
Number of publications potentially relevant per target impact area (according to specific search terms relevant to each section)	340	311	342	274	2
Number of publications excluded after rapid assessment for relevance by title/abstract (non-relevant to specific search terms, excluded literature)	337	299	296	273	2
Number of publications for which detailed assessment of full text are required (considered relevant after rapid assessment)	3	12	46	1	0

4.2.2 Full text assessment

4.2.2.1 Summary of results

During this step, the publications considered relevant after the rapid assessment were evaluated based on full text. Publications were considered as relevant if they meet the relevance criteria described in section 3.3.1. As it was the case during the rapid assessment, in this step publications were excluded if they met the criteria described in section 3.2.

Table 4.2-2: Summary of the number of references after the relevance assessment with the evaluation objectives (Step 2)

Study selection process	Active substance thiamethoxam (2015-03-01 and 2021-04-01)			
	Toxicity to humans	**Residues in crops and livestock products**	**Toxicity to flora and fauna in the human living environment**	**Environmen-tal Fate**
Number of publications for which detailed assessment of full text are required (considered relevant after rapid assessment)	3	12	46	1
Number of publications excluded from further consideration after detailed assessment for relevance (non-relevant, excluded literature)	1	2	16	0
Number of papers from international organisation considered relevant at the full text assessment step	0	1	0	0
Number of publications considered relevant following the two-step process (i.e., after detailed assessment of full-text)	2	9	30	1

Any relevant open literature cited in evaluation documents of international organisations (JMPR, US EPA, ECHA, European Commission and EFSA) were also sorted out at this step. Only one publication from the organisation EFSA was found and the result is described in Table 4.2-16.

Based on full text documents, the relevant articles were further evaluated in accordance with the relevance criteria given in Tables Table 3.3.1-1 - Table 3.3.1-4, and sorted as potentially relevant for risk assessment (Category “a”), as supplemental data (Category “b”), either not applicable (Category “c”). The detailed evaluation results are given in Table 4.2-8 to Table 4.2-15.

Table 4.2-3: Summary of the number of references and their classification in Step 2 of the relevance assessment

Study selection process	Active substance thiamethoxam (2015-03-01 and 2021-04-01)			
	Toxicity to humans	**Residues in crops and livestock products**	**Toxicity to flora and fauna in the human living environment**	**Environmen-tal Fate**
Number of papers considered as relevant classified as category “a” (Literatures that may be used to set or reconsider risk assessment parameters)	0	2	2	0
Number of papers considered as relevant classified as category “b” (Literatures that may be used as supplementary data when setting risk assessment parameters.)	0	5	27	1
Number of papers considered as relevant classified as category “c” (Literatures that are not classified as a or b)	2	2	1	0
Number of publications considered as reliable (Klimisch score if category “a”)	0	2 (all were given Klimisch score 2)	2 (all were given Klimisch score 2)	0

Category “a” = Reference to establish or review risk assessment parameters
Category “b” = Reference available as supplementary data
Category “c” = Not classified

Only the references judged to be Category “a" in Step 2 of the relevance assessment were checked for reliability by applying scores according to Klimisch et al. (997). Furthermore, they were listed with some more detailed - as requested by the Japanese Ministry of Forestry and Fisheries (MAFF) and the Food Safety Commission (FSC) - in separate Tables per scientific field of interest.

4.2.2.2 Detailed results of full text assessment

The following tables provide results obtained during the full text assessment.

Table 4.2-4: List of papers determined "not relevant" in the second phase of relevance assessment and its reason for reason for judgement for the "Toxicity to humans" section

Author	Year	Title	Journal	Reason for judgement
D. Y. Kong, J. D. Zhang, X. H. Hou, S. B. Zhang, J. Tan, Y. S. Chen, W. R. Yang, J. W. Zeng, Y. Han, X. H. Liu, D. L. Xu and R. L. Cai	2017	Acetamiprid inhibits testosterone synthesis by affecting the mitochondrial function and cytoplasmic adenosine triphosphate production in rat Leydig cells	Biology of Reproduction, 96, 1, 254-265	This is an oral subacute study on rat to observe the effect on male testosterone secretion after administration of acetamiprid (a neonicotinoid). This is a non-guideline study with no mechanistic action conclusion from the whole family of neonicotinoid and this is not related to Thiamethoxam. Thus, this study is not applicable for the dossier.

Table 4.2-5: List of papers determined "not relevant" in the second phase of relevance assessment and its reason for the "residues in crops and livestock products" section

Author	Year	Title	Journal	Reason for judgement
W. T. Jiao, G. Q. Ge, R. M. Hua, J. Sun, Y. Y. Li and R. Y. Hou	2019	Study on the Metabolism of Six Systemic Insecticides in a Newly Established Cell Suspension Culture Derived from Tea (Camellia Sinensis L.) Leaves	Jove-Journal of Visualized Experiments, 148,	This study presents the advantages to study metabolic pathways using plant cells rather than intact plant from field. The study does not address the metabolic pathway of thiamethoxam. The induction of callus from leaves harvested from field-grown tea trees and from leaves excised from tea plantlets grown *In vitro* in a sterile environment was compared by measuring contamination, browning, and induction after 28 days of cultivation on MS media. No detail on the concentration of thiamethoxam or its metabolites are indicated. This study does not meet the requirements for the metabolism residue study.
C. C. Wu, F. S. Dong, X. D. Mei, J. Ning and D. M. She	2019	Distribution, Dissipation, and Metabolism of Neonicotinoid Insecticides in the Cotton Ecosystem under Foliar Spray and Root Irrigation	Journal of Agricultural and Food Chemistry, 67, 45, 12374-12381	Field trials of cotton were conducted in 2017 under open conditions in Liaocheng, Shandong Province, China; and in accordance with the Guidelines for Testing Pesticide Residues issued by the Ministry of Agriculture of the People's Republic of China.

Table 4.2-6: List of papers determined "not relevant" in the second phase of relevance assessment and its reason for judgement for the "Toxicity to flora and fauna in the human living environment" section

Author	Year	Title	Journal	Reason for judgement
B. A. Woodcock, J. M. Bullock, R. F. Shore, M. S. Heard, M. G. Pereira, J. Redhead, L. Ridding, H. Dean, D. Sleep, P. Henrys, J. Peyton, S. Hulmes, L. Hulmes, M. Sarospataki, C. Saure, M. Edwards, E. Genersch, S. Knabe and R. F. Pywell	2017	Country-specific effects of neonicotinoid pesticides on honey bees and wild bees	Science, 356, 6345, 1393-+	This study is large-scale field experiment aiming to assess the effects of neonicotinoid-treated crops (winter oilseed rape grown with either seed coatings containing clothianidin or thiamethoxam or control with no seed treatment) on honeybee species *Apis mellifera*, *Bombus terrestris* and *Osmia bicornisacross* across three countries (Hungary, Germany, and the United Kingdom). Thiamethoxam was applied at 10.07 to 11.14 g a.i./ ha and combined with the fungicides fludioxonil and metalaxyl-M (trade name Cruiser). All treatments received typical commercial inputs of pesticides (e.g., lambda-cyhalothrin) and fertilizers. Residues of thiamethoxam were quantified both in the nests of bee species and those expressed in the crop. Results of the study suggest that exposure to neonicotinoid seed treatments can have negative effects on the interannual reproductive potential of both wild and managed bees, but that these effects are not consistent across countries. This is a non-guideline study. Thiamethoxam seed treatment was combined with other pesticides, and the effects observed cannot be attributed to thiamethoxam alone. The study therefore is not considered further.
J. C. Miles, J. Hua, M. S. Sepulveda, C. H. Krupke and J. T. Hoverman	2017	Effects of clothianidin on aquatic communities: Evaluating the impacts of lethal and sublethal exposure to neonicotinoids	Plos One, 12, 3,	This study evaluated the effects of clothianidin on aquatic communities in a combination of field surveys conducted in USA and mesocosm experiments at field-relevant concentrations. Thiamethoxam was detected in water samples during the field survey along with other pesticides. The effects of thiamethoxam cannot be distinguished from the effects of other pesticides and environmental stressors. The aim of mesocosm experiment was to evaluate interactive effects of clothianidin and predation on aquatic communities. The article is not considered further.
R. Zemeckis, A. Dautarte, J. Kretavicius and J. Drozdz	2019	Effects of winter and spring rape seed treatment with neonicotinoids on honey bees	Zemdirbyste-Agriculture, 106, 2, 173-182	In this study the impact of winter and spring rape seed treatment with thiamethoxam and clothianidin on the development, wintering and productivity of bee colonies, as well as neonicotinoid residues in rape pollen, nectar and bee

Author	Year	Title	Journal	Reason for judgement
				bread were investigated in 2016-2018 under field conditions in Lithuania. The research provides a methodology for the establishment of bee colonies, setting of test fields and the determination of neonicotinoid residues in nectar, pollen and bee bread. The impact of neonicotinoids on honey bees was observed in fully developed bee colonies after overwintering. The study also aimed to quantify the levels of neonicotinoids in the dust released during the sowing operation. In the summer of 2017 and 2018 (June and July), the effects of neonicotinoids on bees were investigated during the flowering stage of spring rape (*Brassica napus L*.). Neonicotinoid residues were analytically identified in nectar, pollen, bee bread and soil dust. As a source of thiamethoxam, formulation thiamethoxam 280 g/L+ fludioxonil 8.0 g/L + metalaxyl-M 32.3 g/L was used. The seeds were coated simultaneously with thiamethoxam and clothianidin. As sources of these two neonicotinoids, two insecticides: beta-cyfluthrin 80 g/L + clothianidin 400 g/L and thiamethoxam 280 g/L + fludioxonil 8.0 g/L + metalaxyl-M 32.3 g/L and were used. Because the seeds were treated with several systemic pesticides, the effects observed cannot be attributed to thiamethoxam alone. The study is not considered further.
L. W. Atwood, D. A. Mortensen, R. T. Koide and R. G. Smith	2018	Evidence for multi-trophic effects of pesticide seed treatments on non targeted soil fauna	Soil Biology & Biochemistry, 125, 144-155	In this study corn and soybean was grown in the field conditions with and without pesticide seed treatment for three years. The field experiment was conducted at the Pennsylvania State University Russell A. Larson Agricultural Research Center in Rock Springs, PA, USA. The response of the soil faunal detritivore, herbivore, mixed, and predator feeding guilds, nitrogen mineralization, and surface litter decomposition at three time points each year was evaluated. Maize seeds planted in the pesticide seed treatment were pre-coated with a mixture of systemic insecticide thiamethoxam (0.25 mg ai/seed), the contact fungicide fludioxonil, and the systemic fungicides mefenoxam, azoxystrobin, and thiabendazole. The soybean seed planted in the pesticide seed treatment was coated with a pesticide mixture that included systemic insecticide thiamethoxam (0.25-0.5 mg ai/seed), the contact fungicide fludioxonil, and the systemic

Author	Year	Title	Journal	Reason for judgement
				fungicides mefenoxam and sedaxane. The maize and soybean seeds planted in the control did not contain the coating. The experiment continued for three years. Each year the same genotype of a glyphosate resistant crop was planted either with or without pesticide seed treatment in a completely randomized design with five replications. The response of the soil fauna at the whole community and feeding guild levels (detritivore, herbivore, mixed, and predator groups), surface litter decomposition, plant available soil nitrogen, and crop yields. The study provides information on the effects of pesticide seed treatments on soil fauna under field conditions, however thiamethoxam seed treatment was applied in combination with other pesticides, and the effects observed cannot be attributed to thiamethoxam alone. The study therefore is not considered further.
J. A. Mustard, A. Gott, J. Scott, N. L. Chavarria and G. A. Wright	2020	Honeybees fail to discriminate floral scents in a complex learning task after consuming a neonicotinoid pesticide	Journal of Experimental Biology, 223, 5,	This study evaluated the effect on the cognitive processes of honeybees when exposed to thiamethoxam (TMX) and other neonicotinoids. The bees were fed with the pesticide dissolved in sucrose syrup (2.736 ng/bee) and were subjected to differential conditioning to make them associate distinct olfactory conditioned stimuli with a positive reinforce or a punishment. Honeybees fed for 48 h with a field-relevant concentration of thiamethoxam had difficulty to distinguish the stimuli associated with a reward and with punishment (i.e., 1-hexanol and 1-decanol odours, respectively). The trained and thiamethoxam-exposed bees had difficulty to respond and distinguish a gradient of odours according to their similarity to 1-hexanol and 1-decanol. An additional simple olfactory conditioning task showed that TMX did not interrupt the ability to learn, but impairs the olfactory processing, since they were more likely to generalize the previous gradient of odours. This is a non-guideline study, and the used method significantly differs from the regular approach set by agreed guidance. The test is designed to provide a qualitative outcome and no regulatory endpoint can be derived from it (mortality not reported). Test concentrations were not analytically verified. Environmental conditions were not

Author	Year	Title	Journal	Reason for judgement
				provided either. This non-guideline study provides information on effects of thiamethoxam on bees olfactory performance, however as the outcome has no relevance for the risk assessment; the article is therefore not further considered.
Y. H. Wang, Y. Zhang, P. Xu, B. Y. Guo and W. Li	2018	Metabolism Distribution and Effect of Thiamethoxam after Oral Exposure in Mongolian Racerunner (Eremias argus)	Journal of Agricultural and Food Chemistry, 66, 28, 7376-7383	This study evaluates the metabolism, distribution, and effect of thiamethoxam in a reptile species Eremias argus after oral exposure to thiamethoxam of known purity at a rate of 20 mg/kg bw. The lizards were euthanized at several timepoints, and randomly selected animals were collected for organs and tissues analysis of concentrations, PCR and enzymatic activity. The elimination of thiamethoxam in lizard blood was fast ($t_{1/2}$ = 2.70 h). The highest concentrations were detected in gonads at 6 h after administration, indicating that it might have potential reproductive toxicity risk to lizards. The gene expression profile indicated that CYP3A4 and AOX played a leading role in thiamethoxam metabolism in liver, while CYP3A7 played a leading role in kidney. The enzyme inhibition test showed that CYP2C9 might also play a key role in the metabolism of TMX. These results can be potentially linked to carcinogenic and hepatic injury risk to lizards. This study does not follow any official guideline and the obtained outcome is not considered relevant or usable for risk assessment and regulatory performance. Moreover, just a single dose was administered, and the results are not directly related with a clear adverse outcome. The article is therefore not further considered.
P. Heneberg, P. Bogusch, A. Astapenkova and M. Rezac	2020	Neonicotinoid insecticides hinder the pupation and metamorphosis into adults in a crabronid wasp	Scientific Reports, 10, 1,	The study evaluates the metamorphosis success of bees and wasps exposed to field-realistic concentrations of thiamethoxam among other neonicotinoid insecticides, and in response to the combined exposure with benzimidazole fungicides. Prepupae of *Pemphredon fabricii* were collected from three different areas and exposed to a commercial formulation of thiamethoxam (Actara 25 WG) at 178.5 ng/cm^2 or 210.0 ng/cm^2, by spraying over 96-well plates. The relative number of individuals that pupated differed from that observed in the water-treated control when treated with the higher concentration of thiamethoxam. The relative number of

Author	Year	Title	Journal	Reason for judgement
				individuals that metamorphosed from pupae into adults differed between the water-treated control and those treated with any of the tested concentrations of thiamethoxam. Generally, all modes of thiamethoxam treatments led to a survival rate below 10%. The longest times to death were also observed in thiamethoxam-treated individuals, which had difficulties with metamorphosis into adults but not pupation. This is a non-guideline study, and the used method significantly differs from the regular approach set by agreed guidance on contact exposure on arthropods. Moreover, thiamethoxam was applied as a formulation, which could contain unknown co-formulants and, therefore, the observed effects are not related to a single test item. Hence, the results obtained are not usable for risk assessment, and the article is therefore not further considered.
M. Rezac, V. Rezacova and P. Heneberg	2019	Neonicotinoid insecticides limit the potential of spiders to re-colonize disturbed agroecosystems when using silk-mediated dispersal	Scientific Reports, 9,	In this study the effects of contact exposure to thiamethoxam (delivered as Actara formulation, 25% a.s. content) on the behaviour (ability to rappel and balloon) of two common farmland spider species, Oedothorax apicatus (Linyphiidae) and Phylloneta impressa (Theridiidae). The outcome of this study has no relevance for the risk assessment as spiders are not considered in risk assessment. The article is therefore not considered further.
M. Parizadeh, B. Mimee and S. W. Kembel	2021	Neonicotinoid Seed Treatments Have Significant Non-target Effects on Phyllosphere and Soil Bacterial Communities	Frontiers in Microbiology, 11,	This study investigated the effects neonicotinoid seed treatment on soil and phyllosphere bacterial community diversity, composition and temporal dynamics in a 3-year soybean/corn rotation in Quebec, Canada (soybean in 2016 and 2018, corn in 2017) using gene sequencing. Four replicates of each non-neonicotinoid (control) and neonicotinoid-treated plots were established alternately and consisted of four rows each. Two extra neonicotinoid-treated plots surrounded the experimental field. Soybean and corn seeds were coated with three fungicides (difenoconazole, metalaxyl-M, and sedaxane) in both control and treated plots. The neonicotinoid-treated seeds, were also covered by thiamethoxam at 0.25 mg/seed. The fields were under no-till farming. Glyphosate was applied twice during each growing season (before seeding and one month after it) to control weeds. Neonicotinoid treatment favored bacterial genera

Author	Year	Title	Journal	Reason for judgement
				known as neonicotinoid biodegraders, and reduced relative abundance of some potentially beneficial soil bacteria (such as those involved in nitrogen cycle). This is a non-guideline study. Thiamethoxam was applied together with fungicides difenoconazole, metalaxyl-M, and sedaxane, and the effects observed cannot be attributed to thiamethoxam alone. Overall, the study provides information on the effects of seed treatments on soil bacterial communities, however because thiamethoxam was mixed with fungicides, the study is not considered further.
O. Samson-Robert, G. Labrie, M. Chagnon and V. Fournier	2017	Planting of neonicotinoid-coated corn raises honey bee mortality and sets back colony development	Peerj, 5,	In this study honey bee mortality from commercial apiaries (honey bee mortality and long-term effects on colony development simulated with population dynamic model) located in two different agricultural settings (corn-dominated areas and corn-free environments) was evaluated during the corn planting season in 2012 and 2013 from 26 bee yards in Quebec, Canada. Exposed apiaries were located within a 500 m radius from a treated-corn field, and within 3 km radius from dominated by neonicotinoid-treated corn fields (exposed treatment). Control apiaries were located in an area where the main crops are hay, wheat, oats, barley and rye and with minimal distance of 3 km from any crop planted with neonicotinoid seed coating. Concentrations of pesticides in honey bee bodies were determined using LC-MS/MS. A total of 32 pesticides and metabolites, with an average of 3.48 chemicals per sample and up to 9 different compounds in a single sample were identified in the study. 31% of samples contained clothianidin and thiamethoxam. The study evaluates the combined impact of different pesticides on honey bee colonies located in proximity of treated fields. The effects of thiamethoxam cannot be distinguished from the effects of other pesticides. The study therefore is not considered further.
D. S. W. Chan and N. E. Raine	2021	Population decline in a ground-nesting solitary squash bee (Eucera pruinosa) following exposure to a neonicotinoid	Scientific Reports, 11, 1,	In this study the effects of realistic exposure to systemic insecticides (applied as seed treatment on squash crops) on ground-nesting bee (Hoary squash bee, Eucera pruinosa) were evaluated in a 3-year semi-field experiment in Ontario, Canada.

Author	Year	Title	Journal	Reason for judgement
		insecticide treated crop (Cucurbita pepo)		Acorn squash seeds were treated with 1) FarMore FI400: neonicotinoid insecticide Cruiser 5FS (47.6% thiamethoxam) + fungicides Apron XL (33.3% mefenoxam), Maxim 480FS (40.3% fludioxonil), and Dynasty (9.6% azoxystrobin); 2) neonicotinoid insecticide Admire 240 (21.4% imidacloprid) and 3) anthranilic diamide insecticide Coragen (21.4% chlorantraniliprole). Thiamethoxam was applied on squash seeds in combination with fungicides, and the effects observed cannot be attributed to thiamethoxam alone. The study is therefore not considered further.
S. K. Arserim, H. Cetin, K. Yetismis, Z. N. Omondi and Y. Ozbel	2020	Toxicity of Thiamethoxam on Field-Collected Sand Flies (Diptera: Psychodidae) From Different Regions of Turkey	Journal of Medical Entomology, 57, 1, 214-217	This study is not considered relevant for the following reasons: 1) the effects of thiamethoxam on sand flies were measured as Knockdown Time 50% (KDT50), which is not a relevant endpoint for the risk assessment for non-target arthropods; 2) the study was not carried out in line with any OECD Test Guidelines; 3) no chemical analysis was described; 4) phlebotomine sand flies are not relevant species for the risk assessment for non-target arthropods; 5) The study was conducted in five different locations in Turkey, which might not be representative for Japan due to the agroclimatic differences between these two countries.
S. Stoyanova, K. Nyeste, E. Georgieva, P. Uchikov, I. Velcheva and V. Yancheva	2020	Toxicological impact of a neonicotinoid insecticide and an organophosphorus fungicide on bighead carp (Hypophthalmichthys nobilis Richardson, 1845) gills: a comparative study	North-Western Journal of Zoology, 16, 1, 64-73	The main aim of the present study was to compare the toxicological effects of thiamethoxam on the gill histological structure of bighead carp. This study is not considered relevant for the following reasons: 1) the effects of agrochemicals on fish gill histology do not provide specific data on acute or chronic toxicity. Effects on mortality and reproduction are usually the main effects considered to assess the toxicity of agrochemicals on fish; 2) no chemical analysis was used in the study to verify the test concentration; and 3) bighead carp is usually not a relevant fish species used in the aquatic risk assessment.
A. Alford and C. H. Krupke	2017	Translocation of the neonicotinoid seed treatment clothianidin in maize.	Plos One, 12, 3,	The article describes a two-year field study that compared concentrations of clothianidin seed treatments in maize to that of maize without neonicotinoid seed treatments.

Author	Year	Title	Journal	Reason for judgement
Mitchell, E. A. D.Mulhauser, B.Mulot, M.Mutabazi, A.Glauser, G.Aebi, A.	2017	A worldwide survey of neonicotinoids in honey	Science, Vol 358, Issue 6359	This study is not considered relevant for the following reasons: 1) it focused on clothianidin as an active substance, and not as a metabolite of thiamethoxam; 2) the scientific article measured the translocation of clothianidin into plant tissue, which is not relevant for the ecotoxicological risk assessment for non-target plants; and 3) the field study was conducted in the United States, which might not be representative for Japan due to the agroclimatic differences between these two countries.
C. D. E. Silva, W. de Rooij, R. A. Verweij and C. A. M. van Gestel	2020	Toxicity in Neonicotinoids to Folsima candida and Eisenia andrei	Environmental Toxicology and Chemistry, 39, 3, 548-555 DOI: 10.1002/etc.4634	This study provides relevant toxicity endpoints for soil organisms by technical active thiamethoxam and also the formulation 'Actara' containing 25% of thiamethoxam. The study was conducted with two species (Eisenia Andrei and Folsomia candida). The test organisms is not target organisms in Japan.

The study notes that the controls of thiamethoxam tests did not meet the OECD criterion of the minimum number of juvenile earthworms for the validity of the test.

Table 4.2-7: List of papers determined "not relevant" in the second phase of relevance assessment and its reason for judgement for the "Environmental section"

Author	Year	Title	Journal	Reason for judgement
No references were rejected during the step 2 for the environmental fate section.				

Table 4.2-8. List of references judged as Category “b" and Category “c” in Step 2 in the second phase of relevance assessment and the reasons for the judgments - Toxicity to humans

List No.	Author	Year	Title	Journal	Reason for judgement
Category “b”					
No papers were ranked as category “b” for the section toxicity to humans.					
Category “c”					
1	Z. W. Nie, Y. J. Niu, W. Zhou, Y. H. Kim, K. T. Shin and X. S. Cui	2019	Thiamethoxam inhibits blastocyst expansion and hatching via reactive-oxygen species induced G2 checkpoint activation in pigs	Cellular Signalling, 53, 294-303 doi.org/10.1016/j.cellsig.2018.08.014	This is a non-guideline *In vitro* study to confirm the hypothesis that Thiamethoxam induces adverse effect on porcine preimplantation embryonic development via an ROS-dependent DNA damage checkpoint response. Early porcine embryos were exposed to a concentration gradient of Thiamethoxam and then cultured for 7 days. Observations were done on blastocysts morphology, numbers of cells, the ROS content and potential DNA damage checkpoint and other indication of DNA damage due to ROS. The results of the study suggest that thiamethoxam induces oxidative stress and disrupts mitochondrial functions. As this study doesn’t follow OECD guideline and gives no clear relation about dose related to effect it cannot be used as supportive. Nevertheless, this study gives indications of how works the thiamethoxam toxicity and could be an additional data and therefore classified as [category “c”].
2	D. Q. Yang, X. T. Zhang, L. Yue, H. L. Hu, X. J. Wei, Q. Guo, B. Y. Zhang, X. P. Fan, Y. Xin, Y. R. Oh and N. Gu	2021	Thiamethoxam induces nonalcoholic fatty liver disease in mice via methionine metabolism disturb via nicotinamide N-methyltransferase overexpression	Chemosphere, 273, doi.org/10.1016/j.chemosphere.2021.129727	This is a 12-week oral toxicity study in ICR mice, non GLP or OECD guideline compliant. Mice were divided into three groups, control, treated with 4 mg/kg or 12 mg/kg of thiamethoxam. At the end of the study the observations were done almost only on liver (histopathological and biochemistry modifications). As this study doesn’t follow OECD guideline and gives no clear relation about dose related to effect it cannot be used as supportive. Nevertheless, this study gives indications of how works the thiamethoxam toxicity and could be an additional data and therefore classified as [category “c”].

Table 4.2-9: List of references judged as "Category b" and "Category c" in Step 2 in the second phase of relevance assessment and the reasons for the judgments - Residue in crops and livestock products

List No.	Author	Year	Title	Journal	Reason for judgement
Category "b"					
3	Y. L. Bian, G. Guo, F. M. Liu and X. H. Li	2023	Residue extrapolation and group maximum residue level recommendation for four pesticides in the four kinds of vegetable crop groups	International Journal of Environmental Analytical Chemistry, 103, 5, 995-1010 DOI: 10.1080/03067319.2020.1866564	In this Chinese study, crop field trials and residue analysis were conducted to investigate the residue fate and risk assessments for difenoconazole, bifenthrin, thiamethoxam and its metabolite clothianidin in the Fruiting Vegetables, Cucurbits Group (cucumber, bitter gourd, loofah, zucchini), the Fruiting Vegetables, other than Cucurbits Group (tomato, cherry tomato, eggplant), the Legume Vegetables Group (cowpea, kidney bean) and the Stalk and Stem Vegetables Group (celery, fennel). OECD calculator was used to evaluate and to recommend MRLs of these pesticides in the studied vegetables. No details on the rate applied were given. In this work, the HPLC-MS/MS and GC-MS methods with the modified QuEChERS preparation were developed to investigate the four pesticides (difenoconazole, thiamethoxam, clothianidin and bifenthrin) residue behaviours in the eleven vegetable crops (cucumber, bitter gourd, loofah, zucchini, tomato, cherry tomato, eggplant, cowpea, kidney bean, celery, and fennel) under open field conditions, and to study the crop classification and residue extrapolation between these different vegetable groups and subgroups. Results showed that it was more reasonable to extrapolate the Fruiting vegetables, other than Cucurbit group to the Fruiting vegetables, Cucurbits group because of the higher residue levels. Furthermore, the residue extrapolation between subgroups was also possible, cherry tomato and eggplant could be extrapolated to tomato, bitter gourd and loofah could be extrapolated to cucumber and zucchini. In addition, the different edible parts led to a large difference in pesticide residues, celery and fennel had higher residue risk in the four vegetable groups because the edible parts of them are whole plants including the leaves. The residue difference in the same edible parts of the different crop groups was not obvious, such as the Fruiting vegetables, Cucurbits group and the Fruiting vegetables, other than Cucurbit group. The PFs extrapolation was more reasonable than residue extrapolation because of fewer uncontrollable factors in processing

List No.	Author	Year	Title	Journal	Reason for judgement
					experiments. The PFs could be extrapolated between cucumber, bitter gourd, loofah and zucchini. However, no detail is given on the product application rate. It is only mentioned that applications were done according to the GAPs or highest recommended dosage, but no GAP was given in the article. In addition, this study was not conducted in Japan. Moreover no table with residue data before and after processing allows to calculate a real PF value. The purpose of this study is only to conclude on the possible extrapolation from 1 crop to another. Thus, this study can be used as supplementary data to facilitate extrapolation between some crops [category “b”]
4	G. Ramadan, M. Shawir, A. El-Bakary and S. Abdelgaleil	2016	Dissipation of four insecticides in tomato fruit using high performance liquid chromatography and QuEChERS methodology	Chilean Journal of Agricultural Research, 76, 1, 129-133 doi:10.4067/S0718-58392016000100018	Study conducted in Egypt under open field conditions in 2013. In the study, thiamethoxam was applied at recommended rates to evaluate the dissipation, the residue levels, and the preharvest intervals for this insecticide in tomato fruits grown under Egyptian field conditions. Samplings were done 1, 3, 5, 7, 10 and 15 days after application on marketable sized fruit. Residue analysis was performed using HPLC-DAD. The study was not conducted in Japan field conditions. Moreover some information need to be clarified: the real concentrations of abamectin and TMX in the formulated product. Indeed it is indicated that "the following commercial formulations: 18.6% abamectin (152.4 g L-1) + thiamethoxam (33.2 g L-1) (Agri-Flex, Syngenta, Basel, Switzerland)" were tested. But in searching this product would contain abamectin (33.2 g L-1)+ thiamethoxam (152.4 g L-1). Therefore, the study is regarded as supplementary data [category b] if the rate of thiamethoxam applied is confirmed, otherwise the study will not be considered as reliable.
5	G. M. Telo, S. A. Senseman, E. Marchesan, E. R. Camargo, T. Jones and G. McCauley	2015	Residues of Thiamethoxam and Chlorantraniliprole in Rice Grain	Journal of Agricultural and Food Chemistry, 63, 8, 2119-2126 DOI: 10.1021/jf5042504	Study conducted in the USA, Texas in 2012. The objective was to analyse residues of thiamethoxam in rice hull, bran, and polished grains when applied on the aerial part of the rice plants following application of thiamethoxam at 30 g a.i./ha (N) and 2N rates at 5, 15, 25 and/or 35 days after flowering (DAF). 10 different treatments were evaluated: 1 application: 30 g TMX/ha applied at 5 DAF 1 application: 30 g TMX/ha applied at 15 DAF 1 application: 30 g TMX/ha applied at 25 DAF 1 application: 30 g TMX/ha applied at 35 DAF

List No.	Author	Year	Title	Journal	Reason for judgement
					2 applications: 30 g TMX/ha at 5 DAF + 30 g TMX/ha applied at 25 DAF 3 applications: 30 g TMX/ha at 5 DAF + 30 g TMX/ha at 25 DAF + 30 g TMX/ha applied at 35 DAF 1 application: 60 g TMX/ha applied at 5 DAF 1 application: 60 g TMX/ha applied at 15 DAF 1 application: 60 g TMX/ha applied at 25 DAF 1 application: 60 g TMX/ha applied at 35 DAF--Thiamethoxam residues were quantified in Rice Hull, Bran, and Polished Grains and results are presented for all analyzed treatments. Analysis was performed using UPLC/MS/MS. Sufficient information on the method and protocol are presented. Depending on the intended application rate and the intended number of applications, this study could be considered as supplementary data for the magnitude of residues in plants [category b] because it was not conducted in Japan.
6	Z. Tong, J. S. Duan, Y. C. Wu, Q. Q. Liu, Q. B. He, Y. H. Shi, L. S. Yu and H. Q. Cao	2018	Evaluation of Highly Detectable Pesticides Sprayed in Brassica napus L.: Degradation Behaviour and Risk Assessment for Honeybees	Molecules, 23, 10, doi:10.3390/molecules23102482	This study determines the residue of thiamethoxam in oilseed rape flowers. In this Chinese study, oilseed rape was treated during flowering with 30 g thiamethoxam/ha. The mixture water volume was 900 L/ha which is higher than the appropriate volume/ha (usually 200 L/ha). Flowers were sampled at 0, 1, 3, 5, 7, 10, and 14 days after spraying. All the samples were frozen immediately and stored at -20°C (up to 15 days) until extraction for residue determination using UPLC-MS/MS analysis. Residue levels, method validation and information on the storage stability are presented in this study but the study was not conducted in Japan. Therefore, the study is regarded as supplementary data for the data requirement on residues in pollen and bee products [Category b].
7	R. Zemeckis, A. Dautarte, J. Kretavicius and J. Drozdz	2019	Effects of winter and spring rape seed treatment with neonicotinoids on honey bees	Zemdirbyste-Agriculture, 106, 2, 173-182 doi:10.13080/z-a.2019.106.023	The topic of this study was to assess under Lithuanian environmental conditions the potential adverse effects of dust on bee colonies (effects of neonicotinoids on bee vitality and health...) following seed treatments on oilseed rape during 2 years. The impact of neonicotinoids on honey bees was observed in fully developed bee colonies after overwintering. In the summer of 2017 and 2018 (June and July), the effects of neonicotinoids on bees were investigated during the flowering stage of spring rape (Brassica napus L.). Spring and winter rape seeds were dressed simultaneously with two tested neonicotinoids – thiamethoxam and

List No.	Author	Year	Title	Journal	Reason for judgement
					clothianidin. As sources of these two neonicotinoids, two insecticides: a.i. beta-cyfluthrin 80gl-1 + clothianidin 400 g l-1 + fludioxonil 8.0 g l-1 + metalaxyl-M 32.3 g l-1 and thiamethoxam 280 g l-1 (Syngenta International AG, Switzerland) were used. Individual dose used for dressing each seed was calculated. Theoretical content of clothianidin was 20 µg and thiamethoxam – 12.6 µg per seed. The nectar samples were collected from the uncapped honeycomb using a 10 ml disposable syringe with a rabbled and grinded needle of 1.2 mm outside thickness. Pollen was collected using pollen collectors, placed on the bee-entrance of the hive. All samples were taken once in the middle of rape flowering. In 2017 and 2018, besides nectar and pollen, the bee bread samples were also collected. Residues of thiamethoxam and clothianidin in bee bread, pollen and nectar were measured in 2017 and 2018. No residues were detected in nectar and pollen but some hives showed some residues in bee bread. Some doubts on residues on pollen can be expected as it is very difficult to identify the time when neonicotinoid residues appear in pollen loads. Pollen was collected only once during the flowering period. Moreover this study was not conducted in Japan. Thus, the article can be classified in [category b].
Category "c"					
8	M. M. Rahman, W. Farha, A. M. Abd El-Aty, M. H. Kabir, S. J. Im, D. I. Jung, J. H. Choi, S. W. Kim, Y. W. Son, C. H. Kwon, H. C. Shin and J. H. Shim	2015	Dynamic behaviour and residual pattern of thiamethoxam and its metabolite clothianidin in Swiss chard using liquid chromatography-tandem mass spectrometry	Food Chemistry, 174, 248-255 dx.doi.org/10.1016/j.foodchem.2014.11.052	Study conducted in Korea. The aim was to investigate at which pre-harvest intervals Thiamethoxam residues in Swiss chard are MRL compliant. For this purpose, measurements of the residue levels of Thiamethoxam and its metabolite Clothianidin in Swiss chard grown under greenhouse conditions were performed, using QuEChERS extraction method and liquid chromatography–tandem mass spectrometry (LC/MS/MS). The dissipation pattern of both analytes was determined in two different areas (Gwangju and Naju) over 14 days to estimate the pre-harvest residue limit. The crop was sampled at 0, 1, 2, 3, 5, 7, 10, 14 days after application. The product Actara (10% thiamethoxam WG) was applied at the recommended dose of 10 g/20 L but it is not clear if 10 g is the quantity of formulated product or 10 g of active ingredient.

List No.	Author	Year	Title	Journal	Reason for judgement
					Based on this, no clear conclusion on residue levels can be drawn. [Category c]
42	G. Q. Ge, W. T. Jiao, C. J. Cui, G. Q. Liao, J. Sun and R. Y. Hou	2019	Thiamethoxam Metabolism and Metabolic Effects in Cell Suspension Culture of Tea (Camellia sinensis L.)	Journal of Agricultural and Food Chemistry, 67, 26, 7538-7546	This report is a new study that uses a non-targeted metabolomics strategy to investigate global metabolic changes in a tea cell suspension culture treated with the insecticide thiamethoxam. This method is not reported in OECD 501. Although this study can help to understand the interactions of thiamethoxam with tea cells, results of this study are not relevant for the residue part as it does not give sufficient information on the metabolism (i.e. not considered similar to an OECD 501 study). Based on this, this public article can be classified in [Category c]

Table 4.2-10: List of references judged as "Category b" and "Category c" in Step 2 in the second phase of relevance assessment and the reasons for the judgments- Toxicity to flora and fauna in the human living environment.

List No.	Author	Year	Title	Journal	Reason for judgement
Category "b"					
9	I. Ohta and M. Takeda	2015	Acute toxicities of 42 pesticides used for green peppers to an aphid parasitoid, Aphidius gifuensis (Hymenoptera: Braconidae), in adult and mummy stages	Applied Entomology and Zoology, 50, 2, 207-212 DOI 10.1007/s13355-015-0323-1	In this study acute toxicity of Thiamethoxam WG formulation (10% thiamethoxam content) applied at the highest recommended field rate (single dose, dilution magnification 3000) on parasitoid Aphidius gifuensis adult mortality and emergence of A. gifuensis adults from Sitobion akebiae (pest) mummies has been evaluated after 48h and 7 days exposure, respectively. It is reported that experimental procedure was set up according to Mead-Briggs (A laboratory method for evaluating the side effects of pesticides on the cereal aphid parasitoid Aphidius rhopalosiphi (Destefani-Perez). Asp Appl Biol 31:179–189. 1992). Negative control treatment contained water without thiamethoxam. Malathion and permethrin were tested as positive control toxic reference. It is not reported whether the sprayer equipment was calibrated accordingly. The relevant guidance Mead-Briggs (A laboratory test for evaluating the effects of plant protection products on the parasitic wasp, Aphidius rhopalosiphi (DeStephani-Perez) (Hymenoptera: Braconidae) 13-23, in Candolfi et al., 2000: Guidelines to evaluate side-effects of plant protection products to NTA), is validated for A. rhopalosiphi, while the study is conducted with A. gifuensis. Fecundity assessment was done differently than recommended in Mead-Briggs (2000), according to which a minimum of 15 surviving females are taken after 48h and individually confined over untreated aphid-infested plants. After 24h, the wasps are removed and plants are left for 10-12 days further. While in this study, S. akebiae mummies from the stock culture collected within 48 h after mummification were used. Barley leaves with mummies (50 per treatment) were dipped in pesticide solution for 5 s and left in a room to dry. It is reported A. gifuensis adults from acute toxicity test were examined. Living and dead emerged parasitoids were counted daily and removed from the container until 1 week after chemical treatment. The A. gifuensis mortality observed at Thiamethoxam WG treatment was 95.8%, and there was statistically significant effect on the number of emerged parasitoids compared to control.

List No.	Author	Year	Title	Journal	Reason for judgement
					A single dose was tested in the experiment and it is not possible therefore to derive ER50 or NOEC. The study is therefore regarded as supplemental information [Category b].
10	P. Butcherine, B. P. Kelaher, M. D. Taylor, C. Lawson and K. Benkendorff	2021	Acute toxicity, accumulation and sublethal effects of four neonicotinoids on juvenile Black Tiger Shrimp (Penaeus monodon)	Chemosphere, 275, doi.org/10.1016/j.chemosphere.2021.129918	In this study acute 48-h static toxicity tests were used to assess the effects of imidacloprid, clothianidin, acetamiprid and thiamethoxam on mortality, uptake and recovery of saltwater shrimp Penaeus monodon. Mortality was estimated in acute 48h tests, with 5 exposure concentrations, and 3 replicates per test concentration. Uptake and recovery were estimated after 4 days exposure followed by 4 days depuration, including determination of neonicotinoid tissue concentrations and activity of acetylcholinesterase and glutathione S transferase enzymes. Shrimps were acclimated to test conditions 4 days before the start of the test. Thiamethoxam of analytical grade was used for the experiment. Tested concentrations were 0 (control), 5, 25, 125, 250 and 500 ug/L. Exposure concentrations were confirmed by analytical analysis (LC-MS-MS) and were within 7.5% of nominal concentrations. Concentration of dissolved oxygen and/or oxygen saturation is not reported. Thiamethoxam 48-hr LC50 was 390 ug/L. Thiamethoxam concentrations in abdominal tissues were not significantly different from the control group at the end of the depuration phase, indicating rapid depuration from abdominal tissues of shrimp. This is a non-guideline study. The study provides evidence of fast recovery of saltwater shrimps after exposure to thiamethoxam. The study is classified as supplemental information [Category b].
11	D. S. W. Chan, R. S. Prosser, J. L. Rodriguez-Gil and N. E. Raine	2019	Assessment of risk to hoary squash bees (Peponapis pruinosa) and other ground-nesting bees from systemic insecticides in agricultural soil	Scientific Reports, 9 doi.org/10.1038/s41598-019-47805-1,	This study provides probabilistic risk assessment of exposure to systemic insecticides clothianidin, thiamethoxam and imidacloprid (neonicotinoids) and chlorantraniliprole (anthranilic diamide) in soil for ground-nesting bees using the hoary squash bee (Peponapis pruinosa) as a model species. Concentrations of clothianidin, thiamethoxam, imidacloprid, and chlorantraniliprole in cropped soil (Cucurbita and field crops in Ontario, Canada) were plotted to produce an environmental exposure distribution for each insecticide. The probability of exceedance of several exposure endpoints (for acute and chronic exposure scenario's) was compared to an acceptable risk threshold (5%). This field study is regarded representative for a specific

List No.	Author	Year	Title	Journal	Reason for judgement
					location, time and agroclimatic conditions in Canada. An assessment of agroclimatic conditions should be done before the study can be considered as supporting information in risk assessment [Category b].
12	S. C. Kessler, E. J. Tiedeken, K. L. Simcock, S. Derveau, J. Mitchell, S. Softley, J. C. Stout and G. A. Wright	2015	Bees prefer foods containing neonicotinoid pesticides	Nature, 521, 7550, 74-U145 doi:10.1038/nature14414	This study aimed to identify whether honeybee, Apis mellifera, and the buff-tailed bumblebee, Bombus terrestris, avoid sucrose solutions containing neonicotinoids imidacloprid, thiamethoxam, and clothianidin using a two-choice test designed to identify the bumblebee's gustatory detection thresholds for nectar toxins. Individual foraging-age worker bumblebees or cohorts of 25 were housed in plastic boxes for 24 h and fed two types of diet: one containing sucrose solution and one containing sucrose solution with neonicotinoid. The concentrations used included values in the range reported from nectar and pollen (0.5–150 nM). It was also tested whether neonicotinoids inhibited the feeding reflex (proboscis extension) or caused honeybees to retract the proboscis once extended. It was shown that honeybee Apis mellifera, and bumblebee Bombus terrestris do not avoid nectar-relevant concentrations of imidacloprid, thiamethoxam and clothianidin in food. This is a non-guidance study. Concentrations of imidacloprid, thiamethoxam and clothianidin in sucrose solution were not analytically verified. Reference item was not tested to verify sensitivity of the test organisms. Bees of both species preferred to eat more of sucrose solutions with insecticides than sucrose alone. Stimulation with insecticides did not cause spiking responses from gustatory neurons in the bees mouthparts and did not inhibit the responses of sucrose-sensitive neurons. The data indicate that bees cannot taste neonicotinoids and are not repelled by them. The study can be used as supporting information in risk assessment [Category b].
13	S. Stoyanova, V. Yancheva, I. Iliev, T. Vasileva, V. Bivolarski, I. Velcheva and E. Georgieva	2016	Biochemical, histological and histochemical changes in Aristichthys nobilis Rich. liver exposed to thiamethoxam	Periodicum Biologorum, 118, 1, 29-36 DOI: 10.18054/pb.2016.118.1.2828	This study investigated the effects of thiamethoxam on biochemical, histological (hepatic activity of lactate dehydrogenase, aspartate and alanine aminotransferases) and histochemical parameters of bighead carp liver (Aristichthys nobilis). The fish were acclimatized for 1 week before experiment. Three test concentrations (6.6 mg/L, 10 mg/L, 20 mg/L) and control were tested, with 10 fish at each treatment without replication. Exposure

List No.	Author	Year	Title	Journal	Reason for judgement
					lasted 96h. Environmental conditions during the test (T, pH, dissolved oxygen concentration, oxygen saturation, conductivity) are reported. Exposure concentrations were not analytically verified. The developmental stage of fish is not reported, while according to OECD 203, juvenile fish should be used in acute toxicity test (mean length of the fish was 18.65 cm, which corresponds more to adult stage). The study shows that there is a relation between the concentration of thiamethoxam and biochemical changes, as well the severity of expression of the histological and histochemical alterations in the bighead carp liver. However, mortality is not reported and LD50 cannot be derived. The study can be used as supporting information in risk assessment [Category b].
14	D. A. Stanley, K. E. Smith and N. E. Raine	2015	Bumblebee learning and memory is impaired by chronic exposure to a neonicotinoid pesticide	Scientific Reports, 5, DOI: 10.1038/srep16508	This study investigated the effects of acute and chronic exposure to field-realistic levels of thiamethoxam, on bumblebee odour learning and memory (at the level of individual and entire colony). The olfactory learning performance of individual bees was estimated using the proboscis extension reflex (PER) conditioning paradigm, a common method to assess olfactory learning performance in honeybees. The estimated parameters included: (1) trainability - whether bees learn the association between odour and reward (higher concentration of sucrose solution), (2) learning level - total number of learnt responses (proboscis extensions in anticipation of reward), (3) learning speed - the first odour presentation during the training period to which a bee first showed the learned association by proboscis extension. Concentrations of 2.4 and 10 ppb (plus untreated control) were chosen to be within field-relevant ranges. Thiamethoxam was added to sucrose solutions supplied to bees. Concentrations of thiamethoxam in sucrose solution were not analytically verified. Reference item was not tested to verify sensitivity of the test organisms. No difference in the number of individuals able to learn at field-realistic acute exposure. However, following chronic pesticide exposure, bees exposed to field-realistic levels learnt more slowly and their short-term memory was significantly impaired following exposure to 2.4 ppb pesticide. This is a non-guideline study. The study provides information on

List No.	Author	Year	Title	Journal	Reason for judgement
					olfactory learning performance of bumble bees (odour learning and memory) and can be regarded as supplemental data [Category b].
15	M. Gauthier, P. Aras, J. Paquin and M. Boily	2018	Chronic exposure to imidacloprid or thiamethoxam neonicotinoid causes oxidative damages and alters carotenoid-retinoid levels in caged honey bees (Apis mellifera)	Scientific Reports, 8, DOI:10.1038/s41598-018-34625-y	In this study, honey bees were orally exposed for 10 days to low field- realistic concentrations imidacloprid and thiamethoxam (did not exceed 3% of the LD50, 3.7–6.12 ng/bee). Selected biomarkers were measured such as acetylcholinesterase (AChE) activity, lipid peroxidation (LPO), α-tocopherol as well as several forms of vitamin A (retinoids) and carotenoids. Test concentrations in sugar solution supplied to bees were analytically verified. Reference item was not tested to establish sensitivity of test organisms. This is a non-guideline study. The study provides information on biochemical mechanisms of thiamethoxam toxicity. The article is considered supporting information [Category b].
16	S. Tosi and J. C. Nieh	2017	A common neonicotinoid pesticide, thiamethoxam, alters honey bee activity, motor functions, and movement to light	Scientific Reports, 7, DOI:10.1038/s41598-017-15308-6	This study investigates the sublethal effects of thiamethoxam on locomotion and movement to light of honeybee, Apis mellifera. All doses tested were lower than the worst-case scenario thresholds defined using calculations from the European Food Safety Authority (EFSA). Reference item was not tested to verify sensitivity of the test organisms. Test concentrations in sucrose solution were not analytically verified. This is a non-guideline study. Acute exposure to thiamethoxam (1.34 ng/ bee) impaired locomotion of honeybees, caused hyperactivity shortly after exposure (in 30 min), and impaired motor functions over a longer period (60 min). A 2-day chronic exposure with field-relevant daily intakes of 1.42–3.48 ng/bee/day impaired bee ability to ascend. The study shows that thiamethoxam can harm worker locomotion and, potentially, alter division of labour if bees move outside or remain outdoors. This is a non-guideline study. The study can be used as supporting information [Category b].
17	S. Tosi, G. Burgio and J. C. Nieh	2017	A common neonicotinoid pesticide, thiamethoxam, impairs honey bee flight ability	Scientific Reports, 7, DOI:10.1038/s41598-017-01361-8	The study investigated the effects of acute or chronic exposure to thiamethoxam on the flight ability of forager honeybee, Apis mellifera in flight mills. All doses tested were lower than the worst-case scenario thresholds for acute and chronic exposure (defined by the European Food Safety Authority (EFSA)), and did not increase mortality as compared to controls. Test concentrations in sucrose

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					solution were not verified with chemical analyses. Reference item was not tested to verify the sensitivity of the test organisms. Within 1 h of consuming a single sublethal dose (1.34 ng/bee), foragers showed excitation and significantly increased flight duration and distance. Chronic exposure significantly decreased flight duration, distance, and average velocity after either one or two days of continuous exposure that resulted in bees ingesting field-relevant thiamethoxam doses of 1.96–2.90 ng/bee/day. The results show that thiamethoxam can significantly affect bee flight. This is a non-guideline study. The study is regarded as supplemental data [Category b].
18	S. C. Wood, I. V. Kozii, R. V. Koziy, T. Epp and E. Simko	2018	Comparative chronic toxicity of three neonicotinoids on New Zealand packaged honey bees	Plos One, 13, 1, doi.org/10.1371/journal.pone.0190517	This study compared the effects of chronic, sublethal exposure to thiamethoxam, clothianidin, and imidacloprid on honeybees Apis mellifera obtained from New Zealand in a field study conducted in Canada. Experimental colonies were installed within an approximately 0.2 km2 area within an alfalfa field surrounded by pasture and fields of canola and cereals. Pollen patties were prepared from a mixture of soybean flour and brewer's yeast, sucrose syrup and pollen obtained from pollen traps. The neonicotinoid stock solutions were diluted in sucrose syrup to a concentration of either 20 nmol/L (~5 ng/g) or 80 nmol/L (~20 ng/g). Aliquots of the pollen patties and sugar solutions from treatment and control groups were submitted for measurement of neonicotinoid concentration by LC-MS/MS. The evaluated parameters included colony weight gain, capped brood area, and population size. There was a significant negative effect on colony weight gain (honey production) after 9 and 12 weeks of exposure to 80 nM of thiamethoxam and on bee cluster size after 12 weeks. This is a non-guideline study representative of agroclimatic conditions in Canada. A comparison of agroclimatic conditions with Japan should be done before the study can be regarded as supplemental data [Category b].
19	E. E. W. Samuelson, Z. P. Chen-Wishart, R. J. Gill and E. Leadbeater	2016	Effect of acute pesticide exposure on bee spatial working memory using an analogue of the radial-arm maze	Scientific Reports, 6, DOI: 10.1038/srep38957	This study investigated the effect of acute thiamethoxam exposure on spatial working memory in the bumblebee Bombus terrestris, using an adaptation of the radial-arm maze (RAM) method. Thiamethoxam concentrations used in the experiment reflected a range that can be found in the field: 2.4ppb, based on residues found in B. terrestris nectar pots and oilseed rape nectar in

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					honeybee crops and 10ppb, based on residues in nectar of treated plants. An additional high dose of 2.5 ng per bee (half the acute oral toxicity LD50 for honeybees) was used to test for effects at non-field-realistic levels, as a positive control. Thiamethoxam was added to sucrose solution supplied to bees. Concentrations were not analytically confirmed. The high dose caused bees to make more and earlier spatial memory errors and take longer to complete the task than unexposed bees. For the low doses, the negative effects were smaller but statistically significant, and dependent on bee size. This is a non-guideline study that provides information on bee spatial working memory under exposure to field-relevant concentrations of thiamethoxam. The study can be regarded as supporting information [Category b].
20	Q. Zeb, M. Naeem, S. A. Khan and S. Ahmad	2016	Effect of Insecticides on the Population of Aphids, Natural Enemies and Yield Components of Wheat	Pakistan Journal of Zoology, 48, 6, 1839-1848 Doi: N/A	This study is a field experiment conducted at Agricultural Research Institute-Tarnab Peshawa (Pakistan) to determine the effect of four different insecticides including formulation Actara 25 WG formulation containing thiamethoxam at a rate of 24 g/acre on the population of wheat aphids, its natural enemies and yield, and yield components of wheat in wheat crops. Two wheat varieties, one susceptible and other partially resistant selected after laboratory and field screening against wheat aphids, were sown in the main plots in a Randomize Complete Block design (RCBD) in split plot arrangement with three replicates. One replicate consisted of two main plots where the wheat varieties were assigned at random. Each main plot was further divided into five subplots where insecticides were applied at random. All tested insecticides were effective in controlling wheat aphids. Both varieties showed increase in grain yield and also increase in yield components in sprayed plots. Aphid density, mortality and parasitation rate at treatment groups and control are presented, however the taxonomic classification and species names are not reported. This is a non-guideline study that is regarded representative for a specific location, agroclimatic conditions in Pakistan. An assessment of agroclimatic conditions should be done before the study can be considered as supporting information [Category b] in risk assessment.

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21	R. Afza, M. Afzal, M. Z. Majeed and M. A. Riaz	2019	Effect of Intra-Guild Predation and Sub Lethal Concentrations of Insecticides on the Predation of Coccinellids	Pakistan Journal of Zoology, 51, 2, 611-617 dx.doi.org/10.17582/journal.pjz/2019.51.2.611.617	This study evaluated the intraguild predation (IGP) in the presence and absence of extraguild prey (aphids) among Coccinella septempunctata and Coccinella transversalis. Further, the effect of sublethal concentrations of insecticides (including thiamethoxam) on IGP of two coccinellids was studied under the laboratory conditions. To study the effects of pesticides on intraguild predation, canola leaves were treated with two sublethal concentrations (LC10 and LC30) of insecticides. Predators were starved for 24 h before test. Predation efficacy was evaluated for all treatments/combinations. There were 5 replicates for each treatment along with control treatment in which potential of escape and natural mortality was evaluated. At thiamethoxam treatment relatively higher aphid consumption compared to other insecticides was observed, but remained significantly lower than control. This is a non-guideline study. Positive control (reference item) was not tested to verify sensitivity of test organisms. The study provides information on the effects of thiamethoxam on natural enemies used in Integrated Pest Managment (IPM) systems, and can be regarded as supporting information [Category b].
22	K. Basley, B. Davenport, K. Vogiatzis and D. Goulson	2018	Effects of chronic exposure to thiamethoxam on larvae of the hoverfly Eristalis tenax (Diptera, Syrphidae)	Peerj, 6, DOI 10.7717/peerj.4258	This study evaluated the effects of exposure on the aquatic larval stages of the hoverfly Eristalis tenax L. (Diptera: Syrphidae) to a range of thiamethoxam concentrations. Six different levels with analytical grade thiamethoxam using stock solutions were tested: 0 (control), 5, 15, 50, 100 and 500 ppb (positive control). Larvae were randomly assigned to treatment groups with 10 individual replicates per treatment group (60 larvae in total per full experiment). Larvae were exposed to thiamethoxam from the day they were introduced to the treatment lagoon, to the day they started to pupate. The full experiment was repeated 4 times (240 larvae), and each separate experiment was populated with eggs from a different female. Estimated parameters included larval and pupal mass, date of pupation, behaviour of emerged adults. Survival was significantly lower when exposed to 500 ppb thiamethoxam. No effect on survival, development or any latent effects on adult activity budgets was observed at lower concentrations (up to 100 ppb). Test concentrations were not analytically verified. Concentration of dissolved oxygen/oxygen saturation and other environmental conditions during the study are not reported. V This non-guideline

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					study provides information on effects of thiamethoxam on aquatic larval stages of Diptera, and can be used as supplemental information [Category b].
23	Z. Tong, J. S. Duan, Y. C. Wu, Q. Q. Liu, Q. B. He, Y. H. Shi, L. S. Yu and H. Q. Cao	2018	Evaluation of Highly Detectable Pesticides Sprayed in Brassica napus L.: Degradation Behavior and Risk Assessment for Honeybees	Molecules, 23, 10, doi:10.3390/molecules23102482	This study aimed to assess the risk of contact exposure to carbendazim, prochloraz, pyrimethanil, fenpropathrin, chlorpyrifos, imidacloprid, thiamethoxam, and acetamiprid to honeybees following spraying in rape fields. Thiamethoxam was supplied as thiamethoxam 25% water-dispersible granules (WDG). Pesticides were sprayed in the field conditions using an automatic sprayer over experimental plots containing flowering rape plants. Three replicate plots were designated for each pesticide, in addition to an untreated control plot. Flower sampling was done 0, 1, 3, 5, 7, 10, and 14 days after spraying. Analytical determination of pesticide residues was done in the whole rape flowers. The risk was quantified using the flower hazard quotient (FHQ) value. It is concluded that thiamethoxam poses unacceptable risk to honeybees after spraying in fields. This is a non-guideline study. Field experiments were conducted in China. An comparison of agroclimatic conditions should be done brefore results of the study can be used as supporting information [Category b].
24	M. Charreton, A. Decourtye, M. Henry, G. Rodet, J. C. Sandoz, P. Charnet and C. Collet	2015	A Locomotor Deficit Induced by Sublethal Doses of Pyrethroid and Neonicotinoid Insecticides in the Honeybee Apis mellifera	Plos One, 10, 12, DOI:10.1371/journal.pone.0144879	The study compares the deleterious effects of sublethal doses of thiamethoxam, among other insecticides, on the locomotion of honeybees in their first day of adult life. Three different dose levels of technical-grade thiamethoxam were tested and applied to the dorsal part of the thorax: 0, 3.8 and 7.5 ng/bee, being negative control, sub-lethal dose at 48h (SLD48h) and two-fold SLD48h. 240 to 270 bees distributed in two replicates were used in the test. A significant decrease in distance is observed after exposure to a SLD48h of thiamethoxam (3.8 ng/bee). Mortality rates were stable between 24 and 48 h and the SLD48h was sublethal at 120 h as well and did not induce mortality more than their respective controls. The test concentrations were directly applied on the bees and the purity of the test item was provided. The number of tested organisms per group exceeds the recommendations in the guideline for contact exposure (OECD TG 214). Data about the environmental conditions was provided, but differed from the recommended parameters of temperature,

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					feeding and humidity. No positive control was tested. Since the showed effects are directly related to thiamethoxam, and quantitative information about behaviour and mortality effects can be obtained, this study can be used as supplemental information [Category b].
25	D. Schlappi, N. Kettler, L. Straub, G. Glauser and P. Neumann	2020	Long-term effects of neonicotinoid insecticides on ants	Communications Biology, 3, 1, doi.org/10.1038/s42003-020-1066-2	This study shows that chronic exposure to sublethal doses of thiamethoxam results in smaller colonies of black garden ant with fewer workers and larvae. Two field-realistic treatments of technical thiamethoxam were selected (4.5 µg/L= treatment low; 30 µg/L= treatment high) and distilled water for the controls. A total of 30 individual laying ant queens were allocated to each of the three treatment groups (each n = 10), subjected to overwintering and exposed to freshly prepared treatment solutions twice during the 64 weeks of the experiment. Nesting tubes were analysed to confirm the presence of thiamethoxam in the colonies. Until the end of the experiment (week 64), there were significant differences in the average worker body mass. Before the second overwintering (week 64), there was a significant difference in the number of workers and larvae. Exposure route is clearly defined and the concentrations of residues at each treatment were determined for each stage. However, the selected species and exposure stage are not commonly used in soil-dwelling organisms tests. Therefore, the validity criteria and the used method significantly differs the regular approach set by agreed guidance on soil-dwelling organisms. However, since a quantitative relationship was stablished between the exposure to thiamethoxam and seasonal long-term effects on ant colony sizes, this study can be used as supplemental information [Category b].
26	G. A. Wright, S. Softley and H. Earnshaw	2015	Low doses of neonicotinoid pesticides in food rewards impair short-term olfactory memory in foraging-age honeybees	Scientific Reports, 5, DOI: 10.1038/srep15322	In this study investigates the negative impacts of low doses of thiamethoxam on honeybees olfaction and rewarding memories. Honeybees were trained and subjected to olfactory conditioning. The conditioned stimulus was the odour, 1-hexanol and the unconditioned stimulus was a reward of 0.4 µL of treatment solution: 0.7 M sucrose (control), or 0.7 M sucrose containing 0.1 nM, 1 nM, 10 nM of thiamethoxam. Bees were orally exposed to the above concentrations and had a slower rate of learning than the control when exposed to 1 nM thiamethoxam. Also, bees fed

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					thiamethoxam were less likely to respond to the test odour at 10 min than at 24 h and got the short-term appetitive memory significantly impaired. This is a non-guideline study, and the used method significantly differs from the regular approach set by agreed guidance. Although a range of doses was used in the protocol, no regulatory endpoint can be derived from it (mortality not reported). However, field-relevant doses can be linked to significant sub-lethal effects, specifically behavioural outputs related to olfactory performance. Therefore, this study can be used as supplemental information [Category b].
27	P. R. Whitehorn, C. Wallace and M. Vallejo-Marin	2017	Neonicotinoid pesticide limits improvement in buzz pollination by bumblebees	Scientific Reports, 7, DOI:10.1038/s41598-017-14660-x	This study assessed the effect of field-realistic, chronic exposure to the widely-used neonicotinoid thiamethoxam on the development of sonication buzz characteristics of bumble bee Bombus terrestris audax over time, as well as the collection of pollen from buzz-pollinated flowers. The concentrations of 2 ppb and 10 ppb tested supplied to nectar provided to microcolonies were chosen to reflect the range of values found in the nectar and pollen of crop and wild plants in the field. Initial stock solution was made by diluting pure thiamethoxam in acetone. In control treatment an equivalent volume of acetone in purified water was added to the control sucrose solution. Control treatment without acetone was not tested. The queenless microcolonies (consisted of worker bees) were exposed to the treated or control nectar for nine days before the buzz pollination trials began. Exposure to field realistic doses of the neonicotinoid thiamethoxam negatively impacted buzz pollination. Exposed bees showed exposure to thiamethoxam resulted in less improvement in pollen collection with increasing experience than control bees (47% and 56% less pollen collected at 2ppb and 10ppb treatments, respectively). This is a non-guideline study. Reference item was not tested to verify sensitivity of the test organisms. The study is regarded as supplemental data [Category b].
28	D. Baines, E. Wilton, A. Pawluk, M. de Gorter and N. Chomistek	2017	Neonicotinoids act like endocrine disrupting chemicals in newly-	Scientific Reports, 7, DOI:10.1038/s41598-017-	This study investigated the effects of oral acute and chronic exposure of acetamiprid, clothianidin, imidacloprid, and thiamethoxam to worker bumble bees (Bombus impatiens), worker

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			emerged bees and winter bees	10489-6 DOI:10.1038/s 41598-017- 10489-6	honey bees (Apis mellifera) and leafcutter bees (Megachile rotundata). Analytical grade thiamethoxam was used in the experiments. Stock solution was prepared with dimethylsulfoxide (DMSO) shown to have no influence on feeding behaviour of bees. Thiamethoxam was added to honey water solution. In the acute tests the following concentrations were used: 8.55 mM, 0.43 mM, 21.3 µM, 1.06 µM, 53.43 nM, 2.67 nM, 133.59 pM, 6.68 pM. In acute toxicity experiments mortality was recorded at 24, 48, 72, and 96 h according to OECD guidelines, but was also extended to include 10 additional days. Neurological impairments were recorded at 24, 48, 72, 96 h, as indicated in the OECD guidelines, but also extended to include 10 additional days. In the chronic test, the lowest 4 concentrations were used. Bees were allowed to consume ad libitum, the test solutions over 14 days. Changes in bee survival and neurological impairment was recorded daily for 14 days (10 days according to OECD guidelines). The time period to ensure that late neurological dysfunctions would not be missed and also to ensure that recovery could be documented. Bees were monitored daily to identify time-based neurological symptoms as features of EDC (endocrine disruption chemical) induced behaviour. The median dorsal vessel or heart, tracheae/air sacs, thoracic muscles, fat body, foregut, midgut and hindgut were examined and scored. LD50 and NOAEL values were calculated in the study for the three testes species. In the acute toxicity studies, delayed symptom, such as ataxia, was recorded as non-lethal endpoint for all three bee species. Chronic exposure reduced the survival and caused significant delayed symptoms for all three bee species. This is a non-guideline study. Thiamethoxam concentrations in honey water were not analytically verified. Honey water was used as a food source and not a standard sucrose solution according to OECD guidelines. Reference item was not tested to verify sensitivity of the test organisms. The studies provide information on the effects of neonicotinoids on EDC-like behaviour in bees in acute and chronic experiments. The study is considered supporting information for the use in risk assessment [Category b].

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29	M. C. Tackenberg, M. A. Giannoni-Guzman, E. Sanchez-Perez, C. A. Doll, J. L. Agosto-Rivera, K. Broadie, D. Moore and D. G. McMahon	2020	Neonicotinoids disrupt circadian rhythms and sleep in honey bees	Scientific Reports, 10, 1 doi.org/10.1038/s41598-020-72041-3,	This study tested the effects of thiamethoxam and clothianidin on honey bee circadian rhythms and sleep, which are important to regulate critical behaviours, such as foraging orientation, navigation, learning and memory processes. Thiamethoxam and clothianidin were added to bee candy (ground white cane sugar and honey), control treatment consisted of bee candy with no pesticide. All bees used for experiments came from healthy colonies with a mated queen not previously exposed to neonicotinoids. Analysed parameters included locomotor activity rhythms and sleep data. Concentrations of thiamethoxam were analytically-verified using LC-MS/MS. Neonicotinoids disrupted honey bee circadian rhythms and sleep, and potentially impaired honey bee navigation, time-memory, and social communication. This is a non-guidance study. Reference item was not tested to verify sensitivity of the test organisms. The study can be used as supporting information in risk assessment [Category b].
30	C. Moffat, S. T. Buckland, A. J. Samson, R. McArthur, V. C. Pino, K. A. Bollan, J. T. J. Huang and C. N. Connolly	2016	Neonicotinoids target distinct nicotinic acetylcholine receptors and neurons, leading to differential risks to bumblebees	Scientific Reports, 6, DOI: 10.1038/srep24764	This study addressed the specificity and effects of imidacloprid, thiamethoxam, and clothianidin on bumblebees Bombus terrestris at field-relevant levels (2.5 ppb) at all levels of individual cells, individual bees and whole colonies in semi-field conditions. First, the ability of neonicotinoids to reach their site of action, the bee brain was studied by feeding bees sugar syrup with honey at concentration 2.5 ppb thiamethoxam for 3 days, followed by analytical determination of neonicotinoid residue levels in bee brain determined using LC-MS/MS. To study the relative acute toxicity of imidacloprid, thiamethoxam, and clothianidin, bees (~30) were exposed to each neonicotinoid at 1 dose 100 ppb) for 1–3 days to estimate mortality. As a second step, it was investigated whether a chronic exposure to field-relevant levels of neonicotinoids (2.5 ppb imidacloprid, thiamethoxam, or clothianidin for 7 days) might increase their sensitivity to subsequent exposure to toxic levels of clothianidin (at 50 ppb). Untreated sugar syrup or treated with neonicotinoids (imidacloprid, thiamethoxam, or clothianidin) was provided to B. terrestris audax microcolonies as sugar source. Third, response of Kenyon cell neurones in culture (Ca2+ responses from single cells) was measured (but not for thiamethoxam). Forth, entire bee colonies were exposed to neonicotinoids (provided at 2.5 ppb in sugar syrup) over 5 weeks.

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					The performance of 75 colonies was investigated using 5 distinct sites across Scotland over 5 separate overlapping periods during the summer. At the end of the experiment the following parameters were estimated: the number of live bees, weight of bees, count of viable brood, number of queens, sex ratio determination. This is a non-guideline study. The field study is representative for a specific time frame, location, and condition in Scotland, but not representative for Japan. An assessment of agroclimatic conditions is required to assess the relevance of the study. The study can be used as supporting information in risk assessment [Category b].
31	T. N. Allakhverdiyeva and A. A. Mekhtiev	2017	The preconditioning phenomenon and its mechanisms in the common carp as affected by Actara insecticide	Journal of Evolutionary Biochemistry and Physiology, 53, 5, 380-383 DOI: 10.1134/S0022093017050039	In this study the effects of Actara insecticide on the common carp (Cyprinus carpio Linnaeus) were studied, including estimation of sublethal concentration (LC50) and the levels of serotonin-modulated anticonsolidation protein (SMAP) in the brain and liver (linked to antimutagenic and antitoxic protection against toxic chemical and bacterial compounds). The following Actara concentration were used in trials to estimate LC50: 250, 320, 350, 370, 400, and 450 mg/L. At each concentration 6 individuals were exposed. The fish in the experiment were 7 months old. In the second experiment, fish were divided into 3 groups: 1) control (n = 6); 2) exposed to 400 mg/L of Actara in freshwater (n = 6), and (3) pre-exposed to 100 mg/L of Actara in freshwater after 1 day 1 day transferred to freshwater with 400 mg/L of Actara (n = 6). The duration of acute test to determine LC50 is not reported. Dissolved oxygen concentration/oxygen saturation and other environmental parameters (T, pH, hardness, photoperiod) are not reported. Test concentrations were not analytically determined. Validity criteria according to OECD 203 therefore cannot be verified. Adult fish were used for the experiment, while OECD guideline recommends using juveniles. LD50 for Actara formulation was estimated as 360 mg/L. It is found that pre-exposure elevates SMAP tissue levels and promotes protection of the organism against damaging effects of lethal Actara concentrations. Due to the limitations listed above the study is classified as supplemental information [Category b].
32	D. M. Alano, E. S. Araujo, J. M. Miras-Avalos, I. C.	2021	Sublethal effects of insecticides used in strawberry on	Spanish Journal of Agricultural	This study aimed to assess the toxicity and sublethal effects of insecticides registered and used in strawberry cultivation in Brazil on T. pretiosum (parasitoids) by applying them on D. Fovealis (pest)

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	Pimentel and M. A. C. Zawadneak		Trichogramma pretiosum (Hymenoptera: Trichogrammatidae)	Research, 19, 1, doi.org/10.5424/sjar/2021191-17235	eggs. Previously non-parasitized D. Fovealis eggs were treated by dipping the cards into the insecticide dilutions or control solution. Then, the cards were air-dried and transferred to glass plates to remove moisture excess at ambient temperature. Each card was offered to a T. pretiosum female. After 24 h of exposure, the cards were removed and transferred to a clean glass vial until parasitoid emergence. The estimated parameters included: mortality of T. Pretiosum females in 24 h, longevity of the females after the exposure to the insecticides, parasitism rate, emergence rate and offspring sex ratio. After emergence, female T. Pretiosum offspring were isolated in glass vials and a card with 20 untreated D. fovealis eggs was offered to each female for parasitism during 24 h. The estimated parameters, observed on a daily basis, were progenitor mortality rate, number of parasitized eggs, emergence rate, sex ratio of the offspring and longevity (survival time until death). Distilled water was used as a control. Thiamethoxam was provided as Actara formulation at the dose 0.1 g/L (the highest authorized for application in strawberry crops). No significant effects on survival of T. Pretiosum females of F0 and F1 generations were found for thiamethoxam. Thiamethoxam was slightly toxic to longevity of females, and did not affect parasitism rate by T. Pretiosum females from the F0 and F1 generations, and emergence rate of F2 generation. It is concluded tha under laboratory conditions, thiamethoxam can be considered compatible with T. Pretiosum. This is a non-guideline study. Reference item was not tested to determine sensitivity of the test organisms. The study provides information on the effects of thiamethoxam on insects used in biological control and can be used as supporting information in risk assessment [Category b].
33	F. J. Demares, K. L. Crous, C. W. W. Pirk, S. W. Nicolson and H. Human	2016	Sucrose Sensitivity of Honey Bees Is Differently Affected by Dietary Protein and a Neonicotinoid Pesticide	Plos One, 11, 6, DOI:10.1371/journal.pone.0156584	This study evaluated the effects of thiamethoxam on survival, food consumption and sucrose sensitivity (proboscis extension reflex, PER) of honeybees (Apis mellifera) fed different proportions of protein, carbohydrate (P and C) in the form of casein and sucrose, respectively, and sucrose concentrations. The experiments continued for 14 days. Ecologically relevant doses 1 ppb, 10 ppb and 100 ppb were tested (0.25%, 2.5% and 25% of LD50 4–5 ng/bee, equivalent to LC50 400–500 ppb when average food consumption of 10 mg/bee/day is taken into account).

List No.	Author	Year	Title	Journal	Reason for judgement
					Concentrations of thiamethoxam in the diet were not analytically verified. Control treatment consisted of diet without thiamethoxam. Positive control (reference item) was not tested to establish sensitivity of the test organisms. Thiamethoxam did not affect protein and carbohydrate intake, but decreased responses to high concentrations of sucrose. Both thiamethoxam and dietary protein influenced survival. These findings suggest that, in the presence of a pesticide and unbalanced food, honeybee health may be severely challenged. This non-guideline study provides information on combined effects of thiamethoxam and diet composition on the performance of honeybees. The study can be used as supporting information in risk assessment [Category b].
34	R. Hussain, A. Ghaffar, G. Abbas, G. Jabeen, I. Khan, R. Z. Abbas, S. Noreen, Z. Iqbal, I. R. Chaudhary, H. M. Ishaq, M. T. Ghori and A. Khan	2022	Thiamethoxam at sublethal concentrations induces histopathological, serum biochemical alterations and DNA damage in fish (Labeo rohita)	Toxin Reviews, 41, 1, 154-164 DOI: 10.1080/15569543.2020.1855655	In this article the effects of sublethal concentrations of thiamethoxam (0, 0.5, 1.0, 1.5, and 2.0 mg/L) on genotoxic potential, hystopatological changes in liver and kidneys and serum biochemical parameters (liver function, kidneys function tests, lipid peroxidation product (MDA), cholesterol, and triglycerides) of freshwater fish Labeo rohita in 120h experiment are studied. Mortality was not evaluated in this study, therefore the study cannot be used to derive LD50. Concentrations of thiamethoxam were not analytically verified. Results of the study demonstrate that thiamethoxam induces blood biochemical, genotoxic, and histopathological abnormalities in exposed fish. This non-guideline study can be used as supporting information in risk assessment [Category b].
35	M. A. Farooqi, H. Mansoor ul and M. Arshad	2016	Toxicity of Three Commonly Used Nicotinoids and Spinosad to Apis mellifera L. (Hymenoptera: Apidae) Using Surface Residual Bioassays	Pakistan Journal of Zoology, 48, 6, 1983-1987 DOI: N/A	This study is considered relevant because provides data that could be used as a supplementary information for the approval of thiamethoxam and the registration of products containing thiamethoxam in Japan. In this study, the acute contact toxic effects of thiamethoxam (as formulated product) were determined on honeybees at 3,6,12 and 24 hours after exposure. The laboratory study, however, was not carried out in line with the OECD TG 214 (Acute Contact Toxicity Test). In addition, no mortality was assessed at 48 hours as recommended by the OECD TG 214. It should be also checked whether the formulation used in the study (i.e. Actara25 WG) is

List No.	Author	Year	Title	Journal	Reason for judgement
					registered in Japan. For all these reasons, the scientific publication is classified as relevant with a [Category b].
Category "c"					
43	S. T. Gul, A. Khan, M. Farooq, S. Niaz, M. Ahmad, A. Khatoon, R. Hussain, M. K. Saleemi and M. F. Hassan	2017	Effect of Sub Lethal Doses of Thiamethoxam (A Pesticide) on Hemato-Biochemical Values in Cockerels	Pakistan Veterinary Journal, 37, 2, 135-138 https://www.researchgate.net/publication/316550418_Effect_of_Sub_Lethal_Doses_of_Thiamethoxam_A_Pesticide_on_Hemato-Biochemical_Values_in_Cockerels	In this study the effects of thiamethoxam on haematological and biochemical parameters of adult poultry birds were investigated. Thiamethoxam was supplied though crop tube. Haematological parameters included total erythrocyte counts and total leukocyte counts, haemoglobin and haematocrit. Biochemical parameters included serum total proteins, albumin, alanine aminotransferase, aspartate aminotransferase, creatinine and blood urea, globulin. Concentration of thiamethoxam tested were 250, 500 and 750 mg/kg bw/d plus control. Blood and sera were collected at the 15th and 30th day of the experiment. Mortality or effects on reproduction were not estimated in the study, and LD50 cannot be derived. Also, this study doesn't follow OECD guideline. Therefore, the study cannot be used for supporting data. Therefore, the article could be classified into [category c].

Table 4.2-11: List of references judged as "Category b" and "Category c" in Step 2 in the second phase of relevance assessment and the reasons for the judgments- Environmental fate

List No.	Author	Year	Title	Journal	Reason for judgement
Category "b"					
36	D. Browne, J. Levison, V. Limay-Rios, K. Novakowski and A. Schaafsma	2021	Neonicotinoids in groundwater: presence and fate in two distinct hydrogeologic settings in Ontario, Canada	Hydrogeology Journal, 29, 2, 651-666 doi.org/10.1007/s10040-020-02250-7	Although these field data were not collected in Japan, analytical and numerical models were used to analyze the patterns of clothianidin and thiamethoxam transport to groundwater. The extrapolation or comparison of the results could be used, as supplementary information, to Japan aquifers conditions. Therefore, this study could be classified into [category b], supportive information.
Category "c"					
No papers were ranked as category "c" for the section Environmental fate					

Table 4.2-12: List of references judged as "Category a" in the second phase of relevance assessment and the result of reliability assessment - Toxicity to humans

List No.	Author	Year	Title	Journal	Reason for judgement in "category a"	Klimisch Score	Reason for judgement of Klimisch Score
No papers were ranked as category "a" for the section Toxicity to humans							

Table 4.2-13: List of references judged as "Category a" in the second phase of relevance assessment and the result of reliability assessment - Residue in crops and livestock products

List No.	Author	Year	Title	Journal	Reason for judgement in "category a"	Klimisch Score	Reason for judgement of Klimisch Score
37	M. Dusek, V. Jandovska and J. Olsovska	2018	Tracking, Behavior and Fate of 58 Pesticides Originated from Hops during Beer Brewing	Journal of Agricultural and Food Chemistry, 66, 38, 10113-10121 DOI: 10.1021/acs.jafc.8b03416	Hops were artificially spiked with the mixture of 58 pesticides, including fungicides, insecticides, and their metabolites. The laboratory brewing trial of bottom fermented Pilsner-type of beer was conducted to maximally simulate in the industrial scale production. Pesticide residues were determined and quantitated using HPLC−HR-MS/MS in the samples collected within the whole brewing process. Analytical method and sample preparation were detailed. Quantitation of pesticide residues was achieved using matrix matched standard calibration curves with isotopically labelled standards at a concentration of 0.050 mg/L. Concentrations (mg/kg or mg/L) of each Pesticide in Treated Hops, Spent Hops, Hopped Wort, Green Beer, and Beer was determined and stability of pesticides during boiling was evaluated. These allow to investigate the residue transfer during the hopping and also the behaviour of residues during fermentation. Finally, those data allow to calculate PF for each processed commodity. This study was not conducted in Japan but it can be considered as relevant because it was performed at laboratory scale. [Category a]	2	This crop is not relevant for the Japanese GAPs
38	N. Liu, X. L. Pan, Q. X. Yang, M.	2018	The dissipation of thiamethoxam and its main metabolite	Scientific Reports, 8,	Chinese study conducted in 2017 in greenhouse strawberries.	2	No information on the storage stability of the

List No.	Author	Year	Title	Journal	Reason for judgement in "category a"	Klimisch Score	Reason for judgement of Klimisch Score
	S. Ji and Z. H. Zhang		clothianidin during strawberry growth and jam-making process (Trials + process of TMX in strawberry --> See if crop relevant for Japan)	DOI:10.1038/s41598-018-33334-w	The objectives were to (1) evaluate the dissipation of thiamethoxam and formation of its main metabolite clothianidin (dissipation study) and (2) investigate the residues of thiamethoxam and clothianidin in processed strawberry parts (jam making process) to provide Processing factors (PFs) for the different steps of strawberry jam making process. Analysis was performed using UPLC-MS/MS analysis. For the dissipation study (1), thiamethoxam 25% WG was applied at dosage of 337.5 g/ha (1.5 times of recommended higher dosage) during the strawberries' growth to half size. Strawberry samples were sampled after 2 h, 1, 3, 5, 7, 10, 14, 21, 28 and 35 days. For the processing study (2), to ensure sufficient pesticide primary deposit, thiamethoxam 25% WG was applied under greenhouse conditions at dosage of 1125 g/ha (5 times of recommended higher dosage) during strawberry maturation. Two kilograms of strawberry samples per plot were sampled at 3 days after the treatment. The presented levels of residues in strawberries and the derived processing factors are relevant for the consumer risk assessment [category a]		analytical samples.

Table 4.2-14 List of references judged as "Category a" in the second phase of relevance assessment and the result of reliability assessment - Toxicity to flora and fauna in the human living environment

List No.	Author	Year	Title	Journal	Reason for judgement in “category a”	Klimisch score	Reason for judgement of Klimisch Score
39	D. A. Stanley and N. E. Raine	2017	Bumblebee colony development following chronic exposure to field-realistic levels of the neonicotinoid pesticide thiamethoxam under laboratory conditions	Scientific Reports, 7, DOI:10.1038/s41598-017-08752-x	In this study mature bumblebee (Bombus terrestris) colonies were exposed to field-realistic levels of thiamethoxam (2.4ppb & 10ppb) over 4 weeks under laboratory conditions. The lower concentration (2.4ppb) corresponds to the concentration measured in nectar pots of bumblebee colonies foraging in agricultural areas in the UK and in pollen collected by honeybees in France, while the higher concentration (10ppb) is within the range measured in the nectar and pollen of a variety of treated crops and wild plants. Each colony was exposed for a period of 26–27 days in a laboratory setting, and all sucrose solutions was actively consumed. The estimated parameters included the numbers of produced workers, males and queens (gynes), average dry mass of individuals of each caste in each colony (as a proxy for total colony size including brood), and the total dry mass of each caste. There was no impact of insecticide exposure on colony weight gain, or the number or mass of sexuals produced, although colonies exposed to 2.4 ppb produced larger males. The study can be used to support higher-tier risk assessment, and is assigned [Category a].	2	According to Appendix P of EFSA Bee Guidance (EFSA Journal 2013;11(7):3295), it is recommended to conduct a laboratory test with queenless microcolonies as a second step in risk assessment to bumble bees when either HQ or an ETR trigger is breached, or the active substance indicates the potential for accumulative effects. Such study is recommended to be performed on worker bees (queenless microcolonies of five workers per nest box), while experimental colonies in the current study were relatively large at

List No.	Author	Year	Title	Journal	Reason for judgement in "category a"	Klimisch score	Reason for judgement of Klimisch Score
							the time of pesticide exposure (containing a queen and an average of 99 workers), suggesting different sensitivity that at the earlier stage of colony cycle during larval development (with less worker bees). Study duration was 26-27 instead of 60 days recommended in the guidance. Environmental conditions during the study are not reported. The study is assigned Reliability score 2 (reliable with restrictions).
40	D. Kocamaz and E. Oruc	2020	Effect of Thiamethoxam and lambda Cyhalothrin, Administered Individually and in Mixture on the Endocrine Function and Antioxidant Defense of Gonads of Oreochromis niloticus	Pakistan Journal of Zoology, 52, 3, 1085-1093 dx.doi.org/10.17582/journal.pjz/20181014161054	In this study endocrine disrupting effects of thiamethoxam (Actara formulation, 25g/L) and λ cyhalothrin were investigated by using Oreochromis niloticus as a model organism. The fish exposed to 1/20, 1/10 of 96-h LC50 value of thiamethoxam and λ cyhalothrin, individually and in mixtures. For experimental design, a total 126 male fish were first divided into 2 groups; control and exposure groups, and then	2	This is a non-guideline study that provides information on endocrine-disrupting properties of thiamethoxam. Details of analytical method to determine

List No.	Author	Year	Title	Journal	Reason for judgement in “category a”	Klimisch score	Reason for judgement of Klimisch Score
					the exposure groups were divided into 6 subgroups (individual thiamethoxam and λ cyhalothrin treatments at 1/20, 1/10 of 96-h LC50, and a mixture). Concentrations at test treatments were quantified at the beginning of each chemical renewal period by GC-ECD, with recoveries >90% of the nominal value for each concentration. Experimental fish were exposed to pesticides on day 7 and 15. Subsequently, fish were transferred into pesticide-free water for 7 days in order to determine the potential reversibility of pesticide toxicity. The experiments were combined from 2 replicated independent experiments. No mortality was observed during the experiments. The following biochemical parameters were measured: activities of acetylcholinesterase (AChE), ethoxyresorufinO-deethylase (EROD), superoxide dismutase (SOD), catalase (CAT) and glutathione S-transferase (GST) activities, glutathione (GSH), malondialdehyde (MDA), protein carbonil (PCO) levels and protein content. The study is considered relevant for the assessment of endocrine-disrupting properties of thiamethoxam, as [Category a].		thiamethoxam concentrations are not reported.

Table 4.2-15 List of references judged as "Category a" in the second phase of relevance assessment and the result of reliability assessment – Environmental fate

List No.	Author	Year	Title	Journal	Klimisch classification	Reason for judgement
No papers were ranked as category "a" for the section Environmental fate.						

Table 4.2-16 Papers determined as "relevant" in the second phase of relevance assessment and the results are cited in assessment reports of EFSA, USEPA, and JMPR

List No.	Author(s)	Year of publication	Title of paper	Names, issues, page numbers, etc. of magazines	Evaluation agency	Reason for judgment
41	-	2018	Peer review of the pesticide risk assessment for bees for the active substance thiamethoxam considering the uses as seed treatments and granules	EFSA (European Food Safety Authority), 2018. Conclusions on the peer review of the pesticide risk assessment for bees for the active substance thiamethoxam considering the uses as seed treatments and granules. EFSA Journal 2018;16(2):5179, 59 pp. https://doi.org/10.2903/j.efsa.2018.5179	EFSA	Magnitude of thiamethoxam residues on bee products are available in this publication. Data presented could be used for the consumer risk assessment.

4.3 Conclusion

In conclusion, for the period (2015-03-01 and 2021-04-01), 1779 articles were extracted. After the two-step process (i.e., after detailed assessment for relevance and reliability of these articles) the results are:

- 2 studies were found relevant to the section “Toxicity to humans” but were classified as category “c” and therefore not further assessed for reliability.

- 9 studies were found relevant to the section “Residues in crops and livestock products”. 2 studies were classified category “a” and all were coted Klimisch score 2 (reliable with restriction).

- 30 studies were found relevant to the section “Toxicity to flora and fauna in the human living environment”. Among these 30 studies, only 2 studies were classified as category “a” and were coted Klimisch score 2 (reliable with restriction).

- 1 study was found relevant to the section “Environmental Fate”, but was classified as category “b” and therefore not further assessed for reliability.

- 1 EFSA study was obtained at the full text assessment step in the section “Residues in crops and livestock products”. This publication was sorted out in a separate table of results as part of the assessment report of an international authority.

CHAPTER 5 APPENDICES

5.1.1 Appendix I: Annexed Results

Results of assessment of Epidemiological and toxicological assessment are provided in the attached format:

- Non- Epidemiology FSC format