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Thiophanate-methyl & Carbendazim– Literature search report according to JMAFF Guidelines for the period 01.04.2009 – 31.03.2024

NIPPON SODA CO., LTD.

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1. Introduction:

This document presents the result of a systematic search of the open scientific literature in English language, following JMAFF Guidelines, for the active substances Thiophanate-methyl and Carbendazim, for the period 01.04.2009 – 31.03.2024. For both substances, the 15-year search period was covered by three separate searches, with the following search periods:

- First search (including JMAFF update): 01.01.2010 – 30.06.2022
- Second search: 01.07.2022 – 31.03.2024
- 2009 update: 01.04.2009 – 31.12.2009

An analysis of the relevance and reliability of each article relevant to the two active substances is also presented.

2. Methodology:

The literature search was performed according to the recommendations presented in the JMAFF Guidelines, using Web of Science (Core Collection) as the searched database.

The method consists of several steps:

- Definition of a search strategy which consist of selecting search keywords
- Performance of the search using Web of Science and sorting out of results
- Systematic review of the retrieved literature including relevance and reliability evaluations
- Reporting of results

2.1. Search strategy:

The keyword selection is performed via a 3-step approach:

- **Step 1**: selection of keywords relative to the target active substance using:
  - Common name
  - IUPAC name
  - CAS name
  - CAS number
  - EC number
  - Other available names
  - Formulation product names

  The following resources were used to search for active substance name and identification:
  - ChemIDplus: https://chem.nlm.nih.gov/chemidplus/
  - Pubchem: https://pubchem.ncbi.nlm.nih.gov/
  - CAS registry: https://commonchemistry.cas.org/

- **Step 2**: selection of keywords relative to observed effects according to four areas:
  - Toxicity/adverse effects on human
  - Crop and livestock residue
  - Ecotoxicity and animal toxicity
  - E-fate

In Web of Science, this keyword selection is performed by refining the search from step 1, selecting the relevant category field for each area of search (see section "b. Search process"), according to the following table:

Effect area	**Category field**
Toxicity/adverse effects on human	agriculture multidisciplinary allergy biochemistry molecular biology cell biology clinical neurology critical care medicine developmental biology emergency medicine endocrinology metabolism environmental sciences genetic heredity immunology medicine general internal medicine research experimental multidisciplinary sciences neurosciences oncology pediatrics pharmacology pharmacy physiology public environmental occupational health reproductive biology toxicology veterinary science
Crop and livestock residue	agriculture multidisciplinary agriculture dairy animal science environmental sciences food science technology multidisciplinary sciences pharmacology pharmacy plant sciences veterinary sciences zoology
Ecotoxicity and animal toxicity	agriculture multidisciplinary biochemistry molecular biology biodiversity conservation biology cell biology developmental biology ecology endocrinology metabolism entomology environmental sciences environmental studies fisheries marine freshwater biology microbiology multidisciplinary sciences neurosciences

	ornithology pharmacology pharmacy plant sciences reproductive biology toxicology veterinary sciences zoology
E-fate	agriculture multidisciplinary ecology environmental sciences environmental studies fisheries limnology marine freshwater biology multidisciplinary sciences soil science water resources

- **Step 3**: selection of keywords relative to target species relative to the four effect area categories:

  In Web of Science, this keyword selection is performed by refining the search from step 2, selecting the relevant species-specific keywords for each area of search (see section "b. Search process"), according to the following table:

Effect area	**Species-specific keywords**
Toxicity/adverse effects on human	Rat, mouse, dog, rabbit, monkey, pig, human, hen, S.typhimurim, E.coli
Crop and livestock residue	Crop, commodity, feed, livestock, hen, cattle, goat, pig, ruminant, cow, poultry
Ecotoxicity and animal toxicity	Avian, bird, mallard duck, quail, bobwhite, lemna, algae, fish, crustacean, aquatic, chironomus, bumble/honey/solitary bee, pollinator, apis,
E-fate	Soil, water, sediment

2.2. Literature search:

The literature searches were independently performed for each of the two substances Thiophanate-methyl and Carbendazim on 14.08.2023, 16.04.2024 and 25.04.2025, for the first search (including JMAFF update), second search and 2009 update, respectively. The 3-step approach described above was followed in all searches.

2.3. Systematic review of retrieved literature

The open literature searched and collected according to methodology described previously was then classified based on its relevance to the purpose of the evaluation. In addition, the relevance evaluation

was carried out in two stages as follows, and the relevant literature was then classified into three provisional categories, and then the reliability was evaluated.

2.3.1. Relevance evaluation

- Step 1: Initial rapid assessment:

The first step of the relevance evaluation is based on screening the title and abstracts of obtained hits. Irrelevant literature/publications are ruled out based on the following reasons:

① Publication of no relevance to the agrochemicals (as an alternative to the agrochemicals for example)

② Publication relevant to policy, society and economic analysis

③ Publication relevant to the production and distribution of agricultural products etc.

④ Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance

⑤ Publication relevant to analytical methods and their development

⑥ Publication relevant to new synthesis methods or basic chemistry

⑦ Publication relevant to patents

⑧ Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment

⑨ Written opinion that it is not showing any new data useful for risk assessment

⑩ Secondary source: introduction relevant to scientific publication or regulation that is not confirmed in the primary source (original)

⑪ Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical)

⑫ Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients

⑬ Publication not relevant to 4 effect areas described in section 1.a. step 2

⑭ Publication relevant to unregistered formulation products (different formulation) in Japan

⑮ Publication regarding dry lab (*In silico* methods, computer simulations)

- Step 2: Detailed assessment:

The second step of the relevance evaluation is based on screening the full text of obtained hits. Irrelevant literature/publications are ruled out based on the following reasons:

① to ⑮ Same as described above during the initial rapid assessment

⑯ Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation, as follows:

a) Study methods are not (sufficiently) documented.

b) The test was conducted according to a study type other than one that can be evaluated appropriately.

c) The test substance has not been dosed/treated by an appropriate route.

d) The dose or treatment equipment is not (sufficiently) documented.

e) The agent for adding of test substance are not confirmed.

f) The chemical analysis method is not documented.

⑰ Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.)

- Step 3: Relevance category classification:

Publication not excluded after the initial rapid and detailed assessments were then regarded as relevant, and the full text of literatures were reviewed by setting classification criteria and by classifying them into the following three categories:

Category	Relevant literature of the classification
a	Literature/publication is judged as available for the setting or reviewing risk assessment parameters［ADI, ARfD, AOEL, MRL, Registration standard of human living environment (meaning flora and fauna), PEC］
b	It is literature that can be used as supplementary data when setting risk assessment parameters
c	Not classified literature to a and b

The following items were considered as the classification criteria:

- The test environment being conducted matches the conditions specified in the test guidelines.
- The test material (including its purity and impurity profile) is well defined
- The number of animals per group is sufficient to establish a statistical significance
- Several dose levels (at least 3) are tested
- A control was set for the test, and the result compared with the test guideline was appropriate
- Analytical methods and results have been well reported.

In deciding whether or not a literature/publication meets the "category a" criteria and regarding the "Toxicity/adverse effects on human" category, the following criteria classified as "quantitative data" presented by the Food Safety Commission of Japan (FSC) were referred to:

- The dose used in publish literature is lower than the lowest dose used in the safety study, which is comparable to the study.
- Research results from open literature are reported using units that can be compared with other test results
- Sufficient information is provided in the open literature to demonstrate that the conclusions, endpoints and dose are accurate, reliable and valid. Moreover, it can be judged that there is a possibility of reproducibility for the research results

2.3.2. Reliability evaluation

Literature/publications classified as "Category a" in the evaluation of relevance described above were then subjected to the classification of the Klimisch standard (see table below), which is widely enforced internationally as a method for evaluating the reliability of literatures.

Score	Reliability	Standard for judgment
1	Reliable without restriction	・guideline study (preferably performed according to GLP) ・comparable to guideline study ・test procedure in accordance with national standard methods ・ test procedure in accordance with generally accepted scientific standards and described in detail
2	Reliable with restriction	・guideline study with acceptable restrictions ・comparable to guideline study with acceptable restrictions ・test procedure in accordance with national standard methods with acceptable restrictions ・study well documented, meets generally accepted scientific principles and acceptable for assessment
3	Not reliable	・significant methodological deficiencies for expert judge ・unsuitable system for expert judge
4	Not assignable	・abstract ・secondary literature (book, Overview etc.) ・documentation insufficient for assessment

More specifically, Klimisch scores were established as follows, for each effect area category:

(1) For the “Toxicity/adverse effects on human” effect area category, ToxRtool (Toxicological data Reliability assessment Tool) was used

(2) For the “Crop and livestock residue” effect area category, the following subsequent criteria were used:
- the test crop is the main crop by test guideline
- condition of test system (grow stage of crop, field condition, amount of treatment, Dose rate, use period, PHI, sampling method) are adequate
- the sample storage stability is verified after sampling
- the storage condition for the sample after sampling is described
- the cultivation condition (density and raising method) is appropriate
- the dose rate is within the limits of GAP specified by the registration

(3) For the "Ecotoxicity and animal toxicity" effect area category, the following subsequent criteria were used:
- the test item dissolves in water, for aquatic organism test
- the origin of test species, rearing condition, route, age, weight or length, etc. is clearly described
- the test environment (temperature etc.) is comparable to the recommendations of the test guideline during the whole test
- the concentration of the test sample is maintained as planned throughout the exposure period
- time-dependant results and observation are observed

(4) For the "E-fate" effect area category, the following subsequent criteria were used:
- test conditions (type of substrate, type of soil, pH, total organic carbon content, density, water content, activating microorganism etc) are clearly described.
- test conditions (e.g. condition of the used soil etc.) satisfy the test guideline.
- the sampling method satisfies the test guideline.
- the sample storage stability is verified after sampling
- the storage condition for the sample after sampling is described

2.4. Reporting of results

Apart from the result section of this literature report, which provides a summary of the findings, including the detailed relevance and reliability assessment, individual excel files presenting all the literature retrieved (including initial relevance assessment) for each field of search (Toxicity/adverse effects on human, Crop and livestock residue, Ecotoxicity and animal toxicity and E-fate) are also provided. Furthermore, all the publications that have undergone the detailed relevance assessment and potential subsequent reliability assessments are also provided. ToxRtool files for the reliability assessment of publication related to the "Toxicity/adverse effects on human" field are also provided

3. Results:

3.1. Thiophanate-methyl search:

3.1.1. Search strategy: keyword selection and summary of search strategy

Step 1 of the keyword selection process was performed as described in Table 1 and Table 2

Table 1: Retrieved keywords for the active substance Thiophanate-methyl

Common name	Thiophanate-methyl
IUPAC/CAS name	methylN-((2-(methoxycarbonylcarbamothioylamino)phenyl)carbamothioyl)carbamate OR Dimethyl 4,4'-(o-phenylene)bis(3-thioallophanate) /Thiophanate methyl
CAS Number / EC number	23564-05-8 / 245-740-7
Other names	Thiophanate methyl OR Methylthiofanate OR 1,2-Bis(3-(methoxycarbonyl)-2-thioureido)benzene OR 1,2-Di-(3-methoxycarbonyl-2-thioureido)benzene OR Dimethyl((1,2-phenylene)bis-(iminocarbonothioyl))bis(carbamate) OR Carbamic acid,N,N′-(1,2-phenylenebis(iminocarbonothioyl))bis-,C,C′-dimethylester OR Allophanic acid,4,4′-o-phenylenebis3-thio-,dimethylester

Table 2: Retrieved keywords for the formulation product containing the active substance Thiophanate-methyl

Common name	Topsin M 500 SC OR Topsin M OR Thiophanate-methyl 500 SC
IUPAC/CAS name	methyl N-[[2-(methoxycarbonylcarbamothioylamino)phenyl]carbamothioyl]carbamate

The summary of the search strategy for Thiophanate-methyl, including search dates and the various steps of the search process and number of hits obtained, are presented in Table 3 (first search (including JMAFF update)), Table 4 (second search) and Table 5 (2009 update).

Table 3: Summary of the search strategy for the active substance Thiophanate-methyl for the first search (including JMAFF update)

Database name	Web of Science (Core Collection) / All editions		
Date of the search	14.08.2023		
Date span of the search	From 01.01.2010 to 30.06.2022		
Used keyword to Retrieve	① AND ② AND ③		
	①	②*	③
Toxicity/adverse effects on human	Common name OR IUPAC/CAS name OR CAS Number / EC number OR Other names (see Table 1) OR Formulation product name (see Table 2)	agriculture multidisciplinary OR biochemistry molecular biology OR Cell Biology OR Environmental Sciences OR Immunology OR medicine research experimental OR multidisciplinary sciences OR pharmacology pharmacy OR physiology OR Toxicology OR public environmental occupational health OR veterinary sciences	Rat OR mouse OR dog OR rabbit OR monkey OR pig OR human OR hen OR S.typhimurium OR E. coli
Crop and livestock residue		agriculture multidisciplinary OR Environmental sciences OR food science technology OR multidisciplinary sciences OR pharmacology pharmacy OR plant sciences OR veterinary science OR zoology	Crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry
Ecotoxicity and animal toxicity		agriculture multidisciplinary OR biochemistry molecular biology OR biodiversity conservation OR biology OR cell biology OR ecology OR	Avian OR bird OR mallard duck OR quail OR bobwhite OR lemma OR algae OR fish OR crustacean OR aquatic OR chironomus OR bumble bee OR honeybee OR solitary

		entomology OR Environmental sciences OR environmental studies OR fisheries OR marine freshwater biology OR microbiology OR multidisciplinary sciences OR pharmacology pharmacy OR plant sciences OR toxicology OR veterinary sciences OR zoology	bee OR pollinator OR apis
E-fate		agriculture multidisciplinary OR ecology OR Environmental sciences OR fisheries OR limnology OR marine freshwater biology OR multidisciplinary sciences OR soil science OR water resources	Soil OR water OR sediment
Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literatures for target active substance name	598	NA	NA
Toxicity/adverse effects on human	NA	155	16
Crop and livestock residue	NA	367	86
Ecotoxicity and animal toxicity	NA	390	16
E-fate	NA	133	39

NA: not applicable

*: only the categories that were available in the search from the full list of categories to be selected for the 4 respective effect areas at step 2 of the keyword selection process are listed.

Table 4: Summary of the search strategy for the active substance Thiophanate-methyl for the second search

Database name	Web of Science (Core Collection) / All editions		
Date of the search	16.04.2024		
Date span of the search	From 01.07.2022 to 31.03.2024		
Used keyword to Retrieve	① AND ② AND ③		
	①	②*	③
Toxicity/adverse effects on human	Common name OR IUPAC/CAS name OR CAS Number / EC number OR Other names (see Table 1) OR Formulation product name (see Table 2)	agriculture multidisciplinary OR biochemistry molecular biology OR cell biology OR environmental Sciences OR multidisciplinary sciences pharmacology pharmacy OR physiology OR public environmental occupational health OR toxicology	rat OR mouse OR mice OR dog OR rabbit OR monkey OR pig OR human OR hen OR typhimurium OR E coli
Crop and livestock residue		agriculture multidisciplinary OR environmental sciences OR food science technology OR multidisciplinary sciences OR pharmacology pharmacy OR plant sciences	Crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry
Ecotoxicity and animal toxicity		agriculture multidisciplinary OR biochemistry molecular biology OR biology OR cell biology OR ecology OR entomology OR environmental sciences OR environmental studies OR microbiology OR multidisciplinary sciences OR pharmacology pharmacy OR	avian OR wild OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR daphnia OR fish OR crustacean OR aquatic OR chironomus OR bee OR pollinator OR apis

		plant sciences OR toxicology	
E-fate		agriculture multidisciplinary OR ecology OR environmental sciences OR environmental studies OR multidisciplinary sciences OR water resources	Soil OR water OR sediment
Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literatures for target active substance name	115	NA	NA
Toxicity/adverse effects on human	NA	29	5
Crop and livestock residue	NA	77	12
Ecotoxicity and animal toxicity	NA	82	6
E-fate	NA	23	11

NA: not applicable

*: only the categories that were available in the search from the full list of categories to be selected for the 4 respective effect areas at step 2 of the keyword selection process are listed.

Table 5: Summary of the search strategy for the active substance Thiophanate-methyl for the 2009 update search

Database name	Web of Science (Core Collection) / All editions		
Date of the search	25.04.2025		
Date span of the search	From 01.04.2009 to 31.12.2009		
Used keyword to Retrieve	① AND ② AND ③		
	①	②*	③
Toxicity/adverse effects on human	Common name OR IUPAC/CAS name OR CAS Number / EC number OR Other names (see Table 1) OR Formulation product name (see Table 2)	agriculture multidisciplinary OR toxicology	rat OR mouse OR mice OR dog OR rabbit OR monkey OR pig OR human OR hen OR typhimurium OR E coli
Crop and livestock residue		agriculture multidisciplinary OR food science technology OR plant sciences	Crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry
Ecotoxicity and animal toxicity		agriculture multidisciplinary OR ecology OR entomology OR marine freshwater biology OR plant sciences OR toxicology	avian OR wild OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR daphnia OR fish OR crustacean OR aquatic OR chironomus OR bee OR pollinator OR apis
E-fate		agriculture multidisciplinary OR ecology OR limnology OR marine freshwater biology	Soil OR water OR sediment
Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literatures for target active substance name	24	NA	NA
Toxicity/adverse effects on human	NA	2	1
Crop and livestock residue	NA	7	2
Ecotoxicity and animal toxicity	NA	10	1

E-fate	NA	2	1

NA: not applicable

*: only the categories that were available in the search from the full list of categories to be selected for the 4 respective effect areas at step 2 of the keyword selection process are listed.

3.1.2. Systematic review of retrieved literature

A summary of the relevance assessment for the Thiophanate-methyl search is presented in Table 6 for all 3 searches combined.

Table 6: Summary of results of the relevance assessment (Step 1, Step 2) of obtained hits for the active substance Thiophanate-methyl

Field	**Total number of Available literatures**	**Step 1**		**Step 2**	
		Non-relevant	**Potentially Relevant (Go to Step2)**	**Non-relevant**	**Relevant**
Toxicity/adverse effects on human					
First search (including JMAFF update)	16	9	7	5	2
Second search	5	5	0	0	0
2009 update	1	0	1	0	1
Total	22	14	8	5	3
Crop and livestock residue					
First search (including JMAFF update)	86	82	4	2	2
Second search	12	10	2	0	2
2009 update	2	1	1	0	1
Total	100	93	7	2	5
Ecotoxicity and animal toxicity					
First search (including JMAFF update)	19	10	9	9	0
Second search	7	4	3	3	0
2009 update	1	1	0	0	0
Total	27	15	12	12	0
E-fate					
First search (including JMAFF update)	31	30	1	1	0
Second search	10	10	0	0	0
2009 update	1	1	0	0	0
Total	42	41	1	1	0
Total					
First search (including JMAFF update)	152	131	21	17	4
Second search	34	29	5	3	2
2009 update	5	3	2	0	2
Grand total	191	163	28	20	8

Note: every literature hit that was originally found in an inadequate field was moved to the field it falls under (for example, a literature hit falling under the "Ecotoxicity and animal toxicity" field but originally found in the "Crop and livestock residue" search was moved to the "Ecotoxicity and animal toxicity" field). Duplicate literature hits between the various fields were also deleted (for example, a literature hit falling under the "Ecotoxicity and animal toxicity" field but found in both the "Ecotoxicity and animal toxicity" and the "Crop and livestock residue" searches was deleted from the "Crop and livestock residue" search. The counts provided in the table above account for these moves and duplicate deletions.

Table 7 presents the list of non-relevant hits/literature studies after step 2 of the relevance assessment and the reason for the decision to justify non-relevance for all 3 searches combined.

Table 7: List of non-relevant hits/literature studies after step 2 of the relevance assessment and reason for decision for the active substance Thiophanate-methyl

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
First search (including JMAFF update)									
T-5-1	Toxicity/adverse effects on human	NA	da Silva, JN; Monteiro, NR; Antunes, PA; Favareto, APA	2020	Maternal and developmental toxicity after exposure to formulation of chlorothalonil and thiophanate-methyl during organogenesis in rats	Anais da Academia Brasileira de Ciencias, 92 (4): 1 - 16	⑫ - Test substance applied as a mixture, not relevant for substance specific evaluation.	Yes	10.1590/0001-3765202020191026
T-5-2	Toxicity/adverse effects on human	NA	Feki, A; Ben Saad, H; Jaballi, I; Magne, C; Boudawara, O; Zeghal, KM; Hakim, A; Ben Ali, Y; Ben Amara, I	2017	Methyl thiophanate-induced toxicity in liver and kidney of adult rats: a biochemical, molecular and histopathological approach	Cellular and Molecular Biology, 63(2): 20 - 28	⑯c - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test substance has not been dosed/treated by an appropriate route. Test substance applied via IP and only one dose tested, no information on source of material and no analytical verification. At this dose level, excessive toxicity effects such as significant decrease in kidney weight were observed, indicating that the study design was not appropriate. The possibility of	No	10.14715/cmb/2017.63.2.4

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							nonspecific toxic effects, including genotoxicity, is also suggested.		
T-5-3	Toxicity/adverse effects on human	KIIA 5.9.3	Lombardi, C; Thompson, S; Ritz, B; Cockburn, M; Heck, JE	June 2021	Residential proximity to pesticide application as a risk factor for childhood central nervous system tumors.	Environmental Research, 197: 111078.	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical). Epidemiological study not specific to Thiophanate-methyl, multiple chemical exposures, not relevant.	No	10.1016/j.envres.2021.111078
T-5-4	Toxicity/adverse effects on human	NA	Liu, ZY; Chen, Y; Han, JH; Chen, D; Yang, GQ; Lan, TT; Li, JM; Zhang, KK	October 2021	Determination, dissipation dynamics, terminal residues and dietary risk assessment of thiophanate-methyl and its metabolite carbendazim in cowpeas collected from different locations in China under field conditions	Journal of the Science of Food and Agriculture, 101 (13): 5498 - 5507	⑯c - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test substance has not been dosed/treated by an appropriate route. Field study, no relevant information on toxicological effects. As noted, above, this was a field study that measured residues in a crop (cowpea). There was not a toxicological assessment of exposure to the	No	10.1002/jsfa.11198

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							test substance in mammals. Therefore, the study is not applicable to measuring adverse effects in mammals/humans.		
T-5-5	Toxicity/adverse effects on human	NA	Ye, ML; Nie, JY; Li, ZX; Cheng, Y; Zheng, LJ; Xu, GF; Yan, Z	2016	Health risks of consuming apples with carbendazim, imidacloprid, and thiophanate-methyl in the Chinese population: Risk assessment based on a nonparametric probabilistic evaluation model	Human and ecological risk assessment, 22(4): 1106 - 1121	⑯c - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test substance has not been dosed/treated by an appropriate route. Field study, no relevant information on toxicological effects. As noted, above, this was a field study that measured residues in a crop (cowpea). There was not a toxicological assessment of exposure to the test substance in mammals. Therefore, the study is not applicable to measuring adverse effects in mammals/humans.	No	10.1080/10807039.2015.1138091
T-5-6	Crop and livestock residue	KIIA 6.3	Fan, SF; Zhao, PY; Zhang,	April 2013	Spinach or amaranth may represent highest residue of thiophanate-methyl	Bulletin of Environmental Contaminat	⑯d - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the	No	10.1007/s00128-012-0925-z

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			FZ; Yu, CS; Pan, CP		with open field application on six leaf vegetables.	ion and Toxicology, 90 (4): 477 - 481	viewpoint of utilisation for the evaluation. The dose or treatment equipment is not (sufficiently) documented. The formulation tested was not described. The source of the formulation tested was not described. The application equipment, method was not fully described. The GAP used in terms of dilution of the formulation was not fully described.		
T-5-7	Crop and livestock residue	KIIA 6.3	Soliman, AS; Helmy, RMA; Nasr, IN; Abbas, MS; Mahmoud, HA; Jiang, WN	May 2017	Behavior of thiophanate methyl and propiconazole in grape and mango fruits under the Egyptian field conditions.	Bulletin of Environmental Contamination and Toxicology, 98 85): 720 -725	⑭- Publication relevant to unregistered formulation products (different formulation) in Japan.	No	10.1007/s00128-017-2066-x
T-5-8	Ecotoxicity and animal toxicity	KIIA 8.2.1	Jia, K; Cheng, B; Huang, LR; Xiao, JH; Bai, ZH; Liao, XJ; Cao, ZG; Shen, TZ; Zhang, CP;	June 2020	Thiophanate-methyl induces severe hepatotoxicity in zebrafish	Chemosphere, 248: 125941	⑯b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation.	No	10.1016/j.chemosphere.2020.125941

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			Hu, CY; Lu, HQ				The test was conducted according to a study type other than one that can be evaluated appropriately. Although the test species (zebrafish) is included in the JMAFF Guidelines No. 6278 (following OECD 203 guideline), the study is not sufficiently documented to determine if it is compliant with existing guideline (OECD TG 236 for test with embryos and OECD TG 203 for test with adult fish) and since the LC50 values are calculated with regard to the Fish Embryo Acute Toxicity (FET) Test and not the acute test. The study is considered not relevant with regards to acute fish test (OECD TG 203) for the following reasons: 1. very little information on test conditions (temperature, dissolved oxygen, pH) 2. several methological deficiencies: only 3 test concentrations used not allowing determination of		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							96h-LC50 values, not possible to determine test validity/performance criteria 3. No analytical verification of test concentrations. 4. size (wet weight and total length) is not described and developmental stage (juvenile, sub-adult, adult stage) is unclear.		
T-5-9	Ecotoxicity and animal toxicity	KIIA 8.2.1	Wang, YH; Lv, L; Xu, C; Wang, D; Yang, GL; Wang, XQ; Weng, HB; Wang, Q	Februar y 2021	Mixture toxicity of thiophanate-methyl and fenvalerate to embryonic zebrafish (*Danio rerio*) and its underlying mechanism.	Science Of the Total Environme nt, 756: 143754	⑯f - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The chemical analysis method is not documented. Not clear if the analytical verification of test concentrations has been performed. No information on chemical analysis provided and no detailed information about test conditions (test concentrations used, measured test conditions e.g. Temperature, pH and dissolved oxygen)	No	10.1016/j.scitotenv.2020.143754

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
T-5-10	Ecotoxicity and animal toxicity	KIIA 8.2.1	Khan, M; Ahmad, M; Ghayyur, S; Mahmood, S; Akhtar, N; Ullah, Z; Tabassum, S; Yasmin, S; Badshah, K; Hussain, H; Saira, S; Gul, A	2022	Comparative effects of selected agrochemicals on biochemical profile and histopathology of grass-carp (*Ctenopharyngodon idella*).	Polish Journal of Environmental Studies, 31 (2): 1679 - 1691	⑯a - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. Study methods are not (sufficiently) documented. No information on: - substance purity (which is tested as a formulation) - test item preparation and method of delivery/dosing - test diluent (water) parameters No analytical verification of test concentration Only one test concentration not allowing determination of LC_{50}	Yes	10.15244/pjoes/142145
T-5-11	Ecotoxicity and animal toxicity	KIIA 8.7	Tschoeke, PH; Oliveira, EE; Dalcin, MS; Silveira-Tschoeke, MCAC; Sarmento, RA; Santos, GR	August 2019	Botanical and synthetic pesticides alter the flower visitation rates of pollinator bees in Neotropical melon fields.	Environmental Pollution, 251: 591 - 599	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients. Bee flower visitation rate tests conducted with the	No	10.1016/j.envpol.2019.04.133

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							commercial mixture of the synthetic fungicides thiophanate-methyl (200 g a.i./kg) and chlorothalonil (200 g a.i./kg). No analytical verification of test concentrations.		
T-5-12	Ecotoxicity and animal toxicity	KIIA 8.7	Tome, HVV; Ramos, GS; Araujo, MF; Santana, WC; Santos, GR; Guedes, RNC; Maciel, CD; Newland, PL; Oliveira, EE	January 2017	Agrochemical synergism imposes higher risk to Neotropical bees than to honeybees	Royal Society Open Science, 4(1)	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients Study in which Thiophanate-methyl is never tested alone but always in conjunction with another active substance (imidacloprid or deltamethrin)	Yes	10.1098/rsos.160866
T-5-13	Ecotoxicity and animal toxicity	KIIA 8.8.2.5	Heneberg, P; Svoboda, J; Pech, P	February 2021	Claustral colony founding does not prevent sensitivity to the detrimental effects of azole fungicides on the fecundity of ants.	Journal of Environmental Management, 280: 111740	⑯b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. No or little information about: - test item preparation and method of delivery/dosing	No	10.1016/j.jenvman.2020.111740

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							- analytical verification of test concentration Test not close to any existing test guidelines and performed with a non-standard species (ants).		
T-5-14	Ecotoxicity and animal toxicity		Pratissoli, D; Milanez, AM; Barbosa, WF; Celestino, FN; Andrade, GS; Polanczyk, RA	April-June 2010	Side effects of fungicides used in cucurbitaceous crop on *trichogramma atopovirilia* oatman & platner (hymenoptera: trichogramatidae).	Chilean Journal of Agricultural Research, 70 (2): 323 - 327	⑯ b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not following any test guideline or using any standard test species of non-target arthropods and that does not provide any useful endpoint for risk assessment. Study of very limited relevance.	Yes	https://www.scielo.cl/pdf/chiljar/v70n2/AT16.pdf
T-5-15	Ecotoxicity and animal toxicity	KIIA 8.12	Li, M; Li, B; Zhang, HY; Chen, CJ; Li, JL; Liang, XY; Gu, YY	2022	Effects of fungicides on seedling and root growth of *Suaeda Salsa*.	Fresenius Environmental Bulletin, 31 (3A): 3316 - 3321	⑯b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation.	Yes	https://www.prt-parlar.de/download_list/?c=FEB_2022

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							The test was conducted according to a study type other than one that can be evaluated appropriately. Study performed with a non-standard salt-tolerant species. Study not following any current guideline and exposure performed in water when test guideline indicates soil tests. No analytical verification of test item concentrations.		
T-5-16	Ecotoxicity and animal toxicity	KIIA 8.16.2	Hanlon, SM; Lynch, KJ; Kerby, JL; Parris, MJ	September 2015	The effects of a fungicide and chytrid fungus on anuran larvae in aquatic mesocosms.	Environmental Science and Pollution Research, 22 (17): 12929 - 12940	⑯b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. No information on: - substance purity (which is tested as a formulation) - test item preparation and method of delivery/dosing	No	10.1007/s11356-015-4566-8

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							- test diluent (water) parameters No analytical verification of test concentration Only one test concentration not allowing determination of LC_{50} Several confounding factors studied such as the pathogenic fungus *Batrachochytrium dendrobatidis* and animal density not allowing the evaluation of the effect s of Thiophanate-methyl alone on amphibians.		
T-5-17	E-fate	KIIA 7.3	Hockemeyer, KR; Latin, R	May-June 2015	Spatial and temporal distribution of fungicides applied to creeping bentgrass.	Journal of Environmental Quality, 44 (3): 841 - 848	⑭- Publication relevant to unregistered formulation products (different formulation) in Japan. The paper used thiophanate-methyl formulation "3336F" manufactured by Cleary Chemical Corp., which is a flowable formulation containing 41.25% active ingredient. While thiophanate-methyl products for turf applications are registered in Japan, this specific	No	10.2134/jeq2014.08.0335

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							formulation (3336F) is not registered in Japan. The paper's methods did not follow the standard guidelines for field soil dissipation trials (e.g. sample plots were cropped, sampling depth). Additionally, the half-life was calculated from the residual concentration of methyl thiophanate; the half-life was not calculated from the total residue including other degradants. Therefore, the values from the paper are not reliable degradation values and cannot be compared with data generated by the applicant or used in the environmental risk assessments.		
Second search									
T-5-18	Ecotoxicity and animal toxicity	NA	Touzout, N; Ainas, M; Alloti, R; Boussahoua, C; Douma, A; Hassein-Bey, AH; Brara, Z; Tahraoui, H;	2023	Unveiling the impact of thiophanate-methyl on *Arthrospira platensis*: growth, photosynthetic pigments, biomolecules, and detoxification enzyme activities.	Frontiers in bioscience-Landmark, 28(10):264	⑯b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other	Yes	10.31083/j.fbl2810264

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			Zhang, J; Amrane, A				than one that can be evaluated appropriately. The cyanobacteria used in this study were collected from a unique environment: the Sahara region of Algeria. The study was conducted under unique conditions of 34 ± 3 °C and a 12-hour light/dark cycle. These conditions are not recommended by the testing guidelines. End points not estimated and parameters assessed are non-conventional. Exposure period 96 hrs. No analytical verification.		
T-5-19	Ecotoxicity and animal toxicity	NA	Perkins, JA; Kim, K; Gut, LJ; Sundin, GW; Wilson, JK	2023	Fungicide exposure in honey bee hives varies by time, worker role, and proximity to orchards in spring.	Journal of Economic Entomology, 116 (2): 435 - 446	⑤ - Publication relevant to analytical methods and their development. No residues of Thiophanate-methyl determined in any matrix assessed.	Yes	10.1093/jee/toad008
T-5-20	Ecotoxicity and animal toxicity	NA	Che, XF; Huang, Y; Zhong, KY; Jia, K; Wei, Y; Meng, YL;	2023	Thiophanate-methyl induces notochord toxicity by activating the PI3K-mTOR pathway in zebrafish	Environmental pollution, 318: 120861	⑯b - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation.	No	10.1016/j.envpol.2022.120861

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			Yuan, W; Lu, HQ		(*Danio rerio*) embryos.		The test was conducted according to a study type other than one that can be evaluated appropriately. Non-standard exposure regime. Exposure period up to 72 hrs for acute toxicity is lower than guideline requirements. No analytical verification.		

The number of hits/literature studies classified as “Category a”, ”Category b” or “Category c” after step 2 and step 3 of the relevance assessment for the active substance Thiophanate-methyl for the 3 searches combined is presented in Table 8.

Table 8: Number of hits/literature studies classified as “Category a”, ”Category b” or “Category c” after step 2 and step 3 of the relevance assessment for the active substance Thiophanate-methyl

Field	**Total number of Available literatures**		
	Category a	**Category b**	**Category c**
Toxicity/adverse effects on human			
First search (including JMAFF update)	0	0	2
Second search	0	0	0
2009 update	0	0	1
Total	0	0	3
Crop and livestock residue			
First search (including JMAFF update)	2	0	0
Second search	0	2	0
2009 update	1	0	0
Total	3	2	0
Ecotoxicity and animal toxicity			
First search (including JMAFF update)	0	0	0
Second search	0	0	0
2009 update	0	0	0
Total	0	0	0
E-fate			
First search (including JMAFF update)	0	0	0
Second search	0	0	0
2009 update	0	0	0
Total	0	0	0
Total			
First search (including JMAFF update)	2	0	2
Second search	0	2	0
2009 update	1	0	1
Grand total	3	2	3

Table 9 and Table 10 presents the detailed list of hits/literature studies classified as “Category b” and ”Category c”, respectively, after step 3 of the relevance assessment and the reasons for this classification for the 3 searches combined. Studies are ordered by data points.

Table 11 presents the detailed list of hits/literature studies classified as ”Category a” after step 3 of the relevance assessment and the reasons for this classification for the 3 searches combined. The Klimisch rating of such studies is also provided with the reasons for the obtained score.

Table 9: Literature classified as ”Category b” after step 3 of the relevance assessment and reason for the classification for the active substance Thiophanate-methyl

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
Second search									
T-6-1-1	Crop and livestock residue	KIIA 6.3	Rutkowska, E; Wolejko, E; Kaczynski, P; Luniewski, S; Lozowicka, B	2023	High and low temperature processing: Effective tool reducing pesticides in/on apple used in a risk assessment of dietary intake protocol.	Chemosphere, 313	The publication provides relevant information about the processing techniques of baking and freeze-drying in apples. Apple field trials were conducted in EU by applying Topsin M 500 SC (active substance - thiophanate methyl). The analytical method was validated following EU method performance criteria of SANTE/11312/2021 (2021). The extraction and quantification of thiophanate-methyl residues is	No	10.1016/j.chemosphere.2022.137498

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							described in detail. Processing factors were determined and were calculated in accordance with accepted methods and equations. In an EU consumer risk assessment, the acute (short) dietary intakes were calculated using EFSA PRIMo 3.1. The publication is considered as containing supplementary data that could be used to set risk assessment parameters in Japan. The study was conducted according to EU-accepted guidelines and methods.		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
T-6-1-2	Crop and livestock residue	KIIA 6.3	Kaczynski, P; Iwaniuk, P; Hrynko, I; Luniewski, S; Lozowicka, B	2024	The effect of the multi-stage process of wheat beer brewing on the behavior of pesticides according to their physicochemical properties.	Food Control, 160: 110356	The publication provides relevant information about the processing technique of brewing. Samples (1 kg) of wheat grain were submerged for 4 h in a solution containing 500 g/L thiophanate-methyl. No field trials were conducted. The active substance was diluted in 1 L of water to achieve a working solution in an artificial bath according to the label of the plant protection product. The analytical method was validated following EU method performance criteria of SANTE/11312/2021 (2021). The	No	10.1016/j.foodcont.2024.110356

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							extraction and quantification of thiophanate-methyl residues is described in detail. Processing factors were calculated in accordance with accepted methods and equations. The study was conducted according to EU-accepted guidelines and methods.		

Table 10: Literature classified as ”Category c” after step 3 of the relevance assessment and reason for the classification for the active substance Thiophanate-methyl

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
First search (including JMAFF update)									
T-6-2-1	Toxicity/adverse effects on human	KIIA 5.4	Saquib, Q; Al-Khedhairy, AA; Singh, BR; Arif, JM; Musarrat, J	2010	Genotoxic fungicide methyl thiophanate as an oxidative stressor inducing 8-oxo-7,8-dihydro-2 '-deoxyguanosine adducts in DNA and mutagenesis	Journal of Environmental Science and Health part b-Pesticides Food Contaminants and Agricultural Wastes, 45 (1): 40 - 45	Literature presented to characterize the toxicological mechanisms induced by thiophanate-methyl. Publication not presenting any information or data useful for setting risk assessment parameters. No information on purity and source of test substance. Inadequate description of statistical methods. Non-guideline study.	No	10.1080/03601230903404325

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
T-6-2-2	Toxicity/adverse effects on human	KIIA 5.4	Moo-Munoz, AJ; Azorin-Vega, EP; Ramirez-Duran, N; Moreno-Perez, PA	2021	Evaluation of the cytotoxic and genotoxic potential of the captan-based fungicides, chlorothalonil-based fungicides and methyl thiophanate-based fungicides in human fibroblasts BJ	Journal of Environmental Science and Health part b-Pesticides Food Contaminants and Agricultural Wastes, 56 (10): 877 - 883	Literature presented to characterize the toxicological mechanisms induced by thiophanate-methyl. Publication not presenting any information or data useful for setting risk assessment parameters. Formulations were used in the evaluation. Inadequate description of statistical methods (Dunnett's analysis not performed). Non-guideline study.	No	10.1080/03601234.2021.1972721
2009 update									

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
T-6-2-3	Toxicity/adverse effects on human	KIIA 5.4.4	Saquib, Q; Al-Khedhairy, AA; Al-Arifi, S; Dhawan, A; Musarrat, J	2009	Assessment of methyl thiophanate-Cu (II) induced DNA damage in human lymphocytes.	Toxicology in Vitro, 23 (5): 848 - 854	Literature presented to characterize the toxicological mechanisms induced by thiophanate-methyl. Publication not presenting any information or data useful for setting risk assessment parameters. The experimental design has not yet been validated as test guideline and has not yet been published.	No	10.1016/j.tiv.2009.04.017

Table 11: Literature classified as ”Category a” after step 3 of the relevance assessment and reason for the classification for the active substance Thiophanate-methyl

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
First search (including JMAFF update)										
T-7-1	Crop and livestock residue	KIIA 6.3	EFSA	April 2012	Reasoned opinion on the modification of the existing MRLs for thiophanate-methyl and carbendazim in apples and pears European Food Safety Authority.	EFSA Journal, 10 (4): 2685	4	EU review document with relevant information on residues, MRLs, risk assessment (consumer; animals) and analytical methods. Not a study document but an EU authority review document with information relating to MRLs and consumer risk assessment on the active substance.	Yes	10.2903/j.efsa.2012.2685
T-7-2	Crop and livestock residue	KIIA 6.3	EFSA	December 2014	Reasoned opinion on the review of the existing maximum residue levels (MRLs) for thiophanate-methyl and carbendazim	EFSA Journal, 12 (12): 3919	4	EU review document with relevant information on residues, MRLs, risk assessment (consumer; animals) and analytical methods.	Yes	10.2903/j.efsa.2014.3919

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
					according to Article 12 of Regulation (EC) No 396/2005 European Food Safety Authority			Not a study document but an EU authority review document with information relating to MRLs and consumer risk assessment on the active substance		
2009 update										
T-7-3	Crop and livestock residue	KIIA 6.3	EFSA	June 2009	Refined risk assessment regarding certain MRLs of concern for the active substances carbendazim and thiophanate-methyl.	EFSA Scientific Report, 289: 1 -29	4	Literature publication from approved independent reviewing authority relating to the review of MRLs for carbendazim and thiophanate-methyl in the EU in 2008, for a number of commodities. The data is considered as supplementary considering the uses are outside of Japan. This publication from EFSA (2009) can be used as supplementary data when setting risk assessment parameters	Yes	10.2903/j.efsa.2009.289r

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
								at JMAFF for thiophanate-methyl and/or the metabolite carbendazim. Publication from EFSA is not assignable according to Klimisch: EFSA document with regard to residues, MRL setting and consumer risk assessment.		

3.2. Carbendazim search:

3.2.1. Search strategy: keyword selection and summary of search strategy

Step 1 of the keyword selection process was performed as described in Table 12 and Table 13.

Table 12: Retrieved keywords for the active substance Carbendazim

Common name	Carbendazim
IUPAC/CAS name	methyl N-(1H-benzimidazol-2-yl)carbamate / Carbendazim
CAS Number / EC number	10605-21-7 / 234-232-0
Other names	1H-benzimidazole-2-carbamic acid, methyl ester OR 2-(methoxycarbonylamino)benzimidazole OR carbendazole OR benzimidazolecarbamate methyl ester OR Carbamic acid, N-1H-benzimidazol-2-yl-, methyl ester OR 2-Benzimidazolecarbamic acid, methyl ester OR Carbamic acid, 1H-benzimidazol-2-yl-, methyl ester OR HOE 017411 OR CF-27

Table 13: Retrieved keywords for the formulation product containing the active substance Carbendazim

Common name	Contrast CS OR Punch CS OR Escudo Forte OR Punch C OR Harvesan OR Punch SE OR DPX-N7872-205
IUPAC/CAS name	methyl N-(1H-benzimidazol-2-yl)carbamate / Carbendazim

The summary of the search strategy for Carbendazim, including search dates and the various steps of the search process and number of hits obtained, are presented in Table 14 ((first search (including JMAFF update)), Table 15 (second search) and Table 16 (2009 update).

Table 14: Summary of the search strategy for the active substance Carbendazim for the first search (including JMAFF update)

Database name	Web of Science (Core Collection) / All editions		
Date of the search	14.08.2023		
Date span of the search	From 01.01.2010 to 30.06.2022		
Used keyword to Retrieve	① AND ② AND ③		
	①	②*	③
Toxicity/adverse effects on human	Common name OR IUPAC/CAS name OR CAS Number / EC number OR Other names (see Table 12) OR Formulation product name (see Table 13)	agriculture multidisciplinary OR allergy OR biochemistry molecular biology OR cell biology OR clinical neurology OR critical care medicine OR developmental biology OR emergency medicine OR endocrinology metabolism OR environmental sciences OR immunology OR medicine general internal OR medicine research experimental OR multidisciplinary sciences OR neurosciences OR oncology OR paediatrics OR pharmacology pharmacy OR physiology OR Toxicology OR public environmental occupational health OR reproductive biology OR toxicology OR veterinary sciences	Rat OR mouse OR dog OR rabbit OR monkey OR pig OR human OR hen OR S.typhimurium OR E.coli
Crop and livestock residue		agriculture multidisciplinary OR agriculture dairy animal science OR food science technology OR multidisciplinary sciences OR pharmacology pharmacy OR plant sciences OR veterinary sciences OR zoology OR Environmental	Crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry

		sciences OR plant sciences	
Ecotoxicity and animal toxicity		agriculture multidisciplinary OR biochemistry molecular biology OR biodiversity conservation OR biology OR cell biology OR developmental biology OR ecology OR endocrinology metabolism OR entomology OR environmental sciences OR environmental studies OR fisheries OR marine freshwater biology OR microbiology OR multidisciplinary sciences OR neurosciences OR pharmacology pharmacy OR plant sciences OR reproductive biology OR toxicology OR veterinary sciences OR Zoology	Avian OR bird OR mallard duck OR quail OR bobwhite OR lemma OR algae OR fish OR crustacean OR aquatic OR chironomus OR bumble bee OR honeybee OR solitary bee OR pollinator OR apis
e-fate		agriculture multidisciplinary OR ecology OR Environmental sciences OR environmental studies OR fisheries OR limnology OR marine freshwater biology OR multidisciplinary sciences OR soil science OR water resources	Soil OR water OR sediment
Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literature for	24203	NA	NA

target active substance name			
Toxicity/adverse effects on human	NA	7172	2881
Crop and livestock residue	NA	4073	494
Ecotoxicity and animal toxicity	NA	6857	582
e-fate	NA	2954	1234

NA: not applicable

*: only the categories that were available in the search from the full list of categories to be selected for the 4 respective effect areas at step 2 of the keyword selection process are listed.

Table 15: Summary of the search strategy for the active substance Carbendazim for the second search

Database name	Web of Science (Core Collection) / All editions		
Date of the search	16.04.2024		
Date span of the search	From 01.07.2022 to 31.03.2024		
Used keyword to Retrieve	① AND ② AND ③		
	①	②*	③
Toxicity/adverse effects on human	Common name OR IUPAC/CAS name OR CAS Number / EC number OR Other names (see Table 12) OR Formulation product name (see Table 13)	agriculture multidisciplinary OR allergy OR biochemistry molecular biology OR cell biology OR clinical neurology OR critical care medicine OR developmental biology OR emergency medicine OR endocrinology metabolism OR environmental sciences OR genetic heredity OR immunology OR medicine general internal OR medicine research experimental OR multidisciplinary sciences OR neurosciences OR oncology OR pediatrics OR pharmacology pharmacy OR physiology OR public environmental occupational health OR reproductive biology OR toxicology OR veterinary sciences	rat OR mouse OR mice OR dog OR rabbit OR monkey OR pig OR human OR hen OR typhimurium OR E coli
Crop and livestock residue		agriculture multidisciplinary OR agriculture dairy animal science OR environmental sciences OR food science technology OR multidisciplinary sciences OR pharmacology pharmacy OR plant sciences OR veterinary sciences OR	Crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry

		zoology	
Ecotoxicity and animal toxicity		agriculture multidisciplinary OR biochemistry molecular biology OR biodiversity conservation OR biology OR cell biology OR developmental biology OR ecology OR endocrinology metabolism OR entomology OR environmental sciences OR environmental studies OR fisheries OR marine freshwater biology OR microbiology OR multidisciplinary sciences OR neurosciences ornithology OR pharmacology pharmacy OR plant sciences OR reproductive biology OR toxicology OR veterinary sciences OR zoology	avian OR wild OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR daphnia OR fish OR crustacean OR aquatic OR chironomus OR bee OR pollinator OR apis
e-fate		agriculture multidisciplinary OR ecology OR environmental sciences OR environmental studies OR fisheries OR limnology OR marine freshwater biology OR multidisciplinary sciences OR soil science OR water resources	Soil OR water OR sediment
Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literature for	3356	NA	NA

target active substance name			
Toxicity/adverse effects on human	NA	1105	359
Crop and livestock residue	NA	748	107
Ecotoxicity and animal toxicity	NA	1101	135
e-fate	NA	511	209

NA: not applicable

*: only the categories that were available in the search from the full list of categories to be selected for the 4 respective effect areas at step 2 of the keyword selection process are listed.

Table 16: Summary of the search strategy for the active substance Carbendazim for the 2009 update search

Database name	Web of Science (Core Collection) / All editions		
Date of the search	25.04.2025		
Date span of the search	From 01.04.2009 to 31.12.2009		
Used keyword to Retrieve	① AND ② AND ③		
	①	②*	③
Toxicity/adverse effects on human	Common name OR IUPAC/CAS name OR CAS Number / EC number OR Other names (see Table 12) OR Formulation product name (see Table 13)	agriculture multidisciplinary OR allergy OR biochemistry molecular biology OR cell biology OR clinical neurology OR critical care medicine OR developmental biology OR emergency medicine OR endocrinology metabolism OR environmental sciences OR genetic heredity OR immunology OR medicine general internal OR medicine research experimental OR multidisciplinary sciences OR neurosciences OR oncology OR pharmacology pharmacy OR physiology OR public environmental occupational health OR reproductive biology OR toxicology OR veterinary science	rat OR mouse OR mice OR dog OR rabbit OR monkey OR pig OR human OR hen OR typhimurium OR E coli
Crop and livestock residue		agriculture multidisciplinary OR agriculture dairy animal science OR environmental sciences OR food	Crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry

		science technology OR multidisciplinary sciences OR pharmacology pharmacy OR plant sciences OR veterinary sciences OR zoology	
Ecotoxicity and animal toxicity		agriculture multidisciplinary OR biochemistry molecular biology OR biodiversity conservation OR biology OR cell biology OR developmental biology OR ecology OR endocrinology metabolism OR entomology OR environmental sciences OR fisheries OR marine freshwater biology OR microbiology OR multidisciplinary sciences OR neurosciences OR pharmacology pharmacy OR plant sciences OR reproductive biology OR toxicology OR veterinary sciences OR zoology	avian OR wild OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR daphnia OR fish OR crustacean OR aquatic OR chironomus OR bee OR pollinator OR apis
e-fate		agriculture multidisciplinary OR ecology OR environmental sciences OR fisheries OR limnology OR marine freshwater biology OR multidisciplinary sciences OR soil science OR water resources	Soil OR water OR sediment

Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literature for target active substance name	784	NA	NA
Toxicity/adverse effects on human	NA	239	135
Crop and livestock residue	NA	96	15
Ecotoxicity and animal toxicity	NA	242	33
e-fate	NA	53	27

NA: not applicable

*: only the categories that were available in the search from the full list of categories to be selected for the 4 respective effect areas at step 2 of the keyword selection process are listed.

3.2.2. Systematic review of retrieved literature strategy

A summary of the relevance assessment for the Carbendazim search is presented in Table 17 for all 3 searches combined.

Table 17: Summary of results of the relevance assessment (Step 1, Step 2) of obtained hits for the active substance Carbendazim

Field	Total number of Available literatures	Step 1		Step 2	
		Non-relevant	Potentially Relevant (Go to Step2)	Non-relevant	Relevant
Toxicity/adverse effects on human					
First search (including JMAFF update)	2878	2843	35	10	25
Second search	359	353	6	1	5
2009 update	135	134	1	1	0
Total	3372	3330	42	12	30
Crop and livestock residue					
First search (including JMAFF update)	481	462	19	17	2
Second search	107	105	2	1	1
2009 update	15	14	1	0	1
Total	603	581	22	18	4
Ecotoxicity and animal toxicity					
First search (including JMAFF update)	618	564	54*	47	7
Second search	141	134	7	7	0
2009 update	33	32	1	1	0
Total	792	730	62	55	7
E-fate					
First search (including JMAFF update)	1186	1173	13	9	4
Second search	201	198	3	3	0
2009 update	27	26	1	1	0
Total	1414	1397	17	13	4
Total					
First search (including JMAFF update)	5163	5042	121	83	38
Second search	808	790	18	12	6
2009 update	210	206	4	3	1
Grand total	6181	6038	143	98	45

Note: every literature hit that was originally found in an inadequate field was moved to the field it falls under (for example, a literature hit falling under the "Ecotoxicity and animal toxicity" field but originally found in the "Crop and livestock residue" search was moved to the "Ecotoxicity and animal toxicity" field). Duplicate literature hits between the various fields were also deleted (for example, a literature hit falling under the "Ecotoxicity and animal toxicity" field but found in both the "Ecotoxicity and animal toxicity" and the "Crop and livestock residue" searches was deleted from the "Crop and livestock residue" search. The counts provided in the table above account for these moves and duplicate deletions.

*: these include 10 studies that were not obtained in the main literature search but that were cited in some of the literature retrieved in the main search and that were deemed potentially relevant to the "Ecotoxicity and animal toxicity"field.

Table 18 presents the list of non-relevant hits/literature studies after step 2 of the relevance assessment and the reason for the decision to justify non-relevance. Studies are ordered by data points for all 3 searches combined.

Table 18: List of non-relevant hits/literature studies after step 2 of the relevance assessment and reason for decision for the active substance Carbendazim

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
First search (including JMAFF update)									
C-5-1	Toxicity /adverse effects on human	KIIA 5.4.4	Itoh, S; Nagata, M; Hattori, C; Takasaki, W	February 2015	Effect of buprenorphine on genotoxicity evaluation of chemicals by the rat liver micronucleus test with partial hepatectomy.	Journal of Toxicological Sciences, 40 (1): 109 - 114	⑬ - Publication not relevant to 4 effect areas described in section 1.a. step 2. Study not specific to Carbendazim.	Yes	10.2131/jts.40.109
C-5-2	Toxicity /adverse effects on human	KIIA 5.5.2	Lisovska, V; Nedopytanska, N; Bagley, E; Reshavska, O	October 2017	Endocrine disruption and carcinogenesis: Evaluation of neoplasms in endocrine organs of rat in Carbendazim carcinogenic chronic study.	Toxicology Letters, 280:167	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment. Abstract with insufficient information.	No	10.1016/j.toxlet.2017.07.467
C-5-3	Toxicity /adverse effects on human	KIIA 5.6	Adedara, IA; Vaithinathan, S; Jubendradass, R; Mathur, PP; Farombi, EO	August 2011	Inhibition of carbendazim-induced steroidogenic dysfunction and apoptosis in rat testis by kolaviron, a natural biflavonoid from Garcinia kola seed	Toxicology Letters, 205:247	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment. Abstract with insufficient information.	No	10.1016/j.toxlet.2011.05.843
C-5-4	Toxicity /adverse effects	KIIA 5.6	Ebedy, YA; Hassanen, EI; Hussien, AM;	July 2022	Neurobehavioral toxicity induced by Carbendazim in rats	Neurochemical Research, 47(7): 1956-1971	⑭ - Publication relevant to unregistered formulation	No	10.1007/s11064-022-03581-5

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
	on human		Ibrahim, MA; Elshazly, MO		and the role of iNOS, Cox-2, and NF-kappa B signalling pathway.		products (different formulation) in Japan. In this literature, CBZ pesticide formulation is used as the test substance. Since the registration of CBZ has expired in Japan, it is classified as not relevant. The use of pesticide formulation is not mentioned in the title and abstract, and is only revealed in the Material and Methods section.		
C-5-5	Toxicity /adverse effects on human	KIIA 5.6.8	Campion, SN; Catlin, N; Houseman, EA; Hensley, J; Sui, YX; Gaido, KW; Wu, ZJ; Boekelheide, K	June 2012	Molecular alterations underlying the enhanced disruption of spermatogenesis by 2,5-hexanedione and carbendazim co-exposure.	Reproductive Toxicology, 33 (3): 382 - 389	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients. Co-exposures - not relevant for studying Carbendazim alone.	No	10.1016/j.reprotox.2012.01.014
C-5-6	Toxicity /adverse effects on human	NA	Freire, PF; Paredes, J; Peropadre, A; Repetto, G; Hazen, M	September 2016	Carbendazim induces cytotoxic and cytostatic effects in non-tumoral human cells.	Toxicology Letters, 258:248	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment. Abstract with insufficient information.	No	10.1016/j.toxlet.2016.06.1879

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-7	Toxicity /adverse effects on human	NA	Daundkar, PS; Rampal, S	November 2014	Evaluation of ameliorative potential of selenium on carbendazim induced oxidative stress in male goats.	Environmental Toxicology and Pharmacology, 38 (3): 711 - 719	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Animal species is goat, and an appropriate toxicity assessment cannot be conducted. Although this literature uses a CBZ pesticide formulation, CBZ registration in Japan has expired.	No	10.1016/j.etap.2014.09.007
C-5-8	Toxicity /adverse effects on human	NA	Ebedy, YA; Elshazly, MO; Hassan, NH; Ibrahim, MA; Hassanen, EI	August 2022	Novel insights into the potential mechanisms underlying carbendazim-induced hepatorenal toxicity in rats.	Journal of Biochemical and Molecular Toxicology, 36 (8): 23079	⑭ - Publication relevant to unregistered formulation products (different formulation) in Japan. Although this literature uses a CBZ pesticide formulation, CBZ registration in Japan has expired.	No	10.1002/jbt.23079
C-5-9	Toxicity /adverse effects on human	NA	Mo, E; Ebedy, YA; Ibrahim, MA; Farroh, KY; Hassanen, EI	June 2022	Newly synthesized chitosan-nanoparticles attenuate carbendazim hepatorenal toxicity in rats via activation	Scientific Reports, 12 (1):9986	⑬ - Publication not relevant to 4 effect areas described in section 1.a. step 2	Yes	10.1038/s41598-022-13960-1

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					of Nrf2/HO1 signalling pathway.				
C-5-10	Toxicity /adverse effects on human	NA	Zhang, Y; Zhou, Y; Duan, TT; Kaium, A; Li, XG	March 2022	Dissipation and dietary risk assessment of Carbendazim and epoxiconazole in citrus fruits in China.	Journal of the Science of Food and Agriculture	⑬ - Publication not relevant to 4 effect areas described in section 1.a. step 2	No	10.1002/jsfa.11474
C-5-11	Crop and livestock residue	KIIA 6.3	Wu, JL; Wei, HD; Sui, XF; Lin, J; Wang, TY; Fen, GQ; Xue, J	April 2010	Dynamics of carbendazim residue in *Panax notoginseng* and soil.	Bulletin of Environmental Contamination and Toxicology, 84 (4): 469 - 472	⑯a - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. Study methods are not (sufficiently) documented.	No	10.1007/s00128-010-9970-7
C-5-12	Crop and livestock residue	KIIA 6.3	Fan, SF; Zhao, PY; Zhang, FZ; Yu, CS; Pan, CP	April 2013	Spinach or amaranth may represent highest residue of thiophanate-methyl with open field application on six leaf vegetables.	Bulletin of Environmental Contamination and Toxicology, 90 (4): 477 - 481	⑯d - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The dose or treatment equipment is not (sufficiently) documented. The formulation tested was not described. The source of the formulation tested was not described.	No	10.1007/s00128-012-0925-z

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							The application equipment, method was not fully described. The GAP used in terms of dilution of the formulation was not fully described.		
C-5-13	Crop and livestock residue	KIIA 6.3	Arora, S; Mukherjee, I; Kumar, A; Garg, DK	January 2014	Comparative assessment of pesticide residues in grain, soil, and water from IPM and non-IPM trials of basmati rice.	Environmental Monitoring and Assessment, 186 (1): 261 - 366	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical).	No	10.1007/s10661-013-3380-3
C-5-14	Crop and livestock residue	KIIA 6.3	Mohapatra, S; Lekha, S	July 2016	Residue level and dissipation of carbendazim in/on pomegranate fruits and soil	Environmental Monitoring and Assessment, 188 (7): 406	⑭ - Publication relevant to unregistered formulation products (different formulation) in Japan.	No	10.1007/s10661-016-5404-2
C-5-15	Crop and livestock residue	KIIA 6.3	Bhandari, G; Zomer, P; Atreya, K; Mol, HGJ; Yang, XM; Geissen, V	May 2019	Pesticide residues in Nepalese vegetables and potential health risks.	Environmental Research, 172: 511 - 521	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical).	No	10.1016/j.envres.2019.03.002
C-5-16	Crop and livestock residue	KIIA 6.3	Neelab; Asi, MR; Kali, S; Riaz, MA; Waseem, A; Iqbal, MM; Ahmad, N; Iqbal, M; Masood, N; Zafar, MI	November 2020	Comparative efficacy of mitigation techniques for the detoxification of *Prunus persica* (L.) from selected pesticide residues.	Environmental Science and Pollution Research, 27 (32): 39786 - 39794	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical).	No	10.1007/s11356-020-08720-5

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-17	Crop and livestock residue	KIIA 6.3	Chen, LP; Wu, CX; Xu, MF; Cang, T; Wang, XQ; Zhao, XP; Zhang, CP	August 2021	Assessment of carbendazim residues and safety in celery under different cultivation conditions.	Bulletin of Environmental Contamination and Toxicology, 107 (2): 276 - 280	⑭ - Publication relevant to unregistered formulation products (different formulation) in Japan.	No	10.1007/s00128-020-02785-1
C-5-18	Crop and livestock residue	KIIA 6.3	Valderrama, L; Valderrama, P; Carasek, E	January 2022	A semi-quantitative model through PLS-DA in the evaluation of carbendazim in grape juices.	Food Chemistry, 368: 130742	⑤ - Publication relevant to analytical methods and their development.	No	10.1016/j.foodchem.2021.130742
C-5-19	Crop and livestock residue	KIIA 6.3	Eslami, Z; Mahdavi, V; Mofrad, AA	July 2022	Simultaneous multi-determination of pesticide residues in barberry: A risk assessment study.	Journal of Food Composition and Analysis, 110: 104576	⑤ - Publication relevant to analytical methods and their development.	No	10.1016/j.jfca.2022.104576
C-5-20	Crop and livestock residue	KIIA 6.3	Pareja, L; Colazzo, M; Perez-Parada, A; Besil, N; Heinzen, H; Bocking, B; Cesio, V; Fernandez-Alba, AR	May 2012	Occurrence and distribution study of residues from pesticides applied under controlled conditions in the field during rice processing.	Journal of Agricultural and Food Chemistry, 60(18): 4440 - 4448	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical).	No	10.1021/jf205293j
C-5-21	Crop and livestock residue	KIIA 6.3	Bakirci, GT; Acay, DBY; Bakirci, F; Otles, S	October 2014	Pesticide residues in fruits and vegetables from the Aegean region, Turkey.	Food chemistry, 160: 379-392	⑰ - Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.). The publication by Bakirci et al. (2014) describes the application of a multi-residue method on 1423 crop	No	10.1016/j.foodchem.2014.02.051

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							samples collected from a market in the Aegean region of Turkey from 2010-2012. The results showed that carbendazim/benomyl was found in mushrooms at a range of 0.012-3.53 mg/kg, which exceeded the MRL established by Turkish Regulation. However, relevant information of residues in the crops under consideration should be obtained from residue trials conducted in the geographical zone relevant to the GAP, and the results presented in this publication cannot be accepted as representative of residues expected under the climatic conditions in Japan. Additionally, the agricultural practices, cultivation methods, and pest management strategies in Turkey likely differ from those in Japan. The magnitude of any residues depends also on the formulation type, the application type and the pre-harvest interval based on the cGAP in Japan. The publication provides		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							information about carbendazim residues in several commodities but mainly reports the development and use of an analytical multi residue-method. Consequently, the paper could also be categorised under the criterion for exclusion '⑤ Publication relevant to analytical methods and their development'.		
C-5-22	Crop and livestock residue	KIIA 6.3	Zeid, MIA; Awad, MK; Melki, KC; Abou Jawdah, Y; Jammoul, AM	December 2021	Pesticides residues on Loquat: Aaminor crop in Lebanon.	Food Control, 130: 108297	⑰ - Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.). The aim of the publication by Zeid et al. (2021) was to screen and quantify the range of pesticide residues in 128 loquat samples gathered from a Lebanese market between 2017 and 2019, study the dissipation behavior of penconazole on apple and loquat in the field, confirm the cGAP of penconazole on apples and propose a pre-harvest interval (PHI) for penconazole on Loquat in Lebanon. The samples were	No	10.1016/j.foodcont.2021.108297

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							analysed using a validated multi-residue method on apple with GC-MS/MS and LC-MS/MS determination. Thiophanate-methyl was detected in loquat at 0.03 mg/kg. Carbendazim was detected at concentrations ranging from 0.08 to 0.096 mg/kg in loquat. However, relevant information on residues in the crops under consideration should be obtained from residue trials conducted in the geographical zone relevant to the GAP, and consequently the results presented in this publication cannot be considered relevant to the climatic conditions in Japan. The study focuses primarily on screening for pesticide residues in market samples rather than controlled field trials for thiophanate-methyl or carbendazim. In fact, both thiophanate-methyl and carbendazim were detected as unauthorized pesticides in Lebanon, classified as "contaminated" samples in the study, with no information on their application conditions, rates,		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							or timing. The study provides no data on field conditions, application methods, or use patterns that led to these residues, making it impossible to relate these findings to typical application conditions in Japan. Furthermore, the study does not include any controlled residue trials for thiophanate-methyl or carbendazim, focusing instead on penconazole, which is not the compound of interest for the current evaluation. The quantity of any residues depends also on the formulation type, the application type and the pre-harvest interval based on the cGAP in Japan. Without specific information on how, when, or in what quantities thiophanate-methyl or carbendazim were applied to produce the detected residues, these findings cannot be used to evaluate typical application conditions or residue behavior under Japanese agricultural practices. The detected residues represent unauthorized use or		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							environmental contamination in Lebanon, not controlled applications that could be compared to Japanese GAP. The publication provides information about thiophanate-methyl and carbendazim residues in loquat but mainly reports the development and use of an analytical multi residue-method to study the behaviour of penconazole residues in loquat and apples.		
C-5-23	Crop and livestock residue	KIIA 6.3	Jardim, ANO; Caldas, ED	June 2012	Brazilian monitoring programs for pesticide residues in food - Results from 2001 to 2010.	Food Control, 25(2): 607 - 616	⑰ - Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.). The objective of the paper by Jardim and Caldas (2012) is to present and discuss the results obtained by the PARA (Program on Pesticide Residue Analysis in Food) and the PNCRC (National Residue and Contaminant Control Program) pesticide residue monitoring programs in Brazil for the period between 2001 and 2010. A total of 13,556 samples of 22 fruit and vegetable crops,	No	10.1016/j.foodcont.2011.11.001

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							rice, and beans were analysed by applying multi-residue methods. Carbendazim was the single compound most frequently detected (26.7% of the samples) but further details on the commodities where residues have been detected, and their quantity were not reported. For this reason, no relation to the typical application (conditions of use) and intended uses of thiophanate-methyl and/or carbendazim products in Japan and possible residues can be drawn. Additionally, the study lacks specific information on application methods, rates, timing, or field conditions that led to the detected residues. Without crop-specific residue data and details on agricultural practices, which differ significantly between Brazil and Japan, it is impossible to relate the findings to typical application conditions in Japan. Further, relevant information on residues in the crops under consideration should be performed with		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							residue trials conducted in the geographical zone relevant to the GAP and the results presented in this publication cannot be considered as representative to the climatic conditions in Japan. The quantity of any residues depends also on the formulation type, the application type and the pre-harvest interval based on the cGAP in Japan.		
C-5-24	Crop and livestock residue	KIIA 6.3	Yang, YT; Wang, HY; Li, W; Chen, Y; Guo, W; Gu, X; Ye, QF	January 2020	Phytoavailability of bound residue of Carbendazim to Chinese cabbage (*Brassica campestris ssp.chinensis*) coexisted with superabsorbent polymers.	Scientific Reports,	④ - Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance.	Yes	10.1038/s41598-020-57488-8
C-5-25	Crop and livestock residue	KIIA 6.4	Hirunrussamee, J; Wongwit, W; Tharnpoophasiam, P; Worakhunpiset, S; Tantrakarnapa, K; Thetkathuek, A	2022	Agrochemical residues in soil, water, chicken's blood and worker's urine samples in rose farms, Tak province, Thailand.	Journal of Environmental Science and Management, 25 (1): 39 - 47	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical).	No	None
C-5-26	Crop and livestoc	KIIA 6.4	de Souza, LFCB; Montagner, CC; Almeida, MB; Kuroda, EK;	May-June 2019	Determination of pesticides in the source and drinking	Semina-Ciencias Agrarias	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals	Yes	10.5433/1679-0359.2019v40n3p1153

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
	k residue		Vidal, C; Freire, RL		waters in Londrina, Parana, Brazil.		without limiting the focus to the target agrochemical).		
C-5-27	Crop and livestock residue	NA	Zhang, Y; Zhou, Y; Duan, TT; Kaium, A; Li, XG	March 2022	Dissipation and dietary risk assessment of Carbendazim and epoxiconazole in citrus fruits in China.	Journal of the Science of Food and Agriculture	⑰ - Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.)	No	10.1002/jsfa.11474
C-5-28	Ecotoxicity and animal toxicity	KIIA 8.2.1	Ludwikowska, A; Bojarski, B; Socha, M; Lutnicka, H; Trzeciak, KB	2013	The effect of carbendazim on embryonic Prussian carp (*Carassius gibelio*) development and hatching.	Archives of Polish Fisheries, 21 (4): 367 - 371	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study with non-standard fish species (Prussian carp), inspired but not following the OECD TG 236 (Fish Embryo Acute Toxicity (FET) Test with major deficiencies (exposure time not adequate, inadequate replication and endpoint measurements, no analytical verification of test item concentrations). No useful endpoints (96-hr LC_{50} value and EC_{50} values for sublethal) provided for	Yes	10.2478/aopf-2013-0038

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							use in aquatic risk assessment. Furthermore, the Fish Embryo Acute Toxicity (FET) method is not included in the JMAFF Guideline No. 6278. and the study is therefore considered as not relevant.		
C-5-29	Ecotoxicity and animal toxicity	KIIA 8.2.1 & KIIA 8.3.1	Rico, A; Waichman, AV; Geber-Correa, R; van den Brink, PJ	June 2011	Effects of malathion and carbendazim on Amazonian freshwater organisms: comparison of tropical and temperate species sensitivity distributions.	Ecotoxicology, 20 (4): 625 - 634	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study providing endpoints about the acute toxicity of Carbendazim to temperate freshwater fish and invertebrates. Focus on higher tier risk assessment with determination of HC5 values for freshwater fish and invertebrates taken from SSD evaluations. However, according to JMAFF Guideline No. 6278, in Japan, SSD/HC5 are not	Yes	10.1007/s10646-011-0601-9

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							allowed to be used for the risk assessment. Only the part about temperate species is of relevance to Japan and therefore the part about tropical (Amazonian) species should be ignored. Furthermore, the test species used in the study are not included in the OECD Guideline 203 mentioned in the JMAFF Guideline No. 6278. Therefore, study considered as not relevant.		
C-5-30	Ecotoxicity and animal toxicity	KIIA 8.2.1	Andrade, TS; Henriques, JF; Almeida, AR; Machado, AL; Koba, O; Giang, PT; Soares, AMVM; Domingues, I	January 2016	Carbendazim exposure induces developmental, biochemical and behavioural disturbance in zebrafish embryos.	Aquatic Toxicology, 170: 390 - 399	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study with fish following the OECD TG 236 (Fish Embryo Acute Toxicity (FET)) Test, with some minor deviations. Study providing endpoints (96-hr LC50 value and EC50	No	10.1016/j.aquatox.2015.11.017

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							values for sublethal endpoints) to determine the acute toxicity of Carbendazim in freshwater fish. However, the Fish Embryo Acute Toxicity (FET)) (OECD TG 236) method is not included in the JMAFF Guideline No. 6278. Therefore, study considered as not relevant.		
C-5-31	Ecotoxicity and animal toxicity	KIIA 8.2.1	Schmidt, S; Busch, W; Altenburger, R; Kuster, E	June 2016	Mixture toxicity of water contaminants-effect analysis using the zebrafish embryo assay (*Danio rerio*).	Chemosphere, 152: 503 - 512	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study providing endpoint (96-hr LC50 value) about the acute toxicity of Carbendazim to zebrafish embryos (Fish Embryo Acute Toxicity (FET) test). However, the Fish Embryo Acute Toxicity (FET)) (OECD TG 236) method is	No	10.1016/j.chemosphere.2016.03.006

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							not included in the JMAFF Guideline No. 6278. Therefore, study considered as not relevant.		
C-5-32	Ecotoxicity and animal toxicity	KIIA 8.2.2	Govindassamy, P; Tiroumavalavane, M; Marcelline, SO; Ramalingam, V	August 2011	Toxic influence of endocrine disruptor, carbendazim, on brain biochemical and haematological changes in the freshwater fish, *Cyprinus carpio*.	Toxicology Letters, 205: S125	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment. Abstract of paper with insufficient information.	No	10.1016/j.toxlet.2011.05.447
C-5-33	Ecotoxicity and animal toxicity	KIIA 8.2.2	Jiang, JH; Wu, SG; Wang, YH; An, XH; Cai, LM; Zhao, XP; Wu, CX	October 2015	Carbendazim has the potential to induce oxidative stress, apoptosis, immunotoxicity and endocrine disruption during zebrafish larvae development.	Toxicology In Vitro, 29 (7): 1473 - 1481	⑯a - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. Study methods are not (sufficiently) documented. No analytical verification of test concentrations. No endpoints useful for environmental risk assessment. No reference substance used to evaluate the performance of the test. No reference to any test guideline provided.	No	10.1016/j.tiv.2015.06.003

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-34	Ecotoxicity and animal toxicity	KIIA 8.2.2	Jiang, JH; Wu, SG; Wu, CX; An, XH; Cai, LM; Zhao, XP	December 2014	Embryonic exposure to carbendazim induces the transcription of genes related to apoptosis, immunotoxicity and endocrine disruption in zebrafish (*Danio rerio*).	Fish & Shellfish Immunology, 41(2): 493 - 500	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not performed according to any current accepted test guideline. Study not providing any useful endpoint for ecotoxicological risk assessment.	No	10.1016/j.fsi.2014.09.037
C-5-35	Ecotoxicity and animal toxicity	KIIA 8.2.2	Bao, ZW; Zhao, Y; Wu, AY; Lou, Z; Lu, HH; Yu, QX; Fu, ZW; Jin, YX	October 2020	Sub-chronic carbendazim exposure induces hepatic glycolipid metabolism disorder accompanied by gut microbiota dysbiosis in adult zebrafish (*Daino rerio*).	Science of The Total Environment, 739: 140081	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study with fish not following any current test guideline (test design not even close to an OECD TG 210 (Fish, Early -life Stage Toxicity	No	10.1016/j.scitotenv.2020.140081

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							test) or an OECD TG 230 (21-say Fish Assay) or an OECD TG 234 (Fish Sexual Development Test)). Study not providing any useful endpoints for ecotoxicological risk assessment.		
C-5-36	Ecotoxicity and animal toxicity	KIIA 8.2.1	Palanikumar, L; Kumaraguru, AK; Ramakritinan, CM; Anand, M	April 2014	Toxicity, biochemical and clastogenic response of chlorpyrifos and carbendazim in milkfish *Chanos chanos*.	International Journal of Environmental Science and Technology, 11 (3): 765 – 774	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study providing endpoints (96-hr LC_{50} value) about the acute toxicity of Carbendazim to milkfish (*Chanos chanos*). However, *Chanos chanos* is not considered as a suitable fish test species according to JMAFF Guideline No. 6278 and the study is therefore considered as not relevant.	No	10.1007/s13762-013-0264-6
C-5-37	Ecotoxicity and animal toxicity	KIIA 8.2.1	Nwani, C; Omah, MC; Ivoke, N; Nwamba, HO; Ani, C; Ogbonna, SU	April 2015	Biochemical, haematological and morphological variations in juvenile *Clarias*	African Journal of Aquatic Science, 40 (1): 63 - 71	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the	No	10.2989/16085914.2015.1014022

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					gariepinus exposed to Carbendazim (R) fungicide		viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study providing endpoints (96-hr LC_{50} value) about the acute toxicity of Carbendazim to African catfish (*Clarias gariepinus*). However, due to significant deficiencies and limited reliability, the fact that this is fish has a tropical and subtropical distribution and that African catfish is not considered as a suitable fish test species according OECD TG 203 and to JMAFF Guideline No. 6278, the study is therefore considered as not relevant.		
C-5-38	Ecotoxicity and animal toxicity	KIIA 8.2.1	Ezeoyili, IC; Mgbenka, BO; Atama, CI; Ngwu, GI; Madu, JC; Nwani, CD	Decembre 2019	Changes in Brain Acetylcholinesterase and Oxidative Stress Biomarkers in African Catfish Exposed to Carbendazim	Journal of Aquatic Animal Health, 31 (4): 371 - 379	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type	No	10.1002/aah.10089

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							other than one that can be evaluated appropriately. Study making reference to the study of Nwani et al., 2015 with regard to the acute toxicity (96-hr LC_{50} value) of Carbendazim to African catfish (*Clarias gariepinus*). However, due to significant deficiencies and limited reliability, the fact that this is fish has a tropical and subtropical distribution and that African catfish is not considered as a suitable fish test species according to OECD TG 203 and JMAFF Guideline No. 6278, the study is therefore considered as not relevant.		
C-5-39	Ecotoxicity and animal toxicity	KIIA 8.2.2	Gotte, JY; Carrizo, JC; Panzeri, AM; Ame, MV; Menone, ML	December 2020	Sublethal effects of carbendazim in *Jenynsia multidentata* detected by a battery of molecular, biochemical and genetic biomarkers.	Ecotoxicology and Environmental Safety, 205: 111157	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately.	No	10.1016/j.ecoenv.2020.111157

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Study not performed according to any current existing guideline. Study not providing any useful endpoints for ecotoxicological risk assessment.		
C-5-40	Ecotoxicity and animal toxicity	KIIA 8.3.1	Del Arco, AI; Parra, G; Rico, A; Van den Brink, PJ	October 2015	Effects of intra- and interspecific competition on the sensitivity of aquatic macroinvertebrates to carbendazim.	Ecotoxicology and Environmental Safety, 120: 27 - 34	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Non-standard test species used. No test guideline followed. Confounding factors (intra- and interspecific competition) tested not allowing to determine the effect of Carbendazim only on aquatic organisms. No determination of any ecotoxicologically-relevant endpoints (LC_{50}, NOEC etc.).	No	10.1016/j.ecoenv.2015.05.001
C-5-41	Ecotoxicity and animal toxicity	KIIA 8.3.1.1 & KIIA 8.3.2.1	Silva, ARR; Santos, CSA; Ferreira, NGC; Morgado, R; Cardoso, DN;	February 2019	Multigenerational effects of carbendazim in *Daphnia magna*:	Environmental Toxicology and Chemistry, 38 (2): 412 - 422	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the	No	10.1002/etc.4307

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			Cruz, A; Mendo, S; Soares, AMVM; Loureiro, S		from a subcellular to a population level.		viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not providing any useful endpoint for ecotoxicological risk assessment. Although focused on *Daphnia magna*, no acute (48-h L/EC_{50}) or chronic (21-d EC_{50}) endpoints are provided in this study.		
C-5-42	Ecotoxicity and animal toxicity	KIIA 8.3.1.1	Silva, ARR; Cardoso, DN; Cruz, A; Mendo, S; Soares, AMVM; Loureiro, S	June 2019	Long-term exposure of *Daphnia magna* to carbendazim: how it affects toxicity to another chemical or mixture.	Environmental Science and Pollution Research, 26 (16): 16289 - 16302	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients. Although the focal point of this study is *Daphnia magna*, with some acute toxicity endpoints measured (48 L/EC_{50} values), the main acute toxicity tests are either focusing on triclosan alone or on a mixture of triclosan and carbendazim, with or without multigenerational pre-exposure to carbendazim,	No	10.1007/s11356-019-05040-1

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							which makes it irrelevant to this literature search.		
C-5-43	Ecotoxicity and animal toxicity	KIIA 8.3.1.1	Encina, F; Escalante, PD; Salazar, K	2017	Acute toxicity (LC_{50}) of a pesticide (carbendazim) on two native crustacean zooplankton species: *Daphnia pulex* leydig, 1860 and *Tumeodiaptomus diabolicus* (brehm, 1935) from northern patagonian lakes (chile)	Crustaceana, 90(2): 199 - 206	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study providing endpoint (48-hr LC_{50} value) about the acute toxicity of Carbendazim to *Daphnia pulex* and the copepod species *Tumeodiaptomus diabolicus*, although there are no claims that the study has been performed according to OECD TG 202 and the data for the copepod species are not acceptable according to JMAFF guideline No. 6278. In this test, adult specimens were used in the bioassay even though the JMAFF guidelines require *Daphnia magna* juvenile less than 24 hours old or adult at 7 days old. Additionally, no measured concentrations were provided.	No	10.1163/15685403-00003637

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							Therefore, the species cannot be used for evaluation by JMAFF. Study considered partly reliable with restriction, as some deviations from current test guideline were noted, as follows: - there is no estimation of test sensitivity with the use of a reference substance (no data provided) and standard deviations for the 48h LC_{50} values have been provided instead of 95% confidence intervals. - there is no evidence that the test item concentrations have been maintained within the 80 - 100% range of nominal values, and, according to both OECD TG 202, mean measured concentrations or time-weighted average concentrations should have been used for the determination of toxicity endpoints, while in this study, it would appear that nominal concentrations were used for the determination of the acute toxicity endpoints.		
C-5-44	Ecotoxicity and	KIIA 8.3.1.3	Zubrod, JP; Baudy, P; Schulz, R; Bundschuh, M	May 2014	Effects of current-use fungicides and their mixtures on the	Aquatic Toxicology, 150: 13 - 143	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not	No	10.1016/j.aquatox.2014.03.002

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
	animal toxicity				feeding and survival of the key shredder *Gammarus fossarum*.		appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study providing endpoints (7-d LC_{50} value) about the acute toxicity of Carbendazim to *gammarus* (*Gammarus fossarum*). However, the study is not following any current test guideline and is using a non-standard species. Furthermore, the test species and test method used in this study are not recognised as suitable according to the JMAFF Guideline No. 6278. Therefore, the study is considered as not relevant.		
C-5-45	Ecotoxicity and animal toxicity	KIIA 8.3.1.3	Moreira, RA; Mansano, AD; Rocha, O; Daam, MA	June 2016	The use of rotifers as test species in the aquatic effect assessment of pesticides in the tropics	Hydrobiologia, 773 (1): 1 - 9	① - Publication of no relevance to the agrochemicals (as an alternative to the agrochemicals for example)	No	10.1007/s10750-016-2675-0
C-5-46	Ecotoxicity and animal toxicity	KIIA 8.4	Suarez-Serrano, A; Ibanez, C; Lacorte, S; Barata, C	November 2010	Ecotoxicological effects of rice field waters on selected planktonic species: comparison between	Ecotoxicology, 19 (8): 1523 - 1535	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming	No	10.1007/s10646-010-0537-5

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					conventional and organic farming.		from different active ingredients. Field study focusing on mixture of plant protection products applied as mixture. Therefore, study not specific to Carbendazim.		
C-5-47	Ecotoxicity and animal toxicity	KIIA 8.4	Tousova, Z; Froment, J; Oswald, P; Slobodnik, J; Hilscherova, K; Thomas, KV; Tollefsen, KE; Reid, M; Langford, K; Blaha, L	September 2018	Identification of algal growth inhibitors in treated wastewater using effect-directed analysis based on non-target screening techniques.	Journal of Hazardous Materials, 358: 494 - 502	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients. Monitoring field study focusing on mixture of plant protection products applied as mixture. Therefore, study not specific to Carbendazim.	No	10.1016/j.jhazmat.2018.05.031
C-5-48	Ecotoxicity and animal toxicity	KIIA 8.4	Minelgaite, G; Stephansen, DA; Simon, M; Fejerskov, ML; Vollertsen, J	November 2020	No clear response in the stormwater phytoplankton community to biocide contamination.	Water, 12: 3120	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not performed according to any current existing guideline.	Yes	10.3390/w12113120

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Study not providing any useful endpoints for ecotoxicological risk assessment.		
C-5-49	Ecotoxicity and animal toxicity	KIIA 8.7	Stanley, J; Sah, K; Jain, SK; Bhatt, JC; Sushil, SN	January 2015	Evaluation of pesticide toxicity at their field recommended doses to honeybees, *Apis cerana* and *A-mellifera* through laboratory, semi-field and field studies.	Chemosphere, 119: 668 - 674	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not following any current test guideline regarding the acute and chronic toxicity of plant protection products to bees. Study not providing any useful endpoints for ecotoxicological risk assessment of Carbendazim in Japan, with a focus on bees.	No	10.1016/j.chemosphere.2014.07.039
C-5-50	Ecotoxicity and animal toxicity	KIIA 8.7	Shi, TF; Burton, S; Zhu, YJ; Wang, YF; Xu, SY; Yu, LS	July 2018	Effects of field-realistic concentrations of carbendazim on survival and physiology in forager honeybees	Journal of Insect Science, 18 (4): 1 - 5	⑯a - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. Study methods are not (sufficiently) documented.	Yes	10.1093/jisesa/iey069

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					(*Hymenoptera: Apidae*).		No analytical verification of test concentrations. No reference substance used to evaluate the performance of the test. No reference to any test guideline provided.		
C-5-51	Ecotoxicity and animal toxicity	KIIA 8.7	Wang, K; Chen, H; Lin, ZG; Niu, QS; Wang, Z; Gao, FC; Ji, T	March 2021	Carbendazim exposure during the larval stage suppresses major royal jelly protein expression in nurse bees (*Apis mellifera*).	Chemosphere, 266: 129011	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Proteomics study not providing any useful information for risk assessment. No analytical verification of test concentrations.	No	10.1016/j.chemosphere.2020.129011
C-5-52	Ecotoxicity and animal toxicity	KIIA 8.7	Chen, H; Wang, K; Ji, WN; Xu, H; Liu, YB; Wang, S; Wang, Z; Gao, FC; Lin, ZG; Ji, T	November 2021	Metabolomic analysis of honey bees (*Apis mellifera*) response to carbendazim based on UPLC-MS.	Pesticide Biochemistry and Physiology, 179: 104975	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type	No	10.1016/j.pestbp.2021.104975

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							other than one that can be evaluated appropriately. Metabolomics study not providing any useful information for risk assessment. No analytical verification of test concentrations.		
C-5-53	Ecotoxicity and animal toxicity	KIIA 8.7	Tong, Z; Duan, JS; Wu, YC; Liu, QQ; He, QB; Shi, YH; Yu, LS; Cao, HQ	October 2018	Evaluation of highly detectable pesticides sprayed in *brassica napus l.*: degradation behavior and risk assessment for honeybees.	Molecules, 23(10): 2-12	⑤ - Publication relevant to analytical methods and their development.	Yes	10.3390/molecules23102482
C-5-54	Ecotoxicity and animal toxicity	KIIA 8.9	Ellis, SR; Hodson, ME; Wege, P	August 2010	Determining the influence of rainfall patterns and carbendazim on the surface activity of the earthworm *Lumbricus terrestris*.	Environmental Toxicology and Chemistry, 29 (8): 1821 - 1827	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not performed according to any current existing guideline (earthworm acute test, OECD TG 207 or earthworm reproduction test, OECD TG 222)	Yes	10.1002/etc.219

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Only 1 test concentration used, not allowing to determine LC_{50} values. No reproductive endpoint measured.		
C-5-55	Ecotoxicity and animal toxicity	KIIA 8.9	Ellis, SR; Hodson, ME; Wege, P	September 2010	The soil-dwelling earthworm *Allolobophora chlorotica* modifies its burrowing behaviour in response to carbendazim applications.	Ecotoxicology and Environmental Safety, 73 (6): 1424 - 1428	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not following any current test guideline. Study using non-standard species (*Allolobophora chlorotica*). Study using only a single test dose, not providing any useful endpoints for ecotoxicological risk assessment.	No	10.1016/j.ecoenv.2010.05.010
C-5-56	Ecotoxicity and animal toxicity	KIIA 8.9	Achiorno, CL; de Villalobos, C; Ferrari, L	November 2018	Susceptibility of *Chordodes nobilii* (Gordiida, Nematomorpha) to three pesticides: Influence of the water used for dilution on	Environmental Pollution, 242: 1427 - 1435	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type	No	10.1016/j.envpol.2018.08.006

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					endpoints in an ecotoxicity bioassay.		other than one that can be evaluated appropriately. Study not performed according to any current test guideline. Study not providing any useful endpoint for ecotoxicological risk assessment.		
C-5-57	Ecotoxicity and animal toxicity	KIIA 8.10.1	Milenkovski, S; Baath, E; Lindgren, PE; Berglund, O	February 2010	Toxicity of fungicides to natural bacterial communities in wetland water and sediment measured using leucine incorporation and potential denitrification.	Ecotoxicology, 19 (2): 285 - 294	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not conducted according to any recognised guideline. No analytical verification of test item concentrations. Non-standard endpoints used (leucine incorporation as a proxy of bacterial growth and denitrification) when standard endpoints used are normally total respiration, heterotrophic respiration and nitrification respiration.	No	10.1007/s10646-009-0411-5

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-58	Ecotoxicity and animal toxicity	KIIA 8.10	Yan, H; Wang, DD; Dong, B; Tang, FF; Wang, BC; Fang, H; Yu, YL	July 2011	Dissipation of carbendazim and chloramphenicol alone and in combination and their effects on soil fungal:bacterial ratios and soil enzyme activities.	Chemosphere, 84 (5): 634 - 641	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not performed according to any current existing guideline (OECD TG 209). No measurement of respiration rate as oxygen uptake (total respiration, heterotrophic respiration, nitrification respiration). Insufficient number of test concentrations (3 minimum required).	No	10.1016/j.chemosphere.2011.03.038
C-5-59	Ecotoxicity and animal toxicity	KIIA 8.10	Kumar, A; Nayak, AK; Shukla, AK; Panda, BB; Raja, R; Shahid, M; Tripathi, R; Mohanty, S; Rath, PC	April 2012	Microbial biomass and carbon mineralization in agricultural soils as affected by pesticide addition.	Bulletin of Environmental Contamination and Toxicology, 88 (4): 538 - 542	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately.	No	10.1007/s00128-012-0538-6

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Study not performed according to any current existing guideline (OECD TG 209). No measurement of respiration rate as oxygen uptake (total respiration, heterotrophic respiration, nitrification respiration) although carbon mineralisation was determined. Insufficient number of test concentrations (3 minimum required). No analytical verification of test item concentrations.		
C-5-60	Ecotoxicity and animal toxicity	KIIA 8.10	Ding, H; Zheng, XZ; Zhang, J; Zhang, YS; Yu, JH; Chen, DL	October 2019	Influence of chlorothalonil and carbendazim fungicides on the transformation processes of urea nitrogen and related microbial populations in soil.	Environmental Science and Pollution Research, 26 (30): 31133 – 31141	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not performed according to any current existing guideline. No useful endpoints. No analytical verification of test item concentrations.	No	10.1007/s11356-019-06213-8

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Test performed with urea not allowing the determination of effect of carbendazim on its own.		
C-5-61	Ecotoxicity and animal toxicity	KIIA 8.10	Wang, CX; Wang, FF; Zhang, QM; Liang, WX	January-February 2016	Individual and combined effects of tebuconazole and carbendazim on soil microbial activity	European Journal of Soil Biology, 72: 6 - 13	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not following any test guideline. Soil respiration rate measured when useful endpoint to be normally measured is soil Nitrogen transformation. No useful endpoints. Therefore, study considered as not relevant.	No	10.1016/j.ejsobi.2015.12.005
C-5-62	Ecotoxicity and animal toxicity	KIIA 8.12	Li, M; Li, B; Zhang, HY; Chen, CJ; Li, JL; Liang, XY; Gu, YY	2022	Effects of fungicides on seedling and root growth of *Suaeda Salsa*.	Fresenius Environmental Bulletin, 31 (3A): 3316 - 3321	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type	Yes	https://www.prt-parlar.de/download_list/?c=FEB_2022

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							other than one that can be evaluated appropriately. Study performed with a non-standard salt-tolerant species. Study not following any current guideline and exposure performed in water when test guideline indicates soil tests. No analytical verification of test item concentrations.		
C-5-63*	Ecotoxicity and animal toxicity	KIIA 8.14	Yoon, CS; Jin, JH; Park, JH; Yeo, CY; Kim, SJ; Hwang, YG; Hong, SJ; Cheong, SW	February 2008	Toxic effects of carbendazim and n-butyl isocyanate, metabolites of the fungicide benomyl, on early development in the African clawed frog, *Xenopus laevis*.	Environmnental Toxicology, 23 (1): 131 - 144	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Study not following any current test guideline regarding the embryotoxicity of carbendazim in amphibians. Study not providing any useful endpoints for aquatic risk assessment of Carbendazim in Japan.	Yes	https://doi.org/10.1002/tox.20338

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-64	Ecotoxicity and animal toxicity	NA	Daam, MA; Van den Brink, PJ	April 2011	Conducting model ecosystem studies in tropical climate zones: Lessons learned from Thailand and way forward.	Environmental Pollution, 159 (4): 940 -946	⑨ - Written opinion that it is not showing any new data useful for risk assessment. Microcosm tropics-specific study. Study focused on microcosm methodology not providing any useful information for the ecotoxicological risk assessment of Carbendazim.	No	10.1016/j.envpol.2010.12.018
C-5-65	Ecotoxicity and animal toxicity	NA	Ccanccapa, A; Masia, A; Navarro-Ortega, A; Pico, Y; Barcelo, D	April 2016	Pesticides in the Ebro river basin: occurrence and risk assessment.	Environmental Pollution, 211: 414 -424	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients. Field study focusing on mixture of plant protection products applied as mixture. Therefore, study not specific to Carbendazim.	No	10.1016/j.envpol.2015.12.059
C-5-66	Ecotoxicity and animal toxicity	NA	Singh, S; Singh, N; Kumar, V; Datta, S; Wani, AB; Singh, D; Singh, K; Singh, J	September 2016	Toxicity, monitoring and biodegradation of the fungicide carbendazim.	Environmental Chemistry Letters, 14 (3): 317 -329	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment. Review paper providing ecotoxicology and toxicology endpoints (including ADI for India) but not providing any	No	10.1007/s10311-016-0566-2

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							details about how endpoints were obtained other than by citing the relevant references. Contains references that may need to be evaluated, as they are not appearing in the main literatures search: - Huan et al., 2016 - Rico et al., 2016 - Yoon et al., 2008 - Ludwikowska et al., 2013		
C-5-67	Ecotoxicity and animal toxicity	NA	Lopez-Doval, JC; Montagner, CC; de Alburquerque, AF; Moschini-Carlos, V; Umbuzeiro, G; Pompeo, M	January 2017	Nutrients, emerging pollutants and pesticides in a tropical urban reservoir: spatial distributions and risk assessment.	Science of The Total Environment, 575: 1307 - 1324	⑫ - Publication relevant to the toxicity of mixtures of formulation products coming from different active ingredients. Monitoring study not providing any useful endpoints for ecotoxicological risk assessment of Carbendazim in Japan, with a focus on aquatic organisms.	No	10.1016/j.scitotenv.2016.09.210
C-5-68	Ecotoxicity and animal toxicity	NA	Daam, MA; Rico, A	May 2018	Freshwater shrimps as sensitive test species for the risk assessment of pesticides in the tropics	Environmental Science and Pollution Research, 25 (14): 13235 - 13243	① - Publication of no relevance to the agrochemicals (as an alternative to the agrochemicals for example). Monitoring study not providing any useful endpoints for	No	10.1007/s11356-016-7451-1

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							ecotoxicological risk assessment of Carbendazim in Japan, with a focus on aquatic organisms. Study not specific to Carbendazim.		
C-5-69	Ecotoxicity and animal toxicity	NA	Carazo-Rojas, E; Perez-Rojas, G; Perez-Villanueva, M; Chinchilla-Soto, C; Chin-Pampillo, JS; Aguilar-Mora, P; Alpizar-Marin, M; Masis-Mora, M; Rodriguez-Rodriguez, CE; Vryzas, Z	October 2018	Pesticide monitoring and ecotoxicological risk assessment in surface water bodies and sediments of a tropical agro-ecosystem.	Environmental Pollution, 241: 800 - 809	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Monitoring study, that includes some ecotoxicological risk assessment, but that is specific to Costa Rica. No determination of endpoints useful for ecotoxicological risk assessment in Japan.	No	10.1016/j.envpol.2018.06.020
C-5-70	Ecotoxicity and animal toxicity	NA	Rico, A; Brock, TCM; Daam, MA	October 2019	Is the effect assessment approach for fungicides as laid down in the European Food Safety Authority aquatic guidance document sufficiently	Environmental Toxicology and Chemistry, 38 (10): 2279 -2293	① - Publication of no relevance to the agrochemicals (as an alternative to the agrochemicals for example). Meta-analysis aiming at evaluating if the effect assessment approach for	Yes	10.1002/etc.4520

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					protective for freshwater ecosystems?		fungicides, as described in the European Food Safety Authority aquatic guidance document is sufficiently protective of freshwater ecosystems. Although the study includes data on Carbendazim, it is not specific to it and it does not provide any useful endpoints for ecotoxicological risk assessment of Carbendazim in Japan, with a focus on aquatic organisms.		
C-5-71	Ecotoxicity and animal toxicity	NA	Xu, L; Granger, C; Dong, HY; Mao, YX; Duan, SL; Li, J; Qiang, ZM	July 2020	Occurrences of 29 pesticides in the Huangpu River, China: highest ecological risk identified in Shanghai metropolitan area.	Chemosphere, 251: 126411	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Monitoring study, that includes some ecotoxicological risk assessment, but that is specific to China. No determination of endpoints useful for ecotoxicological risk assessment in Japan.	No	10.1016/j.chemosphere.2020.126411

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-72	Ecotoxicity and animal toxicity	NA	Onwona-Kwakye, M; Hogarh, JN; Van den Brink, PJ	September 2020	Environmental risk assessment of pesticides currently applied in Ghana.	Chemosphere, 254: 126845	⑨ - Written opinion that it is not showing any new data useful for risk assessment. Ghana-specific risk assessment study that uses publicly available data on aquatic/chronic toxicity of carbendazim and a range of other pesticides (EPA ECOTOX database).	No	10.1016/j.chemosphere.2020.126845
C-5-73	Ecotoxicity and animal toxicity	NA	Werner, I; Schneeweiss, A; Segner, H; Junghans, M	April 2021	Environmental risk of pesticides for fish in small- and medium-sized streams of Switzerland,	Toxics, 9 (4)	⑪ - Publication relevant to typical exposure of agrochemicals (focus on a wide range of agrochemicals without limiting the focus to the target agrochemical). Monitoring study with no focus on Carbendazim. Study not providing any useful endpoints for ecotoxicological risk assessment of Carbendazim in Japan, with a focus on aquatic organisms.	Yes	10.3390/toxics9040079
C-5-74	Ecotoxicity and animal toxicity	NA	Eissa, F; Al-Sisi, M; Ghanem, K	October 2021	Occurrence, human health, and ecotoxicological risk assessment of pesticides in surface waters of the River Nile's Rosetta Branch, Egypt.	Environmental Science and Pollution Research, 28 (39): 55511 - 55525	② - Publication of no relevance to the agrochemicals (as an alternative to the agrochemicals for example). Monitoring study not providing any useful	No	10.1007/s11356-021-14911-5

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							endpoints for ecotoxicological risk assessment of Carbendazim in Japan, with a focus on aquatic organisms.		
C-5-75	E-fate	NA	Raheem, SS; Al-Dossary, MA; AL-Saad, HT	2021	Ability of some fungi to biodegrade carbendazim fungicide.	Iraqi Journal of Agricultural Sciences, 52(1): 259 - 267	④ - Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance	Yes	10.36103/ijas.v52i1.1256
C-5-76	E-fate	KIIA 7.2	Lewandowska, A; Walorczyk, S	2010	Carbendazim residues in the soil and their bioavailability to plants in four successive harvests.	Polish Journal of Environmental Studies, 19 (4): 757 - 761	⑰ - Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.). Study with a design that does not comply with any particular test guideline. Other major deficiencies: - study conducted in Poland, with climatic conditions not reported. - no purity reported for the radiolabelled test substance. - solution of radiolabel not sprayed and in the form of a specific formulation so of unclear relevance to Japan PPP's. - application rate not specified so of unclear relevance to Japan PPPs. - only a single crop evaluated. - no intermediate sampling.	Yes	https://www.pjoes.com/pdf-88444-22302?filename=Carbendazim%20Residues%20in.pdf

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							- assumes greater than a year plant backs (4 seasons stated). - bound residues not exhaustively extracted. - extent of characterisation/identification not sufficient.		
C-5-77	E-fate	KIIA 7.2	Mu, HY; Zhang, JC; Yang, XM; Wang, K; Xu, W; Zhang, HY; Liu, XJ; Ritsema, CJ; Geissen, V	September 2022	Pesticide screening and health risk assessment of residential dust in a rural region of the North China Plain	Chemosphere, 303:135115	⑰ - Literatures that can't be used for evaluation for typical application/condition of use in Japan (Field condition, type of soil, etc.). Although the analytical methods and results have been well reported, this study is a monitoring study with relevance limited to China. Study limited to some areas in China and these data are not relevant to japanese soils. Also the test system is questionable.	No	10.1016/j.chemosphere.2022.135115
C-5-78	E-fate	KIIA 7.4.1	Han, LX; Ge, QQ; Mei, JJ; Cui, YL; Xue, YF; Yu, YL; Fang, H	April 2019	Adsorption and desorption of carbendazim and thiamethoxam in five different agricultural soils.	Bulletin of Environmental Contamination and Toxicology, 102 (4): 550 -554	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately.	No	10.1007/s00128-019-02568-3

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Study providing information about the adsorption-desorption distribution coefficient (Kd)of Carbendazim. However, the study is limited to some areas in China and does not conform to that of Japan. The test system is also questionable. Significant methodological deficiencies noted, as follows: - pure analytical standard used not technical material. - soils from China used so with relevance to japanese soils unclear. - soil pH range within pH 5.24 - 7.36. - OM data instead of OC data presented. - not all soil types assessed. - no mass balances reported and stability of Carbendazim in solutions and soil not reported. - limited information on the validation of the analytical method, with no detaisl regarding linearity and specificity. - non-GLP study.		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-79	E-fate	KIIA 7.4.1	Li, GZ; Li, JM; Tan, W; Yang, M; Wang, HB; Wang, XY	October 2022	Effectiveness and mechanisms of the adsorption of carbendazim from wastewater onto commercial activated carbon.	Chemosphere, 304: 135231	④ - Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance	No	10.1016/j.chemosphere.2022.135231
C-5-80	E-fate	KIIA 7.8	Kaur, T; Toor, AP; Wanchoo, RK	April 2015	Parametric study on degradation of fungicide carbendazim in dilute aqueous solutions using nano TiO_2.	Desalination and Water Treatment, 54 (1): 122-131	④ - Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance	No	10.1080/19443994.2013.879081
C-5-81	E-fate	KIIA 7.8	Rajeswari, R; Kanmani, S	July 2010	Comparative study on photocatalytic oxidation and photolytic zonation for the degradation of pesticide wastewaters.	Desalination and Water Treatment, 19 (1-3): 301-306	④ - Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance	No	10.5004/dwt.2010.1495
C-5-82	E-fate	KIIA 7.8	Minelgaite, G; Nielsen, AH; Pedersen, ML; Vollertsen, J	2017	Photodegradation of three stormwater biocides.	Urban Water Journal, 14(1): 53-60	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Laboratory assessment performed at single	No	10.1080/1573062X.2015.1076489

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							wavelength. Exposure vessels were not constructed with quartz glass as recommended. Carbendazim was not reported to degrade in laboratory and/or outdoor experiments so no useful information for risk assessment		
C-5-83	E-fate	NA	Mojid, MA; Hossain, ABMZ; Wyseure, GCL	May 2019	Impacts of municipal wastewater on the transport characteristics of reactive solutes through agricultural soils.	Communications in Soil Science and Plant Analysis, 50(10): 1199-1213	⑯a - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. Study methods are not (sufficiently) documented. Text cited in paper: Solute-leaching experiments in freshwater-treated soils were described in detail in Mojid et al. (2016). In the study reported here, an additional set of similar experiments was done for wastewater-treated soils. So, only a summary of the experimental details is given here.	No	10.1080/00103624.2019.1604739
Second search									

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-85	Toxicity/adverse effects on human	NA	Sun, YF; Huang, CG; Jiang, Y; Wan, YJ	2023	Urinary concentrations of fungicide carbendazim's metabolite and associations with oxidative stress biomarkers in young children.	Environmental Science and Pollution Research, 30 (7): 18408 - 18418	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Biomonitoring study not useful for characterizing hazards.	No	10.1007/s11356-022-23311-2
C-5-86	Crop and livestock residue	NA	Costa, RM; Chaib, VRME; Domingues, AG; Rubio, KTS; Martucci, MEP	2023	Untargeted metabolomics reveals lipid impairment in the liver of adult zebrafish (*Danio rerio*) exposed to carbendazim.	Environmental Toxicology and Chemistry, 42 (2): 437-448	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. The study was limited to fish liver analysis. The metabolomics approach suggested the identity of putative water and liver	No	10.1002/etc.5534

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							metabolites or at least a proposed molecular formula. Metabolism studies on fish, if required, should be conducted with radiolabeled test item to detect, quantify and identify carbendazim metabolites as such, that the nature of the residues and information on organ-specific accumulation in fish can be investigated in detail.		
C-5-87	Ecotoxicity and animal toxicity	NA	Loureiro, DB; Lario, LD; Herrero, MS; Salvatierra, LM; Novo, LAB; Pérez, LM	2023	Potential of *Salvinia biloba Raddi* for removing atrazine and carbendazim from aquatic environments.	Environmental Science and Pollution Research, 30 (8): 22089 - 22099	④ – Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance	Yes	10.1007/s11356-022-23725-y
C-5-88	Ecotoxicity and animal toxicity	NA	Silva, ARR; Silva, PV; Soares, AR; González-Alcaraz, MN; van Gestel, CAM; Roelofs, D; Moura, G; Soares, AMVM; Loureiro, S	2023	*Daphnia magna* multigeneration exposure to carbendazim: gene transcription responses.	Toxics, 11: 918	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately.	Yes	10.3390/toxics11110918

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Test conducted with only one concentration at the NOEC level, and the observed gene transcription responses, not determine toxic levels. Dose rate selected based on another reference. Replication not consistent with guidance. Multiple generation assessments are not a requirement. Gene analysis data not required.		
C-5-89	Ecotoxicity and animal toxicity	NA	De Oliveira, MRB; Profeta, IV; Lopes, JVSR; Costa, RM; Chaib, VRME; Domingues, AG; Beirao, MV; Rubio, KTS; Martucci, MEP; Eskinazi-Sant'Anna, EM; de Azevedo, CS	2024	Effects of the fungicide carbendazim on the behaviour of the zebrafish *Danio rerio* (Cypriniformes, Cyprinidae).	Acta Ethologica, https://doi.org/10.1007/s10211-024-00438-8	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Findings limited to behavioural observations with no meaningful data for risk assessment.	No	10.1007/s10211-024-00438-8

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-5-90	Ecotoxicity and animal toxicity	NA	Hermann, M; Peeters, ETHM; van den Brink, PJ	2023	Heatwaves, elevated temperatures, and a pesticide cause interactive effects on multi-trophic levels of a freshwater ecosystem.	Environmental Pollution, 327: 121498	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Bespoke study design performed indoors. Variable test chambers. Single dose rate assessed. Trends of population effects presented but no endpoint proposed (NB only single dose rate).	No	10.1016/j.envpol.2023.121498
C-5-91	Ecotoxicity and animal toxicity	NA	Hu, GX; Wang, H; Wan, YJ; Zhou, LL; Wang, Q; Wang, MH	2022	Combined toxicities of cadmium and five agrochemicals to the larval zebrafish (*Danio rerio*).	Scientific Reports, 12 (1): 16045	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately.	Yes	10.1038/s41598-022-20364-8

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							The test was conducted with a mixture of cadmium and agrochemicals. Age of fish not adequate. Exposure method not adequate. No analytical verification.		
C-5-92	Ecotoxicity and animal toxicity	NA	Kocaman, K; Yetis, U; Dilek, FB	2022	Investigating the effect of solids retention time on pesticides removal in an activated sludge process.	Sustainable Chemistry and Pharmacy, 29: 100784	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. Data generated for mixtures and individual active substances. No endpoints estimated. No mention of toxic reference assessment. Evaluation unnecessary as ASRIT testing is not Japanese requirement.	No	10.1016/j.scp.2022.100784
C-5-93	Ecotoxicity and	NA	Costa, RM; Chaib, VRME; Domingues, AG;	2023	Untargeted metabolomics reveals lipid impairment in the	Environmental Toxicology and Chemistry, 42 (2): 437 - 448	⑯b – Study design, study system, study type, test Item, exposure route, etc. are not appropriate from	No	10.1002/etc.5534

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
	animal toxicity		Rubio, KTS; Martucci, MEP		liver of adult zebrafish (*Danio rerio*) exposed to carbendazim.		the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately. The study was limited to fish liver analysis. Metabolite profile for potential biomarkers.		
C-5-94	E-fate	NA	Chauhan, S; Fatima, T; Dubey, A; Chauhan, PS; Prakash, O; Singh, PC	2023	Integrated application of trichoderma and carbendazim affects the carbendazim extractability and microbial functions in the maize rhizosphere.	Journal of Soil Science and Plant Nutrition, 23 (3): 3373 - 3380	④ – Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance.	No	10.1007/s42729-023-01254-y
C-5-95	E-fate	NA	Verdenelli, RA; Dominchin, MF; Barbero, FM; Pérez-Brandán, C; Aoki, A; Gil, SV; Meriles, JM	2023	Effect of two broad-spectrum fungicides on the microbial communities of a soil subjected to different degrees of water erosion.	Applied Soil Ecology, 190: 104984	④ – Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance.	No	10.1016/j.apsoil.2023.104984
C-5-96	E-fate	NA	Hua, LT; Wu, RL; Li, CL;	2024	Experimental study on	Ecological Processes, 13 (1):	⑯b – Study design, study system, study type, test	Yes	10.1186/s13717-024-00503-x

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			Wang, CN; Li, YL; Xu, FL		photodegradation and leaching of typical pesticides in greenhouse soil from Shouguang, Shandong Province, East China.		Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation. The test was conducted according to a study type other than one that can be evaluated appropriately.		
2009 update									
C-5-97	Toxicity /adverse effects on human	KIIA 5.2.1	Alpertunga, B; Catalgol, B; Catalgol, S	2009	Effects of benzimidazole fungicides, benomyl and carbendazim, on lipid peroxidation and antioxidant system in rat.	Toxicology Letters, 189, S212	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment.	No	10.1016/j.toxlet.2009.06.549
C-5-98	Ecotoxicity and animal toxicity	NA	Maltby, L; Brock, TCM; van den Brink, PJ	2009	Fungicide risk assessment for aquatic ecosystems: importance of interspecific variation, toxic mode of action, and exposure regime.	Environmental Science & Technology, 43 (19): 7556 - 7563	⑧ - Summary and review of conference presentations or books, which are not providing enough data or information to conduct risk assessment.	No	10.1021/es901461c
C-5-99	E-fate	KIIA 8.10.1	Wang, YS; Huang, YJ; Chen, WC; Yen, JH	2009	Effect of carbendazim and pencycuron on soil bacterial community	Journal of Hazardous Materials, 172 (1): 84 - 91	⑯a - Study design, study system, study type, test Item, exposure route, etc. are not appropriate from the viewpoint of utilisation for the evaluation.	No	10.1016/j.jhazmat.2009.06.142

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Study methods are not (sufficiently) documented. - Soil mass treated not stated or description of vessels and system soil incubated in. - Soil OC and incubation temperatures outside guideline recommended levels. - Appears to be non-GLP - Analytical methodology validation uncertainty		

*: studies not obtained in the main literature search but cited in some of the literature retrieved in the main search and deemed potentially relevant

The number of hits/literature studies classified as “Category a”, ”Category b” or “Category c” after step 2 and step 3 of the relevance assessment for the active substance Carbendazim for the 3 searches combined is presented in Table 19.

Table 19: Number of hits/literature studies classified as “Category a”, ”Category b” or “Category c” after step 2 and step 3 of the relevance assessment for the active substance Carbendazim

Field	**Total number of Available literatures**		
	Category a	**Category b**	**Category c**
Toxicity/adverse effects on human			
First search (including JMAFF update)	0	2	23
Second search	1	0	4
2009 update	0	0	0
Total	1	2	27
Crop and livestock residue			
First search (including JMAFF update)	2	0	0
Second search	0	1	0
2009 update	1	0	0
Total	3	1	0
Ecotoxicity and animal toxicity			
First search (including JMAFF update)	1	0	6
Second search	0	0	0
2009 update	0	0	0
Total	1	0	6
E-fate			
First search (including JMAFF update)	0	4	0
Second search	0	0	0
2009 update	0	0	0
Total	0	4	0
Total			
First search (including JMAFF update)	3	6	29
Second search	1	1	4
2009 update	1	0	0
Grand total	5	7	33

Table 20 and Table 21 present the detailed list of hits/literature studies classified as “Category b” and ”Category c”, respectively, after step 3 of the relevance assessment and the reasons for this classification for the 3 searches combined. Studies are ordered by data points.

Table 22 presents the detailed list of hits/literature studies classified as ”Category a” after step 3 of the relevance assessment and the reasons for this classification for the 3 searches combined. Studies are ordered by data points. The Klimisch rating of such studies is also provided with the reasons for the obtained score.

Table 20: Literature classified as ”Category b” after step 3 of the relevance assessment and reason for the classification for the active substance Carbendazim

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
First search (including JMAFF update)									
C-6-1-1	Toxicity/adverse effects on human	KIIA 5.4.4	Itoh, S; Hattori, C; Nagata, M; Sanbuissho, A	August 2012	Structural and numerical chromosome aberration inducers in liver micronucleus test in rats with partial hepatectomy	Mutation Research-Genetic Toxicology and Environmental Mutagenesis, 747 (1): 98 -103	Supportive micronucleus test/chromosome aberration test.	No	10.1016/j.mrgentox.2012.04.007
C-6-1-2	Toxicity/adverse effects on human	KIIA 5.6.9	Rama, EM; Bortolan, S; Vieira, ML; Gerardin, DCC; Moreira, EG	August 2014	Reproductive and possible hormonal effects of carbendazim.	Regulatory Toxicology and Pharmacology, 69 (3): 476 - 486	Hershberger and uterotrophic assays. The analysis was conducted using only two dose groups (the 800ppm group was excluded from analysis due to death) in the uterotrophic assay. Therefore, the study is considered only as supportive.	No	10.1016/j.yrtph.2014.05.016
C-6-1-3	E-fate	KIIA 7.2	Paszko, T	August 2014	Adsorption, degradation and mobility of carbendazim in profiles of Polish mineral soils.	Geoderma, 226: 160-169	OECD guideline methodology applied. Data, however, is only Poland-specific. The paper states that in some areas of Poland, the soils are not represented by the FOCUS groundwater scenarios as	No	10.1016/j.geoderma.2014.02.007

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							the prevailing soil types are coarser or contain lower organic carbon contents. On comparison with the recommended soil types in the OECD 106 test method, all of the soils in the Paszko (2014) paper are at the extremely low end of the organic carbon content scale. Eight of the nine soils would be classified as Loamy Sand. This means the soils chosen for the study do not give a reasonable representation of a wide range of soils, so the adsorption and degradation results are only relevant for the areas where the soils were collected and cannot be extrapolated to other areas nor combined in a geometric mean.		
C-6-1-4	E-fate	KIIA 7.4.1	Paszko, T	October 2012	Effect of pH on the adsorption of carbendazim in Polish mineral soils.	Science of The Total Environment, 435: 222 - 229	Study providing useful information about the adsorption-desorption distribution coefficient (Kd)of Carbendazim. Study considered not reliable. Although it claims to follow OECD 106, the	No	10.1016/j.scitotenv.2012.07.013

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							following significant methodological deficiencies are noted: - 3 polish soils used, which makes its relevance to Japanese soils unclear. - Soil pH range between 4.35 - 6.08. - Not all soil types were assessed. - The analytical standard used as the test item is not the technical grade active substance. - No information on the validation or performance of the analytical method during the experiments is provided. - No mass balance information is provided and the stability of test item in solution and soil is not reported. - Organic content (OC) is in the range: 0.03 - 1.23. - Non-GLP study.		
C-6-1-5	E-fate	KIIA 7.4.1	Ahmad, KS	January 2019	Carbendazole lithospheric adsorption, *Saccharum officinarum*-based remediation and microbial degradation in	Environmental Earth Sciences, 78: 31	Study providing useful information about the adsorption-desorption distribution coefficient (Kd)of Carbendazim. Study considered not reliable.	No	10.1007/s12665-018-8000-7

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					heterogeneously composed soils.		Although the method details are given in another paper that claims to have been performed according to OECD 2000 methodology (assumed OECD 106 (2000)), there are significant methodological deficiencies noted, as follows: - no details about test material purity etc. - pakistanese soils used, which makes it of unclear relevance to japanese soils. - no detail regarding the validation or the performance of the analytical method used. - soil pH range: 7.05 - 7.68. - not all soil types assessed. - OM data instead of OC. - non-GLP study.		
C-6-1-6	E-fate	KIIA 7.4.1	Ahmad, KS	2019	*Arachis hypogaea* derived activated carbon steered remediation of Benzimidazole based fungicide adsorbed soils.	Chemistry and Ecology	Study providing useful information about the adsorption-desorption distribution coefficient (Kd)of Carbendazim. Study considered not reliable.	No	10.1080/02757540.2019.1600678

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							Although it claims compliance with OECD 106, there are significant methodological deficiencies noted, as follows: - analytical standard used instead of technical active ingredient. - 7 parkistanese soils used, which makes it of unclear relvance to japanese soils. - validation and performance of the analytical method used not reported. - no mass balance or stability of test item in solution or soil reported. - soil pH range within pH 6.2 - 8.1. - OM data instead of OC data presented. - not all soil types assessed. - GLP status of study not specified.		
Second search									
C-6-1-8	Crop and livestock residue	KIIA 6.3	Rutkowska, E; Wolejko, E; Kaczynski, P; Luniewski,	2023	High and low temperature processing: Effective tool reducing pesticides in/on apple used in	Chemosphere, 313: 137498	The publication provides relevant information about the processing techniques of baking and freeze-drying in apples. Apple field trials were	No	10.1016/j.chemosphere.2022.137498

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
			S; Lozowicka, B		a risk assessment of dietary intake protocol.		conducted in EU by applying Topsin M 500 SC (active substance - thiophanate methyl). The analytical method was validated following EU method performance criteria of SANTE/11312/2021 (2021). The extraction and quantification of thiophanate-methyl residues as well as its metabolite carbendazim is described in detail. Processing factors were determined for both compounds and were calculated in accordance with accepted methods and equations. In a EU consumer risk assessment, the acute (short) dietary intakes were calculated using EFSA PRIMo 3.1. The publication is considered as containing supplementary data that could be used to set risk assessment parameters in Japan. The study was conducted according to EU-accepted guidelines and methods.		

Table 21: Literature classified as ”Category c” after step 3 of the relevance assessment and reason for the classification for the active substance Carbendazim

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
First search (including JMAFF update)									
C-6-2-1	Toxicity/ adverse effects on human	KIIA 5.1	Banyiova, K; Necasova, A; Kohoutek, J; Justan, I; Cupr, P	February 2016	New experimental data on the human dermal absorption of Simazine and Carbendazim help to refine the assessment of human exposure.	Chemosphere, 145: 148 - 156	Study using the compound itself, not the formulation. The test was conducted using a saturated aqueous solution. It is unreasonable to measure the dermal absorption of carbendazim, a metabolite of thiophanate-methyl, using a formulation. Even if proper dermal absorption test data were available for a formulation with carbendazim as the active ingredient, it does not mean that carbendazim, as a metabolite of thiophanate-methyl, would be exposed to humans along with the inert ingredients of that formulation.	No	10.1016/j.chemosphere.2015.11.018
C-6-2-2	Toxicity/ adverse effects on human	KIIA 5.1.3	Breslin, WJ; Paulman, A; Sun-Lin, D; Goldstein, KM; Derr, A	February 2013	The Inhibin B (InhB) response to the testicular toxicants mono-2-ethylhexyl phthalate (MEHP), 1,3 Dinitrobenzene (DNB), or carbendazim (CBZ) following short-term repeat dosing in the male rat.	Birth Defects Research Part b-Developmental and Reproductive Toxicology, 98 (1): 72 - 81	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Only 2 doses tested. Non-guideline study.	No	10.1002/bdrb.21043

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-6-2-3	Toxicity/ adverse effects on human	KIIA 5.1.3	Abolaji, AO; Awogbindin, IO; Adedara, IA; Farombi, EO	May 2017	Insecticide chlorpyrifos and fungicide carbendazim, common food contaminants mixture, induce hepatic, renal, and splenic oxidative damage in female rats.	Human & Experimental Toxicology, 36 (5): 483 - 493	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Only 1 dose tested. Non-guideline study.	Yes	10.1177/0960327116652459
C-6-2-4	Toxicity/ adverse effects on human	KIIA 5.1.3	Aranha, MLG; Garcia, MS; Cavalcante, DND; Silva, APG; Fontes, MK; Gusso-Choueri, PK; Choueri, RB; Perobelli, JE	January 2021	Biochemical and histopathological responses in peripubertal male rats exposed to agrochemicals isolated or in combination: A multivariate data analysis study.	Toxicology, 447: 152636	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Only 1 dose tested. Non-guideline study.	No	10.1016/j.tox.2020.152636
C-6-2-5	Toxicity/ adverse effects on human	KIIA 5.4	Dikic, D; Mojsovic-Cuic, A; Cupor, I; Benkovic, V; Horvat-Knezevic, A; Lisicic, D; Orsolic, N	May 2012	Carbendazim combined with imazalil or cypermethrin potentiate DNA damage in hepatocytes of mice.	Human & Experimental Toxicology, 31 (5): 492 - 505	Study that does not present any data useful for setting risk assessment parameters. Study with insufficient number of observed cells when compared to OECD test guideline 489 (observed: 100 cells, required: 150 cells). Only one dose tested.	Yes	10.1177/0960327111417910
C-6-2-6	Toxicity/ adverse effects on human	KIIA 5.4	Rai, B; Mercurio, SD	April 2020	Environmentally relevant exposures of male mice to carbendazim and thiram cause persistent genotoxicity in male mice.	Environmental Science and Pollution Research International, 27 (10): 10629 - 10641	Study that does not present any data useful for setting risk assessment parameters. Study with insufficient number of observed cells when compared to OECD test guideline 474	No	10.1007/s11356-019-07088-5

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							(observed: 100 cells, required: 150 cells for Comet assay). Only one dose tested. No purity information.		
C-6-2-7	Toxicity/ adverse effects on human	KIIA 5.4	Bowen, DE; Whitwell, JH; Lillford, L; Henderson, D; Kidd, D; McGarry, S; Pearce, G; Beevers, C; Kirkland, DJ	May 2011	Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the Comet assay and the flow-cytometric peripheral blood micronucleus test.	Mutation Research-Genetic Toxicology and Environmental Mutagenesis, 722 (1): 7 – 19	Study that does not present any data useful for setting risk assessment parameters. Study with insufficient number of observed cells when compared to OECD test guidelines 489 and 474 (observed: 100 cells, required: 150 cells for Comet assay and observed: 2000 cells, required: 4000 cells for bone marrow micronucleus assay). No purity information.	No	10.1016/j.mrgentox.2011.02.009
C-6-2-8	Toxicity/ adverse effects on human	KIIA 5.6	Zhou, JH; Xiong, K; Yang, Y; Ye, XQ; Liu, J; Li, FX	January 2015	Deleterious effects of benomyl and carbendazim on human placental trophoblast cells.	Reproductive Toxicology, 51: 64 - 71	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Non-guideline study.	No	10.1016/j.reprotox.2014.12.008
C-6-2-9	Toxicity/ adverse effects on human	KIIA 5.6	Farag, A; Ebrahim, H; ElMazoudy, R; Kadous, E	April 2011	Developmental toxicity of fungicide Carbendazim in female mice.	Birth Defects Research Part b-Developmental and Reproductive Toxicology, 92 (2): 122 - 130	Study that does not present any data useful for setting risk assessment parameters. Mice, which are not recommended in the test guidelines, are being used. Therefore, an appropriate animal species that can be properly evaluated has not been selected.	No	10.1002/bdrb.20290

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-6-2-10	Toxicity/ adverse effects on human	KIIA 5.6.6	Moffit, JS; Her, LS; Mineo, AM; Knight, BL; Phillips, JA; Thibodeau, MS	February 2013	Assessment of Inhibin B as a Biomarker of Testicular Injury Following Administration of Carbendazim, Cetrorelix, or 1,2-Dibromo-3-Chloropropane in Wistar Han Rats	Birth Defects Research Part b-Developmental and Reproductive Toxicology, 98 (1): 17 - 28	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Non-guideline study. Only one dose tested.	No	10.1002/bdrb.21045
C-6-2-11	Toxicity/ adverse effects on human	KIIA 5.6.6	Sakr, SA; Shalaby, SY	April 2014	Carbendazim-induced testicular damage and oxidative stress in albino rats: ameliorative effect of licorice aqueous extract.	Toxicology and Industrial Health, 30 (3): 259 - 267	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Non-guideline study. Only one dose tested. Sampling only 3 times per week.	No	10.1177/0748233712456059
C-6-2-12	Toxicity/ adverse effects on human	KIIA 5.6.6	Durand, P; Martin, G; Blondet, A; Gilleron, J; Carette, D; Janczarski, S; Christin, E; Pointis, G; Perrard, MH	December 2017	Effects of low doses of carbendazim or iprodione either separately or in mixture on the pubertal rat seminiferous epithelium: An *ex vivo* study.	Toxicology In Vitro, 45: 366 - 373	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Non-guideline study.	No	10.1016/j.tiv.2017.05.022
C-6-2-13	Toxicity/ adverse effects on human	KIIA 5.6.6	Li, HT; Zhang, PF; Zhao, Y; Zhang, HF	January 2020	Low doses of carbendazim and chlorothalonil synergized to impair mouse spermatogenesis	Ecotoxicology and Environmental Safety, 188: 109908	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful	No	10.1016/j.ecoenv.2019.109908

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
					through epigenetic pathways.		for setting risk assessment parameters. Non-guideline study. No information on test item purity.		
C-6-2-14	Toxicity/ adverse effects on human	KIIA 5.6.6	Salem, MA; Ismail, RS; Zaki, HF; Arafa, HMM; El-Khatib, ASN	June 2021	L-carnitine extenuates endocrine disruption, inflammatory burst and oxidative stress in carbendazim-challenged male rats via upregulation of testicular StAR and FABP9, and downregulation of P38-MAPK pathways.	Toxicology, 457: 152808	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Non-guideline study. Only one dose tested. Only one dose tested.	No	10.1016/j.tox.2021.152808
C-6-2-15	Toxicity/ adverse effects on human	KIIA 5.6.6	Hsu, YH; Chang, CW; Chen, MC; Yuan, CY; Chen, JH; Ma, JT; Ueng, TH; Lu, SY	December 2011	Carbendazim-induced androgen receptor expression antagonized by flutamide in male rats.	Journal of Food and Drug analysis, 19(4): 418-428	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters.	Yes	10.38212/2224-6614.2198
C-6-2-16	Toxicity/ adverse effects on human	KIIA 5.6.6	Pisani, C; Voisin, S; Arafah, K; Durand, P; Perrard, MH; Guichaoua, MR; Bulet, P; Prat, O	2016	*Ex Vivo* assessment of testicular toxicity induced by carbendazim and iprodione, alone or in a mixture.	Altex-Alternatives to Animal Experimentation	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters.	Yes	10.14573/altex.1601253
C-6-2-17	Toxicity/ adverse effects	KIIA 5.6.6	Upadhyay, J; Rana, M; Bisht, SS; Rana, A;	2019	Biomarker responses (serum biochemistry) in pregnant female wistar rats and histopathology	Brazilian Journal of Pharmaceutical	No purity information. Only one treatment group (10 mg/kg/day) was established.	Yes	10.1590/s2175-97902019000118194

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
	on human		Durgapal, S; Juyal, V		of their neonates exposed prenatally to pesticides	Sciences, 55: 1-9	Biochemical parameters for nephrotoxicity have not been conducted.		
C-6-2-18	Toxicity/ adverse effects on human	KIIA 5.6.6	Ranjan, B; Daundkar, PS; Rampal, S	June 2014	Ameliorative effect of selenium on carbendazim induced oral sub-chronic testicular toxicity in bucks.	Small Ruminant Research, 119 (1-3): 107-113	This is a study using bucks and does not comply with the guideline. Additionally, there is no mention of purity. For these reasons, it is inappropriate as data contributing to risk assessment parameters such as ADI and ARfD.	No	10.1016/j.smallrumres.2014.03.006
C-6-2-19	Toxicity/ adverse effects on human	KIIA 5.6.6	Liu, J; Zhang, PF; Zhao, Y; Zhang, HF	July 2019	Low dose carbendazim disrupts mouse spermatogenesis might be through estrogen receptor related histone and DNA methylation.	Ecotoxicology and Environmental Safety, 176: 242 - 249	The purity of the test item is not described. Mice, which are not recommended in the test guidelines, are being used. Therefore, an appropriate animal species that can be properly evaluated has not been selected. For these reasons, the study is inappropriate as data contributing to risk assessment parameters.	No	10.1016/j.ecoenv.2019.03.103
C-6-2-20	Toxicity/ adverse effects on human	NA	Dikic, D; Landeka, I; Knezevic, F; Mojsovic-Cuic, A; Benkovic, V; Horvat-Knezevic, A; Loncar, G; Teparic, R; Rogic, D	May 2012	Carbendazim Impends Hepatic Necrosis when Combined with Imazalil or Cypermethrin.	Basic & Clinical Pharmacology & Toxicology, 110 (5): 433 - 440	Study that does not present any data useful for setting risk assessment parameters. Only one treatment group (20 mg/kg/day) was established.	Yes	10.1111/j.1742-7843.2011.00831.x

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-6-2-21	Toxicity/ adverse effects on human	NA	Shi, JZ; Zhao, M; Li, KX; Zhao, YJ; Li, W; Peng, Y; Zheng, J	April 2022	Metabolic activation and cytotoxicity of fungicide carbendazim mediated by CYP1A2	Journal of Agricultural and Food Chemistry, 70(13): 4092-4101	Literature suggesting that metabolites are involved in the mechanism of hepatotoxicity. This study cannot be used for risk assessment. There are no study guidelines that describe only the involvement of metabolites in the mechanism of hepatotoxicity.	No	10.1021/acs.jafc.1c08144
C-6-2-22	Toxicity/ adverse effects on human	NA	Helali, I; Ferchichi, S; Maaouia, A; Aouni, M; Harizi, H	September 2016	Modulation of macrophage functionality induced in vitro by chlorpyrifos and carbendazim pesticides.	Journal of Immunotoxicology, 13 (5): 745 - 750	Literature presented to characterize the toxicological mechanisms induced by CBZ. It does not present any data useful for setting risk assessment parameters. Non-guideline study.	Yes	10.1080/1547691X.2016.1181124
C-6-2-23	Toxicity/ adverse effects on human	NA	Viktorov, AV; Yurkiv, VA	February 2013	Effects of Carbendazim on Kupffer cell functioning.	Bulletin of Experimental Biology and Medicine, 154(4): 438-440	Significant methodological deficiencies compared to existing test guideline. Study of limited relevance.	No	10.1007/s10517-013-1971-1
C-6-2-24	Ecotoxicity and animal toxicity	KIIA 8.1.1	Kimaro, WH; Madekurozwa, MC; Groenewald, HB	July 2013	Histomorphometrical and ultrastructural study of the effects of carbendazim on the magnum of the Japanese quail (*Coturnix coturnix japonica*).	Onderstepoort Journal of Veterinary Research, 80 (1): 1 - 8	Study not performed according to any current test guideline. No information available to determine if the study fulfills any of the validity criteria of the closest test guideline (OECD TG 223). No useful endpoints provided (14-day LD_{50}) although histopatological effects were observed after 48 hours of	Yes	10.4102/ojvr.v80i1.579

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							exposure to doses of 400 mg/kg and above.		
C-6-2-25	Ecotoxicity and animal toxicity	KIIA 8.3.1	Del Arco, AI; Rico, A; van den Brink, PJ	August 2015	Effects of intra- and interspecific competition on the sensitivity of *Daphnia magna* populations to the fungicide carbendazim.	Ecotoxicology, 24 (6): 1362 - 1371	Study not following any current guideline but providing useful information about population effects of Carbendazim in *Daphnia magna* with EC50 values. However, in the study, tests were conducted with only 3 concentrations, which is too small to permit to determine reliable EC_{50}s. Study generally not meeting the requirements of the test guideline.	No	10.1007/s10646-015-1512-y
C-6-2-26*	Ecotoxicity and animal toxicity	KIIA 8.3.1.1 & KIIA 8.3.2.1	Silva, ARR; Cardoso, DN; Cruz, A; Pestana, JLT; Mendo, S; Soares, AMVM; Loureiro, S	February 2017	Multigenerational effects of carbendazim in *Daphnia magna*.	Environmental Toxicology and Chemistry, 36 (2): 383 - 394	Study providing endpoints (48-hr LC_{50} and 21-d EC_{50} value) about the acute and chronic toxicity of Carbendazim to *Daphnia magna*, but only for the *Daphnia* not chronically exposed to carbendazim over several generations. However, significant deviations from current test guidelines (OECD TG 202 and OECD TG 211) indicate a very limited relevance for this study. Study considered not reliable, as significant deviations from current test guideline were noted, as follows:	No	10.1002/etc.3541

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							- for the acute data (immobilization test), although adherence to OECD TG 202 is claimed, the replication is not appropriate (only 3 replicates of 5 neonates each when a minimum of 20 individuals is required) and no estimation of test sensitivity with the use of a reference substance has been performed (no data provided). - for the chronic test (reproduction test), although adherence to OECD TG 211 is claimed, the replication is not appropriate (only 5 replicates of individually housed Daphnia when a minimum of 10 individually housed organisms is required). - for both the acute and chronic tests, there is clear evidence that the test item concentrations are not maintained within the 80 - 100% range of nominal values, and, according to both OECD TG 202 and 211, mean measured concentrations or time-weighted average concentrations should have been used for the determination of toxicity endpoints, while in this study, nominal concentrations were used.		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
C-6-2-27	Ecotoxicity and animal toxicity	KIIA 8.3.2.1	Ribeiro, F; Ferreira, NCG; Ferreira, A; Soares, AMVM; Loureiro, S	March 2011	Is ultraviolet radiation a synergistic stressor in combined exposures? The case study of *Daphnia magna* exposure to UV and carbendazim.	Aquatic Toxicology, 102 (1-2): 114 - 122	The part of the study that focuses on single exposure to Carbendazim is useful to assess the long-term effects of carbendazim on aquatic invertebrates as it provides 21-day EC_{50} value with regards to neonate production (reproductive endpoint). However, although reference is made to OECD TG 211 (1998), the lack of analytical verification of test concentrations is not appropriate from the viewpoint of utilisation for the evaluation and indicate a limited relevance. Significant methodological deficiencies have been identified, as follows: - no analytical verification of test item concentrations not permitting to ascertain that the concentration of the test sample is maintained as planned throughout the exposure period - EC_{50} data determined with nominal concentration when using measured concentrations (if they were available) would be more accurate - no 95% confidence interval provided for the EC50 value	No	10.1016/j.aquatox.2011.01.007

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							- no information on test performance (validity criteria) is provided - reference is made to an old guideline (updated in 2012)		
C-6-2-28	Ecotoxicity and animal toxicity	KIIA 8.4	Ding, TD; Li, W; Li, JY	June 2019	Toxicity and metabolic fate of the fungicide carbendazim in the typical freshwater diatom *Navicula* species.	Journal of Agricultural and Food Chemistry, 67(24): 6683 - 6690	Study not performed according to any current test guideline. No information available to determine if the study fulfills any of the validity criteria of the OECD TG 201 and no analytical verification of test item concentrations. Although a 24h EC_{50} has been determined, no effects are observed after 72 hours, with no 72h EC50 determined.	No	10.1021/acs.jafc.8b06179
C-6-2-29	Ecotoxicity and animal toxicity	KIIA 8.2, KIIA 8.3 and KIIA 8.4	Iturburu, FG; Calderon, G; Ame, MV; Menone, ML	November 2019	Ecological Risk Assessment (ERA) of pesticides from freshwater ecosystems in the Pampas region of Argentina: legacy and current use chemicals contribution.	Science of the Total Environment, 691: 476 - 482	Study providing an Argentinian-specific risk assessment approach using already-existing toxicity endpoints (Fish acute and chronic toxicity (96 h LC50 and 21 days NOEC) in rainbow trout *Oncorhynchus mykiss*, aquatic invertebrates' acute and chronic toxicity (48 h EC50 and 21 days NOEC) in water flea *Daphnia magna* and algal acute and chronic toxicity (72 h EC50 and 96 h NOEC) in *Scenedesmus subspicatus*. Study not providing any new endpoints useful for the ecotoxicological risk assessment	No	10.1016/j.scitotenv.2019.07.044

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
							of carbendazim in aquatic organisms.		
Second search									
C-6-2-32	Toxicity/ adverse effects on human	KIIA 5.8	Ma, XR; Chen, X; Hou, HA; Liu, DH; Liu, XK; Wang, P; Zhou, ZQ	2023	Low dose of carbendazim and tebuconazole: accumulation in tissues and effects on hepatic oxidative stress in mice.	Toxics, 11 (326). https://doi.org/10.3390/ toxics11040326	In the study, carbendazim was not detected in the blood of the treated group, and no other toxic effects were observed. The exact amount of drug intake is also unknown, making it inappropriate for use in risk assessment. No test guideline followed in the study.	Yes	10.3390/toxics11040326
C-6-2-33	Toxicity/ adverse effects on human	KIIA 5.6	Ma, C; Yang, ZA; Zhang, SX; Zhang, XK; Wang, SY; Cheng, HR; Liu, Y; Ruan, HZ; Xu, ZY; Liang, CM; Liang, D; Ding, ZM; Liu, YJ; Cao, YX	2023	Carbendazim exposure inhibits mouse oocytes meiotic maturation in vitro by destroying spindle assembly.	Food and Chemical Toxicology, 179: 113966	There are no study guidelines that describe in the mechanism of oocyte maturation toxicity. This study is not appropriate for use in risk assessment. No information of test substance (purity, maker). No test guideline followed in the study.	No	10.1016/j.fct.2023.113966
C-6-2-34	Toxicity/ adverse effects on human	KIIA 5.8	Zhang, SW; Luo, T; Weng, Y; Wang, D; Sun, L; Yu, ZP; Zhao, Y; Liang, SM; Ren, HY; Zheng, XL; Jin, YX; Qi, XJ	2024	Toxicologic effect and transcriptome analysis for sub-chronic exposure to carbendazim, prochloraz, and their combination on the liver of mice.	Environmental Science and Pollution Research, 31 (4): 5500 - 5512	The route of administration for this test is feeding. Although the dose is stated, the exact drug intake is not reported. It is not appropriate to use for risk assessment.	No	10.1007/s11356-023-31412-9
C-6-2-35	Toxicity/ adverse	KIIA 5.8	Bao, ZW; Wang, D; Zhao,	2023	Insights into enhanced toxic effects by the	Science of the Total	The route of administration for this test is feeding.	No	10.1016/j.scitotenv.2023.163648

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision	Open access	DOI
	effects on human		Y; Luo, T; Yang, GL; Jin, YX		binary mixture of carbendazim and procymidone on hepatic lipid metabolism in mice.	Environment, 882: 163648	Although the dose is stated, the exact drug intake is not reported. It is not appropriate to use for risk assessment.		

*: studies not obtained in the main literature search but cited in some of the literature retrieved in the main search and deemed potentially relevant.

Table 22: Literature classified as ”Category a” after step 3 of the relevance assessment and reason for the classification for the active substance Carbendazim

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
First search (including JMAFF update)										
C-7-1	Crop and livestock residue	KIIA 6.3	EFSA	April 2012	Reasoned opinion on the modification of the existing MRLs for thiophanate-methyl and carbendazim in apples and pears European Food Safety Authority.	EFSA Journal, 10 (4): 2685	4	EU review document with relevant information on residues, MRLs, risk assessment (consumer; animals) and analytical methods. Not a study document but an EU authority review document with information relating to MRLs and consumer risk assessment on the active substance.	Yes	10.2903/j.efsa.2012.2685
C-7-2	Crop and livestock residue	KIIA 6.3	Hakme, E; Herrmann, SS; Poulsen, ME	October 2020	Processing factors of pesticide residues in biscuits and their relation to the physicochemical properties of pesticides.	Food Additives and Contaminants Part a-Chemistry Analysis Control Exposure & Risk Assessment, 37(10): 1695 - 1706	2	The publication provides relevant information about the processing technique of baking in a high bran content food product (biscuits). Wheat or other cereal grains (oat, barley, and rye)	Yes	10.1080/19440049.2020.1791975

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
								produced as test material for European Union proficiency tests that contain incurred residues of multiple pesticides were used. Processing factors were determined and supplement the existing available data in the BfR compilation of processing factors. Some requirements from the OECD TG 508 were discussed and considered. The procedure for biscuit preparation that was adopted for this study mimics the representative domestic standard of biscuit in accordance to OECD TG 508. The extraction and quantification of carbendazim residues is		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
								described in detail. The study was performed within the framework of the European Union Reference Laboratory (EURL) for pesticide residues in cereals and feeding stuffs. Processing factors were determined and supplement the existing available data in the BfR compilation of processing factors. The publication provides relevant information about the processing behaviour of carbendazim. The presented data could be relevant for other national consumer risk assessments.		
C-7-3	Ecotoxicity and animal toxicity	KIIA 8.3.1.1 & KIIA 8.3.2.1	Silva, ARR; Cardoso, DN; Cruz,	May 2015	Ecotoxicity and genotoxicity of a binary	Ecotoxicology and Environmental Safety, 115: 279 - 290	2	Study providing endpoint (48-hr L/EC_{50} and 21-d	No	10.1016/j.ecoenv.2015.02.022

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
			A; Lourenço, J; Mendo, S; Soares, AMVM; Loureiro, S		combination of triclosan and carbendazim to *Daphnia magna*.			EC_{50}/NOEC value) about the acute and chronic toxicity of Carbendazim to *Daphnia magna,* may be useful for ecotoxicological risk assessment. Study considered reliable with restriction, as some minor deviations from current test guideline were noted, as follows: - for the acute data (immobilization test), although the study claims to have been performed according to OECD TG 202, there is no estimation of test sensitivity with the use of a reference substance (no data provided) and standard errors for the 48h		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
								L/EC_{50} values have been provided instead of 95% confidence intervals. - for the chronic test (reproduction test), although the study claims to have been performed according to OECD TG 211 is claimed, standard errors for the 21d EC_{50} values have been provided instead of 95% confidence intervals. - for both the acute and chronic tests, there is also clear evidence that the test item concentrations are not maintained within the 80 - 100% range of nominal values, and, according to both OECD TG 202 and 211, mean measured		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
								concentrations or time-weighted average concentrations should have been used for the determination of toxicity endpoints, while in this study, it is not clear if measured or nominal concentrations were used.		
Second search										
C-7-4	Toxicity/adverse effects on human	KIIA 5.4	Iso, T; Suzuki, K; Murata, Y; Hirose, N; Umano, T; Horibata, K; Sugiyama, KI; Hirose, A; Masumura, K; Matsumoto, M	2024	Lack of in vivo mutagenicity of carbendazim in the liver and glandular stomach of MutaMice.	Genes and Environment, 46:7 https://doi.org/10.1186/s41021-024-00299-4	1	Reliable without restrictions (guideline study), based on ToxRtool evaluation.	Yes	10.1186/s41021-024-00299-4
2009 update										
C-7-5	Crop and livestock residue	KIIA 6.3	EFSA	2009	Refined risk assessment regarding certain	EFSA Scientific Report, 289: 1-29	4	Literature publication from approved	Yes	10.2903/j.efsa.2009.289r

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
					MRLs of concern for the active substances carbendazim and thiophanate-methyl			independent reviewing authority relating to the review of MRLs for carbendazim and thiophanate-methyl in the EU in 2008, for a number of commodities. The data is considered as supplementary considering the uses are outside of Japan. This publication from EFSA (2009) can be used as supplementary data when setting risk assessment parameters at JMAFF for thiophanate-methyl and/or the metabolite carbendazim. Publication from EFSA is not assignable according to Klimisch: EFSA document with regard to		

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Klimisch score	Reasons for the decision	Open access	DOI
								residues, MRL setting and consumer risk assessment.		

*: studies not obtained in the main literature search but cited in some of the literature retrieved in the main search and deemed potentially relevant.

4. References:

JMAFF Guideline full reference:

「公表文献の収集、選択等のためのガイドライン」（令和 3 年 9 月 22 日　農業資材審議会農薬分科会決定/令和 5 年 7 月 27 日一部改正）

Appendix 1: Form 8 table for the active substance Thiophanate-methyl and metabolite Carbendazim

EFSA reports:

The following documents were initially screened for literature data about Thiophanate-methyl and Carbendazim:

- EFSA (European Food Safety Authority), 2018. Conclusion on the peer review of the pesticide risk assessment of the active substance thiophanate-methyl. EFSA Journal 2018;16(1):5133, 123 pp. doi:10.2903/j.efsa.2018.5133

- EFSA (European Food Safety Authority). 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance carbendazim. EFSA Journal 2010; 8(5):1598. 76 pp. https:// doi. org/ 10. 2903/j. efsa. 2010. 1598

No literature data was identified during this initial screening.

The following documents were subsequently screened:

- EFSA (European Food Safety Authority), Bellisai, G., Bernasconi, G., Brancato, A., Carrasco Cabrera, L., Ferreira, L., Giner, G., Greco, L., Jarrah, S., Kazocina, A., Leuschner, R., Magrans, J. O., Miron, I., Nave, S., Pedersen, R., Reich, H., Ruocco, S., Santos, M., Scarlato, A. P., Verani, A.2021. Reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. EFSA Journal 2021;19(7):6773. doi: 10.2903/j.efsa.2021.6773
- EFSA (European Food Safety Authority), Bellisai, G., Bernasconi, G., Binaglia, M., Carrasco Cabrera, L., Castellan, I., Castoldi, A., Chiusolo, A., Crivellente, F., Del Aguila, M., Ferreira, L., Giner Santonja, G., Greco, L., Istace, F., Jarrah, S., Lanzoni, A., Leuschner, R., Mangas, I., Mioč, A., Verani, A. 2024a. Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. EFSA Journal, 22(2), 8569. https:// doi. org/ 10. 2903/j. efsa. 2024. 8569
- EFSA (European Food Safety Authority), 2024. Statement on the assessment of quality of data available to EFSA to derive the health-based guidance values for carbendazim. EFSA Journal. 2024;22: e8756. DOI: 10.2903/j.efsa.2024.8756
- Germany. (2009). Renewal Reassessment Report on the active substance carbendazim, prepared by the rapporteur Member State Germany in accordance with Article 5(5) of Council Directive 91/414/EEC, July 2009.
- Germany. (2010). Final Addendum to Assessment Report on carbendazim, compiled by EFSA, March 2010.

- Sweden. (2017). Revised Renewal Assessment Report (RAR) on thiophanate-methyl prepared by the rapporteur Member State Sweden in the framework of Regulation (EU) No 844/2012, October 2017.

A number of publications were identified in the revised Renewal Assessment Report (RAR) on thiophanate-methyl prepared by the rapporteur Member State Sweden in the framework of Regulation (EU) No 844/2012, October 2017 for the active substance Thiophanate-methyl and its metabolite Carbendazim, as illustrated in the RAR exert below:

*Exert from Thiophanate-methyl RAR Volume 3 CA B6, B7, B8 and B*9:

"Databases: TOXCENTER, BIOSIS, AGRICOLA, HCAPLUS, PQSCITECH, MEDLINE, ESBIOBASE, EMBASE, CABA, PASCAL via the service provider STN-International. The search strategy was based on a single concept search. Searches were made for the active substance thiophanate-methyl as well as for the metabolite carbendazim.

Time window: 2002-01-01 -2014-01-27.

Input parameters: CAS number, chemical names, common name, formulation names, code and abbreviation.

The following general criteria were applied to assess the relevance (Klimisch et al, 1997):

1. Publication scientifically sound
2. Does provide relevant information for dossier preparation or risk assessment purpose
3. Method validated
4. Documentation sufficient for assessment
5. Does meet important criteria of today standard methods
6. No relevant methodological deficiencies
7. Suitable test system
8. Document does not contain already identified results

Thiophanate-methyl: In total, 2239 records were retrieved from bibliographic databases and were screened by expert reviewers for relevance. Based on the evaluation of the summary records (titles/abstracts) 2200 publications were assessed as obviously not relevant for the EU-data requirements. 39 full-text documents were assessed in detail. 30 of these publications did not provide relevant information for the dossier preparation or risk assessment purposes and were assessed as not relevant for the EU-data requirements.

9 were selected to provide relevant information and were cited in the supplementary dossier, 2 of which referred to toxicological endpoints. The studies are presented in Volume B3CP as they concern the exposure assessment of thiophanate-methyl. The other 7 studies referred to ecotoxicological endpoints. 5 studies were related to endocrine disruption and are presented in this document. Two studies were related to the risk assessment for non-target terrestrial arthropods and are presented in Annex B.9CP. No studies referred to residue endpoints. Of the 30 publications that the applicant excluded from the risk assessment, 4 were related to environmental fate and behaviour. These 4 publications are described in more detail below.

Carbendazim: In total, 436 records were retrieved from bibliographic databases and were screened by expert reviewers for relevance. Based on the evaluation of the summary records (titles/abstracts) 392 publications were assessed as obviously not relevant for the EU-data requirements. 44 full-text documents were assessed in detail. 32 of these publications did not provide relevant information for the dossier preparation or risk assessment purposes and were as well assessed as obviously not relevant for the EU-data requirements. 12 publications were selected to provide relevant information and were cited in the supplementary dossier, 8 of which referred to toxicological properties, 4 of which referred to ecotoxicological endpoints and 1 of which in part referred to endpoints in fate and behaviour (This study (Yu et al, 2009) has been briefly summarised at the end of section B.8.1.1.1.1). These have been briefly presented in this document. Of the 32 publications that the applicant excluded from the risk assessment, 14 were related to ecotoxicology. No studies referred to residue endpoints."

All relevant studies mentioned above are listed and presented in Table 23 and Table 24 for Thiophanate-methyl and Carbendazim, respectively.

In the Renewal Reassessment Report on the active substance carbendazim, prepared by the rapporteur Member State Germany in accordance with Article 5(5) of Council Directive 91/414/EEC, July 2009, a literature search covering the period 2000 to 2008 was performed and a number of publications were deemed as potential key studies or supplementary studies regarding the genotoxicity, reproductive toxicity and other toxicity of Carbendazim. These studies are listed and presented in Table 24.

In the Reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl (EFSA, 2021) and the update of this evaluation (EFSA, 2024a), a screening of the published literature available (PubMed) has been performed. The list of literature was further screened for studies relevant to assess the aneugenic and in particular the clastogenic potential of carbendazim and thiophanate-methyl. The studies identified as relevant to assess these endpoints (Appendices G for carbendazim and H for thiophanate-methyl) were discussed at the related EFSA experts meeting which was held on 15 January 2021. These studies are presented in Table 23 and Table 24, for thiophanate-methyl and Carbendazim, respectively, if not already listed from the screening of other EFSA documents, as mentioned in the previous paragraphs.

JMPR reports:

The following documents were initially screened for literature data about Thiophanate-methyl and Carbendazim:

- Pesticide residues in food 1998. Evaluations 1998. PART I – RESIDUES. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group (JMPR), Rome, Italy, 21–30 September 1998. WORLD HEALTH ORGANIZATION and FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, Rome, 2004. 1220 pp

- Pesticide residues in food 2004 Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 20–29 September 2004 WORLD HEALTH ORGANIZATION and FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, Rome, 2004. 383 pp
- Pesticide residues in food – 2005 Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 20-29 September 2005 WORLD HEALTH ORGANIZATION and FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, Rome, 2005. 360 pp
- Pesticide residues in food 2006. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Rome, Italy, 3–12 October 2006. FAO PLANT PRODUCTION AND PROTECTION PAPER. 400 pp
- Pesticide residues in food 2017. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues Geneva, Switzerland, 12–21 September 2017. FAO PLANT PRODUCTION AND PROTECTION PAPER. 104 pp
- Joint FAO/WHO meeting on pesticide residues 2023. Summary report. Acceptable Daily Intakes, Acute Reference Doses, Residue Definitions, Recommended Maximum Residue Limits, supervised trials median residue values and other values recorded by the 2023 meeting. WORLD HEALTH ORGANIZATION and FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS, Washington, DC, 19-28 September 2023. 30 pp
- Pesticide residues in food 2023: Joint FAO/WHO meeting on pesticide residues. Evaluation Part II – Toxicological. 2024. Geneva: World Health Organization and Food and Agriculture Organization of the United Nations. Licence: CC BY-NC-SA 3.0 IGO.

Relevant publication listed in these documents are listed and presented in tables 23 and 24 for Thiophanate-methyl and Carbendazim, respectively.

Furthermore, it was noted that some toxicological information (Acceptable Daily Intakes, Acute Reference Doses, Residue Definitions, Recommended Maximum Residue Limits) about Carbendazim is presented in the 2004 and 2005 reports.

US EPA reports:

The following documents were screened for literature data about Thiophanate-methyl and Carbendazim after consultation and screening of the US EPA Docket (https://www.regulations.gov/docket/EPA-HQ-OPP-2014-0004; 9 documents with relevant literature information out of the 74 listed):

- Toxicology Chapter for Thiophanate Methyl and Carbendazim. 2002. EPA-HQ-OPP-2004-0265-0007. United States Environmental Protection Agency. 50 pp

- Reregistration Eligibility Decision – Thiophanate-methyl. 2005. PC-102001. United States Environmental Protection Agency. 219 pp
- Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments in Support of the Registration Review of Thiophanate-Methyl and Carbendazim. 2014. EPA-HQ-OPP-2014-0004-0012. United States Environmental Protection Agency. 99 pp
- Thiophanate-Methyl and Carbendazim (MBC). Human Health Assessment Scoping Document in Support of Registration Review. 2014. EPA-HQ-OPP-2014-0004-0010. United States Environmental Protection Agency. 62 pp
- Registration Review Ecological Portion of the Draft Risk Assessment (DRA) for Antimicrobial Uses of Carbendazim. 2019. EPA-HQ-OPP- 2014-0004-0033. United States Environmental Protection Agency. 26 pp
- Thiophanate-Methyl and Carbendazim: Amended Draft Human Health Risk Assessment for Registration Review. 2020. EPA-HQ-OPP- 2014-0004-0096. United States Environmental Protection Agency. 164 pp
- Thiophanate-methyl and MBC (Carbendazim): Draft Ecological Risk Assessment for Registration Review. 2020. EPA-HQ-OPP-2014-0004-0037. United States Environmental Protection Agency. 178 pp
- Thiophanate-Methyl and Carbendazim: Draft Human Health Risk Assessment for Registration Review. 2020. EPA-HQ-OPP-2014-0004-0038. United States Environmental Protection Agency. 161 pp
- Thiophanate-methyl and Carbendazim: Proposed Interim Registration Review Decision Case Number 2680. 2022. EPA-HQ-OPP-2014-0004-0116. United States Environmental Protection Agency. 178 pp

Relevant publication listed in these documents are listed and presented in Table 23 and Table 24 for Thiophanate-methyl and Carbendazim, respectively.

Table 23: Literature conformed to “Relevance assessment” by Step2 and reference cited the results as peer-reviewed open literature by EFSA, USEPA and JMPR for Thiophanate-methyl

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
T-8-1	Toxicity/adverse effects on human – genotoxicity	Perocco, P; Del Ciello, C; Mazzullo, M; Rocchi, P; Ferreri, A.M; Paolini, M; Pozzetti, L; Cantelli-Forti, G	November 1997	Cytotoxicity and cell transforming activities of the fungicide methyl thiophanate on BALB/c 3T3 cells *in vitro*.	Mutation Research, 394 (1-3): 29-35	US EPA	Toxicology Chapter for Thiophanate Methyl and Carbendazim. 2002 And Reregistration Eligibility Decision – Thiophanate-methyl.	US EPA indicates a significant and reproducible increase in morphologically transformed foci at 25 µg/ml without S9 and ≥20 µg/ml with S9. Cytotoxicity observed at ≥25 µg/ml (pronounced at ≥50 µg/ml) without S9 only weak cytotoxicity with S9 (most pronounced at 100-200 µg/ml). Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s1383-5718(97)00120-4
T-8-2	Toxicity/adverse effects on human – Genotoxicity	Barale, R., Scapoli, C., Meli, C., Casini, D., Minunni, M., Marrazzini, A., Loprieno, N., Barrai, I.	1993	Cytogenetic effects of benzimidazoles in mouse bone marrow.	Mutation Research, 300: 15-28	EFSA / JMPR	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a) / Pesticide residues in food 2023: Joint FAO/WHO meeting on	Study identified by EFSA and JMPR (2024) as relevant to assess aneugenicity/clastogenicity of Thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1218(76)90032-x

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							pesticide residues. Evaluation Part II – Toxicological. (2024)			
T-8-3	Toxicity/adverse effects on human – Genotoxicity	Ben Amara I, Ben Saad H, Cherif B, Elwej A, Lassoued S, Kallel C and Zeghal N	2014	Methyl-thiophanate increases reactive oxygen species production and induces genotoxicity in rat peripheral blood.	Toxicology Mechanisms and Methods, 24 (9): 679-687	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of Thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.	No	10.3109/15376516.2014.961217
T-8-4	Toxicity/adverse effects on human – Genotoxicity	Fimognari C, Nüsse M and Hrelia P	1999	Flow Cytometric Analysis of Genetic Damage, Effect on Cell Cycle Progression, and Apoptosis by Thiophanate-Methyl in Human Lymphocytes.	Environmental and Molecular Mutagenesis 33:173-176	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of Thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/(sici)1098-2280(1999)33:2<173::aid-em10>3.0.co;2-r
T-8-5	Toxicity/adverse effects on human – Genotoxicity	Salamone MF and Mavournin KH,	1994	Bone marrow micronucleus assay: a review of the mouse stocks used and their published mean spontaneous micronucleus frequencies.	Environmental and Molecular Mutagenesis 23:239-273	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of Thiophanate-methyl. Study not found in the current literature	No	10.1002/em.2850230402

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							thiophanate-methyl. (2004a)	search according to JMAFF guidelines.		
T-8-6	Toxicity/adverse effects on human – Genotoxicity	Wang TC, Wu CL, Lin JH, Tarn CY and Lin SY,	1987	Sister chromatid exchanges and chromosome aberrations induced by pesticide combinations in Chinese hamster ovary cells.	Bull. Institute of Zoology, Academia Sinica, 26(4): 317-329	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of Thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.	Yes	https://zoolstud.sinica.edu.tw/Journals/26.4/317.pdf
T-8-7	Toxicity/adverse effects on human – Genotoxicity	Moo-Munoz, AJ; Azorin-Vega, EP; Ramirez-Duran, N; Moreno-Perez, PA	2021	Evaluation of the cytotoxic and genotoxic potential of the captan-based fungicides, chlorothalonil-based fungicides and methyl thiophanate-based fungicides in human fibroblasts BJ	Journal of Environmental Science and Health part b-Pesticides Food Contaminants and Agricultural Wastes, 56 (10): 877 - 883	JMPR	Pesticide residues in food 2023: Joint FAO/WHO meeting on pesticide residues. Evaluation Part II – Toxicological. (2024)	Study identified by JMPR as suggesting that thiophanate-methyl causes secondary genotoxicity *in vitro* as a consequence of severe cytotoxicity. However, JMPR evaluation concludes that the paper is of little relevance to the evaluation of the mutagenicity of thiophanate-methyl which is caused by interference with the mitotic spindle assembly, resulting in aneuploidy Study found in the current literature search according to JMAFF guidelines	NA	NA

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								and classified as relevant Category “c” (hit number T-6-2-2)		
T-8-8	Toxicity/adverse effects on human – Developmental / maternal toxicity	da Silva, JN; Monteiro, NR; Antunes, PA; Favareto, APA	2020	Maternal and developmental toxicity after exposure to formulation of chlorothalonil and thiophanate-methyl during organogenesis in rats	Anais da Academia Brasileira de Ciencias, 92 (4): 1 - 16	JMPR	Pesticide residues in food 2023: Joint FAO/WHO meeting on pesticide residues. Evaluation Part II – Toxicological. (2024)	Study identified by JMPR as “Silva et al., 2020”. JMPR evaluation indicates that the findings of the paper appear inconsistent with those of the rat regulatory study, which identified a NOAEL for developmental toxicity of 1000 mg/kg bw per day. However, as the material tested was a formulation containing other chemicals and another active substance (chlorothalonil), it was not possible to attribute the reported findings to thiophanate-methyl. Overall, the JMPR evaluation indicates that no meaningful conclusions can be drawn from this publication. Study found in the current literature search according to JMAFF guidelines	NA	NA

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								and classified as non-relevant after step 2 (hit number T-5-1)		
T-8-9	Toxicity/adverse effects on human – Induction of liver detoxication enzymes	Paolini, M; Pozzetti, L; Perocco, P; Mazzullo, M; Cantelli-Forti, G	1999	Molecular non-genetic biomarkers of effect related to methyl thiophanate cocarcinogenesis: organ- and sex-specific cytochrome P450 induction in the rat.	Cancer Letters, 135(2):203–213.	JMPR	Pesticide residues in food 2023: Joint FAO/WHO meeting on pesticide residues. Evaluation Part II – Toxicological. (2024)	JMPR evaluation indicates that in this study, thiophanate-methyl induced increases in CYP3A and CYP2B1 in the liver of rats. No conclusion on the usefulness of the paper is provided. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0304-3835(98)00298-5
T-8-10	Toxicity/adverse effects on human – exposure assessment	Mandal, S; Das, S; Bhattacharyya, A	May 2010	Dissipation study of Thiophanate Methyl residue in/on grapes (*Vitis vinifera L.)* in India.	Bulletin of Environmental Contamination and Toxicology, 84(5): 592-595	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. Study performed with a formulation of thiophanate-methyl (75% WP). Since the study is not found as relevant for the dissipation half-life of thiophanate-methyl under European condition, the study was not evaluated in detail by the RMS. It is however noted that	No	10.1007/s00128-010-9985-0

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								the study dissipation half-life is close to the DT_{50} value for thiophanate-metyl of 5 days listed in the in the EFSA Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessments for plant protection products. Study not found in the current literature search according to JMAFF guidelines.		
T-8-11	Toxicity/adverse effects on human – exposure assessment	Fantke, P; Gillespie, BW; Juraske, R; Jolliet, O	June 2014	Estimating half-lives for pesticide dissipation from plants	Environmental Science & Technology, 48(15): 858T-8-8602	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. According to the study, the estimated dissipation half-life for thiophanate-methyl is 9.07 days (geometric mean) when applied on an average plant under field conditions at 20 °C. However, since a DT_{50} of 5 days is listed in the EFSA Guidance on the assessment of exposure of operators,	Yes	doi.org/10.1021/es500434p

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								workers, residents and bystanders in risk assessments for plant protection products 2 as a realistic dissipation rate for thiophanate-methyl under European conditions, RMS is of the opinion that this value is the most relevant to use in the worker exposure assessment. The study was therefore not evaluated in detail by the RMS. It is however noted that the estimated dissipation half-life is in the same order of magnitude as the DT_{50} value listed in the EFSA Guidance. Study not found in the current literature search according to JMAFF guidelines.		
T-8-12	Ecotoxicity and animal toxicity – Genotoxicity	Capriglione T, De Iorio S, Gay F, Capaldo A, Vaccaro MC, Morescalchi MA and Laforgia V	2011	Genotoxic effects of the fungicide thiophanate methyl on Podarcis sicula assessed by micronucleus test, comet assay and chromosome analysis.	Ecotoxicology, 20:885-891	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of Thiophanate-methyl. Study not found in the current literature	No	10.1007/s10646-011-0655-8

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							thiophanate-methyl. (2004a)	search according to JMAFF guidelines.		
T-8-13	Ecotoxicity and animal toxicity – endocrine disruption	Sciarrillo, R; De Falco, M; Virgilio, F; Laforgia, V; Capaldo, A; Gay, F; Valiante, S; Varano, L	January 2008	Morphological and functional changes in the thyroid gland of methyl thiophanate-injected lizards, *Podarcis sicula*.	Archives of Environmental Contamination and Toxicology, 55(2): 254-261	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that the morphological effects and the deceased hormone levels were already pronounced at the lowest tested concentration of 5µg/L, indicating a specific effect on thyroidal function. Study not found in the current literature search according to JMAFF guidelines.	No	10.1007/s00244-007-9116-z
T-8-14	Ecotoxicity and animal toxicity – endocrine disruption	Cardone, A	March 2012	Testicular toxicity of methyl thiophanate in the Italian wall lizard (*Podarcis sicula*): morphological and molecular evaluation.	Ecotoxicology, 21(2):512-23	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that the overall evidence does not allow to rule	No	10.1007/s10646-011-0812-0

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								out a potential endocrine disrupting activity of thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.		
T-8-15	Ecotoxicity and animal toxicity – endocrine disruption	De Falco, M; Sciarrillo, R; Capaldo, A; Russo, T; Gay, F; Valiante, S; Varano, L; Laforgia, V	June 2007	The effects of the fungicide methyl thiophanate on adrenal gland morphophysiology of the lizard, *Podarcis sicula*.	Archives of Environmental Contamination and Toxicology, 53: 241-248	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. The RMS finds it likely that the observations are rather a response to general stress due to the toxic action of the substance than a specific endocrine disrupting mode of action. The observed lymphocyte and macrophage infiltration would support this. Study not found in the current literature search according to JMAFF guidelines.	No	10.1007/s00244-006-0204-2
T-8-16	Ecotoxicity and animal	Capaldo, A; Gay, F; De Falco, M;	May 2006	The newt *Triturus carnifex* as a model for	Comparative Biochemistry and	EFSA / RMS (Sweden)	Renewal Assessment	Study identified during the literature	No	10.1016/j.cbpc.2005.12.005

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
	toxicity – endocrine disruption	Virgilio, F; Valiante, S; Laforgia, V; Varano, L		monitoring the ecotoxic impact of the fungicide thiophanate methyl: adverse effects on the adrenal gland.	Physiology part C Toxicology and Pharmacology, 143(1):86-93		Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B9) – October 2016	search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. The RMS indicates that the endocrine effects are observed at a concentration below but quite close to acute toxicity (100% mortality at 9.6µg/L), whereas lower concentrations were not tested. Study not found in the current literature search according to JMAFF guidelines.		
T-8-17	Ecotoxicity and animal toxicity – endocrine disruption	Padilla, S; Corum, D; Padnos, B; Hunter, DL; Beam, A; Houck, KA; Sipes, N; Kleinstreuer, N; Knudsen, T; Dix, DJ; Reif, DM	April 2012	Zebrafish developmental screening of the ToxCast™ Phase I chemical library.	Reproductive toxicology, 33(2):174-87	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B9) – October 2016	RMS indicates that the most sensitive endpoint in the ELS study was an increased dry weight, but this was not monitored in this study. Further, the lack of analytical verification the exposure levels makes the results unreliable. The study is not considered as useful for the risk assessment.	No	10.1016/j.reprotox.2011.10.018

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								Study not found in the current literature search according to JMAFF guidelines.		
T-8-18	Ecotoxicity and animal toxicity – effect on earthworms	Roark, JH; Dale, JL	1979	The Effect of Turf Fungicides on Earthworms.	Arkansas Academy of Science proceedings, Vol. XXXIII, 1979	US EPA	Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments in Support of the Registration Review of Thiophanate-Methyl and Carbendazim	US EPA indicates that exposure *to Eisenia fetida* to Thiophanate-methyl were also found to cause significant mortality. Study not found in the current literature search according to JMAFF guidelines.	Yes	https://scholarworks.uark.edu/cgi/viewcontent.cgi?article=2710&context=jaas
T-8-19	Ecotoxicity and animal toxicity – effect on earthworms	Stringer, A; Lyons, CH	1974	The Effect of benomyl and Thiophanate-methyl on earthworm populations in apple orchards.	Pesticide Science: 5: 189-196	US EPA	Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments in Support of the Registration Review of Thiophanate-	US EPA indicates five TM spray applications at 0.78 kg/ha resulted in observation of drastic earthworm population reductions in British apple orchards over a 1-3 year period. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/ps.2780050210

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							Methyl and Carbendazim			
T-8-20	Ecotoxicity and animal toxicity – risk to non-target arthropods	Czarnecka, M; Parma, P; Kulec-Płoszczyca, E	2014	Total effects of selected plant protection products applied to different natural substrates on the predatory mite *Typhlodromus pyri* Sch.	IOBC-WPRS Bulletin, 2014, 103, 51-60	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that The results indicate that an EC50 for mortality and reproduction based on the active ingredient is >2.004 kg/ha. However, the lack of detailed information (batch, purity, formulation type) on the test substance makes the results less reliable. Hence, the results must be regarded as supportive information and will not be used further in the risk assessment. Study not found in the current literature search according to JMAFF guidelines.	No	https://iobc-wprs.org/product/total-effects-of-selected-plant-protection-products-applied-to-different-natural-substrates-on-the-predatory-mite-typhlodromus-pyri-sch/
T-8-21	Ecotoxicity and animal toxicity – risk to non-target arthropods	Noernberg, SD; Gruetzmacher, AD; Kovaleski, A; Finatto, JA;	2011	Persistence of pesticides used in integrated production of apple to	Ciencia e Agrotecnologia, 35 (2): 305-313	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for	Study identified during the literature search and submitted by the applicant for the purpose of	No	10.1590/S1413-70542011000200011

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
		Fonseca Paschoal, MD		*Trichogramma pretiosum*.			Thiophanate-methyl (Volume 1 and Volume 3 CP B9) – October 2016	renewal of thiophanate-methyl. The study report was written in Portugese, and the summary was based on the applicant's M-III document. No details were given on the formulated product, except for the content of active ingredient and no information on the treatment rate per hectare. Hence, we agree with the applicant that the study seems to be of limited use for the risk assessment. Study not found in the current literature search according to JMAFF guidelines.		
T-8-22	E-fate	Cycon, M; M. Wojcik, M; Piotrowska-Seget, Z	2011	Biodegradation kinetics of the benzimidazole fungicide thiophanate - methyl by bacteria isolated from loamy sand soil.	Biodegradation, 3: 573-583	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B8) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl RMS agrees with applicant that the study is not relevant for risk assessment purpose.	No	10.1007/s10532-010-9430-4

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								Study not found in the current literature search according to JMAFF guidelines.		
T-8-23	E-fate	Singh, RK; Chakraborty, D; Sharma, DK	2005a	Adsorption behaviour of thiophanate-methyl on soil extracted humic acid.	Indian Journal of Agricultural Sciences, 75: 479-482.	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B8) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl RMS agrees with applicant that the study is not relevant for risk assessment purpose. Study not found in the current literature search according to JMAFF guidelines.	No	None
T-8-24	E-fate	Singh, RK; Chakraborty, D; Sharma, DK	2005b	Studies on adsorption behaviour of thiophanate methyl on soils.	Annals of Agricultural Research, 26: 286-290.	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B8) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl The RMS agrees with applicant to exclude the study. If equilibrium time is not mentioned the documentation is indeed too brief. Additionally, the soils	No	None

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								are not representative for EU. Study not found in the current literature search according to JMAFF guidelines.		
T-8-25	E-fate	Zhang, Z; Shan, W; Jian, Q; Gong, Y; Song, W; Liu, X	2012	Dissipation and residue of thiophanate-methyl and its metabolite in cucumber and soil under open land and greenhouse conditions.	Nongye Huanjing Kexue Xuebao, 6: 1077-1081.	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CP B8) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl The RMS agrees with applicant to exclude the study. In addition to the applicant's arguments, the soils are not representative for EU. Study not found in the current literature search according to JMAFF guidelines.	No	None

NA: not applicable as hits already found in the current literature search according to JMAFF guidelines

Table 24: Literature conformed to “Relevance assessment” by Step2 and reference cited the results as peer-reviewed open literature by EFSA, USEPA and JMPR for Carbendazim

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
C-8-1	Toxicity/adverse effects on human - B.6.1 Absorption, distribution, excretion and metabolism / KIIA 5.1	Jia L, Garza M, Wong H, Reimer D, Redelmeier T, Camden JB, Weitman SD	2002	Pharmacokinetic comparison of intravenous carbendazim and remote loaded carbendazim liposomes in nude mice.	Journal of Pharmaceutical and Biomedical Analysis, 28: 65-72	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study which results have no impact for the risk assessment. Only the serum was analysed for metabolites. Study considered not acceptable. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0731-7085(01)00702-6
C-8-2	Toxicity/adverse effects on human - B.6.1 Absorption, distribution, excretion and metabolism / KIIA 5.1	Jia L, Wong H, Wang Y, Garza M, Weitman SD	2003	Carbendazim: disposition, cellular permeability, metabolite identification, and pharmacokinetic comparison with its nanoparticle.	Journal of Pharmaceutical Sciences, 92: 161-172	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study with the aim of elucidating the influence of different liposomal formulations on the bioavailability of carbendazim as a drug. Study results with no relevance for the risk	No	10.1002/jps.10272

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								characterization. Study considered not acceptable. Study not found in the current literature search according to JMAFF guidelines.		
C-8-3	Toxicity/adverse effects on human - B.6.2.2.6 Additional oral studies / KIIA 5.2.1	Catalgol B, Catalgol S, Alpertunga B	2007	Effects of benomyl and carbendazim on lipid peroxidation and antioxidant system in kidney of rats following acute exposure.	Toxicology Letters, 172: S62-S63	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Benomyl (1 g/kg), carbendazim (0.64 g/kg) and benomyl+carbendazim (0.1+0.064 g/kg) were administered orally for one day to rats (group size, strain, sex and age not reported). In homogenates of kidney, malondialdehyde and GGT were increased, GSH levels were decreased. Superoxide dismutase, catalase, glutathione peroxidise activities were unchanged. The results cannot be assessed independently as no summarising or individual values were presented and are	No	10.1016/j.toxlet.2007.05.186

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								therefore not acceptable. Study not found in the current literature search according to JMAFF guidelines.		
C-8-4	Toxicity/adverse effects on human - B.6.2.2.6 Additional oral studies / KIIA 5.2.1	Lisovska V, Shulyak V, Nedoputanska N	2005	Carbendazim administration to the blood system of rats.	Toxicology Letters, 158: S141-S141	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. A dose of 750 mg/kg bw carbendazim was orally administered to male Wistar rats (6 animals/group). Peripheral blood was analysed. Erythrocytes, haemoglobin and reticulocytes were decreased. Acanthocytes and atypical lymphocytes were seen. The results cannot be assessed independently as no (summarising or individual) values were presented and are therefore not acceptable. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.1016/j.toxlet.2005.05.014

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
C-8-5	Toxicity/adverse effects on human - B.6.2.2.6 Additional oral studies / KIIA 5.2.1	Janardhan, A., Rao, A.B., Sisodia, P.	1986	Species variation in acute toxicity of monocrotophos and methyl benzimidazole carbamate.	Indian Journal of Pharmacology, 18: 102-103	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. LD_{50} and LC_{50} values after seven days were graphically determinated for monocrotophos and carbendazim (methyl benzimidazole carbamate) using different routes and animals. Study not found in the current literature search according to JMAFF guidelines.		https://journals.lww.com/iphr/abstract/1986/18020/species_variation_in_acute_toxicity_of.10.aspx
C-8-6	Toxicity/adverse effects on human - B.6.2.3.4 Additional percutaneous study / KIIA 5.2.2	Muthuvivegandandavel,V., Muthuraman,P., Muthu,S., Srikumar,K.	2008	Toxic effects of carbendazim at low dose levels in male rats.	Journal of Toxicological Sciences, 33: 25-30	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Carbendazim (analytical grade, obtained form Gharada Chemicals, Mumbai, India) was dissolved in corn oil in concentrations of 5, 10 and 50 mM. The solution was administered intradermaly (volume	Yes	10.2131/jts.33.25

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								not given) to male rats (Wistar, C-8-10 wk old, 6 animals/group). After 6 h, haematology, clinical chemistry parameters were measured and liver was fixed and prepared for histological evaluation. Some statistical significant changes were found. Further on, “portal vein congestion, enlargement of sinusoids, increase in the number of liver Kupffer cells and mononuclear cell infiltration in the liver, were observed”. “Hydropic degeneration of hepatocytes was also observed”. The authors interpreted these findings as treatment related, however, no incidences were reported, making it difficult to assess the findings independently. Study not found in the current literature search according to JMAFF guidelines.		

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
C-8-7	Toxicity/adverse effects on human - B.6.3.4 Additional short-term toxicity studies / KIIA 5.3.2	Barlas N, Selmanoglu G, Kockaya A, Songur S	2002	Effects of carbendazim on rat thyroid, parathyroid, pituitary and adrenal glands. and their hormones.	Human and Experimental Toxicology, 21: 217-221	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Only a limited set of parameters was evaluated. Considering the body weight data in each report, it seems as if all results are based on one animal study. Groups of 10 male Wistar Swiss albino rats were treated daily with dose levels of 0, 150, 300 and 600 mg/kg bw/d for 15 weeks. Carbendazim (supplied by Agro-San, Kirklareli, Turkey, purity: 98 %) was dissolved in corn oil once weekly. One control group received no treatment, whereas a second group received vehicle alone. Pituitary and adrenal weight were not changed by the treatment. T3 levels were increased in mid dose group but not in other dose groups. Levels of T4, TSH, ACTH and growth hormone were not	Yes	10.1191/0960327102ht187oa

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								altered. In thyroid, damaged and expanded follicles, lymphoid cell infiltration were seen in all dose levels, congestion and enlargement of interstitial tissue were seen in mid and high dose groups. In parathyroid, cellular degeneration and congestion were observed in all dose groups; amyloid lesions were seen in mid and high dose groups. In adrenal, cellular degeneration and lipid droplets were reported in all dose groups, oedema was reported in mid and high dose groups. Study not found in the current literature search according to JMAFF guidelines.		
C-8-8	Toxicity/adverse effects on human - B.6.3.4 Additional short-term toxicity studies / KIIA 5.3.2	Selmanoglu G, Barlas N, Songur S, Kockaya EA	2001	Carbendazim-induced haematological, biochemical and histopathological changes to the liver and kidney of male rats.	Human and Experimental Toxicology, 20: 625 - 630	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Only a limited set of parameters was evaluated. Considering the body	Yes	10.1191/0960327017188906 03

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								weight data in each report, it seems as if all results are based on one animal study. Groups of 10 male Wistar Swiss albino rats were treated daily with dose levels of 0, 150, 300 and 600 mg/kg bw/d for 15 weeks. Carbendazim (supplied by Agro-San, Kirklareli, Turkey, purity: 98 %) was dissolved in corn oil (275 µL/rat per day) once weekly. One control group received no treatment, whereas a second group received vehicle alone. After 15 weeks of treatment various clinical chemistry values were significantly changed in the high dose group (increased parameters: albumin, glucose, creatinine, cholesterol; decreased parameter: VLDL). Counts of white blood cells and lymphocytes were significantly decreased in all dose groups. In all dose groups in the livers congestion in portal vein and mononuclear cell infiltration were seen,		

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								additionally in mid and high dose group: hydropic degeneration. In kidneys of all dose groups, tubular degeneration, congestion and mononuclear cell infiltration were seen, additionally in mid and high dose groups: fibrosis. Relative (but not absolute) liver weight was decreased. Body weight and kidney weight were comparable to weights in control group. Study not found in the current literature search according to JMAFF guidelines.		
C-8-9	Toxicity/adverse effects on human - B.6.3.4 Additional short-term toxicity studies / KIIA 5.3.2	Songür SH, Kockaya EA, Selmanoglu G, Barlas N	2005	Dose-dependent effects of carbendazim on rat thymus.	Cell Biochemistry and Function,23: 457-460	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Only a limited set of parameters was evaluated. Considering the body weight data in each report, it seems as if all results are based on one animal study. Groups of 10 male Wistar Swiss albino	No	10.1002/cbf.1181

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								rats were treated daily with dose levels of 0, 150, 300 and 600 mg/kg bw/d for 15 weeks. Carbendazim (supplied by Agro-San, Kirklareli, Turkey, purity: 98 %) was dissolved in corn oil once weekly. One control group received no treatment, whereas a second group received vehicle alone. Relative thymus weight was reduced in all dose groups, absolute thymus weight was reduced in high dose group only. Fibrosis and oedema were seen in thymus of mid and high dose groups. Fibronectin localisation in capsules and interstitial connective tissue in all dose groups was more intense than in control group. Study not found in the current literature search according to JMAFF guidelines.		
C-8-10	Toxicity/adverse effects on human - B.6.3.4 Additional	Janardhan, A., Rao, A.B. and Sisodia, P.	1987	Sub-chronic toxicity of methyl benzimidazole carbamate in rats.	Bulletin of Environmental Contamination and Toxicology, 38: 890-898.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for	Study identified during the literature search and submitted by the applicant for	No	10.1007/BF01616717

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	short-term toxicity studies / KIIA 5.3.2						carbendazim (Volume 3 B6)	the purpose of renewal of carbendazim. In a 90-day oral toxicity study in Wistar rats, carbendazim technical was given at 0, 16, 32 or 64 mg/kg bw/d to groups of 10 rats/sex/dose. Decreased body weights were seen in all treated groups. Examination of blood and serum samples revealed adverse effects on haematology as well as clinical biochemistry parameters. Increased organ/body weight ratios were noted, which may also be the result of the decrease seen in body weights. Degenerative lesions in the liver and kidneys and an inflammatory response in the lungs were noted upon microscopic examination. A NOEL could not be established. Study not found in the current literature		

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								search according to JMAFF guidelines.		
C-8-11	Toxicity/adverse effects on human - B.6.3.4 Additional short-term toxicity studies / KIIA 5.3.2	Janardhan, A., Rao, A.B. and Sisodia, P.	1988	Short-term toxicity of methyl benzimidazole carbamate in dogs.	Bulletin of Environmental Contamination and Toxicology, 41: 704-711	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. In a 90-day oral toxicity study in mongrel dogs, carbendazim technical was given at 0, 20, 40 or 80 mg/kg bw/d to groups of 3 dogs/sex/dose. Low haemoglobin, decreased number of leukocytes and variation in erythrocyte count were noted. Clinical biochemistry parameters revealed an increase in ALAT, ASAT, urea and total bilirubin. At necropsy increased liver and spleen weights were noted in males, decreased adrenal, testes and ovary weights in males and/or females and decreased spleen weights in females. Dose related degenerative lesions were noted in the liver and kidneys, in the	No	10.1007/BF02021022

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								liver accompanied with inflammatory reactions. A NOEL was not established. Study not found in the current literature search according to JMAFF guidelines.		
C-8-12	Toxicity/adverse effects on human - B.6.3.4 Additional short-term toxicity studies / KIIA 5.3.2	Lukowicz-Ratjczak, J.; Gadomska, J.; Krechniak, J.	1985	Effect of carbendazim on selected diagnostic indices in rat.	Bromatologia i Chemia Toksykologiczna, 18: 197-201	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. 12-week study, rat. Minimal alterations in blood chemistry were observed. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/jbt.23079
C-8-13	Toxicity/adverse effects on human - B.6.3.4 Additional short-term toxicity studies / KIIA 5.3.2	Cempel, M.; Krechniak, J.	1985	Effect of carbendazim on some blood plasma enzymes activities.	Bromatologia i Chemia Toksykologiczna, 18: 133-136	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. 12-week study, rat. Minimal alterations in blood chemistry occurred. Study not found in the current literature	No	None

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								search according to JMAFF guidelines.		
C-8-14	Toxicity/adverse effects on human – Genotoxicity -B.6.4.2 In vitro genotoxicity testing/ KIIA 5.4.1	de Stoppelaar JM, van de KT, Bedaf M, Verharen HW, Slob W, Mohn GR, Hoebee B, van Benthem J	1999	Increased frequencies of diploid sperm detected by multicolour FISH after treatment of rats with carbendazim without micronucleus induction in peripheral blood erythrocytes.	Mutagenesis, 14: 621-632	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6) And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study on genotoxicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/mutage/14.6.621
C-8-15	Toxicity/adverse effects on human – Genotoxicity -B.6.4.2 In vitro genotoxicity testing/ KIIA 5.4.1	Zdzienicka, M., Kuzma, E. Szymczyk, T.	1983	The mutagenic properties of carbendazime and benomyl in bacteriological systems.	Bromatologia i Chemia Toksykologiczna, 1: 43 - 48	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on mutagenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	None
C-8-16	Toxicity/adverse effects on human –	Banduhn, N. Obe, G.	1985	Mutagenicity of methyl 2-benzimidazolecarba	Mutation Research, 156: 199-218.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of	Study identified during the literature search and submitted	No	10.1016/0165-1218(85)90065-5

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
	Genotoxicity -B.6.4.2 In vitro genotoxicity testing/ KIIA 5.4.2			mate, diethylstilbestrol and estradiol: Structural chromosomal aberrations, sister-chromatid exchanges, C-mitoses, polyploidies and micronuclei.			Council Directive 91/414/EEC for carbendazim (Volume 3 B6) and Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	by the applicant for the purpose of renewal of carbendazim. Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study on mutagenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-17	Toxicity/adverse effects on human – Genotoxicity -B.6.4.3 In vivo genotoxicity testing (somatic cells) – Mouse spot tests/ KIIA 5.4.2; 5.4.4 and 5.4.5	Fahrig, R. and Seiler, J.P.	1979	Dose and effect of methyl-2-benzimidazolylcarbamate in the "mammalian spot test", an in vivo method for the detection of genetic alterations in somatic cells of mice.	Chemical-Biological Interactions, 26: 115-120	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim *in vivo*. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0009-2797(79)90097-8
C-8-18	Toxicity/adverse effects on human – Genotoxicity -B.6.4.3 In vivo genotoxicity testing	Lamb, M.J. Lilly, L.J.	1980	An investigation of some genetic toxicological effects of the fungicide benomyl.	Toxicology, 17: 83-95.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim.	No	10.1016/0300-483x(80)90030-x

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
	(somatic cells) – Studies in insects (Drosophila melanogaster) / KIIA 5.4.2; 5.4.4 and 5.4.5						And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study on genotoxicity of carbendazim *in vivo*. Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-19	Toxicity/adverse effects on human – Genotoxicity -B.6.4.3 In vivo genotoxicity testing (somatic cells) – Studies in insects (Drosophila melanogaster) / KIIA 5.4.4	Mollet, P.	1976	Lack of proof of induction of somatic recombination and mutation in drosophila by methyl-2-benzimidazole carbamate, dimethyl sulfoxide and acetic acid.	Mutation Research, 40: 383-388	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim *in vivo*. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1218(76)90037-9
C-8-20	Toxicity/adverse effects on human – Genotoxicity - B.6.4.3.3 Structural chromosomal aberrations / KIIA 5.4.4 and KIIA 5.8	Seiler, J.P.	1976	The mutagenicity of benzimidazole and benzimidazole derivatives. VI. Cytogenetic effects of benzimidazole derivatives in the bone marrow of the mouse and the Chinese hamster.	Mutation Research, 40, 1976, 339-347.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6) And	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on mutagenicity of carbendazim *in vivo*.	No	10.1016/0165-1218(76)90032-x

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-21	Toxicity/adverse effects on human – Genotoxicity -B.6.4.3.7 Aneuploidy/micronucleus assay in mouse bone marrow/ KIIA 5.4.2 and 5.4.4	Sarrif, A.M., Bentley, K.S., Fu, L.-J., O'Neil, R.M., Reynolds, V.L. Stahl, R.G.	1994	Evaluation of benomyl and carbendazim in the in vivo aneuploidy/ micronucleus assay in BDF1 mouse bone marrow.	Mutation Research, 310: 143-149.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6) And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim *in vivo*. Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0027-5107(94)90018-3
C-8-22	Toxicity/adverse effects on human – Genotoxicity -B.6.4.4.1.3 Additional studies/ KIIA 5.4.1	Matsuo, F., Nakai, M., Nasu, T.	1999	The fungicide carbendazim induces meiotic micronuclei in the spermatids of the rat testis.	The Journal of Veterinary Medical Science, 61: 573-576	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim.	Yes	10.1292/jvms.61.573

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study on genotoxicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-23	Toxicity/adverse effects on human – Genotoxicity -B.6.4.4.1.3 Additional studies/ KIIA 5.4.5	Barale, R., Scapoli, C., Meli, C., Casini, D., Minunni, M., Marrazzini, A., Loprieno, N., Barrai, I.	1993	Cytogenetic effects of benzimidazoles in mouse bone marrow.	Mutation Research, 300: 15-28	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1218(76)90032-x
C-8-24	Toxicity/adverse effects on human – Genotoxicity -B.6.4.4.1.3 Additional studies/ KIIA 5.4.5	Zelesco, P.A., Barbieri, I., Graves, J.A.M.	1990	Use of a cell hybrid test system to demonstrate that benomyl induces aneuploidy and polyploidy.	Mutation Research, 242: 329-335.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim. Study not found in the current literature	No	10.1016/0165-1218(90)90051-3

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								search according to JMAFF guidelines.		
C-8-25	Toxicity/adverse effects on human – Genotoxicity -B.6.4.2.3.2 Additional tests with yeast and fungi/ KIIA 5.4.1	Nirenberg, H.I., Speakman, J.B.	1981	The pH dependence of the mutagenicity of methyl benzimidazol-2-yl carbamate (MBC) towards aspergillus nidulans (Eidam) winter and cladosporium cucumerinum Ellis & Arth.	Mutation Research, 88: 53-59	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1218(81)90089-6
C-8-26	Toxicity/adverse effects on human – Genotoxicity -B.6.4.2.3.2 Additional tests with yeast and fungi/ KIIA 5.4.1	Speakman, J.B. Nirenberg, H.I.	1981	Mutagenicity of methyl benzimidazol-2-yl carbamate (MBC) towards aspergillus nidulans (Eidam) winter and cladosporium cucumerinum Ellis & Arth.	Mutation Research, 88: 45-51	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on genotoxicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1218(81)90088-4
C-8-27	Toxicity/adverse effects on human - Genotoxicity - B.6.4.5 Further data to support the establishment of a threshold level for	Elhajouji, A., Van Hummelen, P., Kirsch-Volders, M.	1995	Indications for a threshold of chemically-induced aneuploidy in vitro in human lymphocytes.	Environmental & Molecular Mutagenesis, 26: 292-304	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6) And	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim.	No	10.1002/em.2850260405

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	aneugenic effects of carbendazim / KIIA 5.4						And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim Study not found in the current literature search according to JMAFF guidelines.		
C-8-28	Toxicity/adverse effects on human – Genotoxocity -B.6.4.5 Further data to support the establishment of a threshold level for aneugenic effects of carbendazim / KIIA 5.4	Georgieva, V., Vachkova, R., Tzoneva, M., Kappas, A.	1990	Genotoxic activity of benomyl in different test systems.	Environmental & Molecular Mutagenesis, 16:32-36	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/em.2850160106
C-8-29	Toxicity/adverse effects on human – Genotoxicity - B.6.4.5 Further data to support the establishment of a threshold level for aneugenic effects of	Jeffay, S.C., Libbus, B.L., Barbee, R.R., Perreault, S.D.	1996	Acute exposure of female hamsters to carbendazim (MBC) during meiosis results in aneuploid oocytes with subsequent arrest of embryonic cleavage and implantation.	Reproductive Toxicology, 10: 183 - 189	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6) And Updated reasoned opinion on the	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim.	No	10.1016/0890-6238(96)00020-2

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
	carbendazim / KIIA 5.4						toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-30	Toxicity/adverse effects on human – Genotoxicity - B.6.4.5 Further data to support the establishment of a threshold level for aneugenic effects of carbendazim / KIIA 5.4	Kochendorfer, U., Stammberger, I., Mayer, D., Schwanitz, G.	1996	A new possible parameter for the detection of aneuploidy inducing substances: the analysis of qualitative and quantitative abnormalities of the spindle apparatus.	Mutation Research, 361: 55-66	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0165-1161(96)90239-3
C-8-31	Toxicity/adverse effects on human – Genotoxicity - B.6.4.5 Further data to support the establishment of a threshold level for aneugenic effects of carbendazim / KIIA 5.4	Parry, J.M.	1998	Detecting chemical aneugens: a commentary to 'Aneuploidy: a report of an ECETOC task force'.	Mutation Research, 410: 117 - 120	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.1016/s1383-5742(97)00031-8

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
C-8-32	Toxicity/adverse effects on human – Genotoxicity - B.6.4.5 Further data to support the establishment of a threshold level for aneugenic effects of carbendazim / KIIA 5.4	Parry, J.M., Fielder, R,J., McDonald, A.	1994	Thresholds for aneuploidy-inducing chemicals. Advisory Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment of the UK Department of Health.	Mutagenesis, 9: 503 504	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/mutage/9.6.503
C-8-33	Toxicity/adverse effects on human – Genotoxicity - B.6.4.5 Further data to support the establishment of a threshold level for aneugenic effects of carbendazim / KIIA 5.4	Parry JM, Jenkins GJ, Haddad F, Bourner R, Parry EM	2000	In vitro and in vivo extrapolations of genotoxin exposures: consideration of factors which influence dose-response thresholds.	Mutation Research, 464: 53-63	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on aneugenic activity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.1016/s1383-5718(99)00166-7
C-8-34	Toxicity/adverse effects on human – Genotoxicity	Amer,S.M., Donya,S.M., and Aly,F.A.E.	2003	Genotoxicity of benomyl and its residues in somatic and germ cells of mice fed on treated stored wheat grains.	Archives of Toxicology, 77:712-721.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with	No	10.1007/s00204-003-0464-9

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								a focus on genotoxicity (induction of aneuploidy) Study not found in the current literature search according to JMAFF guidelines.		
C-8-35	Toxicity/adverse effects on human – Genotoxicity	Ashby,J. and Tinwell,H.	2001	Continuing ability of the rodent bone marrow micronucleus assay to act as a predictor of the possible germ cell mutagenicity of chemicals	Mutation Research, 478:211-213	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on genotoxicity (induction of aneuploidy) Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0027-5107(01)00129-4
C-8-36	Toxicity/adverse effects on human – Genotoxicity	de Stoppelaar, J.M., van de,K.T., Verharen,H.W., Hokse,H., Opperhuizen,A., Mohn,G.R., van Benthem,J.,	2000	In vivo cytokinesis blocked micronucleus assay with carbendazim in rat fibroblasts and comparison with in vitro assays.	Mutagenesis, 15:155-164.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on genotoxicity	No	10.1093/mutage/15.2.155

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		and Hoebee,B.						(induction of aneuploidy) Study not found in the current literature search according to JMAFF guidelines.		
C-8-37	Toxicity/adverse effects on human – Genotoxicity	Mahmood, R. and Parry,J.	2008	Short-term exposure to carbendazim induces micronuclei in cultured human peripheral blood lymphocytes.	Mutagenesis, 16:561	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on genotoxicity (induction of aneuploidy) Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/mutage/16.6.557
C-8-38	Toxicity/adverse effects on human – Genotoxicity	Vanhauwaert,A., Vanparys,P., and Kirsch-Volders,M.	2001	The in vivo gut micronucleus test detects clastogens and aneugens given by gavage.	Mutagenesis, 16:39-50	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on genotoxicity (induction of aneuploidy)	No	10.1093/mutage/16.1.39

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								Study not found in the current literature search according to JMAFF guidelines.		
C-8-39	Toxicity/adverse effects on human – Genotoxicity	Adler,I.D., Schmid,T.E., and Baumgartner,A.	2002	Induction of aneuploidy in male mouse germ cells detected by the sperm-FISH assay: a review of the present data base.	Mutation Research, 504:173-182	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0027-5107(02)00090-8
C-8-40	Toxicity/adverse effects on human – Genotoxicity	Decordier,I., Dillen,L., Cundari,E., and Kirsch-Volders,M.	2002	Elimination of micronucleated cells by apoptosis after treatment with inhibitors of microtubules.	Mutagenesis, 17:337-344	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature	No	10.1093/mutage/17.4.337

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								search according to JMAFF guidelines.		
C-8-41	Toxicity/adverse effects on human – Genotoxicity	Fellows,M., Doherty,A., Hayes,J., Thompson, A., and O'Donovan ,A.R.	2005	In the mouse lymphoma TK assay, are TK-/- mutant clones formed following treatment with the aneugen Carbendazim monosomic for chromosome 11?	Mutagenesis, 20:482	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/toxsci/kfp037
C-8-42	Toxicity/adverse effects on human – Genotoxicity	Igarashi,M., Setoguchi, M., Takada,S., Itoh,S., and Furuhama, K.	2006	Micronucleus induction in the mouse liver by numerical chromosome aberration inducers.	Environmental and Molecular Mutagenesis, 47:437	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/em.20241

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C-8-43	Toxicity/adverse effects on human – Genotoxicity	Igarashi,M., Setoguchi, M., Takada,S., Itoh,S., and Furuhama, K.	2007	Optimum conditions for detecting hepatic micronuclei caused by numerical chromosome aberration inducers in mice.	Mutation Research-Genetic Toxicology and Environmental Mutagenesis, 632:89-98.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/j.mrgentox.2007.04.012
C-8-44	Toxicity/adverse effects on human – Genotoxicity	Kirsch-Volders,M., Vanhauwaert,A., Eichenlaub-Ritter,U., and Decordier,I.	2003	Indirect mechanisms of genotoxicity.	Toxicology Letters, 140:63-74	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0378-4274(02)00498-8
C-8-45	Toxicity/adverse effects on human – Genotoxicity	McCarroll, N.E., Protzel,A., Ioannou,Y.,	2002	A survey of EPA/OPP and open literature on selected pesticide chemicals.	Mutation Research, 512:1-35	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive	Study identified during the level 4 (Demand for further information) of	No	10.1016/s1383-5742(02)00026-1

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		Frank Stack,H.F., Jackson,M. A., Waters,M. D., and Dearfield,K .L.		III. Mutagenicity and carcinogenicity of benomyl and carbendazim.			91/414/EEC for carbendazim (Volume 1)	renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of genotoxicity. Study not found in the current literature search according to JMAFF guidelines.		
C-8-46	Toxicity/adverse effects on human – Genotoxicity	Albertini S,	1989	Influence of different factors on the induction of chromosome malsegregation in Saccharomyces cerevisiae D61.M by bavistan and assessment of its genotoxic property in the Ames test and in Saccharomyces cerevisiae D7.	Mutation research, 216: 327-340	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1161(89)90043-5
C-8-47	Toxicity/adverse effects on human – Genotoxicity	Bowen DE, Whitwell JH, Lillford L, Henderson D, Kidd D, McGarry S, Pearce G, Beevers C and Kirkland DJ,	2011	Evaluation of a multi-endpoint assay in rats, combining the bone-marrow micronucleus test, the Comet assay and the flow-cytometric peripheral blood micronucleus test	Mutation Research 722 (2011) 7–19. doi:10.1016/j.mrgentox.2011.02.009	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study found in the current literature search according to JMAFF guidelines and classified as relevant Category “c” (hit number C-6-2-7	NA	NA

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								)		
C-8-48	Toxicity/adverse effects on human – Genotoxicity	Coffing S, Engel M, Dickinson D, Thiffeault C, Spellman R, Shutsky T and Schuler M,	2011	The rat gut micronucleus assay: a good choice for alternative in vivo genetic toxicology testing strategies.	Environmental and Molecular Mutagenesis 52:269-279	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study found in the current literature search according to JMAFF guidelines and classified as not relevant after initial rapid relevance assessment because not considered as a data requirement according to JMAFF Guidelines No.6278 (hit listed in excel spreadsheet ("Carbendazim after step 3 Tox first search with update - Final after NS October 2024 - with list nb.xlsx") at line 86).	No	10.1002/em.20616
C-8-49	Toxicity/adverse effects on human – Genotoxicity	Elhajouji A, Tibaldi F, Kirsch-Volders	1997	Indication for thresholds of chromosome non-disjunction versus chromosome lagging induced by spindle inhibitors in vitro in human lymphocytes.	Mutagenesis, 12 (3): 133-140	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/mutage/12.3.133

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C-8-50	Toxicity/adverse effects on human – Genotoxicity	Friedman PA and Platzer EG	1978	Interaction of anthelmintic benzimidazoles and benzimidazole derivatives with bovine brain tubulin.	Biochimica et Biophysica Acta, 544: 605-614	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0304-4165(78)90334-3
C-8-51	Toxicity/adverse effects on human – Genotoxicity	Gudi R, Sandhu SS and Athwal RS	1990	Kinetochore identification in micronuclei in mouse bone-marrow erythrocytes: An assay for the detection of aneuploidy-inducing agents.	Mutation Research, 234: 263-268	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1161(90)90038-P
C-8-52	Toxicity/adverse effects on human – Genotoxicity	Marshall RR, Murphy M, Kirkland DJ and Bentley KS	1996	Fluorescence in situ hybridisation with chromosome-specific centromeric probes: a sensitive method to detect aneuploidy.	Mutation Research 372: 233-245	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0027-5107(96)00143-1
C-8-53	Toxicity/adverse effects on human – Genotoxicity	Seiler JP,	1980	Evaluation of some pesticides for mutagenicity	Pesticide Mutagenicity: 39C-8-404.	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim.	No	None

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							substances carbendazim and thiophanate-methyl. (2004a)	Study not found in the current literature search according to JMAFF guidelines.		
C-8-54	Toxicity/adverse effects on human – Genotoxicity	Vigreux C, Poul JM, Deslandes E, Lebailly P, Godard T, Sichel F, Henry-Amar M and Gauduchon P,	1998	DNA damaging effects of pesticides measured by the single cell gel electrophoresis assay (comet assay) and the chromosomal aberration test, in CHOK1 cells.	Mutation Research, 419: 79–90	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s1383-5718(98)00126-0
C-8-55	Toxicity/adverse effects on human – Genotoxicity	Wang TC, Wu CL, Lin JH, Tarn CY and Lin SY,	1987	Sister chromatid exchanges and chromosome aberrations induced by pesticide combinations in Chinese hamster ovary cells.	Bull. Institute of Zoology, Academia Sinica, 26(4): 317-329	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	Yes	https://zoolstud.sinica.edu.tw/Journals/26.4/317.pdf
C-8-56	Toxicity/adverse effects on human – Genotoxicity	Whittaker SG, Moser SF, Maloney DH, Piegorsch WW, Resnick MA and Fogel S,	1990	The detection of mitotic and meiotic chromosome gain in the yeast Saccharomyces cerevisiae: Effects of methyl benzimidazol-2-yl carbamate, methyl methanesulfonate, ethyl methanesulfonate, dimethyl sulfoxide, propionitrile and	Mutation Research, 242: 231-258	EFSA	Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0165-1218(90)90089-k

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				cyclophosphamide monohydrate.						
C-8-57	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.1 and KIIA 5.6.2	Carter, S.D., Hess, R.A., Laskey, J.W.	1987	The fungicide methyl 2-benzimidazole carbamate causes infertility in male Sprague-Dawley rats.	Biology of Reproduction, 37: 709-717	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive and developmental toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1095/biolreprod37.3.709
C-8-58	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.1	Gray, L.E., Ostby, J., Linder, R., Goldman, J., Rehnberg, G. Cooper, R.	1990	Carbendazim-induced alterations of reproductive development and function in the rat and hamster.	Fundamental and Applied Toxicology, 15: 281-297	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0272-0590(90)90055-o
C-8-59	Toxicity/adverse effects on human - B.6.6.4.2 Effects on pregnancy/ KIIA 5.6.2	Cummings, A.M., Ebron-McCoy, M.T., Rogers, J.M.,	1992	Developmental effects of methyl benzimidazolecarbamate followin exposure during early pregnancy.	Fundamental and Applied Toxicology, 18: 28C-8-293.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim.	No	10.1016/0272-0590(92)90057-o

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		Barbee, B.D. Harris, S.T.						Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-60	Toxicity/adverse effects on human - B.6.6.4.2 Effects on pregnancy/ KIIA 5.6.2	Cummings, A.M., Harris, S.T. Rehnberg, G.L.	1990	Effects of methyl benzimidazolecarbamate during early pregnancy in the rat.	Fundamental and Applied Toxicology, 15: 52C-8-535.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0272-0590(90)90039-m
C-8-61	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.2	Lim J., Miller, M.G.	1997	The Role of the Benomyl Metabolite Carbendazim in Benomyl-Induced Testicular Toxicity.	Toxicology and applied Pharmacology 142 Article No. TO968042	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1006/taap.1996.8042

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C-8-62	Toxicity/adverse effects on human - B.6.6.4.2 Effects on pregnancy/ KIIA 5.6.2	Minta, M. and Biernacki, B.	1982	Embryotoxicity of carbendazim in hamsters, rats and rabbits.	Bulletin of the Veterinary Institute in Pulawy, 2 (1-4): 42-52	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on developmental toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	None
C-8-63	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.6	Evenson, D.P., Janca, F.C., Jost, L.K.	1987	Effects of the fungicide methyl-benzimidazol-2-yl carbamate (MBC) on mouse germ cells as determined by flow cytometry.	Journal of Toxicology and Environmental Health, 20: 387-399	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1080/15287398709530992
C-8-64	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.6	Hess, R.A., Moore, B.J., Forrer, J., Linder, R.E. Abuel-Atta, A.A.	1991	The fungicide benomyl (methyl 1-(butylcarbamoyl)-2-benzimidazolecarbamate) causes testicular dysfunction by inducing the sloughing of germ	Fundamental and Applied Toxicology, 17: 733-745.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim.	No	10.1016/0272-0590(91)90181-3

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				cells and occlusion of efferent ductules.				Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.		
C-8-65	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.9	Goldman, J.M., Rehnberg, G.L., Cooper, R.L., Gray, L.E., Hein, J. F. McElroy, W.K.	1989	Effects of the benomyl metabolite, carbendazim, on the hypothalamic-pituitary reproductive axis in the male rat.	Toxicology, 57: 173-182.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0300-483x(89)90163-7
C-8-66	Toxicity/adverse effects on human - B.6.6.4.1.3 Additional mechanistic studies/ KIIA 5.6.6	Rehnberg, G.L., Cooper, R.L., Goldman, J.M., Gray, L.E., Hein, J. F. McElroy, W.K.	1989	Serum and testicular testosterone and androgen binding protein profiles following subchronic treatment with carbendazim.	Toxicology and Applied Pharmacology, 101: 55-61.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on reproductive toxicity effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/0041-008x(89)90211-1

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C-8-67	Toxicity/adverse effects on human – Reproductive toxicity	Correa,L.M., Nakai,M., Strandgaard,C.S., Hess,R.A., and Miller,M.G.	2002	Microtubules of the mouse testis exhibit differential sensitivity to the microtubule disruptors carbendazim and colchicine.	Toxicological Sciences, 69:175-182.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/toxsci/69.1.175
C-8-68	Toxicity/adverse effects on human – Reproductive toxicity	Gotoh,Y., Netsu,J., Nakai,M., and Nasu,T.	1999	Testicular damage after exposure to carbendazim depends on the number of patent efferent ductules.	Journal of Veterinary and Medical Sciences, 61:755-760	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.1292/jvms.61.755
C-8-69	Toxicity/adverse effects on human – Reproductive toxicity	Lu,S.Y., Liao,J.W., Kuo,M.L., Wang,S.C., Hwang,J.S.	2004	Endocrine-disrupting activity in carbendazim-induced reproductive and developmental toxicity in rats.	Journal of Toxicology and Environmental Health-Part A-Current Issues, 67:1501-1515	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim.	No	10.1080/15287390490486833

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		, and Ueng,T.H.					carbendazim (Volume 1)	Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.		
C-8-70	Toxicity/adverse effects on human – Reproductive toxicity	Lu,S.Y., Liao,J.W., Kuo,M.L., Hwang,J.S., and Ueng,T.H.	2006	Antagonistic and synergistic effects of carbendazim and flutamide exposures in utero on reproductive and developmental toxicity in rats.	Journal of Food and Drug Analysis, 14:120-132	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.38212/2224-6614.2491
C-8-71	Toxicity/adverse effects on human – Reproductive toxicity	Maranghi,F., Macri,C., Ricciardi,C., Stazi,A.V., Rescia,M., and Mantovani, A.	2003	Histological and histomorphometric alterations in thyroid and adrenals of CD rat pups exposed in utero to methyl thiophanate.	Reproductive Toxicology, 17:617-623	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity.	No	10.1016/s0890-6238(03)00105-9

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								Study not found in the current literature search according to JMAFF guidelines.		
C-8-72	Toxicity/adverse effects on human – Reproductive toxicity	Markelewicz,R.J., Hall,S.J., and Boekelheide,K.	2004	2,5-hexanedione and carbendazim coexposure synergistically disrupts rat spermatogenesis despite opposing molecular effects on microtubules.	Toxicological Sciences, 80:92-100	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1093/toxsci/kfh140
C-8-73	Toxicity/adverse effects on human – Reproductive toxicity	Moffit,J.S., Bryant,B.H., Hall,S.J., and Boekelheide,K.	2007	Dose-dependent effects of sertoli cell toxicants 2,5-hexanedione, carbendazim, and mono-(2-ethylhexyl) phthalate in adult rat testis.	Toxicologic Pathology, 35:719-727	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1080/01926230701481931

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C-8-74	Toxicity/adverse effects on human – Reproductive toxicity	Nakai,M., Miller,M.G., Carnes,K., and Hess,R.A.	2002	Stage-specific effects of the fungicide carbendazim on Sertoli cell microtubules in rat testis.	Tissue Cell, 34:73-80	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0040-8166(02)00006-x
C-8-75	Toxicity/adverse effects on human – Reproductive toxicity	Rajeswary, S., Mathew,N., Akbarsha, M.A., Kalyanasundram,M., and Kumaran,B.	2007a	Protective effect of vitamin E against carbendazim-induced testicular toxicity-histopathological evidences and reduced residue levels in testis and serum.	Archives of Toxicology, 81:813-821	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1007/s00204-007-0204-7
C-8-76	Toxicity/adverse effects on human – Reproductive toxicity	Rajeswary, S., Kumaran,B., Ilangovan, R.,	2007b	Modulation of antioxidant defense system by the environmental fungicide	Reproductive Toxicolology, 24:371 - 380	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim.	No	10.1016/j.reprotox.2007.03.010

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
		Yuvaraj,S., Sridhar,M., Venkataraman,P., Srinivasan, N., and Aruldhas, M.M.		carbendazim in Leydig cells of rats.			carbendazim (Volume 1)	Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.		
C-8-77	Toxicity/adverse effects on human – Reproductive toxicity	Sitarek,K.	2001	Embryolethal and teratogenic effects of carbendazim in rats.	Teratogenesis, Carcinogenesis, and Mutagenesis, 21:335-340	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potential key study for Annex I renewal with a focus on reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/tcm.1021
C-8-78	Toxicity/adverse effects on human – Reproductive toxicity	Correa,L.M. and Miller,M.G.	2001	Microtubule depolymerisation in rat seminiferous epithelium is associated with diminished tyrosination of alpha-tubulin.	Biology of Reproduction, 64:1644-1652	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better	No	10.1095/biolreprod64.6.1644

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								interpretation of reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.		
C-8-79	Toxicity/adverse effects on human – Reproductive toxicity	Minta,M., Wilk,I., and Zmudzki,J.	2004	Embryotoxicity of carbendazim in rat and hamster micromass cultures.	Bulletin of the Veterinary Institute in Pulawy, 48:481-484	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	None
C-8-80	Toxicity/adverse effects on human – Reproductive toxicity	Petrashenko,L., Shepelskaya,N., and Sapoznikova,S.	2002	The study of fungicide carbendazim effect on reproductive function in Wistar rats.	Toxicology Letters (Shannon), 135:S81	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of reproductive toxicity.	No	10.1016/S0378-4274(02)00258-8

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								Study not found in the current literature search according to JMAFF guidelines.		
C-8-81	Toxicity/adverse effects on human – Reproductive toxicity	Nishizawa, S., Mitsuru,K., Ozawa,N., Kitajima,N., Hata,J., Kaneko,H., and Uno,H.	2003	Induction of brain anomalies in rat fetuses by single dosing of carbendazim.	Congenital anomalies, 43:241	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.1111/j.1741-4520.2003.tb01046.x
C-8-82	Toxicity/adverse effects on human – Reproductive toxicity	Tanaka,R., Sasanami,T., Toriyama, M., and Mori,M.	2000	Effects of carbendazim on mouse oocyte maturation and aneuploidy induction in vitro.	Teratology, 62:32	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as helpful to provide additional information for a better interpretation of reproductive toxicity. Study not found in the current literature search according to JMAFF guidelines.	No	10.1002/1096-9926(200009)62:3%3C

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C-8-83	Toxicity/adverse effects on human - B.6.6.4.2 Effects on pregnancy/ KIIA 5.6.10 & 5.6.11	Janardhan, A., Sattur, P.B. and Sisodia, P.	1984	Teratogenicity of methyl benzimidazole carbamate in rats and rabbits.	Bulletin of Environmental Contamination and Toxicology, 33: 257 - 263	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on teratogenic effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1007/BF01625540
C-8-84	Toxicity/adverse effects on human - B.6.6.4.2 Effects on pregnancy/ KIIA 5.6.10	Vergieva, T.	1985	Behavioral teratology - Results achieved and perspectives of development.	Journal of Hygiene Epidemiology Microbiology and Immunology, 28 (2): 121-127.	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on teratogenic effects of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	None
C-8-85	Toxicity/adverse effects on human - B.6.8.2.4 Further information from open literature / KIIA 5.8	Agarwal, M., Bagga, S., Singhal, L.K., Chauhan, R.S.	2002	Carbendazim down regulates the macrophage functions in poultry.	Toxicology Letters (135) S135-	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on immunotoxicity of carbendazim.	No	10.1016/S0378-4274(02)00258-8

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								Study not found in the current literature search according to JMAFF guidelines.		
C-8-86	Toxicity/adverse effects on human - B.6.8.2.4 Further information from open literature / KIIA 5.8	Singhal, L.K., Bagga, S., Kumar, R., Chauhan, R.S.	2003	Down regulation of humoral immunity in chickens due to carbendazim.	Toxicology in Vitro, 17: 687-692	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 3 B6)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of carbendazim. Study on immunotoxicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s0887-2333(03)00103-6
C-8-87	Toxicity/adverse effects on human – Other toxicological studies	Heneweer, M., van den Berg,M., and Sanderson, J.T.	2004	A comparison of human H295R and rat R2C cell lines as in vitro screening tools for effects on aromatase.	Toxicology Letters, 146:183-194	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potentially relevant by RMS. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/j.toxlet.2003.10.002
C-8-88	Toxicity/adverse effects on human – Other	Morinaga, H., Yanase,T., Nomura,M., Okabe,T.,	2004	A benzimidazole fungicide, benomyl, and its metabolite, carbendazim, induce aromatase activity in	Endocrinology, 145:1860-1869	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for	Study identified during the level 4 (Demand for further information) of	No	10.1210/en.2003-1182

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
	toxicological studies	Goto,K., Harada,N., and Nawata,H.		a human ovarian granulose-like tumor cell line (KGN).			carbendazim (Volume 1)	renewal dossier of carbendazim. Study identified as potentially relevant by RMS. Study not found in the current literature search according to JMAFF guidelines.		
C-8-89	Toxicity/adverse effects on human – Other toxicological studies	Yamada,T., Sumida,K., Saito,K., Ueda,S., Yabushita,S., Sukata,T., Kawamura, S., Okuno,Y., and Seki,T.	2005	Functional genomics may allow accurate categorisation of the benzimidazole fungicide benomyl: lack of ability to act via steroid-receptor-mediated mechanisms.	Toxicology and Applied Pharmacology, 205:11-30	EFSA / RMS (Germany)	Renewal Assessment Report in accordance with Article 5(5) of Council Directive 91/414/EEC for carbendazim (Volume 1)	Study identified during the level 4 (Demand for further information) of renewal dossier of carbendazim. Study identified as potentially relevant by RMS. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/j.taap.2004.09.002
C-8-90	Toxicity/adverse effects on human - B.6.8.1.1.5 Genotoxicity	Elhajouji, A; Lukamowicz, M; Cammerer, Z; Kirsch-Volders, M	January 2011	Potential thresholds for genotoxic effects by micronucleus scoring.	Mutagenesis, 26(1): 199 -204	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. Study not thoroughly evaluated by the RMS as not considered to change the reference values or overall conclusions for carbendazim	No	10.1093/mutage/geq089

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								established by EFSA during the Peer Review (2010) and not though to have any direct impact on the risk assessment of thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.		
C-8-91	Toxicity/adverse effects on human - B.6.8.1.1.5 Genotoxicity	Ermler, S; Scholze, M; Kortenkamp, A	July 2013	Seven Benzimidazole pesticides combined at sub-threshold levels induce micronuclei *in vitro*.	Mutagenesis, 28(4): 417-426	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. Study not thoroughly evaluated by the RMS as not considered to change the reference values or overall conclusions for carbendazim established by EFSA during the Peer Review (2010) and not though to have any direct impact on the risk assessment of thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.	Yes	10.1093/mutage/get019

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C-8-92	Toxicity/adverse effects on human - B.6.8.1.1.5 Genotoxicity	Itoh, S; Hattori, C; Nagata, M; Sanbuissho, A	August 2012	Structural and numerical chromosome aberration inducers in liver micronucleus test in rats with partial hepatectomy.	Mutation Research-Genetic Toxicology and Environmental Mutagenesis, 747 (1): 98 -103	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016 And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not thoroughly evaluated by the RMS as not considered to change the reference values or overall conclusions for carbendazim established by EFSA during the Peer Review (2010) and not though to have any direct impact on the risk assessment of thiophanate-methyl. Study found in the current literature search according to JMAFF guidelines and classified as relevant Category “b” (hit number C-6-1-1)	NA	NA
C-8-93	Toxicity/adverse effects on human - genotoxicity	Barale, R; Scapoli, C; Meli, C; Casini, D; Minunni,	June 1993	Cytogenic effects of benzamidazoles in mouse bone marrow	Mutation Research, 300: 15-28	US EPA	Toxicology Chapter for Thiophanate Methyl and Carbendazim. 2002 And	US EPA indicates a borderline significant increase in polyploidy and hyperploidy with no increase in	No	10.1016/0165-1218(93)90135-z

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
		M; Marrazzini, A; Loprieno, N; Barrai, I					Reregistration Eligibility Decision – Thiophanate-methyl. And Updated reasoned opinion on the toxicological properties and maximum residue levels (MRLs) for the benzimidazole substances carbendazim and thiophanate-methyl. (2004a)	structural chromosomal aberrations. Generally considered as positive results. Study identified by EFSA as relevant to assess aneugenicity/clastogenicity of carbendazim. Study not found in the current literature search according to JMAFF guidelines (same hit as C-8-23)		
C-8-94	Toxicity/adverse effects on human - B.6.8.1. 1.8.2 Developmental toxicity	Farag, A; Ebrahim, H; ElMazoudy, R; Kadous, E	April 2011	Developmental toxicity of fungicide Carbendazim in female mice.	Birth Defects Research Part b-Developmental and Reproductive Toxicology, 92 (2): 122 – 130 DOI: 10.1002/bdrb.20290	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that this study was submitted by the applicant for the purpose of renewal of thiophanate-methyl but has not been thoroughly evaluated by the RMS as it is not considered to change the reference values or overall conclusions for carbendazim established by EFSA during the Peer	NA	NA

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								Review (2010) and will thereby have no direct impact on the risk assessment of thiophanate-methyl. Study found in the current literature search according to JMAFF guidelines and classified as relevant Category “c” (hit number C-6-2-9).		
C-8-95	Toxicity/adverse effects on human - B.6.8.1.1.9 Other toxicological studies	Prashantkumar, W; Sethi, R; Pathak, D; Rampal, S; Saini, S	May 2012	Testicular damage after chronic exposure to carbendazim in male goats.	Toxicological & Environmental Chemistry, 94 (7): 1433-1442	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that this study was identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl but has not been thoroughly evaluated by the RMS as it is not considered to change the reference values or overall conclusions for carbendazim established by EFSA during the Peer Review (2010) and will thereby have no direct impact on the	No	10.1080/02772248.2012.693493

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								risk assessment of thiophanate-methyl. Study not found in the current literature search according to JMAFF guidelines.		
C-8-96	Toxicity/adverse effects on human – Reproductive toxicity	Breslin, W; Paulman, A; Sun-Lin, D; Goldstein, KM; Derr, A	February 2013	The inhibin B (InhB) response to the testicular toxicants mono-2-ethylhexyl phthalate (MEHP), 1,3 dinitrobenzene (DNB), or carbendazim (CBZ) following short-term repeat dosing in the male rat.	Birth Defects Research Part B Developmental and Reproductive Toxicology, 98(1): 72-81	US EPA	Thiophanate-Methyl and Carbendazim: Amended Draft Human Health Risk Assessment for Registration Review.	US EPA indicates that in this study evaluating testicular toxicity in the rat following 2 or 7 gavage doses a dose and duration-dependent incidence of testicular and epididymal degenerative lesions following administration of Carbendazim at 20 and 400 mg/kg/day was observed. US EPA indicates that the LOAEL is 20 mg/kg/day, based on epididymal histopathology. A NOAEL was not established in this study (<20 mg/kg/day). US EPA indicates that this published study in the rat is classified as acceptable/nonguideline and is considered appropriate for qualitative use in the	NA	NA

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								human health risk assessment of Carbendazim. The study is a published report from the open scientific literature, did not include individual animal data and was not conducted to satisfy a guideline data requirement for Carbendazim. The study provides information on toxicity to the testes following repeated gavage dosing that supplements the available information on toxicity of Carbendazim. Study found in the current literature search according to JMAFF guidelines and classified as relevant Category "c" (hit number C-6-2-2)		
C-8-97	Toxicity/adverse effects on human – Reproductive toxicity	Nakai, M; Hess, R.A; Moore, B.J; Guttroff, R.F; Strader, L.F; Linder, RE	November-December 1992	Acute and Long-term Effects of a Single Dose of the Fungicide Carbendazim (Methyl 2-Benzimidazole Carbamate) on the Male Reproductive System in the Rat.	Journal of Andrology. 13(6):507-517	US EPA	Toxicology Chapter for Thiophanate Methyl and Carbendazim. 2002 Reregistration Eligibility Decision – Thiophanate-methyl. Thiophanate-Methyl and Carbendazim:	US EPA indicates that the LOAEL for testicular toxicity is 100 mg/kg based on occluded efferent ductules at 2 and at 70 days' post-dosing, increased testicular weight at 2 days post-dosing, and	Yes	10.1002/j.1939-4640.1992.tb00345.x

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
							Amended Draft Human Health Risk Assessment for Registration Review. 2020	decreased testes weight, decreased seminiferous tubule diameter and increased atrophied tubules at 70 days' post-dosing. The NOAEL is 50 mg/kg based on sloughing (premature release) of immature germ cells 2 days postexposure, and atrophy of a few seminiferous tubules in one testicle, significant decrease in seminiferous tubule diameter, and slight abnormal growth of the efferent ductules at 70 days postexposure. The subtle effects detected in the epididymal sperm at 50 mg/kg may be attributed to the direct effect of Carbendazim on the seminiferous epithelium. This study is classified as acceptable/nonguideline and may be used qualitatively in the hazard characterization of Carbendazim for purposes of human		

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								health risk assessment. It is a published study and was not submitted to satisfy a guideline requirement for Carbendazim but provides supplemental information on the effects of single oral doses to the testes in the male rat. The published report did not include the test material purity and lot number or individual animal data. Study not found in the current literature search according to JMAFF guidelines.		
C-8-98	Toxicity/adverse effects on human - B.6.8.1.1.10 Endocrine disruption	Hsu, YH; Chang, CW; Chen, MC; Yuan, CY; Chen, JH; Ma, JT; Ueng, TH; Lu, SY	December 2011	Carbendazim-induced androgen receptor expression antagonized by flutamide in male rats.	Journal of Food and Drug Analysis,19 (4): 41C-8-428	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that it is considered to provide information indicating a potential for endocrine disruption by carbendazim. The study has however not been thoroughly evaluated by the RMS as it is not considered to change the reference values for	NA	NA

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								carbendazim established by EFSA during the Peer Review (2010) and will thereby have no direct impact on the renewal assessment of thiophanate-methyl. Study found in the current literature search according to JMAFF guidelines and classified as relevant Category "c" (hit number C-6-2-15)		
C-8-99	Toxicity/adverse effects on human - B.6.8.1.1.10 Endocrine disruption	Rama, EM; Bortolan, S; Vieira, ML; Gerardin, DCC; Moreira, EG	August 2014	Reproductive and possible hormonal effects of carbendazim.	Regulatory Toxicology and Pharmacology, 69 (3): 476 – 486	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that it is considered to provide information indicating a potential for endocrine disruption by carbendazim. The study has however not been thoroughly evaluated by the RMS as it is not considered to change the reference values for carbendazim established by EFSA during the Peer Review (2010) and will thereby have no	NA	NA

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								direct impact on the renewal assessment of thiophanate-methyl. Study found in the current literature search according to JMAFF guidelines and classified as relevant Category "b" (hit number C-6-1-2).		
C-8-100	Toxicity/adverse effects on human - B.6.8.1.1.10 Endocrine disruption	Yu, G; Guo, Q; Xie, L; Liu, Y; Wang, X	2009a	Effects of subchronic exposure to carbendazim on spermatogenesis and fertility in male rats.	Toxicology and Industrial Health, 25(1): 41-47	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 1 and Volume 3 CA B6) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that it is considered to provide information indicating a potential for endocrine disruption by carbendazim. The study has however not been thoroughly evaluated by the RMS as it is not considered to change the reference values for carbendazim established by EFSA during the Peer Review (2010) and will thereby have no direct impact on the renewal assessment of thiophanate-methyl.	No	10.1177/0748233709103033

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								Study not found in the current literature search according to JMAFF guidelines.		
C-8-101	Toxicity/adverse effects on human – Other toxicological effects	Selmanoglu, G; Barlas, N; Songür, S; Koçkaya, EA	December 2001	Carbendazim-induced haematological, biochemical and histopathological changes to the liver and kidney of male rats.	Human Experimental Toxicology, 20(12): 625-630	US EPA	Thiophanate-Methyl and Carbendazim: Amended Draft Human Health Risk Assessment for Registration Review.	US EPA indicates that this study evaluating target organ toxicity in male rats following a 15-week oral (gavage) dosing showed a decrease in liver weight and histopathology (portal vein congestion, mononuclear cell infiltration, hydropic degeneration). In this study, a dose-dependent decreases in white blood cells were observed and lymphocytes showed a dose-related decrease. US EPA indicates The LOAEL is 300 mg/kg/day for the parameters evaluated, based on histopathology of the liver and kidney. The NOAEL is 150 mg/kg/day. Furthermore, US EPA indicates that this study is classified as acceptable/nonguideline and is considered appropriate for qualitative use in the	No	10.1191/096032701718890603

List No.	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reviewed organization	Peer-reviewed literature (Date of publication etc.)	Notes	Open access	DOI
								human health risk assessment of Carbendazim. It provides limited information on the effect of carbendazim on the liver, kidney and blood cells that may be considered together with data from other studies in assessing toxicity to target organs. Study not found in the current literature search according to JMAFF guidelines. (same hit as C-8-8)		
C-8-102	Toxicity/adverse effects on human – Other toxicological effects (Developmental toxicity/teratogenicity)	Sitarek, K	August 2001	Embryolethal and teratogenic effects of carbendazim in rats.	Teratogenesis, Carcinogenesis, and Mutagenesis, 21(5): 335-340	US EPA	Thiophanate-Methyl and Carbendazim: Amended Draft Human Health Risk Assessment for Registration Review.	US EPA indicates that he maternal toxicity LOAEL is 35 mg/kg/day, based on decreased placental weight, increased fetal resorptions, including totally resorbed litters, and post-implantation loss. The maternal toxicity NOAEL is 8 mg/kg/day. The developmental toxicity LOAEL is 35 mg/kg/day, based on decreased fetal weight and	NA	NA (same hit as C-8-77)

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								length, decreased live fetuses per litter, increased resorptions and post-implantation loss, delayed skeletal ossification and an increase in external, visceral and skeletal malformations. US EPA indicates that this developmental toxicity study in the rat is acceptable /nonguideline and is appropriate for qualitative use in the human health risk assessment of Carbendazim. Study not found in the current literature search according to JMAFF guidelines. (same hit as C-8-77)		
C-8-103	Toxicity/adverse effects on human – Other toxicological effects	Songür, SH; Koçkaya, EA; Selmanoğlu, G; Barlas, N	December 2004	Dose-dependent effects of carbendazim on rat thymus.	Cell Biochemistry and Function, 23(6): 457-460	US EPA	Thiophanate-Methyl and Carbendazim: Amended Draft Human Health Risk Assessment for Registration Review.	US EPA indicates a decreased thymus weight (16/25%, absolute/relative), and increased fibronectin (FN) immunohistochemical staining in the thymus capsule at the mid-dose of 300 mg/kg/day in this study.	NA	NA (same hit as C-8-9)

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								US EPA indicates that a NOAEL and LOAEL were not established for this study due to the limited parameters Examined. Furthermore, this oral study in male rats is acceptable/nonguideline and is considered to be appropriate for qualitative use in assessing the effect of MBC on the thymus as a potential indicator of immunotoxicity. The study was limited in scope, did not provide individual animal data and only evaluated thymus weight and FN staining, the latter of which is not considered a reliable indicator of thymus toxicity. A dose-dependent decrease in thymus weight, however, was observed. Study not found in the current literature search according to JMAFF guidelines. (same hit as C-8-9)		

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C-8-104	Ecotoxicity and animal toxicity – Toxicity to aquatic organisms	Canton, JH	1976	The Toxicity of Benomyl, Thiophanate-methyl, and BCM to Four Freshwater Organisms.	Bulletin of Environmental Contamination and Toxicology: 16 (2): 214-224	US EPA	Preliminary Problem Formulation for the Environmental Fate, Ecological Risk, Endangered Species, and Human Health Drinking Water Exposure Assessments in Support of the Registration Review of Thiophanate-Methyl and Carbendazim	US EPA indicates a reported EC_{50} of 0.64 ppm for carbendazim for algae. Study not found in the current literature search according to JMAFF guidelines.	No	10.1007/BF01685230
C-8-105	Ecotoxicity and animal toxicity – B.9.1.5 Potential for endocrine disruption	Jiang, JH; Wu, SG; Wu, CX; An, XH; Cai, LM; Zhao, XP	December 2014	Embryonic exposure to carbendazim induces the transcription of genes related to apoptosis, immunotoxicity and endocrine disruption in zebrafish (*Danio rerio*).	Fish & Shellfish Immunology, 41(2): 493 – 500	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. The applicant argues that no clear concentration dependency of any assessed gene could be found. The RMS does not agree, since for the mentjoned most relevant genes (ER and HPG/HPT) a dose response can be seen. The applicant argues furthermore that the results of the endocrine correlated genes were contrary what is disputable as CYP 19	NA	NA

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								gene expression should be estrogen receptor (ER) dependent. While this mjght be the case for estrogen-antagonistic substances, the correlation between CYP 19 and ER might be less predictable for carbendazim, which does not appear to induce the estrogen responsive VTGgene (data inconclusive but pointing towards a down-regulation of VTG gene). Study found in the current literature search according to JMAFF guidelines and classified as not relevant after detailed relevance assessment (hit number C-5-34).		
C-8-106	Ecotoxicity and animal toxicity – B.9.1.5 Potential for endocrine disruption	Miracle, MR; Nandini, S; Sarma SSS; Vicente, E	March 2011	Endocrine disrupting effects, N at different temperatures, on *Moina micrura* (Cladocera: Crustacea) induced by carbendazim, a fungicide.	Hydrobiologia, 668: 155- 170	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. RMS indicates that since high mortality occurred even in controls both in F0	No	10.1007/s10750-011-0638-z

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								and Fl (50% dead at day 7), no conclusions can be made whether the observed decrease in reproductive success might be a result of a specific endocrine mechanism. Hence, study not relevant for endpoint endocrine disruption. Study not found in the current literature search according to JMAFF guidelines.		
C-8-107	Ecotoxicity and animal toxicity – B.9.4.1 Earthworm - sub-lethal effects	Chelinho, S; Domene, X; Campana, P Andrés, P; Römbke, J; Sousa, JP	March 2014	Toxicity of phenmedipham N and carbendazim to *Enchytraeus crypticus* and *Eisenia andrei* (Oligochaeta) in Mediterranean soils.	Journal of Soils and Sediments, 14: 584-599	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. The RMS mentioned that the results from this study indicate that the toxicity of carbendazim to earthworms is relatively consistent between different soil types while avoidance concentrations (AC_{50}) ranged from 1.5 to 9.4 mg/kg soil dry weight and were generally higher for sandy soils with low pH. The NOEC values for reproduction was	NA	NA

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								reported to be 0.58 mg/kg dw soil or lower, which indicate a higher toxicity to earthworm reproduction compared to the previously EU agreed NOEC for carbendazim (l .0 mg/kg dw soil). Study found in the current literature search according to JMAFF guidelines and classified as not relevant after initial rapid relevance assessment because not considered as a data requirement according to JMAFF Guidelines No.6278 (hit listed in excel spreadsheet).		
C-8-108	Ecotoxicity and animal toxicity – B.9.5 Effects on soil nitrogen transformation	Yu, Y; Chu, X; Pang, G; Xiang, Y; Fang, H	2009b	Effects of repeated applications of fungicide carbendazim on its persistence and microbial community in soil.	Journal of Environmental Sciences, 21 (2): 179-185	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. The RMS indicates that this study was not evaluated in detail here, since the methods used and parameters tested were not in accordance	No	10.1016/s1001-0742(08)62248-2

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								with the data requirements and the results do not add further information to the risk assessment for soil microorganisms, which is based on effects on nitrification. The study may however give some information related to microbial degradation in soil, which is referred to the section on Environmental fate. Study not found in the current literature search according to JMAFF guidelines.		
C-8-109	E-fate - B.8.1.1.1 Degradation of the active substance in aerobic soil	Yu, Y; Chu, X; Pang, G; Xiang, Y; Fang, H	2009b	Effects of repeated applications of fungicide carbendazim on its persistence and microbial community in soil.	Journal of Environmental Sciences, 21 (2): 179-185	EFSA / RMS (Sweden)	Renewal Assessment Report under Regulation (EC) 1107/2009 for Thiophanate-methyl (Volume 3 CA B9) – October 2016	Study identified during the literature search and submitted by the applicant for the purpose of renewal of thiophanate-methyl. The RMS indicates that the study seems to have been well conducted. The results indicate that microorganisms may become adapted to degradation of carbendazim. Study not found in the current literature search according to JMAFF guidelines.	No	10.1016/s1001-0742(08)62248-2

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								Same hit as C-8-108 (Ecotoxicity and animal toxicity field area).		

NA: not applicable as hits already found in the current literature search according to JMAFF guidelines