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Pencycuron & metabolites – Literature search report according to JMAFF Guidelines

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Table of Contents

Introduction:.....	3
Methodology:.....	3
Search strategy:	3
Literature search:	5
Systematic review of retrieved literature	5
Relevance evaluation	5
- Step 1: Initial rapid assessment:	5
- Step 2: Detailed assessment:.....	6
- Step 2: Relevance category classification	6
Reliability evaluation.....	7
Reporting of results.....	8
Results:.....	9
Pencycuron search:	9
Search strategy: keyword selection and summary of search strategy.....	9
Systematic review of retrieved literature	11
Pencycuron-PB-amine search:	20
Search strategy: keyword selection and summary of search strategy.....	20
Systematic review of retrieved literature strategy	22
Metabolite AE1371502:.....	23
Search strategy: keyword selection and summary of search strategy.....	23
Systematic review of retrieved literature strategy	24
Metabolite AE R805671:	25
Search strategy: keyword selection and summary of search strategy.....	25
References:.....	26
Appendix 1: Form 8 table for the active substance Pencycuron and its metabolites.....	27
EFSA reports:.....	27
JMPR reports:	28
US EPA reports:.....	29
Appendix 2: FSC table for the active substance pencycuron and its metabolites	33

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 Pencycuron and its metabolites, for the period 01.04.2009 - 31.03.2024. An analysis of the relevance and reliability of each article relevant to the active substance Pencycuron and its metabolites is also presented.

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

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, mice, dog, rabbit, monkey, pig, human, hen, typhimurium, E coli
Crop and livestock residue	Crop, commodity, feed, livestock, hen, cattle, goat, pig, Ruminant, cow, poultry
Ecotoxicity and animal toxicity	Avian, wild, bird, mallard duck, quail, bobwhite, lemna, algae, daphnia, fish, crustacean, aquatic, chironomus, bee, pollinator, apis,
E-fate	Soil, water, sediment

Literature search:

The literature searches were independently performed for the active substance Pencycuron and its metabolites Pencycuron-PB-amine, metabolite AE1371502 and metabolite AE R805671 on 17.06.2024. The 3-step approach described above was followed.

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.

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 2: 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

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

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.

Results:**Pencycuron search:****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 Pencycuron

Common name	Pencycuron
IUPAC name	1-(4-chlorobenzyl)-1-cyclopentyl-3-phenylurea
CAS name	N-[(4-Chlorophenyl)methyl]-N-cyclopentyl-N'-phenylurea
CAS Number / EC number	66063-05-6 / 266-096-3
Other names	1-[(4-chlorophenyl)methyl]-1-cyclopentyl-3-phenylurea Urea, N-[(4-chlorophenyl)methyl]-N-cyclopentyl-N'-phenyl- 4-Chlorophenyl methyl-N-cyclopentyl-N'-phenylurea 1-(4-chlorobenzyl)-1-cyclopentyl-3-phenylurea 1-(p-Chlorobenzyl)-1-cyclopentyl-3-phenylurea N-4-chlorobenzyl-N-cyclopentyl-N'-phenylurea NTN 19701

Table 2: Retrieved keywords for the formulation product containing the active substance Pencycuron

Common name	Monceren Monceren 250SC Teevic WP Cerenturf GR Turfshiba FL Cerenturf WG
IUPAC/CAS name	-

The summary of the search strategy for Pencycuron, including search dates and the various steps of the search process and number of hits obtained, are presented in Table 3.

Table 3: Summary of the search strategy for the active substance Pencycuron

Database name	Web of Science (Core Collection) / All editions		
Field collection	Web of Science Core Collection contains 10 indices, in which there are 254 fields, as follows: Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), Arts & Humanities Citation Index (A&HCI), Emerging sources citation index (ESCI), Conference Proceedings Citation Index Science, Social Sciences & Humanities (CPCI-S/CPCI-SSH), Book Citation Index-Science, Social Sciences & Humanities (BSCI-SSH), Current Chemical Reactions (CCR Expanded) and Index Chemicus (IC).		
Scope of the collection and number of literatures	Over 21,000 Journals, Over 304,000 Proceedings, Over 143,000 Academic books		
Update frequency	5 times/week (Mon-Fri, other than a public holiday in the U.S.A.)		
Date of the search	17.06.2024		
Date span of the search	From 01.04.2009 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	agriculture multidisciplinary OR developmental biology OR environmental sciences OR multidisciplinary sciences OR pharmacology pharmacy 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 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 biology OR developmental biology OR ecology OR entomology OR environmental sciences OR microbiology 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

		multidisciplinary sciences OR pharmacology pharmacy OR plant sciences OR toxicology OR zoology	
E-fate		agriculture multidisciplinary OR ecology OR environmental sciences OR biology OR multidisciplinary sciences	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	52	NA	NA
Toxicity/adverse effects on human	NA	23	2
Crop and livestock residue	NA	35	6
Ecotoxicity and animal toxicity	NA	35	8
E-fate	NA	21	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.

Systematic review of retrieved literature

A summary of the relevance assessment for the Pencycuron search is presented in Table 4.

Table 4: Summary of results of the relevance assessment (Step1, Step2) of obtained hits for the active substance Pencycuron

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	2	0	2	1	1
Crop and livestock residue	6	5	1	0	1
Ecotoxicity and animal toxicity	8 (7)	1	7 (6)	3 (2)	4
E-fate	11 (7)	9 (6)	2 (1)	1(0)	1
Total	27	15	12	5	7
Total without duplicates	22	12	10	3	7

Note: number in parenthesis correspond to hits number after removal of duplicates when compared to other hits obtained in all 4 field areas. Data only presented when duplicate hits were found.

Table 5 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.

Table 5: List of non-relevant hits/literature studies after step 2 of the relevance assessment and reason for decision for the active substance Pencycuron

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision
5-1	Toxicity/adverse effects on human	NA	Kaonga, CC; Chidya, RCG; Kosamu, IBM; Abdel-Dayem, SM; Mapoma, HWT; Thole, B; Mbewe, R; Sakugawa, H	2018	Trends in usage of selected fungicides in Japan between 1962 and 2014: a review.	International Journal of Environmental Science and Technology, 15(8): 1801 - 1814	⑬ - Publication not relevant to 4 effect areas described in section 1.a. step 2. Article provides general use information only
5-2	Ecotoxicity and animal toxicity	NA	Kaonga, CC; Chidya, RCG; Kosamu, IBM; Abdel-Dayem, SM; Mapoma, HWT; Thole, B; Mbewe, R; Sakugawa, H	2018	Trends in usage of selected fungicides in Japan between 1962 and 2014: a review.	International Journal of Environmental Science and Technology, 15(8): 1801 - 1814	⑬ - Publication not relevant to 4 effect areas described in section 1.a. step 2. Article provides general use information only
5-3	Ecotoxicity and animal toxicity	NA	Herrera, R; Núñez, D; Romero, N; Besoain, X; Pérez, LM; Montealegre, J	2012	Sensitivity of wild-type and mutant <i>Trichoderma harzianum</i> strains to fungicides.	Ciencia e Investigacion Agraria, 39(3): 569 - 576	④ - Publication relevant to efficacy, phytotoxicity or physicochemical properties of the active substance. Study focusing on determining the sensitivity of <i>Trichoderma harzianum</i> , a bacterial strain potentially involved in the control (biocontrol)

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision
							of plant pathogens, to pencycuron which is ultimately about to make sure that pencycuron is efficient against pathogens by preserving the beneficial <i>Trichoderma harzianum</i> strain.
5-4	Ecotoxicity and animal toxicity	NA	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	⑬ - Publication not relevant to 4 effect areas described in section 1.a. step 2. Study not following any test guidelines with regards to toxicity towards microorganisms. Study potentially relevant to the environmental fate area.
5-5	E-fate	NA	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 Study methods are not (sufficiently) documented

The number of hits/literature studies classified as “Category a”, ”Category b” or “Category c” after steps 2 of the relevance assessment for the active substance Pencycuron is presented in Table 6.

Table 6: Number of hits/literature studies classified as “Category a”, ”Category b” or “Category c” after steps 2 of the relevance assessment for the active substance Pencycuron

Field	Total number of Available literatures		
	Category a	Category b	Category c
Toxicity/adverse effects on human	1	0	0
Crop and livestock residue	0	1	0
Ecotoxicity and animal toxicity	0	4	0
E-fate	0	1	0
Total	1	6	0

Table 7 presents the detailed list of hits/literature studies classified as ”Category b” after step 2 of the relevance assessment and the reasons for this classification. Studies are ordered by data points.

Table 8 presents the detailed list of hits/literature studies classified as ”Category a” after step 2 of the relevance assessment and the reasons for this classification. Studies are ordered by data points. The Klimisch rating of such studies is also provided with the reasons for the obtained score.

Table 7: Literature classified as "Category b" after step 2 of the relevance assessment and reason for the classification for the active substance Pencycuron

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision
6-1-1	Crop and livestock residue	KIIA 6.3	Brancato, A; Brocca, D; Cabrera, LC; De Lentdecker, C; Erdos, Z; Ferreira, L; Greco, L; Jarrah, S; Kardassi, D; Leuschner, R; Lythgo, C; Medina, P; Miron, I; Molnar, T; Pedersen, R; Reich, H; Riemenschneider, C; Sacchi, A; Santos, M; Stanek, A; Sturma, J; Tarazona, J; Theobald, A; Vagenende, B; Villamar-Bouza, L	2018	Review of the existing maximum residue levels for pencycuron according to Article 12 of Regulation (EC) No 396/2005.	EFSA Journal, 16 (12):5518	Literature publication from approved independent reviewing authority relating to the review of MRLs for pencycuron in the EU in 2018, for a number of crops. The data is considered as supplementary considering the uses are outside of Japan and a new MRL regulation will be adopted in 2024 following the active substance's expiration in the EU. The publication is considered as reliable with restriction (Klimisch 2) considering a new MRL regulation is expected to be enforced in 2024 in the EU for pencycuron, and MRL evaluation was performed on uses outside of Japan.
6-1-2	Ecotoxicity and animal toxicity	KIIA 8.2.1	Ku-Centuri3n, M; Gonz3lez-Mar3n, B; Calder3n-Ezquerro, MC;	2016	DNA damage assessment in zebrafish embryos exposed to Monceren® 250	Zebrafish, 13(5): 442-448	Study not following any test guidelines. No useful endpoint can be derived from this study for aquatic risk assessment although it provides

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision
			Martínez-Valenzuela, MC; Maldonado, E; Calderón-Segura, ME		SC fungicide using the alkaline comet assay.		supportive information regarding the genotoxicity of pencycuron, as the formulated product Monceren 250 SC, in zebrafish embryos. Study considered as supportive only.
6-1-3	Ecotoxicity and animal toxicity	KIIA 8.2.1	Ku-Centurión, M; Calderón-Segura, ME; Maldonado, E	2016	Detection of DNA damage in zebrafish (<i>Danio rerio</i>) embryos exposed to Monceren® 250 SC fungicide through alkaline comet assay.	Toxicology Letters, 259: S183, PP18.12	Study not following any test guidelines. No useful endpoint can be derived from this study for aquatic risk assessment although it provides supportive information regarding the genotoxicity of pencycuron, as the formulated product Monceren 250 SC, in zebrafish embryos. Study considered as supportive only.
6-1-4	Ecotoxicity and animal toxicity	KIIA 8.2.1	Zhou, YX; Shen, C; Du, H; Bao, YY; He, CY; Wang, CG; Zuo, ZH	2019	Bioassay system for the detection of aryl hydrocarbon receptor agonists in waterborne pesticides using zebrafish cyp1a1 promoter-luciferase recombinant hepatic cells.	Chemosphere, 220:61-68	Study not following any test guidelines. No useful endpoint can be derived from this study for aquatic risk assessment although it provides supportive information regarding the effect of pencycuron on luciferase expression (induction). Study considered as supportive only.
6-1-5	Ecotoxicity and animal toxicity	KIIA 8.4	Kumar, JIN; Amb, MK; Bora, A	2010	Chlorobenzyl cyclopentyl-3-phenylurea effects on heterocystous	Journal of Crop Improvement, 24(3):261-270	Study not following any test guidelines.

List No.	Field	Data requirement (Item No.)	Authors	Date of publication	Title of literature	Journal name, No., Page etc.	Reasons for the decision
					filamentous cyanobacteria <i>Westiellipsoidis prolifica</i> Janet.		Test species (Filamentous Cyanobacteria <i>Westiellipsoidis prolifica</i>) not a recognised test species. No useful endpoint can be derived from this study for aquatic risk assessment although the study provides information about the toxicity of pencyuron towards cyanobacteria.
6-1-6	Efate		Fenoll, J; Garrido, I; Hellín, P; Flores, P; Vela, N; Navarro, S	2014	Use of different organic wastes in reducing the potential leaching of propanil, isoxaben, cadusafos and pencyuron through the soil	Journal of Environmental Science and Health part B- Pesticides Food Contaminants, and Agricultural Wastes, 49(8):601-608	The soil studied is not within the specification for OECD 307, 106 or 312. Also, there are insufficient soil types, the soil/solution ratio is not as recommended for an OECD 106 study and there is an absence of reference substance, as normally required for an OECD 312 study.

Table 8: Literature classified as "Category a" after step 2 of the relevance assessment and reason for the classification for the active substance Pencycuron

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
7-1	Toxicity/adverse effects on human	KIIA 5.4	Nagy, K; Zheng, CY; Bolognesi, C; Adám, B	2019	Interlaboratory evaluation of the genotoxic properties of pencycuron, a commonly used phenylurea fungicide.	Science of the total environment, 647:1052-1057	1	Guideline test (OECD 487). Reliable study according to the ToxRtool evaluation.

Pencycuron-PB-amine search:**Search strategy: keyword selection and summary of search strategy**

Step 1 of the keyword selection process was performed as described in Table 9 and Table 10.

Table 9: Retrieved keywords for the metabolite Pencycuron-PB-amine

Common name	Pencycuron-PB-amine
IUPAC	N-[(4-chlorophenyl)methyl]cyclopentanamine
CAS name	4-Chloro-N-cyclopentylbenzenemethanamine
CAS Number / EC number	66063-15-8 / 266-097-9
Other names	N-(4-chlorobenzyl)-N-cyclopentylamine 4-Chloro-N-cyclopentylbenzylamine N-(4-chlorobenzyl)cyclopentanamine Cyclopentylbenzylamine Benzenemethanamine

Table 10: Retrieved keywords for the formulation product containing the metabolite Pencycuron-PB-amine

Common name	-
IUPAC/CAS name	-

The summary of the search strategy for Pencycuron-PB-amine, including search dates and the various steps of the search process and number of hits obtained, are presented in Table 11.

Table 11: Summary of the search strategy for the metabolite Pencycuron-PB-amine

Table 11: Summary of the search strategy for the meta-analyses (one search + 3 online)			
Database name	Web of Science (Core Collection) / All editions		
Field collection	Web of Science Core Collection contains 10 indices, in which there are 254 fields, as follows: Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), Arts & Humanities Citation Index (A&HCI), Emerging sources citation index (ESCI), Conference Proceedings Citation Index Science, Social Sciences & Humanities (CPCI-S/CPCI-SSH), Book Citation Index-Science, Social Sciences & Humanities (BSCI-SSH), Current Chemical Reactions (CCR Expanded) and Index Chemicus (IC).		
Scope of the collection, the number of literatures	Over 21,000 Journals, Over 304,000 Proceedings, Over 143,000 Academic books		
Update frequency	5 times/week (Mon-Fri, other than a public holiday in U.S.A.)		
Date of the search	17.06.2024		
Date span of the search	From 01.04.2009 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	multidisciplinary sciences OR pharmacology pharmacy	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		multidisciplinary 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		multidisciplinary sciences OR pharmacology pharmacy	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		multidisciplinary sciences	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	8	NA	NA

target active substance name			
Toxicity/adverse effects on human	NA	2	1
Crop and livestock residue	NA	2	0
Ecotoxicity and animal toxicity	NA	1	0
e-fate	NA	1	0

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.

Systematic review of retrieved literature strategy

A summary of the relevance assessment for the metabolite Pencycuron-PB-amine search is presented in Table 12.

Table 12: Summary of results of the relevance assessment (Step 1, Step 2) of obtained hits for the metabolite Pencycuron-PB-amine

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	1	1	0	0	0
Crop and livestock residue	0	0	0	0	0
Ecotoxicity and animal toxicity	0	0	0	0	0
e-fate	0	0	0	0	0
Total	1	0	0	0	0

Metabolite AE1371502:**Search strategy: keyword selection and summary of search strategy**

Step 1 of the keyword selection process was performed as described in Table 13 and Table 14.

Table 13: Retrieved keywords for the metabolite AE1371502

Common name	-
IUPAC	1-cyclopentyl-3-phenylurea
CAS name	-
CAS Number / EC number	-
Other names	AE 1371502 des-benzyl pencycuron

Table 14: Retrieved keywords for the formulation product containing the metabolite AE1371502

Common name	NA
IUPAC/CAS name	NA

The summary of the search strategy for metabolite AE1371502, including search dates and the various steps of the search process and number of hits obtained, are presented in Table 15.

Table 15: Summary of the search strategy for the metabolite AE1371502

Database name	Web of Science (Core Collection) / All editions		
Field collection	Web of Science Core Collection contains 10 indices, in which there are 254 fields, as follows: Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), Arts & Humanities Citation Index (A&HCI), Emerging sources citation index (ESCI), Conference Proceedings Citation Index Science, Social Sciences & Humanities (CPCI-S/CPCI-SSH), Book Citation Index-Science, Social Sciences & Humanities (BSCI-SSH), Current Chemical Reactions (CCR Expanded) and Index Chemicus (IC).		
Scope of the collection, the number of literatures	Over 21,000 Journals, Over 304,000 Proceedings, Over 143,000 Academic books		
Update frequency	5 times/week (Mon-Fri, other than a public holiday in U.S.A.)		
Date of the search	17.06.2024		
Date span of the search	From 01.04.2009 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	developmental biology	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		plant sciences 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		developmental biology OR plant 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		-	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	3	NA	NA
Toxicity/adverse effects on human	NA	1	0
Crop and livestock residue	NA	2	1
Ecotoxicity and animal toxicity	NA	2	1
e-fate	NA	0	0

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.

Systematic review of retrieved literature strategy

A summary of the relevance assessment for the metabolite AE1371502 search is presented in Table 16.

Table 16: Summary of results of the relevance assessment (Step 1, Step 2) of obtained hits for the metabolite AE1371502

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	0	0	0	0	0
Crop and livestock residue	1	1	0	0	0
Ecotoxicity and animal toxicity	1	1	0	0	0
e-fate	0	0	0	0	0
Total	2	0	0	0	0

Total without duplicates	2	0	0	0	0
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Metabolite AE R805671:

Search strategy: keyword selection and summary of search strategy

Step 1 of the keyword selection process was performed as described in Table 17 and Table 18.

Table 17: Retrieved keywords for the metabolite AE R805671

Common name	-
IUPAC	N-[(4-chlorophenyl)methylene]cyclopentylamine
CAS name	-
CAS Number / EC number	-
Other names	-

Table 18: Retrieved keywords for the formulation product containing the metabolite AE R805671

Common name	NA
IUPAC/CAS name	NA

The summary of the search strategy for metabolite AE R805671, including search dates and the various steps of the search process and number of hits obtained, are presented in Table 19. The search returned no hits for any of the 4 areas.

Table 19: Summary of the search strategy for the metabolite AE R805671

Database name	Web of Science (Core Collection) / All editions		
Field collection	Web of Science Core Collection contains 10 indices, in which there are 254 fields, as follows: Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), Arts & Humanities Citation Index (A&HCI), Emerging sources citation index (ESCI), Conference Proceedings Citation Index Science, Social Sciences & Humanities (CPCI-S/CPCI-SSH), Book Citation Index-Science, Social Sciences & Humanities (BSCI-SSH), Current Chemical Reactions (CCR Expanded) and Index Chemicus (IC).		
Scope of the collection, the number of literatures	Over 21,000 Journals, Over 304,000 Proceedings, Over 143,000 Academic books		
Update frequency	5 times/week (Mon-Fri, other than a public holiday in U.S.A.)		
Date of the search	17.06.2024		
Date span of the search	From 01.04.2009 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	-	-
Crop and livestock residue		-	-

Ecotoxicity and animal toxicity		-	-
e-fate		-	-
Retrieved results			
Retrieved condition (Keyword)	①	① AND ②	① AND ② AND ③
Total number of retrieved literature for target active substance name	0	NA	NA
Toxicity/adverse effects on human	NA	-	-
Crop and livestock residue	NA	-	-
Ecotoxicity and animal toxicity	NA	-	-
e-fate	NA	-	-

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.

Form 8:

Appendix 1 present the findings for Form 8 for the active substance Pencycuron and its metabolites.

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 Pencycuron and its metabolites

EFSA reports:

The following documents were screened for literature data about pencycuron and its metabolites:

- EFSA (European Food Safety Authority), 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance pencycuron. EFSA Journal 2010;8(10):1828, 53pp. doi:10.2903/j.efsa.2010.1828.
- EFSA (European Food Safety Authority), 2017. Reasoned opinion on the modification of the existing maximum residue level for pencycuron in potatoes. EFSA Journal 2017; 15(1):4692, 20 pp. doi:10.2903/j.efsa.2017.4692
- EFSA (European Food Safety Authority), Brancato A, Brocca D, Carrasco Cabrera L, De Lentdecker C, Erdos Z, Ferreira L, Greco L, Jarrah S, Kardassi D, Leuschner R, Lythgo C, Medina P, Miron I, Molnar T, Pedersen R, Reich H, Riemenschneider C, Sacchi A, Santos M, Stanek A, Sturma J, Tarazona J, Theobald A, Vagenende B and Villamar-Bouza L, 2018. Reasoned opinion on the review of the existing maximum residue levels for pencycuron according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2018;16(12):5518, 43 pp. <https://doi.org/10.2903/j.efsa.2018.5518>
- The Netherlands, 2005. Draft Assessment Report (DAR) on the active substance pencycuron prepared by the rapporteur Member State the Netherlands in the framework of Directive 91/414/EEC, October 2005.
- The Netherlands, 2009. Additional Report to the Draft Assessment Report on the active substance pencycuron prepared by the rapporteur Member State the Netherlands in the framework of Commission Regulation (EC) No 33/2008, November 2009.
- The Netherlands, 2010. Final Addendum to the Draft Assessment Report and Additional Report on pencycuron, compiled by EFSA, August 2010.

No publications on pencycuron or its metabolites was identified in the form the open peer-reviewed literature in any of these documents.

During the screening of all DAR volumes (Volume 1 – Volume 3 B1-B9), an assessment of literature search in various databases (Heimann, K.G. (2004)) is mentioned in volume B6. No literature hits coming from this literature search is nevertheless mentioned in any of the various DAR volumes. In the DAR volume B6, there is also a mention that no literature was identified in that search with regards to clinical cases of poisoning incidents with pencycuron (see section B.6.9.2 Clinical cases of poisoning incidents), observations on exposure of the general population to pencycuron (see section B.6.9.3 Observations on exposure of the general population), clinical signs and symptoms of poisoning and details of clinical tests on pencycuron (see section B.6.9.4 Clinical signs and symptoms of poisoning and details of clinical tests), first aid measures and therapeutic regimes with respect to poisoning with pencycuron (see section B.6.9.5 First aid measures and therapeutic regimes) or expected effects of poisoning by pencycuron (see section B.6.9.6 Expected effects of poisoning).

JMPR reports:

The Food and Agriculture Organization of the United Nations was screened for the list of pesticides evaluated by JMPR (<https://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/lpe/lpe-p/en/>) and no JMPR reports were found for Pencycuron and its metabolites (see screenshot below).

NSP - P - List of Pesticide Evaluated by JMPR and JMPS

List of Pesticides evaluated by JMPR and JMPS - P

Below is a list of pesticides that have been evaluated by the Joint FAO/WHO Meeting on Pesticide Residues (JMPS) and the Joint FAO/WHO Meeting on Pesticide Specifications (JMPS).

All compounds are listed alphabetically in the JMPS report and evaluation column; click on Report to download either the Toxicological Evaluation or the Residue Evaluation in the JMPS Report in the related year; and click on Evaluation to download the Residue Evaluation in the related year.

In the specification column, click on the year indicated in each cell to download the latest specification evaluated by the JMPS.

Pesticide	JMPS Report and Evaluation	Specification
Parquat	JMPS no. (557) 2003 (T) Report 2004 (R) Report, Evaluation 2005 (R) Report, Evaluation	
Parquat dichloride		2021
Parathion	JMPS no. (558) 1991 (R) Report 1995 (R, R) Report, Evaluation 1997 (R) Report, Evaluation 2000 (R) Report, Evaluation	1999 PIC
Parathion-methyl	JMPS no. (559) 1991 (R) Report 1992 (R) Report 1994 (R) Report, Evaluation 1995 (T) Report 2000 (R) Report, Evaluation 2003 (R) Report, Evaluation	2001
Pencycuron	JMPS no. (152) 1992 (T, R) Report 1995 (R) Report, Evaluation 2010 (R) Report 2016 (R) Report, Evaluation	
Pendimethalin	JMPS no. (282) 2010 (T, R) Report	
Penthiopyrad	JMPS no. 283 2012 (R) Report 2013 (R) Report	

Core Themes

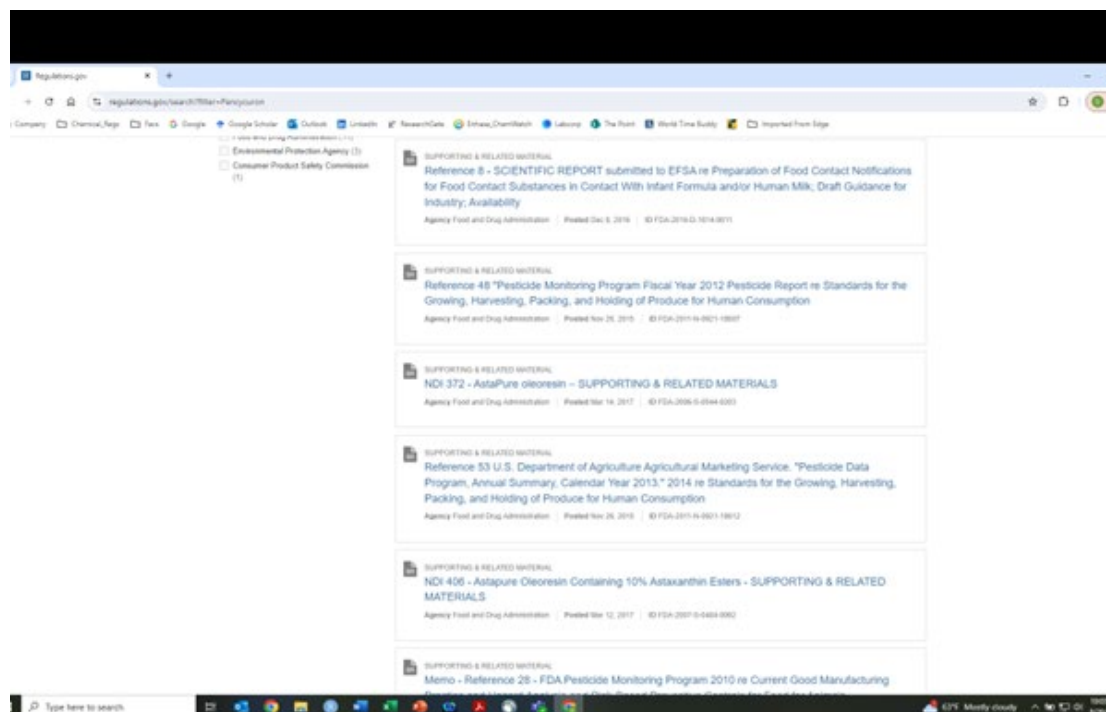
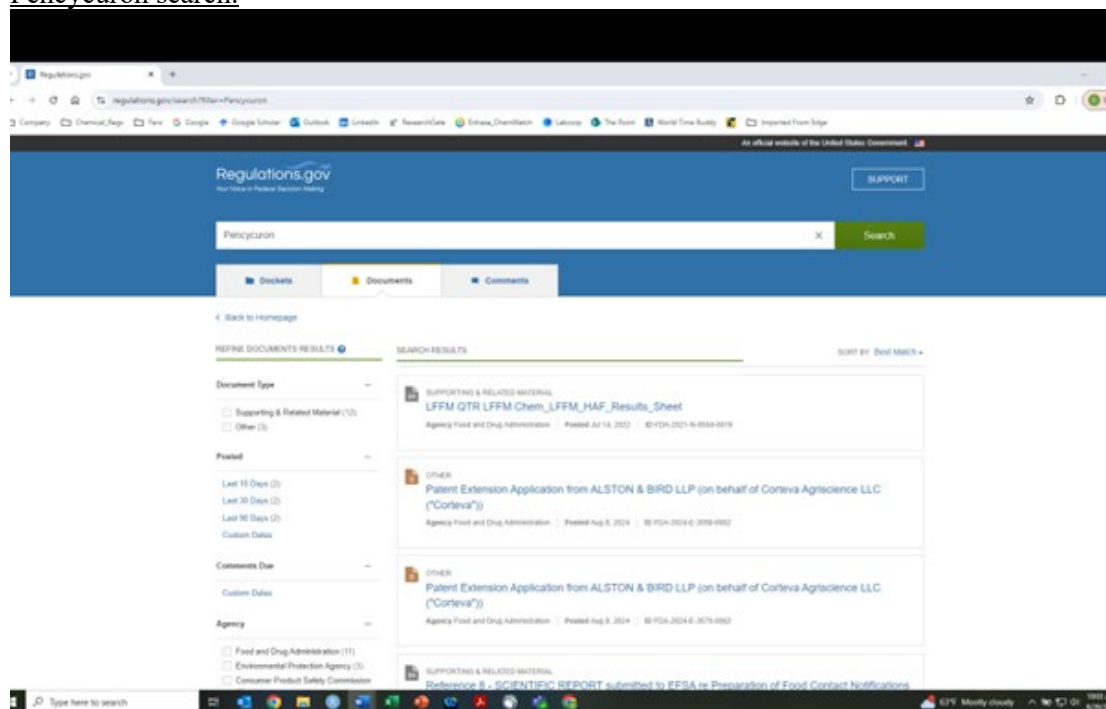
- Sustainable Crop Production Intensification
- Seeds and Plant Genetic Resources
- Biodiversity and Ecosystem Services
- Plant Production and Climate Change
- Horticulture and Diversification
- International Treaties, Conventions, Advisory Bodies

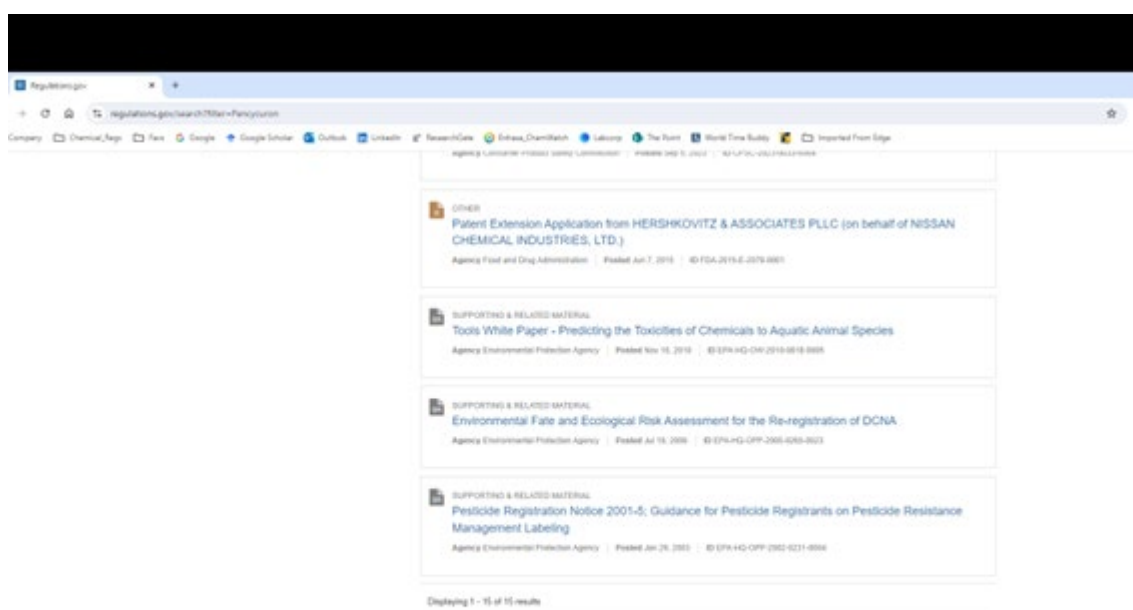
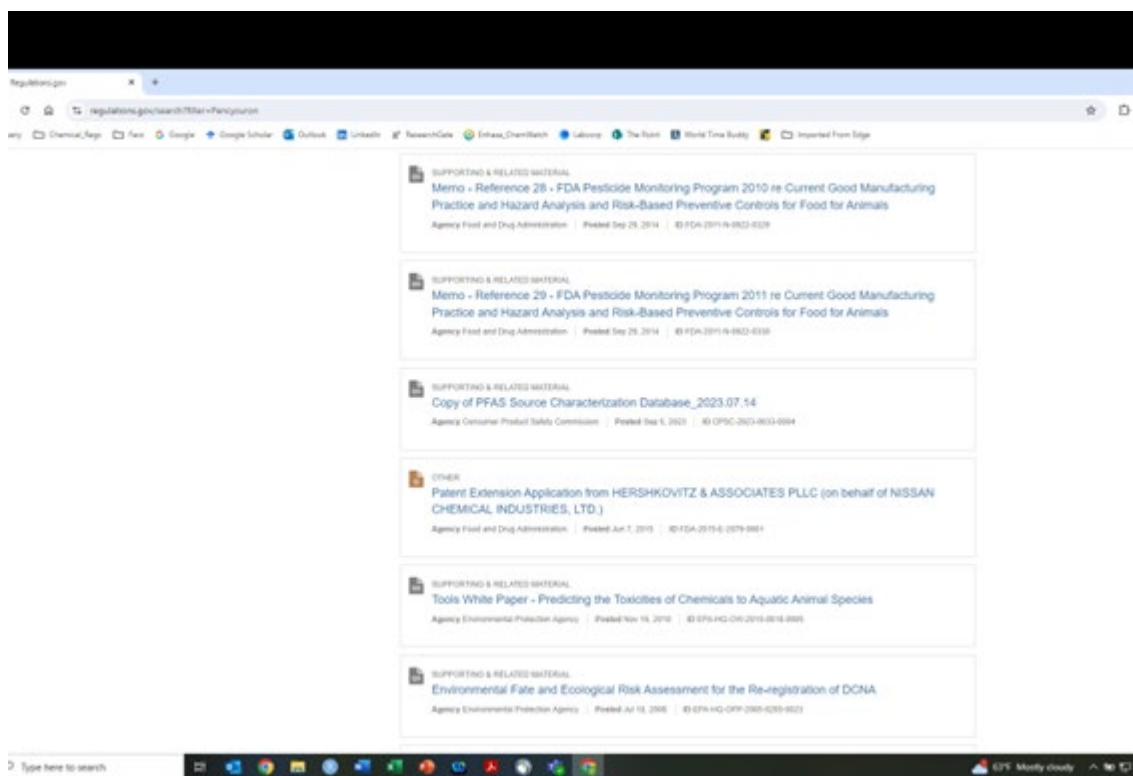
US EPA reports:

The US EPA database and docket was screened (<https://www.regulations.gov>) for Pencycuron using the common name, full chemical name, CAS number or product name. The obtained hits were all not relevant.

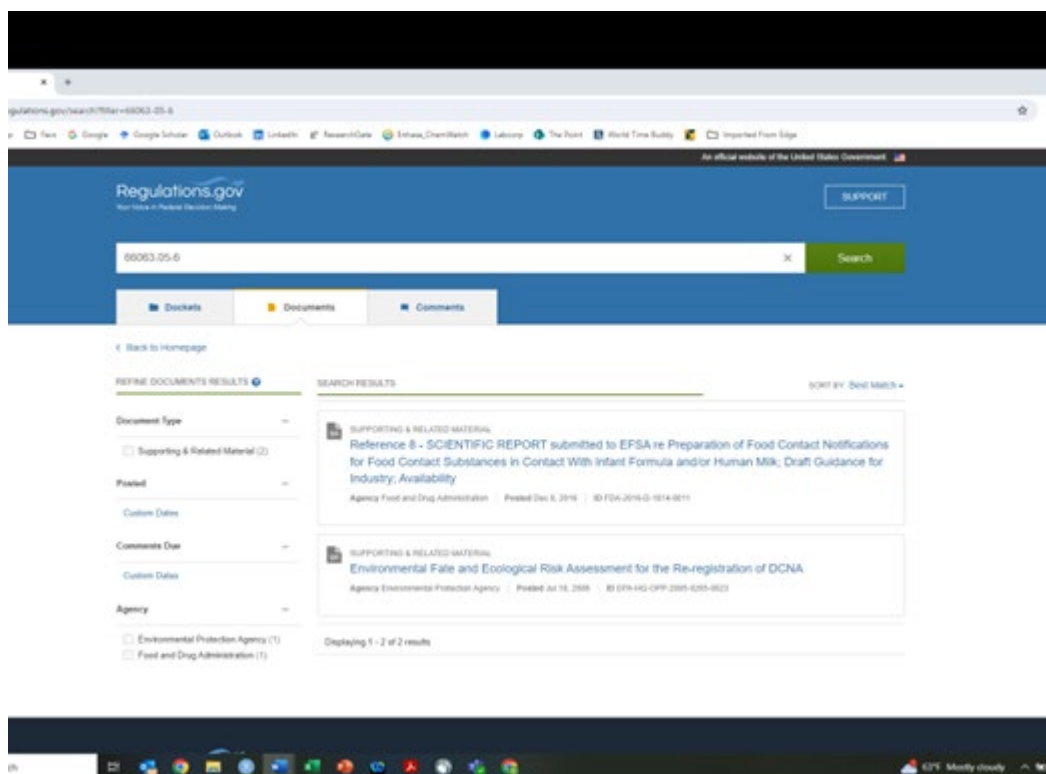
Some screenshots of the various searches are provided below:

Pencycuron search:

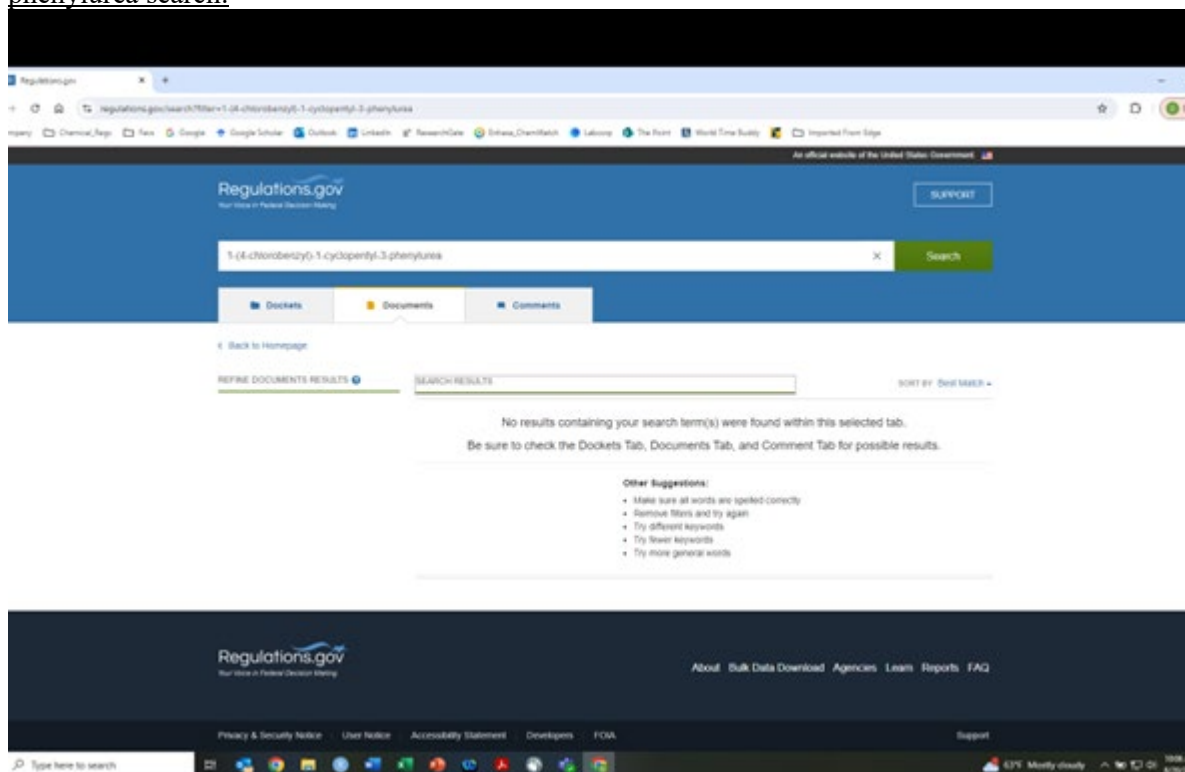




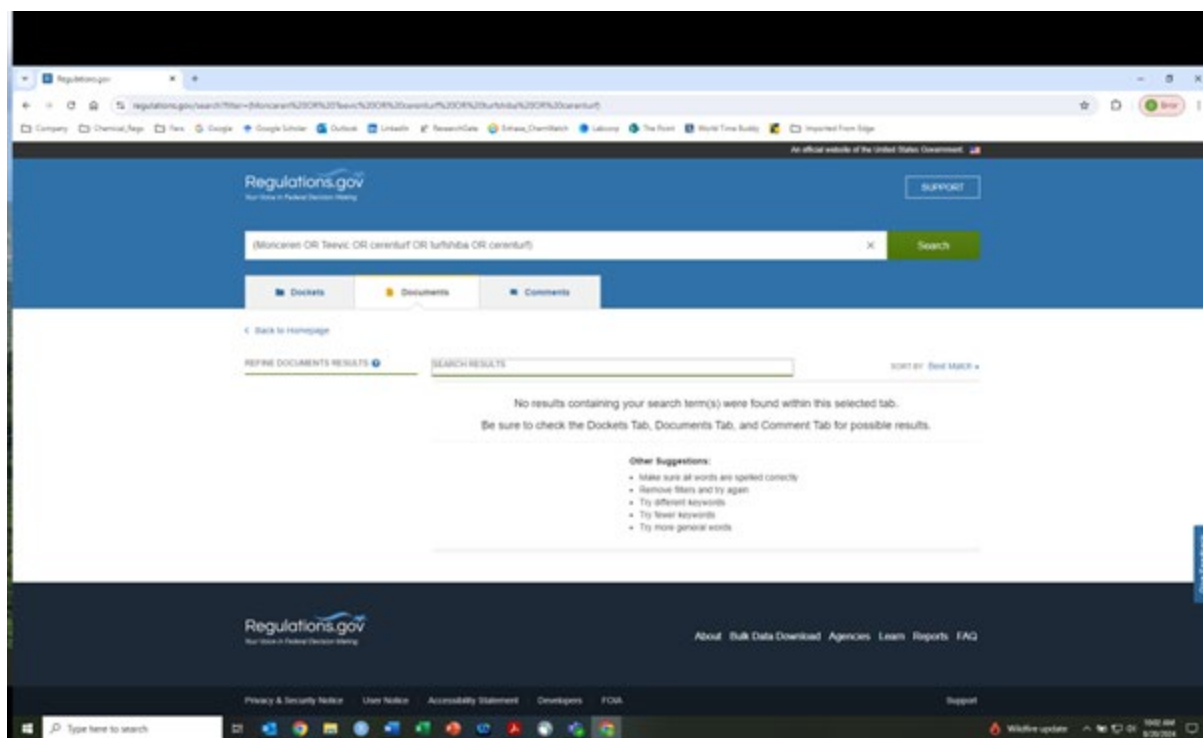
CAS number: 66063-05-6 search:



1-(4-chlorobenzyl)-1-cyclopentyl-3-phenylurea OR N-[(4-Chlorophenyl)methyl]-N-cyclopentyl-N'-phenylurea search:



(Monceren OR Teevic OR cerenturf OR turfshiba OR cerenturf) search:



Appendix 2: FSC table for the active substance pencycuron and its metabolites

No.	Title of literature	Journal name	Publication year	Author name	Author's Institution	Bibliographic information	Field of study	Original /Review article	Whether or not It is used in overseas evaluation reports	Presence or absence of citation in dossier	<i>in vivo</i> (animal species)/ <i>in vitro</i>	Dose (mg/kg body weight or mg/kg body weight/day)	NOAEL /NOEL	LOAEL /LOEL	Klimisch Code	Information about conformity for evaluation purposes	remarks
7-1	Interlaboratory evaluation of the genotoxic properties of pencycuron, a commonly used phenylurea fungicide.	Science of the Total Environment 647 (2019) 1052–1057	2019	Nagy et al.	Department of Preventive Medicine, Faculty of Public Health, University of Debrecen, Debrecen, Hungary	https://doi.org/10.1016/j.scitotenv.2018.08.067	General toxicity/metabolism	Original	—	—	<i>in vitro</i> (five non-smoking male human mononuclear white blood cells (MWBCs) / hepatocytes (HepG2)) comment assay and cytokinesis-block micronucleus (CBMN) assay	0, 1, 5, 10, 25, 50 and 100 µg/mL	—	—	1	Guideline test (OECD 487). Reliable study according to the ToxRtool evaluation. The combined results of the two labs showed a dose-dependent DNA damage detected by micronucleus frequency, which reached statistical significance at 100 µg/ml concentration after 21-h exposure in HepG2 cells (p=0.048). Significant genotoxic effect could also be observed in the comet assay from 50 µg/ml concentration in MWBCs, and at 100 µg/ml concentration in HepG2 cells in one lab. Nevertheless, this finding was not confirmed by the other lab in HepG2 cells, where Fpg-dependent oxidative DNA damage could also not be detected.	Provides information on genotoxicity. Relevance category classification (JMAFF guideline): a