S-メトラクロール

公表文献調査結果について

提出：令和 5 年 9 月 26 日
第 1 回修正：令和 6 年 1 月 16 日

シンジェンタジャパン株式会社

1.　概要

S-メトラクロールに関して、再評価資料提出期限の始期（2023 年 7 月 1 日）の 6 ヶ月前から過去15年間を含む期間に発行された公表文献について検索し、適合性及び信頼性の評価を行った。

2004 年 8 月 22 日～2014 年 8 月 22 日の期間に発行された英文文献については、EU において提出された調査報告書の結果を「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 日農薬資材審議会農薬分科会決定、令和 5 年 7 月 27 日一部改正）」に基づき再評価した。追加調査として Web of Science Core Collection を用いて 2014 年 8 月 1 日～2023 年 2 月 13 日の期間に発行された英文文献を対象とした検索を実施した。また、J-STAGE を用いて 2014 年 1 月 1 日～2023 年 2 月 22 日の期間に発行された文献に対して英文キーワード検索を、2008 年 1 月 1 日～2023 年 2 月 22 日の期間に発行された文献に対して和文キーワード検索を実施した。

また、2023 年 6 月 13 日時点において、海外の評価機関（欧州食品安全機関（EFSA）、米国環境保護庁（USEPA）及び FAO/WHO 合同残留農薬専門家会議（JMPR））が発行した S-メトラクロールに関する評価書を収集し、評価書中で引用されている公表文献を確認した。

2.　報告書の構成について

S-メトラクロールの公表文献に関する報告書及びその概要については以下のとおりである。

2.1　公表文献の調査結果について

2004 年 8 月 22 日～2014 年 8 月 22 日の期間については、EU において提出された公表文献調査報告書の結果を「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 日農薬資材審議会農薬分科会決定、令和 5 年 7 月 27 日一部改正）」に基づき適合性及び信頼性の再評価をした。該当フォルダ中に各分野における公表文献調査結果報告書、再評価報告書及び適合性ありと判断した文献の写し（オープンアクセスの文献を除く）を収載している。「ヒトに対する毒性」の分野において適合性ありと判断した公表文献については、疫学研究に関する文献とそれ以外に分類し、食品安全委員会より提供されているフォーマットに準じた資料を作成し収載している。

追加調査として、Web of Science Core Collection を用いて 2014 年 8 月 1 日～2023 年 2 月 13 日の期間に発行された英文文献を対象とした検索を行った。また、J-STAGE を用いて 2014 年 1 月 1 日～2023 年 2 月 22 日の期間に発行された文献に対して英文キーワード検索を、2008 年 1 月 1 日～2023 年 2 月 22 日の期間に発行された文献に対して和文キーワード検索を実施した。該当フォルダ中に公表文献に関する報告書及び適合性ありと判断された文献の写し（オープンアクセスの文献を除く）を収載している。「ヒトに対する毒性」の分野において適合性ありと判断した公表文献については、疫学研究に関する文献とそれ以外に分類し、食品安全委員会より提供されているフォーマットに準じた資料を作成し収載している。

2.2　海外の評価機関が発行した評価書中で引用されている公表文献について

2023 年 6 月 13 日時点において、当該有効成分は米国及び欧州において除草剤として登録がある。なお、JMPR による評価は行われていない。

「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 日農薬資材審議会農薬分科会決定、令和 5 年 7 月 27 日一部改正）」に基づき該当する評価書を調査したところ、欧州食品安全機関（EFSA）及び米国環境保護庁（USEPA）発行の S-メトラクロールに関する評価書が確認され、報告書中の公表文献の引用を確認した。該当フォルダ中の公表文献に関する報告書及びその別添資料にて調査結果を報告するとともに、引用文献の写しを収載している。「ヒトに対する毒性」の分野の引用文献については、疫学研究に関する文献とそれ以外に分類し、食品安全委員会より提供されているフォーマットに準じた資料を作成し収載している。

3.　検索結果のまとめ

3.1　公表文献の調査結果

検索をおこなった全期間の調査結果のまとめを表 3.1-1～3.1-5 に示す。

表 3.1-1　評価目的との適合性評価（第 1 段階、第 2 段階）の結果のまとめ①
（2004 年 8 月 22 日～2014 年 8 月 22 日）

分野	データベース間の重複を除いた総論文数	第 1 段階		第 2 段階	
		適合性なし	それ以外（第 2 段階へ）	適合性なし	適合性あり（区分 a+b+c）
ヒトに対する毒性	1059	940	119	90 [c]	29 [c]
農作物及び畜産物への残留	1629	1620	9	9	0
生活環境動植物及び家畜に対する毒性	1296 [a]	1136	160 [a]	106 [d]	43 [a), d)]
環境動態	4283 [b]	4230	53 [b]	52 [b]	1
上記以外	0	0	0	11 [d]	0 [d]
合計	**8267**	**7926**	**341**	**268**	**73**

a)　EFSA の要求により追加で評価した 1 報を含む。
b)　EFSA の要求により追加で評価した 2 報を含む。
c)　2023 年に実施した適合性及び信頼性の再評価結果を反映したもの。EU に提出した報告書において適合性ありと判断された公表文献 33 報のうち、4 報は適合性なしと判断した。
d)　2023 年に実施した適合性及び信頼性の再評価結果を反映したもの。EU に提出した報告書において適合性ありと判断された公表文献 57 報のうち、3 報は適合性なしと判断し、11 報は作物への薬効及び薬害に関する文献として「4 分野以外」に分類し直し、いずれも適合性なしと判断した。

表 3.1-2　評価目的との適合性評価（第 1 段階、第 2 段階）の結果のまとめ②

（Web of Science Core Collection を用いた英文文献検索：2014 年 8 月 1 日～2023 年 2 月 13 日）

分野	データベース間の重複を除いた総論文数	第 1 段階		第 2 段階	
		適合性なし	それ以外（第 2 段階へ）	適合性なし	適合性あり (区分 a+b+c)
ヒトに対する毒性	45*	37*	8	1	7
農作物及び畜産物への残留	226*	213*	13	10	3
生活環境動植物及び家畜に対する毒性	133*	90*	43	12	32
環境動態	534*	397*	137	23	113
上記以外	267* a)	267*	0	0	0
合計	**1012**	**811**	**201**	**46**	**155**

*4 分野間での重複あり

a)　4 分野に該当しないことが明白な文献等は第 1 段階の評価以前に「上記以外」に分類した。

表 3.1-3　評価目的との適合性評価（第 1 段階、第 2 段階）の結果のまとめ③

（J-STAGE を用いた英文キーワード検索：2014 年 1 月 1 日～2023 年 2 月 22 日）

分野	データベース間の重複を除いた総論文数	第 1 段階		第 2 段階	
		適合性なし	それ以外（第 2 段階へ）	適合性なし	適合性あり (区分 a+b+c)
ヒトに対する毒性	21*	21*	0	0	0
農作物及び畜産物への残留	19*	19*	0	0	0
生活環境動植物及び家畜に対する毒性	15*	15*	0	0	0
環境動態	37*	37*	0	0	0
上記以外	0	0	0	0	0
合計	**46**	**46**	**0**	**0**	**0**

*4 分野間での重複あり

表 3.1-4　評価目的との適合性評価（第 1 段階、第 2 段階）の結果のまとめ④

（J-STAGE を用いた和文キーワード検索：2008 年 1 月 1 日～2023 年 2 月 22 日）

分野	データベース間の重複を除いた総論文数	第 1 段階		第 2 段階	
		適合性なし	それ以外（第 2 段階へ）	適合性なし	適合性あり (区分 a+b+c)
ヒトに対する毒性	26*	26*	0	0	0
農作物及び畜産物への残留	63*	63*	0	0	0
生活環境動植物及び家畜に対する毒性	43*	41*	2	2	0
環境動態	40*	38*	2	1	1
上記以外	0	0	0	0	0
合計	**68**	**64**	**4**	**3**	**1**

*4 分野間での重複あり

表 3.1-5　適合性評価第 2 段階で適合性ありとされた文献の分類結果及び信頼性評価結果

分野	該当する論文数		
	区分 a	区分 b	区分 c
ヒトに対する毒性	0	16	20
農作物及び畜産物への残留	0	2	1
生活環境動植物及び家畜に対する毒性	2	20	53
環境動態	1	17	97
合計	**3**	**55**	**171**

信頼性評価結果 (Klimisch 分類)		
信頼性評価結果 (Klimisch 分類)	Klimisch 1	1
	Klimisch 2	2
	Klimisch 3	0
	Klimisch 4	0
合計		**3**

3.2　海外の評価機関が発行した評価書中で引用されている公表文献の調査結果

2023 年 6 月 13 日時点において、S-メトラクロールに関して 3 件の欧州食品安全機関（EFSA）発行の評価書及び 18 件の米国環境保護庁（USEPA）の評価書が認められた（表 3.2-1）。これらの評価書中において計 258 件の文献の引用が確認された。

表 3.2-1　S-メトラクロールに関する海外の評価機関が発行した評価書（2023 年 6 月 13 日時点）

発行機関	評価書名	発行年
EFSA	Review of the existing maximum residue levels (MRLs) for S-metolachlor according to Article 12 of Regulation (EC) No 396/20051	2012
	Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted	2018
	Peer review of the pesticide risk assessment of the active substance S-metolachlor excluding the assessment of the endocrine disrupting properties	2023
USEPA	Metolachlor　Health Advisory Office of Drinking Water, USEPA	1987
	GUIDANCE FOR THE REREGISTRATION OF PESTICIDE PRODUCTS CONTAINING AS THE ACTIVE INGREDIENT METOLACHLOR	1987
	Reregistration Eligibility Decision (RED) Metolachlor	1995
	R.E.D. FACTS Metolachlor	1995
	Toxicology Chapter for Metolachlor/S-Metolachlor	2002
	SECONDARY VALUES FOR METOLACHLOR (CAS No. 51218-45-2)	2003
	Regulatory Determinations Support Document for Selected Contaminants from the Second Drinking Water Contaminant Candidate List (CCL 2) Part III: What About the Remaining CCL 2 Contaminants?	2008
	Registration Review Problem Formulation for Metolachlor and S-Metolachlor	2014
	Metolachlor: Tier 1 Review of Human Incidents	2014
	EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays for the List 1 Chemicals	2015
	Response to Public Comments on the EFED Registration Review Problem Formulation for Metolachlor and S-Metolachlor	2015

（次頁につづく）

表 **3.2-1　S-**メトラクロールに関する海外の評価機関が発行した評価書（**2023** 年 **6** 月 **13** 日時点）

（つづき）

発行機関	評価書名	発行年
USEPA	BEAD Response to Public Comments in Support of Registration Review (EPA Docket ID No.: EPA-HQ-OPP-2014-0772)-Metolachlor Case [S-metolachlor (108800) and Metolachlor (108801)]	2015
	Metolachlor/S-metolachlor: Report of the Cancer Assessment Review Committee (5th Evaluation)	2017
	Region 4 Ecological Risk Assessment Supplemental Guidance	2018
	Metolachlor & S-metolachlor: Drinking Water Exposure Assessment for Registration Review	2018
	Metolachlor and S-Metolachlor: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment	2019
	Metolachlor/S-Metolachlor: Draft Ecological Risk Assessment for Registration Review	2019
	Metolachlor/S-Metolachlor: Draft Human Health Risk Assessment for Registration Review	2020

以上

S-Metolachlor

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CA, Section 9

Toxicological and Toxicokinetic Studies

LITERATURE DATA

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

Table of Contents

CA 9 LITERATURE DATA

CA 9.1 Title

This document is a Literature Review Report for S-metolachlor, relevant metabolite(s) and EU representative formulation A9396G (Dual Gold®).

CA 9.2 Author(s) of the review

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CA 9.3 Summary: A brief summary indicating the purpose of the report, the methodology employed and the results obtained

This report summarises the search for "scientific peer-reviewed open literature on S-metolachlor and its potentially relevant metabolites(s) dealing with side effects on health and published within the last ten years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

The search strategy is detailed in the tables below. In summary, initially a very broad search was done to look for any references which included the active substance S-metolachlor, or its major metabolites, in conjunction with any of the key words set out in Table 9.5-1. The names searched for were:

```
L1      QUE  (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2      QUE  (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3      QUE  (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4      QUE  (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5      QUE  (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6      QUE  (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7      QUE  (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8      QUE  (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9      QUE  (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10     QUE  (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11     QUE  (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12     QUE  (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13     QUE  (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14     QUE  (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15     QUE  (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16     QUE  (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17     QUE  (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18     QUE  (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19     QUE  (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))
L20     QUE  ((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21     QUE  (55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22     QUE  (METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23     QUE  ((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24     QUE  (CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
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L25      QUE  (L1-L20)   METABOLITES
L26      QUE  (L21 OR L22 OR L23 OR L24)   METOLACHLOR
L27      QUE  (L25 OR L26)   METOLACHLOR & METABOLITES
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An overview of the results is summarised in the table below and further details are provided in Section 9.5.

Data requirement(s) captured in the search	**Number (Initial Search)**
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	1059
Number of *summary records* excluded from the search results after rapid assessment for relevance	940
Total number of *full-text* documents assessed in detail	119
Number of *studies* excluded from further consideration after detailed assessment for relevance	86
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	33

*both from bibliographic databases and other sources of peer-reviewed literature

CA 9.4 Protocol

CA 9.4.1 Statement of the objective of the review

The review has the objective of identifying “scientific peer-reviewed open literature on S-metolachlor and its potentially relevant metabolites(s) dealing with side effects on health and published within the last ten years before the date of submission of the dossier” in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

CA 9.4.2 Criteria for relevance with which decisions to select studies in the dossier were made

Table 9.4.2-1: List of Criteria for relevance for toxicological and toxicokinetic studies

Data requirements(s) (indicated by the correspondent CA data point (s))	**Criteria for relevance**
*CA 5.1 ADME studies	1. Well identified test material including purity and impurity profile 2. Relevant test species e.g. rodent – rat/mouse – non-rodent – dog 3. Relevant endpoint e.g. ADME measurement or metabolite identification 4. Well described condition of the test and quantitative assessment of results to substantiate and evaluate whether the study conclusions and endpoints are robust
*CA 5.2 Acute toxicity	1. Well identified test material including purity and impurity profile 2. Test species likely to be relevant to mammalian toxicology assessment – rats and mice, rabbit, guinea pig 3. Relevant route of administration for risk assessment 4. Describe observations, examinations, analyses performed or necropsy 5. Different outcome to those studies currently reported

Data requirements(s) (indicated by the correspondent CA data point (s))	Criteria for relevance
*CA 5.4 Genotoxicity	1. Well identified test material including purity and impurity profile 2. Relevant cell line or species used 3. "validated" or widely used test method 4. In vitro observation not addressed by in vivo data (including tissue specific effects) 5. In vivo effect in somatic or germs cells in relevant species 6. Relevant route of exposure to test substance 7. Contradicts submitted studies, impacts WoE. 8. Recognised methods for scoring studies outcomes used where applicable
*CA 5.3, 5.5, 5.6, 5.7, 5.8.1 Short term, chronic, reproductive and neurotoxicity, studies on metabolites	1. Well identified test material including purity and impurity profile 2. Test species likely to be relevant to mammalian toxicology assessment – rodents rats and mice, non- rodent dog is preferred 3. Sufficient number of animals per group to establish statistical significance 4. Test several dose levels (minimum 3) 5. Relevant route of administration for risk assessment 6. Include negative control (preferable) 7. Establish dose response 8. Describe observations, examinations, analyses performed or necropsy 9. Contradicts submitted studies and/or changes key endpoints
CA 5.8.2 Supplementary studies on the active substance	1. Identified test material 2. Unusual routes of exposure acceptable as they may introduce important information on other possible toxicological effects 3. Regulatory use usually limited to addressing species sensitivity /safety factors etc. 4. Examples of studies a. Effects of combined exposures b. Hormonal effects (if not guideline studies or included in 5.8.3) c. Hypersensitivity of specific sub-populations d. Gender and age variation in susceptibility (if not included in 5.6 Reproductive studies) e. Mode of action investigations
CA 5.8.3 Endocrine disrupting properties	1. Identified test material 2. All studies considered relevant at this stage – need to be checked for reliability 3. Relevant to ED assessment
CA 5.9 Medical data (including epidemiology) CP 7.2 to 7.4	1. Identified test material 2. All records considered relevant at this stage - need to be checked for reliability 3. Deemed relevant following review from epidemiologist

* Recommended protocols under each data point include but are not limited to those listed in the Commission Communications 2013/C 95/01 and 2013/C 95/02

In addition to the above, the criteria for relevance were expanded to consider whether the publication described any effect that was adverse, novel, or likely to affect the risk assessment, or impact on classification or labelling. Where this judgement has been used it is clearly explained in Table 9.6-4.

Any documents deemed relevant will be checked for reliability according to the criteria described by Klimisch *et al* (1997)[1] using the ToxRTool (http://ihcp.jrc.ec.europa.eu/our_labs/eurl-ecvam/archive-publications/toxrtool). Other criteria may also be used to complete the evaluation. Details of reliability evaluations will be included in the relevant part of the MCA Section 5.

[1] Klimisch H-J, Andreae M and Tillmann U (1997) A Systematic Approach for Evaluating the Quality of Experimental Toxicological and Ecotoxicological Data. Reg Tox Pharmacol 25, 1-5

Table 9.4.2-2: List of Criteria for relevance for operator exposure information/studies

Data requirements(s) (indicated by the correspondent CP data point (s))	Criteria for relevance
General criteria CP 7.2 all sections	5. Sufficient replicates must be included in the study to demonstrate statistical robustness 6. Agronomic practices must be relevant to scenario in submission, including: crop type ,application method and parameters (e.g. boom height), application rate 7. Leaf type and plant growth stage must be relevant to scenario in submission 8. Climactic/meteorological conditions of study must be relevant to scenario in submission, including rainfall, wind speed and temperature 9. Raw data must be available for analysis 10. Statistical analysis must be robust and relevant 11. Assessment of outliers/extreme values must be robust and relevant
Operator/worker exposure studies CP 7.2.1.2 and CP 7.2.3.2	1. Studies should follow accepted OECD protocol 2. Studies performed to GLP are preferred 3. Replicates should be minimum of 10
Biomonitoring studies CP 7.2.1.2, CP 7.2.2.2 and CP 7.2.3.2	1. Internal exposures must be clearly related to specific external doses 2. Replicates should be minimum of 10
Air monitoring studies CP 7.2.2.2	10. Monitoring parameters must be relevant to bystander/resident exposures, including monitoring distance, height and duration: 11. Accurate logs of relevant local activity must be available (e.g. crop spraying) 12. Accurate logs of local climactic/meteorological conditions must be available for the duration of the monitoring period, including rainfall, wind speed, wind direction, temperature and humidity
Dislodgeable foliar residue studies CP 7.2.3.2	1. Study must have been conducted on a similar formulation 2. Application number and interval must be relevant 3. Replicates must be minimum of 40
Foliar decline studies CP 7.2.3.2	4. Data must demonstrate minimum of two clear half lives 5. Sufficient data points must be provided to demonstrate decline curves between repeat applications 6. Studies with significant rainfall in first 48 hours should be discounted 7. Replicates must be minimum of 10

* Recommended protocols under each data point include but are not limited to those listed in the Commission Communications 2013/C 95/01 and 2013/C 95/02

CA 9.5 Search methods

Date of initial search	22.08.2014
Date of most recent update to search	-
Date span of the search	10 years

Table 9.5-1: Detailed Search Parameters for Toxicological and Toxicokinetic studies (CA 5.1 to 5.9)

Search Strategy	
L1	QUE (MUTAG? OR CANCER? OR TERATO? OR GENETOX? OR CARCIN?)
L2	QUE (TUMOUR? OR TUMOR? OR CYTOTOX? OR GENOTOX? OR MELANOM?)
L3	QUE (NEUROTOXI? OR LD50 OR IC50 OR ((LD OR IC)(W)50))
L4	QUE (((LONG OR SHORT)(W)TERM?)(L)(EFFECT? OR STUD? OR TOXIC?))
L5	QUE (ENDOCRIN? OR INHALAT? OR IRRITAT? OR REPROTOX?)
L6	QUE (PERCUTANEOU? OR DERMAL? OR ORAL? OR INTOXICAT? OR INGEST?)
L7	QUE (((REPRODUCT? OR EMBRYO? OR FOET? OR DEVELOP?)(5A)TOXI?))
L8	QUE ((ACUTE? OR CHRONIC?)(5A)(EFFECT? OR TOXIC? OR TOXIN#))
L9	QUE (GIRL# OR CHILD OR CHILDREN OR PATIENT# OR HUMAN# OR MAN)
L10	QUE (MEN OR WOM!N OR BOY# OR WORKER# OR OPERATOR# OR FARMER#)
L11	QUE (APPLICATOR# OR PERSONNEL? OR WORKFORCE OR EMPLOYEE#)
L12	QUE (MAMMAL? OR RODENT# OR RAT OR RATS OR MOUSE OR MICE)
L13	QUE (ACCIDENT? OR POISON? OR ALLERG? OR EXPOSURE? OR EXPOSE#)
L14	QUE (OCCUPAT? OR EPIDEMIOL? OR SENSITIZ? OR SENSITIS?)
L15	QUE ((HEALTH OR ADVERSE)(5A)(EFFECT# OR RISK#))
L16	QUE (MEDICAL OR (FIRST(W)AID) OR (TOXIC?(3A)STUD?) OR THERAPE?)
L17	QUE (TOXICOKINETIC# OR EXTRACTAB? OR (RADIO(W)LABEL?))
L18	QUE (DOG# OR (GUINEA(W)PIG#) OR RABBIT# OR SKIN? OR EYE#)
L19	QUE (HAND# OR DERMAL? OR BYSTANDER# OR RESIDENT#)
L20	QUE ((ROTAT? OR SUCCEDING OR FOLLOWING)(3A)CROP#)
L21	QUE ((DIETARY OR CONSUM? OR CUMULAT? OR AGGREGAT?)(5A)RISK?)
L22	QUE (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21)

Table 9.5-1: Detailed Search Parameters for Toxicological and Toxicokinetic studies (CA 5.1 to 5.9)

Provider	Database	Justification	Limits applied
Host STN	MEDLINE	Contains information on every area of medicine providing comprehensive coverage from 1948 to present. Sources include journals and chapters in books or symposia. The database is updated 5 times each week with an annual reload and therefore stays very current in its cover.	None
	EMBASE	The database, covers worldwide literature in the biomedical and pharmaceutical fields, including biological science, biochemistry, human medicine, forensic science, pediatrics, pharmacy, pharmacology and drug therapy, pharmacoeconomics, psychiatry, public health, biomedical engineering and instrumentation, and environmental science. Sources include more than 4,000 journals from approximately 70 countries, monographs, conference proceedings, dissertations, and reports. The databases covers data from 1974-present and is updated daily.	
	EMBAL	The database provides early access to bibliographic data and the abstracts for references that will appear in EMBASE. Bibliographic information for references is available in EMBAL for the latest 8 weeks of EMBASE data. The database covers the worldwide literature on the biomedical and pharmaceutical fields. Bibliographic information, abstracts, and author keywords are searchable. Sources include over 4,000 journals. The database covers current data and is updated daily.	
	ESBIOBASE	A database providing comprehensive coverage of the entire spectrum of biological research worldwide. Coverage includes the following areas: applied microbiology, biotechnology, cancer research, cell & developmental biology, clinical chemistry, ecological & environmental sciences, endocrinology, genetics, immunology, infectious diseases, metabolism, molecular biology, neuroscience, plant and crop science, protein biochemistry, and toxicology. Records are selected from over 1,700 international scientific journals, books, and conference proceedings. The database covers the period 1994 - present and is updated weekly.	
	AGRICOLA	A bibliographic database containing selected worldwide literature of agriculture and related fields. Coverage of the database includes agricultural economics and rural sociology, agricultural production, animal sciences, chemistry, entomology, food and human nutrition, forestry, natural resources, pesticides, plant science, soils and fertilizers, and water resources. Also covered are related areas such as biology and biotechnology, botany, ecology, and natural history. The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. It covers the period 1970-present and is updated monthly.	
	BIOSIS	A large and comprehensive worldwide life science database covers original research reports, reviews, and selected U.S. patents in biological and biomedical areas, with subject coverage ranging from aerospace biology to zoology. Sources include periodicals, journals, conference proceedings, reviews, reports, patents, and short communications. Nearly 6,000 life source journals, 1,500 international meetings as well as review articles, books, and monographs are reviewed for inclusion. It covers the period 1926 – present and is updated weekly.	
	CABA	Covers worldwide literature from all areas of agriculture and related sciences including biotechnology, forestry, and veterinary medicine. Sources include journals, books, reports, published theses, conference proceedings, and patents. It covers the period 1973-present and is updated weekly.	

Provider	Database	Justification	Limits applied
	CAPLUS	Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences including applied, macromolecular, organic, physical, inorganic, and analytical chemistry. Current sources include over 8,000 journals, patents, technical reports, books, conference proceedings, dissertations, product reviews, bibliographic items, book reviews, and meeting abstracts. Electronic-only journals and Web preprints are also covered. Cited references are included for journals, conference proceedings and basic patents from the U.S., EPO, WIPO, and German patent offices added to the CAS databases from 1999 to the present. Also provides early access to the bibliographic information, abstracts and CAS Registry Numbers for documents in the process of being indexed by CAS. Covers the period 1907 – present and is updated daily	
	FSTA	The database provides worldwide coverage of all scientific and technological aspects of the processing and manufacture of human food products including basic food sciences, biotechnology, hygiene and toxicology, engineering, packaging, and all individual foods and food products. Sources include more than 2,200 journals, books, reviews, conference proceedings, patents, standards, and legislation. It covers the period 1969 – present and is updated weekly.	
	FROSTI	The database contains citations to the worldwide literature on food science and technology including food and beverages, analytical methods, quality control, manufacturing, microbiology, food processing, health and nutrition, recipes, and additives. Sources include approximately 800 scientific and technical journals, bulletins, technical reports, conference proceedings, grey literature, and British, European (EP), U.S., Japanese, and international (PCT) patent applications. Covers the period 1972 – present and is updated twice weekly.	
	GEOREF	Covers international literature on geology and geosciences. Sources include the Bibliography of North American Geology, Bibliography and Index of Geology Exclusive of North America, Geophysical Abstracts, Bibliography of Fossil Vertebrates, selected records from Geoline and from geology sections of PASCAL and state and national geological surveys. Covers the period 1669 – present and is updated twice a month.	
	TOXCENTER	Covers the pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals. It is composed of the following subfiles: BIOSIS, CAplus, IPA and MEDLINE and sources include abstracts, books and book chapters, bulletins, conference proceedings, journal articles, letters, meetings, monographs, notes, papers, patents, presentations, research and project summaries, reviews, technical reports, theses, translations, unpublished material, web reprints. Covers the period 1907 – present and is updated weekly	
	PQSCITECH	Is a huge resource in all areas of science and technology from engineering to lifescience. The file is a merge of 25 STN databases formerly known as CSA databases (Cambridge Scientific Abstracts): AEROSPACE, ALUMINIUM, ANTE, AQUALINE, AQUASCI, BIOENG, CERAB, CIVILENG, COMPUAB, CONFSCI, COPPERLIT, CORROSION, ELCOM, EMA, ENVIROENG, HEALSAFE, LIFESCI, LISA, MATBUS, MECHENG, METADEX, OCEAN, POLLUAB, SOLIDSTATE, and WATER. Sources are journals, patents, books, reports, and conference proceedings spanning the period 1962 – present and it is updated monthly.	

Provider	Database	Justification	Limits applied
	PASCAL	The database provides access to the world's scientific and technical literature including physics and chemistry, life sciences (biology, medicine, and psychology), applied sciences and technology, earth sciences, and information sciences. French and European literature is particularly well represented. Approximately 5,000 journal titles are indexed. References to theses and to conference proceedings are also included. Spans the period 1977 to present and is updated weekly	
	SCISEARCH	Is an international index to the literature covering virtually every subject area within the broad fields of science, technology, and biomedicine. SciSearch contains all the records published in Science Citation Index Expanded™ and additional records from the Current Contents series of publications. Bibliographic information and cited references from over 5,600 scientific, technical, and medical journals are contained in the database. Spans the period 1974 to present and is updated weekly.	
	ANABST	Covers worldwide literature on analytical chemistry. The ANABSTR file contains bibliographic records with abstracts (since 1984) for documents reported in printed Analytical Abstracts. Sources for ANABSTR include journals, books, conference proceedings, reports, and standards. Spans the period 1980 to present and is updated weekly.	

* Total number of summary records retrieved after removing duplicates

Table 9.5-3: Detailed Search Parameters for Web searches

Website name and service publisher	URL	Justification	Search terms	Limits applied	Number*
A web search has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-4: Detailed Search Parameters for Journal Table of Contents

Journal name	Journal URL or publisher	Dates, volumes and issues searched	Method of searching	Search terms	Number*
A search for journal table of contents has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-5: Detailed Search Parameters for Reference Lists

Bibliographic details of documents whose reference lists were scanned	Number*
A search for reference lists has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.	

* Total number of summary records or full-text documents retrieved after removing duplicates

CA 9.6 Results

Table 9.6-1: Results of study selection process

Data requirement(s) captured in the search	Number (Initial Search)
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	1059
Number of *summary records* excluded from the search results after rapid assessment for relevance	940
Total number of *full-text* documents assessed in detail	119
Number of *studies* excluded from further consideration after detailed assessment for relevance	86
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	33

*both from bibliographic databases and other sources of peer-reviewed literature

For the initial rapid assessment, study titles were scanned to identify the relevance of studies for mammalian toxicology. Studies dismissed immediately included those clearly not related to toxicology and those unambiguously belonging to other section (ecotoxicology, residue data). In some cases the title did not provide sufficient information to dismiss the reference and in these cases the abstract was checked to confirm whether the full paper should be reviewed.

Table 9.6-2: List of references for all relevant and unclear studies listed by data point number

CA data point number	Author(s)	Year	Title	Source
Initial search				
Not applicable	Gordon A	2012	Review of toxicological effects caused by episodic stressor exposure.	Environmental Toxicology and Chemistry, (May 2012) Vol. 31, No. 5, pp. 1169-1174.
Not applicable	Pressman J	2010	Concentration, Chlorination, and Chemical Analysis of Drinking Water for Disinfection Byproduct Mixtures Health Effects Research: U.S. EPA's Four Lab Study	Environmental Science & Technology (2010), 44 (19), 7184-7192.
CA 5.1	Endo S	2011	Serum Albumin Binding of Structurally Diverse Neutral Organic Compounds: Data and Models	Chemical Research in Toxicology (2011), 24(12), 2293-2301.
CA 5.2.6	Gorski J	2012	An in vitro method for detecting chemical sensitization using human reconstructed skin models and its applicability to cosmetic, pharmaceutical, and medical device safety testing.	Cutaneous and Ocular Toxicology, (December 2012) Vol. 31, No. 4, pp. 292-305.
CA 5.3.2	Zhou M	2009	Observation on toxicity experiment of S-metolachlor	Zhiye Yu Jiankang (2009), 25(24), 2657-2661
CA 5.3.3	Val S *et al.*	2011	Role of size and composition of traffic and agricultural aerosols in the molecular responses triggered in airway epithelial cells.	Inhalation Toxicology (2011), 23 (11), 627-640.
CA 5.3.3	Val S *et al.*	2011	Role of size and composition of traffic and agricultural aerosols in the molecular responses triggered in airway epithelial cells [Erratum to document cited in CA156:382398]	Inhalation Toxicology (2011), 23 (14), 957.

CA data point number	Author(s)	Year	Title	Source
CA 5.4.1	Nikoloff N *et al.*	2013	Comparative study of cytotoxic and genotoxic effects induced by herbicide S-metolachlor and its commercial formulation Twin Pack Gold® in human hepatoma (HepG2) cells.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013 Dec) Vol. 62, pp. 777-81.
CA 5.4.2	Bokan K *et al.*	2010	Application of the SMART mutagenicity test and an aquatic toxicity biotest on pesticides as environmental stressors.	Noevenytermeles (2010), Volume 59, Number Supplement, pp. 187-190.
CA 5.5	Kleinstreuer N, *et al.*	2013	In Vitro Perturbations of Targets in Cancer Hallmark Processes Predict Rodent Chemical Carcinogenesis	Toxicological Sciences (2013), 131(1), 40-55
CA 5.6.2	Kleinstreuer N, *et al.*	2011	Environmental impact on vascular development predicted by high-throughput screening.	Environmental Health Perspectives, (November 2011) Vol. 119, No. 11, pp. 1596-1603.
CA 5.6.2	Padilla S *et al.*	2012	Zebrafish developmental screening of the ToxCast Phase I chemical library	Reproductive Toxicology (2012), 33 (2), 174-187.
CA 5.6.2	Zhou B *et al.*	2008	Study on zebrafish embryo-toxicity of four pesticides	Zhejiang Gongye Daxue Xuebao (2008), 36 (2), 136-140.
CA 5.8.1	Kubatova A *et al*.	2006	Genotoxicity of polar fractions from a herbicide-contaminated soil does not correspond to parent contaminants.	Environmental Toxicology and Chemistry, (JUL 2006) Vol. 25, No. 7, pp. 1742-1745.
CA 5.8.1	Rodriguez C *et al.*	2012	Assessing health risks from pesticides in recycled water: a case study of augmentation of drinking water supplies in Perth, Western Australia.	Human and Ecological Risk Assessment (2012), Volume 18, Number 6, pp. 1216-1236
CA 5.8.2	Ait-Aissa S *et al.*	2010	Anti-androgenic activities of environmental pesticides in the MDA-kb2 reporter cell line	Toxicology in Vitro (2010), 24(7), 1979-1985.
CA 5.8.2	Baldwin W *et al.*	2009	A Concentration Addition Model for the Activation of the Constitutive Androstane Receptor by Xenobiotic Mixtures	Toxicological Sciences (2009), 107 (1), 93-105.
CA 5.8.2	Cho H-Y	2008	Study on the biochemical characterization of herbicide detoxification enzyme, glutathione S-transferase	BioFactors, (2007) Vol. 30, No. 4, pp. 281-7.
CA 5.8.2	Crettaz P	2004	In silico methods used in a weight of evidence approach for assessing the human health effects of plant protection products.	Toxicology and Applied Pharmacology, (JUN 15 2004) Vol. 197, No. 3, pp. 284.
CA 5.8.2	Cunningham A *et al.*	2009	A structure-activity relationship (SAR) analysis for the identification of environmental estrogens: the categorical-SAR (cat-SAR) approach	Endocrine Disruption Modeling (2009), 173-198.

CA data point number	Author(s)	Year	Title	Source
CA 5.8.2	Genter M *et al*.	2009	Comparison of rat olfactory mucosal responses to carcinogenic and non-carcinogenic chloracetanilides.	Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association, (2009 Jun) Vol. 47, No. 6, pp. 1051-7.
CA 5.8.2	Genter M *et al.*	2010	Chloroacetanilide-induced nasal carcinogenesis in rats	Nose and Viral Cancer (2010), 427-434.
CA 5.8.2	Gohill V *et al.*	2010	Nutrient-sensitized screening for drugs that shift energy metabolism from mitochondrial respiration to glycolysis	Nature Biotechnology (2010), 28 (3), 249-255.
CA 5.8.2	Greenlee E *et al.*	2004	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9.
CA 5.8.2	Hartnett S *et al.*	2013	Cellular effects of metolachlor exposure on human liver (HepG2) cells.	Chemosphere, (2013 Jan) Vol. 90, No. 3, pp. 1258-66
CA 5.8.2	Hu J	2009	Immunotoxicity effect of metolachlor on mice	Harbin Yike Daxue Xuebao (2009), 43(1), 53-55
CA 5.8.2	Hu L-L *et al.*	2011	Predicting biological functions of compounds based on chemical-chemical interactions	PLoS One (2011), 6 (12), e29491.
CA 5.8.2	Judson R *et al*.	2010	In Vitro Screening of Environmental Chemicals for Targeted Testing Prioritization: The ToxCast Project	Environmental Health Perspectives (2010), 118 (4), 485-492.
CA 5.8.2	Kale V	2007	Mechanistic studies on hepatotoxicity of chloroacetanilide herbicides and hematotoxicity of munitions compound RDX and environmental degradation product MNX.	Dissertation Abstracts International. Vol. 68, no. 12. 2007
CA 5.8.2	Kale V *et al.*	2008	Comparative cytotoxicity of alachlor, acetochlor, and metolachlor herbicides in isolated rat and cryopreserved human hepatocytes.	Journal of biochemical and molecular toxicology, (2008 Feb) Vol. 22, No. 1, pp. 41-50.
CA 5.8.2	Kojima H *et al.*	2011	Comparative study of human and mouse pregnane X receptor agonistic activity in 200 pesticides using in vitro reporter gene assays	Toxicology (2011), 280(3), 77-87
CA 5.8.2	Kueblbeck J *et al.*	2011	Use of comprehensive screening methods to detect selective human CAR activators	Biochemical Pharmacology (2011), 82(12), 1994-2007
CA 5.8.2	Lemaire G *et al*.	2006	Activation of α- and β-estrogen receptors by persistent pesticides in reporter cell lines	Life Sciences (2006), 79(12), 1160-1169.
CA 5.8.2	Lemaire G *et al.*	2006	Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system.	Toxicological sciences : an official journal of the Society of Toxicology, (2006 Jun) Vol. 91, No. 2, pp. 501-9.
CA 5.8.2	Leslie E	2005	Multidrug resistance proteins: Role of P-glycoprotein, MRP1, MRP2, and BCRP (ABCG2) in tissue defense.	Toxicology and Applied Pharmacology, (2005) Vol. 204, No. 3, pp. 216-237.

CA data point number	Author(s)	Year	Title	Source
CA 5.8.2	Lowry D *et al.*	2013	Mechanism of metolachlor action due to alterations in cell cycle progression	Cell biology and toxicology, (2013 Aug) Vol. 29, No. 4, pp. 283-91.
CA 5.8.2	Miranda S *et al.*	2007	Cytotoxicity of chloroacetanilide herbicide alachlor in HepG2 cells independent of CYP3A4 and CYP3A7	Food and Chemical Toxicology (2007), 45 (5), 871-877.
CA 5.8.2	Oosterhuis B *at al.*	2008	Specific interactions of chloroacetanilide herbicides with human ABC transporter proteins.	Toxicology, (2008 Jun 3) Vol. 248, No. 1, pp. 45-51.
CA 5.8.2	Pereira S et al.	2009	Toxicity assessment of the herbicide metolachlor comparative effects on bacterial and mitochondrial model systems.	Toxicology in vitro : an international journal published in association with BIBRA, (2009 Dec) Vol. 23, No. 8, pp. 1585-90.
CA 5.8.2	Rotroff D *et al.*	2010	Xenobiotic-Metabolizing Enzyme and Transporter Gene Expression in Primary Cultures of Human Hepatocytes Modulated by Toxcast Chemicals	Journal of Toxicology and Environmental Health, Part B: Critical Reviews (2010), 13(2-4), 329-346
CA 5.8.2	Sinclair C *et al.*	2006	Prioritization of pesticide environmental transformation products in drinking water supplies	ENVIRONMENTAL SCIENCE & TECHNOLOGY, (1 DEC 2006) Vol. 40, No. 23, pp. 7283-7289.
CA 5.8.2	Sipes N *et al.*	2013	Profiling 976 ToxCast Chemicals across 331 Enzymatic and Receptor Signaling Assays	Chemical Research in Toxicology (2013), 26 (6), 878-895.
CA 5.8.2	Smital T	2011	Assessment of toxicological profiles of the municipal wastewater effluents using chemical analyses and bioassays	Ecotoxicology and Environmental Safety (2011), 74 (4), 844-851.
CA 5.8.2	Takeuchi S *et al.*	2006	In vitro screening of 200 pesticides for agonistic activity via mouse peroxisome proliferator-activated receptor (PPAR)α and PPARγ and quantitative analysis of in vivo induction pathway	Toxicology and Applied Pharmacology (2006), 217 (3), 235-244
CA 5.8.2	Takeuchi S *et al.*	2008	In vitro screening for aryl hydrocarbon receptor agonistic activity in 200 pesticides using a highly sensitive reporter cell line, DR-EcoScreen cells, and in vivo mouse liver cytochrome P450-1A induction by propanil, diuron and linuron	Chemosphere (2008), 74(1), 155-165
CA 5.8.2	Toccalino P *et al.*	2012	Chemical mixtures in untreated water from public-supply wells in the U.S. - Occurrence, composition, and potential toxicity	Science of the Total Environment (2012), 431, 262-270.
CA 5.8.2	Yoshida M *et al.*	2013	Simulation of acute reference dose (ARfD) settings for pesticides in Japan	Journal of Toxicological Sciences (2013), 38 (2), 205-214.
CA 5.8.3	Bishop P *et al.*	2014	The Use and Acceptance of Other Scientifically Relevant Information (OSRI) in the U.S. Environmental Protection Agency (EPA) Endocrine Disruptor Screening Program	Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2014), 101 (1), 3-22.

CA data point number	Author(s)	Year	Title	Source
CA 5.8.3	Hayes T	2006	Chemical mixtures: Hayes responds [4].	Environmental Health Perspectives, (Sep 2006) Vol. 114, No. 9, pp. A518-A519.
CA 5.8.3	Jarosova B *et al.*	2012	Changes in concentrations of hydrophilic organic contaminants and of endocrine-disrupting potential downstream of small communities located adjacent to headwaters	Environment International (2012), 45, 22-31.
CA 5.8.2	Kojima H *et al.*	2004	Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using chinese hamster ovary cells	Environmental Health Perspectives (2004), 112 (5), 524-531.
CA 5.8.2	Laville N *et al*.	2006	Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line.	Toxicology, (2006 Nov 10) Vol. 228, No. 1, pp. 98-108.
CA 5.8.3	Mathias *F et al.*	2012	Herbicide Metolachlor Causes Changes in Reproductive Endocrinology of Male Wistar Rats	ISRN Toxicology (2012) 130846.
CA 5.8.3	Mnif W	2011	Effect of endocrine disruptor pesticides: A review.	International Journal of Environmental Research and Public Health, (June 2011) Vol. 8, No. 6, pp. 2265-2303.
CA 5.8.3	Reif D *et al*.	2010	Endocrine profiling and prioritization of environmental chemicals using ToxCast data.	Environmental Health Perspectives (2010), 118(12), 1714-1720.
CA 5.8.3	Rotroff D *et al.*	2014	Predictive Endocrine Testing in the 21st Century Using in Vitro Assays of Estrogen Receptor Signaling Responses.	Environmental Science & Technology (2014), 48 (15), 8706-8716.
CA 5.8.3	Wambaugh J *et al*.	2013	High-Throughput Models for Exposure-Based Chemical Prioritization in the ExpoCast Project.	Environmental Science & Technology (2013), 47 (15), 8479-8488.
CA 5.9.2	Beard J *et al.*	2011	Suicide and pesticide use among pesticide applicators and their spouses in the Agricultural Health Study.	Environmental Health Perspectives, (November 2011) Vol. 119, No. 11, pp. 1610-1615.
CA 5.9.2	Hsu B-G	2009	Late-onset Methemoglobinemia Induced by Metobromuron/metolachlor.	Tzu Chi Medical Journal, (December 2009) Vol. 21, No. 4, pp. 334-338
CA 5.9.4	Alavanja M *et al.*	2004	Pesticides and lung cancer risk in the agricultural health study cohort.	American journal of epidemiology, (2004 Nov 1) Vol. 160, No. 9, pp. 876-85.
CA 5.9.4	Andreotti G *et al.*	2009	Agricultural pesticide use and pancreatic cancer risk in the Agricultural Health Study Cohort	International Journal of Cancer (2009), 124(10), 2495-2500
CA 5.9.4	Andreotti G *et al.*	2010	Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort.	Cancer causes & control: CCC, (2010 Nov) Vol. 21, No. 11, pp. 1759-75.
CA 5.9.4	Barr D	2010	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	The Science of the total environment, (2010 Jan 15) Vol. 408, No. 4, pp. 790-5.

CA data point number	Author(s)	Year	Title	Source
CA 5.9.4	Barry K *et al.*	2011	Genetic variation in base excision repair pathway genes, pesticide exposure, and prostate cancer risk	Environmental Health Perspectives (2011), 119(12), 1726-1732
CA 5.9.4	Bonner M *et al.*	2005	The Agricultural Health Study biomarker workshop on cancer etiology.	Journal of Biochemical and Molecular Toxicology, (2005) Vol. 19, No. 3, pp. 169-171.
CA 5.9.4	Dayton S *et al.*	2010	Pesticide use and myocardial infarction incidence among farm women in the agricultural health study.	Journal of Occupational and Environmental Medicine, (July 2010) Vol. 52, No. 7, pp. 693-697.
CA 5.9.4	Dennis L *et al.*	2010	Pesticide use and cutaneous melanoma in pesticide applicators in the agricultural heath study	Environmental Health Perspectives (2010), 118(6), 812-817
CA 5.9.4	Fantke P *et al.*	2012	Health impact and damage cost assessment of pesticides in Europe	Environment International (2012), 49, 9-17.
CA 5.9.4	Flower K *et al*.	2004	Cancer risk and parental pesticide application in children of agricultural health study participants	Environmental Health Perspectives (2004), 112(5), 631-635.
CA 5.9.4	Freeman L *et al*.	2011	Atrazine and cancer incidence among pesticide applicators in the agricultural health study (1994-2007)	Environmental Health Perspectives (2011), 119 (9), 1253-1259.
CA 5.9.4	Gallois J	2011	DNA adduct variations in non-smoking crop farmers: Potential relationship with occupational exposure to pesticides?	Environmental Toxicology and Pharmacology, (July 2011) Vol. 32, No. 1, pp. 1-9.
CA 5.9.4	Hoppin J *et al.*	2006	Pesticides and adult respiratory outcomes in the agricultural health study.	Annals of the New York Academy of Sciences, (Sep 2006) Vol. 1076, pp. 343-354.
CA 5.9.4	Hou L	2013	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Environmental health perspectives, (2013 Aug) Vol. 121, No. 8, pp. 919-24.
CA 5.9.4	Huijbregts M *et al.*	2005	Human toxicological effect and damage factors of carcinogenic and noncarcinogenic chemicals for life cycle impact assessment	Integrated Environmental Assessment and Management (2005), 1(3), 181-244.
CA 5.9.4	Kamel F *et al.*	2012	Pesticide exposure and amyotrophic lateral sclerosis	NeuroToxicology (2012), 33(3), 457-462
CA 5.9.4	Koutros S *et al.*	2010	Pesticide Use Modifies the Association Between Genetic Variants on Chromosome 8q24 and Prostate Cancer	Cancer Research (2010), 70(22), 9224-9233
CA 5.9.4	Koutros S *et al.*	2011	Xenobiotic-metabolizing gene variants, pesticide use, and the risk of prostate cancer	Pharmacogenetics and Genomics (2011), 21(10), 615-623
CA 5.9.4	Koutros S	2013	Genetic susceptibility loci, pesticide exposure and prostate cancer risk	PLoS One (2013), 8 (4), e58195.
CA 5.9.4	Landgren O *et al.*	2009	Pesticide exposure and risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study	Blood (2009), 113(25), 6386-6391

CA data point number	Author(s)	Year	Title	Source
CA 5.9.4	Lee W *et al.*	2004	Agricultural pesticide use and adenocarcinomas of the stomach and oesophagus	Occupational and Environmental Medicine (2004), 61(9), 743-749
CA 5.9.4	Lee W *et al.*	2005	Agricultural pesticide use and risk of glioma in Nebraska, United States	Occupational and Environmental Medicine (2005), 62(11), 786-792
CA 5.9.4	Lee W *et al.*	2007	Pesticide use and colorectal cancer risk in the Agricultural Health Study	International Journal of Cancer (2007), 121(2), 339-346
CA 5.9.4	Metayer C	2013	Exposure to herbicides in house dust and risk of childhood acute lymphoblastic leukemia	Journal of exposure science & environmental epidemiology, (2013 Jul) Vol. 23, No. 4, pp. 363-70
CA 5.9.4	Migeot V	2013	Drinking-water exposure to a mixture of nitrate and low-dose atrazine metabolites and small-for-gestational age (SGA) babies: A historic cohort study.	Environmental Research (2013), 122, 58-64.
CA 5.9.4	Pellizzari E	2004	Assessment of data quality for the NHEXAS - Part II: Minnesota children's pesticide exposure study (MNCPES). [Erratum to document cited in CA140:308309]	Journal of Exposure Analysis and Environmental Epidemiology (2004), 14(1), 108
CA 5.9.4	Perry M	2008	Effects of environmental and occupational pesticide exposure on human sperm: A systematic review.	Human Reproduction Update, (2008) Vol. 14, No. 3, pp. 233-242.
CA 5.9.4	Phillips K	2008	Human exposure to endocrine disrupters and semen quality.	Journal of Toxicology and Environmental Health - Part B: Critical Reviews, (Mar 2008) Vol. 11, No. 3-4, pp. 188-220.
CA 5.9.4	Red R	2011	Environmental toxicant exposure during pregnancy.	Obstetrical and Gynecological Survey, (March 2011) Vol. 66, No. 3, pp. 159-169.
CA 5.9.4	Rosenfeld P *et al.*	2011	Pesticides.	Rosenfeld, PE; Feng, LGH. (2011) pp. 127-154. Risks of Hazardous Wastes.
CA 5.9.4	Ruder A *et al.*	2004	Gliomas and farm pesticide exposure in men: The upper midwest health study.	Archives of Environmental Health, (Dec 2004) Vol. 59, No. 12, pp. 650-657.
CA 5.9.4	Rusiecki J *et al.*	2005	Cancer incidence among pesticide applicators exposed to metolachlor in the agricultural health study	EPIDEMIOLOGY, (SEP 2005) Vol. 16, No. 5, pp. S98-S98.
CA 5.9.4	Rusiecki J	2006	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	International journal of cancer. Journal international du cancer, (2006 Jun 15) Vol. 118, No. 12, pp. 3118-23.
CA 5.9.4	Sathiakumar N *et al.*	2011	A review of epidemiologic studies of triazine herbicides and cancer.	Critical Reviews in Toxicology, (April 2011) Vol. 41, No. SUPPL. 1, pp. 1-34.

CA data point number	Author(s)	Year	Title	Source
CA 5.9.4	Slager R	2010	Rhinitis associated with pesticide use among private pesticide applicators in the agricultural health study.	Journal of toxicology and environmental health. Part A, (2010) Vol. 73, No. 20, pp. 1382-93.
CA 5.9.4	Thorpe N	2005	Herbicides and nitrates in groundwater of Maryland and childhood cancers: a geographic information systems approach.	Journal of environmental science and health. Part C, Environmental carcinogenesis & ecotoxicology reviews, (2005) Vol. 23, No. 2, pp. 261-78.
CA 5.9.4	Wang N *et al.*	2012	Pollution level and human health risk assessment of some pesticides and polychlorinated biphenyls in Nantong of Southeast China.	Journal of Environmental Sciences (2012), Volume 24, Number 10, pp.1854-1860.
CA 5.9.4	Weichenthal *et al.*	2010	A review of pesticide exposure and cancer incidence in the Agricultural Health Study cohort.	Environmental health perspectives, (2010 Aug) Vol. 118, No. 8, pp. 1117-25.
CA 5.9.4	Wells K et al.	2010	Development of a gis-based model for estimating residential agricultural pesticide exposure and its application to a study of prostate cancer incidence and pesticide exposure.	American Journal of Epidemiology, (JUN 1 2010) Vol. 171, No. Suppl. 11, pp. S84.
CA 5.9.4	Wickerham E et al.	2012	Reduced birth weight in relation to pesticide mixtures detected in cord blood of full-term infants.	Environment International, (OCT 15 2012) Vol. 47, pp. 80-85.
CA 5.9.4	Wofford P et al.	2014	Community air monitoring for pesticides. Part 3: using health-based screening levels to evaluate results collected for a year.	Environmental monitoring and assessment, (2014 Mar) Vol. 186, No. 3, pp. 1355-70.
CA 5.9.4	Yan X *et al.*	2009	Pesticide concentrations in matrices collected in the perinatal period in a population of pregnant women and newborns in New Jersey, USA	Human and Ecological Risk Assessment (2009), 15(5), 948-967
CA 5.9.7	Seok S-J *et al.*	2012	Acute oral poisoning due to chloracetanilide herbicides.	Journal of Korean medical science, (2012 Feb) Vol. 27, No. 2, pp. 111-4.
CP 7.2.1.2,	Hayat K. *et al.*	2010	Determination of pesticide residues in blood samples of villagers involved in pesticide application at District Vehari (Punjab), Pakistan	African Journal of Environmental Science and Technology Vol. 4(10), pp. 666-684, October 2010
CP 7.2.1.2, CP 7.2.3.2	Panuwet P. *et al.*	2008	Concentrations of urinary pesticide metabolites in small-scale farmers in Chiang Mai Province, Thailand.	Sci. Total Environ. (2008 Dec) 15;407(1):655-68
CP 7.2.1.2, CP 7.2.2.2, CP 7.2.3.2	Curwin B. et al.	2005	Urinary and hand wipe pesticide levels among farmers and nonfarmers in Iowa	Journal of Exposure Analysis and Environmental Epidemiology (2005) 15, 500–508

CA data point number	Author(s)	Year	Title	Source
CP 7.2.1.2, CP 7.2.2.2, CP 7.2.3.2	Curwin B. et al.	2007	Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in iowa.	Ann. Occup. Hyg. (2007 Jan);51(1):53-65
CP 7.2.1.2, CP 7.2.3.2	Schummer C. et al.	2012	Determination of farm workers' exposure to pesticides by hair analysis.	Toxicol. Lett. (2012 Apr) 25;210(2):203-10
CP 7.2.1.2, CP 7.2.3.2	Arcury T. et al.	2010	Repeated pesticide exposure among North Carolina migrant and seasonal farmworkers	Am. J. Ind. Med. (2010 Aug);53(8):802-13
CP 7.2.1.2, CP 7.2.3.2	Arcury T. et al.	2009	Seasonal Variation in the Measurement of Urinary Pesticide Metabolites among Latino Farmworkers in Eastern North Carolina	Int. J. Occup. Environ. Health. (2009 Oct–Dec); 15(4): 339–350
CP 7.2.2.2	Curwin B. et al.	2005	Pesticide contamination inside farm and nonfarm homes.	J. Occup. Environ. Hyg. (2005 Jul);2(7):357-67
CP 7.2.2.2	Ward M. et al.	2006	Proximity to crops and residential exposure to agricultural herbicides in iowa.	Environ. Health Perspect. 2006 Jun;114(6):893-7
CP 7.2.2.2	Curwin B. et al.	2007	Pesticide dose estimates for children of Iowa farmers and non-farmers	Environmental Research, Volume 105, Issue 3, (November 2007), Pages 307–315
CP 7.2.2.2	Arcury T. et al.	2007	Pesticide urinary metabolite levels of children in eastern North Carolina farmworker households.	Environ. Health Perspect. (2007 Aug);115(8):1254-60
CP 7.2.2.2	Aulagnier F et al.	2008	Pesticides measured in air and precipitation in the Yamaska Basin (Québec): occurrence and concentrations in 2004.	Sci. Total Environ. (2008 May) 15;394 (2-3) 338-48
CP 7.2.2.2	Peck A. et al.	2005	Gas-Phase Concentrations of Current-Use Pesticides in Iowa	Environ. Sci. Technol. (**2005**), 39, 2952-2959
CA 5.9.4	Swan	2003	Semen Quality in Relation to Biomarkers of Pesticide Exposure	Environmental Health Perspectives, vol 111, 12 September 2003.
CA 5.9.4	Munger	2007	Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies	Environmental Health Perspectives, Volume 105, Number 3, March 1997
CA 5.9.4	Chevrier Gwendolina	2011	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Environmental health perspectives, (2011 Jul) Vol. 119, No. 7, pp. 1034-41.
CA 5.9.4	Alavanja M *et al.*	2003	Use of Agricultural Pesticides and Prostate Cancer Risk in the Agricultural Health Study Cohort	Am J Epidemiol 2003;157:800–814

Table 9.6-3: List of references for all relevant and unclear studies listed by Author

Author(s)	Year	CA data point number	Title	Source
Initial Search				
Ait-Aissa S *et al.*	2010	CA 5.8.2	Anti-androgenic activities of environmental pesticides in the MDA-kb2 reporter cell line	Toxicology in Vitro (2010), 24(7), 1979-1985.
Alavanja M *et al.*	2003	CA 5.9.4	Use of Agricultural Pesticides and Prostate Cancer Risk in the Agricultural Health Study Cohort	Am J Epidemiol 2003;157:800–814
Alavanja M *et al.*	2004	CA 5.9.4	Pesticides and lung cancer risk in the agricultural health study cohort.	American journal of epidemiology, (2004 Nov 1) Vol. 160, No. 9, pp. 876-85.
Andreotti G *et al.*	2009	CA 5.9.4	Agricultural pesticide use and pancreatic cancer risk in the Agricultural Health Study Cohort	International Journal of Cancer (2009), 124(10), 2495-2500
Andreotti G *et al.*	2010	CA 5.9.4	Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort.	Cancer causes & control: CCC, (2010 Nov) Vol. 21, No. 11, pp. 1759-75.
Arcury T. et al.	2007	CP 7.2.2.2	Pesticide urinary metabolite levels of children in eastern North Carolina farmworker households.	Environ. Health Perspect. (2007 Aug);115(8):1254-60
Arcury T. et al.	2010	CP 7.2.1.2, CP 7.2.3.2	Repeated pesticide exposure among North Carolina migrant and seasonal farmworkers	Am. J. Ind. Med. (2010 Aug);53(8):802-13
Arcury T. et al.	2009	CP 7.2.1.2, CP 7.2.3.2	Seasonal Variation in the Measurement of Urinary Pesticide Metabolites among Latino Farmworkers in Eastern North Carolina	Int. J. Occup. Environ. Health. (2009 Oct–Dec); 15(4): 339–350
Aulagnier F et al.	2008	CP 7.2.2.2	Pesticides measured in air and precipitation in the Yamaska Basin (Québec): occurrence and concentrations in 2004.	Sci. Total Environ. (2008 May) 15;394 (2-3) 338-48
Baldwin W *et al.*	2009	CA 5.8.2	A Concentration Addition Model for the Activation of the Constitutive Androstane Receptor by Xenobiotic Mixtures	Toxicological Sciences (2009), 107 (1), 93-105.
Barr D	2010	CA 5.9.4	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	The Science of the total environment, (2010 Jan 15) Vol. 408, No. 4, pp. 790-5.
Barry K *et al.*	2011	CA 5.9.4	Genetic variation in base excision repair pathway genes, pesticide exposure, and prostate cancer risk	Environmental Health Perspectives (2011), 119(12), 1726-1732
Beard J *et al.*	2011	CA 5.9.2	Suicide and pesticide use among pesticide applicators and their spouses in the Agricultural Health Study.	Environmental Health Perspectives, (November 2011) Vol. 119, No. 11, pp. 1610-1615.
Bishop P *et al.*	2014	CA 5.8.3	The Use and Acceptance of Other Scientifically Relevant Information (OSRI) in the U.S. Environmental Protection Agency (EPA) Endocrine Disruptor Screening Program	Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2014), 101 (1), 3-22.

Author(s)	Year	CA data point number	Title	Source
Bokan K *et al.*	2010	CA 5.4.2	Application of the SMART mutagenicity test and an aquatic toxicity biotest on pesticides as environmental stressors.	Noevenytermeles (2010), Volume 59, Number Supplement, pp. 187-190.
Bonner M *et al.*	2005	CA 5.9.4	The Agricultural Health Study biomarker workshop on cancer etiology.	Journal of Biochemical and Molecular Toxicology, (2005) Vol. 19, No. 3, pp. 169-171.
Chevrier Gwendolina	2011	CA 5.9.4	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Environmental health perspectives, (2011 Jul) Vol. 119, No. 7, pp. 1034-41.
Cho H-Y	2008	CA 5.8.2	Study on the biochemical characterization of herbicide detoxification enzyme, glutathione S-transferase	BioFactors, (2007) Vol. 30, No. 4, pp. 281-7.
Crettaz P	2004	CA 5.8.2	In silico methods used in a weight of evidence approach for assessing the human health effects of plant protection products.	Toxicology and Applied Pharmacology, (JUN 15 2004) Vol. 197, No. 3, pp. 284.
Cunningham A *et al.*	2009	CA 5.8.2	A structure-activity relationship (SAR) analysis for the identification of environmental estrogens: the categorical-SAR (cat-SAR) approach	Endocrine Disruption Modeling (2009), 173-198.
Curwin B. et al.	2005	CP 7.2.2.2	Pesticide contamination inside farm and nonfarm homes.	J. Occup. Environ. Hyg. (2005 Jul);2(7):357-67
Curwin B. et al.	2005	CP 7.2.1.2, CP 7.2.2.2, CP 7.2.3.2	Urinary and hand wipe pesticide levels among farmers and nonfarmers in Iowa	Journal of Exposure Analysis and Environmental Epidemiology (2005) 15, 500–508
Curwin B. et al.	2007	CP 7.2.2.2	Pesticide dose estimates for children of Iowa farmers and non-farmers	Environmental Research, Volume 105, Issue 3, (November 2007), Pages 307–315
Curwin B. et al.	2007	CP 7.2.1.2, CP 7.2.2.2, CP 7.2.3.2	Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in iowa.	Ann. Occup. Hyg. (2007 Jan);51(1):53-65
Dayton S *et al.*	2010	CA 5.9.4	Pesticide use and myocardial infarction incidence among farm women in the agricultural health study.	Journal of Occupational and Environmental Medicine, (July 2010) Vol. 52, No. 7, pp. 693-697.
Dennis L *et al.*	2010	CA 5.9.4	Pesticide use and cutaneous melanoma in pesticide applicators in the agricultural heath study	Environmental Health Perspectives (2010), 118(6), 812-817
Endo S	2011	CA 5.1	Serum Albumin Binding of Structurally Diverse Neutral Organic Compounds: Data and Models	Chemical Research in Toxicology (2011), 24(12), 2293-2301.
Fantke P *et al.*	2012	CA 5.9.4	Health impact and damage cost assessment of pesticides in Europe	Environment International (2012), 49, 9-17.
Flower K *et al.*	2004	CA 5.9.4	Cancer risk and parental pesticide application in children of agricultural health study participants	Environmental Health Perspectives (2004), 112(5), 631-635.

Author(s)	Year	CA data point number	Title	Source
Freeman L *et al*.	2011	CA 5.9.4	Atrazine and cancer incidence among pesticide applicators in the agricultural health study (1994-2007)	Environmental Health Perspectives (2011), 119 (9), 1253-1259.
Gallois J	2011	CA 5.9.4	DNA adduct variations in non-smoking crop farmers: Potential relationship with occupational exposure to pesticides?	Environmental Toxicology and Pharmacology, (July 2011) Vol. 32, No. 1, pp. 1-9.
Genter M *et al*.	2009	CA 5.8.2	Comparison of rat olfactory mucosal responses to carcinogenic and non-carcinogenic chloracetanilides.	Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association, (2009 Jun) Vol. 47, No. 6, pp. 1051-7.
Genter M *et al.*	2010	CA 5.8.2	Chloroacetanilide-induced nasal carcinogenesis in rats	Nose and Viral Cancer (2010), 427-434.
Gohill V *et al.*	2010	CA 5.8.2	Nutrient-sensitized screening for drugs that shift energy metabolism from mitochondrial respiration to glycolysis	Nature Biotechnology (2010), 28 (3), 249-255.
Gordon A	2012	Not applicable	Review of toxicological effects caused by episodic stressor exposure.	Environmental Toxicology and Chemistry, (May 2012) Vol. 31, No. 5, pp. 1169-1174.
Gorski J	2012	CA 5.2.6	An in vitro method for detecting chemical sensitization using human reconstructed skin models and its applicability to cosmetic, pharmaceutical, and medical device safety testing.	Cutaneous and Ocular Toxicology, (December 2012) Vol. 31, No. 4, pp. 292-305.
Greenlee E *et al.*	2004	CA 5.8.2	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9.
Hartnett S *et al.*	2013	CA 5.8.2	Cellular effects of metolachlor exposure on human liver (HepG2) cells.	Chemosphere, (2013 Jan) Vol. 90, No. 3, pp. 1258-66
Hayat K. *et al.*	2010	CP 7.2.1.2,	Determination of pesticide residues in blood samples of villagers involved in pesticide application at District Vehari (Punjab), Pakistan	African Journal of Environmental Science and Technology Vol. 4(10), pp. 666-684, October 2010
Hayes T	2006	CA 5.8.3	Chemical mixtures: Hayes responds [4].	Environmental Health Perspectives, (Sep 2006) Vol. 114, No. 9, pp. A518-A519.
Hoppin J *et al.*	2006	CA 5.9.4	Pesticides and adult respiratory outcomes in the agricultural health study.	Annals of the New York Academy of Sciences, (Sep 2006) Vol. 1076, pp. 343-354.
Hou L	2013	CA 5.9.4	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Environmental health perspectives, (2013 Aug) Vol. 121, No. 8, pp. 919-24.
Hsu B-G	2009	CA 5.9.2	Late-onset Methemoglobinemia Induced by Metobromuron/metolachlor.	Tzu Chi Medical Journal, (December 2009) Vol. 21, No. 4, pp. 334-338
Hu J	2009	CA 5.8.2	Immunotoxicity effect of metolachlor on mice	Harbin Yike Daxue Xuebao (2009), 43(1), 53-55

Author(s)	Year	CA data point number	Title	Source
Hu L-L *et al.*	2011	CA 5.8.2	Predicting biological functions of compounds based on chemical-chemical interactions	PLoS One (2011), 6 (12), e29491.
Huijbregts M *et al.*	2005	CA 5.9.4	Human toxicological effect and damage factors of carcinogenic and noncarcinogenic chemicals for life cycle impact assessment	Integrated Environmental Assessment and Management (2005), 1(3), 181-244.
Kleinstreuer N, *et al.*	2011	CA 5.6.2	Environmental impact on vascular development predicted by high-throughput screening.	Environmental Health Perspectives, (November 2011) Vol. 119, No. 11, pp. 1596-1603.
Kleinstreuer N, *et al.*	2013	CA 5.5	In Vitro Perturbations of Targets in Cancer Hallmark Processes Predict Rodent Chemical Carcinogenesis	Toxicological Sciences (2013), 131(1), 40-55
Kubatova A *et al.*	2006	CA 5.8.1	Genotoxicity of polar fractions from a herbicide-contaminated soil does not correspond to parent contaminants.	Environmental Toxicology and Chemistry, (JUL 2006) Vol. 25, No. 7, pp. 1742-1745.
Jarosova B *et al.*	2012	CA 5.8.3	Changes in concentrations of hydrophilic organic contaminants and of endocrine-disrupting potential downstream of small communities located adjacent to headwaters	Environment International (2012), 45, 22-31.
Judson R *et al.*	2010	CA 5.8.2	In Vitro Screening of Environmental Chemicals for Targeted Testing Prioritization: The ToxCast Project	Environmental Health Perspectives (2010), 118 (4), 485-492.
Kale V	2007	CA 5.8.2	Mechanistic studies on hepatotoxicity of chloroacetanilide herbicides and hematotoxicity of munitions compound RDX and environmental degradation product MNX.	Dissertation Abstracts International. Vol. 68, no. 12. 2007
Kale V *et al.*	2008	CA 5.8.2	Comparative cytotoxicity of alachlor, acetochlor, and metolachlor herbicides in isolated rat and cryopreserved human hepatocytes.	Journal of biochemical and molecular toxicology, (2008 Feb) Vol. 22, No. 1, pp. 41-50.
Kamel F *et al.*	2012	CA 5.9.4	Pesticide exposure and amyotrophic lateral sclerosis	NeuroToxicology (2012), 33(3), 457-462
Kojima H *et al.*	2004	CA 5.8.2	Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using chinese hamster ovary cells	Environmental Health Perspectives (2004), 112 (5), 524-531.
Kojima H *et al.*	2011	CA 5.8.2	Comparative study of human and mouse pregnane X receptor agonistic activity in 200 pesticides using in vitro reporter gene assays	Toxicology (2011), 280(3), 77-87
Koutros S *et al.*	2010	CA 5.9.4	Pesticide Use Modifies the Association Between Genetic Variants on Chromosome 8q24 and Prostate Cancer	Cancer Research (2010), 70(22), 9224-9233
Koutros S *et al.*	2011	CA 5.9.4	Xenobiotic-metabolizing gene variants, pesticide use, and the risk of prostate cancer	Pharmacogenetics and Genomics (2011), 21(10), 615-623
Koutros S	2013	CA 5.9.4	Genetic susceptibility loci, pesticide exposure and prostate cancer risk	PLoS One (2013), 8 (4), e58195.

Author(s)	Year	CA data point number	Title	Source
Kueblbeck J *et al.*	2011	CA 5.8.2	Use of comprehensive screening methods to detect selective human CAR activators	Biochemical Pharmacology (2011), 82(12), 1994-2007
Landgren O *et al.*	2009	CA 5.9.4	Pesticide exposure and risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study	Blood (2009), 113(25), 6386-6391
Laville N *et al.*	2006	CA 5.8.2	Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line.	Toxicology, (2006 Nov 10) Vol. 228, No. 1, pp. 98-108.
Lee W *et al.*	2004	CA 5.9.4	Agricultural pesticide use and adenocarcinomas of the stomach and oesophagus	Occupational and Environmental Medicine (2004), 61(9), 743-749
Lee W *et al.*	2005	CA 5.9.4	Agricultural pesticide use and risk of glioma in Nebraska, United States	Occupational and Environmental Medicine (2005), 62(11), 786-792
Lee W *et al.*	2007	CA 5.9.4	Pesticide use and colorectal cancer risk in the Agricultural Health Study	International Journal of Cancer (2007), 121(2), 339-346
Lemaire G *et al.*	2006	CA 5.8.2	Activation of α- and β-estrogen receptors by persistent pesticides in reporter cell lines	Life Sciences (2006), 79(12), 1160-1169.
Lemaire G *et al.*	2006	CA 5.8.2	Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system.	Toxicological sciences : an official journal of the Society of Toxicology, (2006 Jun) Vol. 91, No. 2, pp. 501-9.
Leslie E	2005	CA 5.8.2	Multidrug resistance proteins: Role of P-glycoprotein, MRP1, MRP2, and BCRP (ABCG2) in tissue defense.	Toxicology and Applied Pharmacology, (2005) Vol. 204, No. 3, pp. 216-237.
Lowry D *et al.*	2013	CA 5.8.2	Mechanism of metolachlor action due to alterations in cell cycle progression	Cell biology and toxicology, (2013 Aug) Vol. 29, No. 4, pp. 283-91.
Mathias *F et al.*	2012	CA 5.8.3	Herbicide Metolachlor Causes Changes in Reproductive Endocrinology of Male Wistar Rats	ISRN Toxicology (2012) 130846.
Metayer C	2013	CA 5.9.4	Exposure to herbicides in house dust and risk of childhood acute lymphoblastic leukemia	Journal of exposure science & environmental epidemiology, (2013 Jul) Vol. 23, No. 4, pp. 363-70
Migeot V	2013	CA 5.9.4	Drinking-water exposure to a mixture of nitrate and low-dose atrazine metabolites and small-for-gestational age (SGA) babies: A historic cohort study.	Environmental Research (2013), 122, 58-64.
Miranda S *et al.*	2007	CA 5.8.2	Cytotoxicity of chloroacetanilide herbicide alachlor in HepG2 cells independent of CYP3A4 and CYP3A7	Food and Chemical Toxicology (2007), 45 (5), 871-877.
Mnif W	2011	CA 5.8.3	Effect of endocrine disruptor pesticides: A review.	International Journal of Environmental Research and Public Health, (June 2011) Vol. 8, No. 6, pp. 2265-2303.

Author(s)	Year	CA data point number	Title	Source
Munger	2007	CA 5.9.4	Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies	Environmental Health Perspectives, Volume 105, Number 3, March 1997
Nikoloff N *et al.*	2013	CA 5.4.1	Comparative study of cytotoxic and genotoxic effects induced by herbicide S-metolachlor and its commercial formulation Twin Pack Gold® in human hepatoma (HepG2) cells.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013 Dec) Vol. 62, pp. 777-81.
Oosterhuis B *at al.*	2008	CA 5.8.2	Specific interactions of chloroacetanilide herbicides with human ABC transporter proteins.	Toxicology, (2008 Jun 3) Vol. 248, No. 1, pp. 45-51.
Padilla S *et al.*	2012	CA 5.6.2	Zebrafish developmental screening of the ToxCast Phase I chemical library	Reproductive Toxicology (2012), 33 (2), 174-187.
Panuwet P. *et al.*	2008	CP 7.2.1.2, CP 7.2.3.2	Concentrations of urinary pesticide metabolites in small-scale farmers in Chiang Mai Province, Thailand.	Sci. Total Environ. (2008 Dec) 15;407(1):655-68
Peck A. et al.	2005	CP 7.2.2.2	Gas-Phase Concentrations of Current-Use Pesticides in Iowa	Environ. Sci. Technol. (**2005**), 39, 2952-2959
Pellizzari E	2004	CA 5.9.4	Assessment of data quality for the NHEXAS - Part II: Minnesota children's pesticide exposure study (MNCPES). [Erratum to document cited in CA140:308309]	Journal of Exposure Analysis and Environmental Epidemiology (2004), 14(1), 108
Pereira S et al.	2009	CA 5.8.2	Toxicity assessment of the herbicide metolachlor comparative effects on bacterial and mitochondrial model systems.	Toxicology in vitro : an international journal published in association with BIBRA, (2009 Dec) Vol. 23, No. 8, pp. 1585-90.
Perry M	2008	CA 5.9.4	Effects of environmental and occupational pesticide exposure on human sperm: A systematic review.	Human Reproduction Update, (2008) Vol. 14, No. 3, pp. 233-242.
Phillips K	2008	CA 5.9.4	Human exposure to endocrine disrupters and semen quality.	Journal of Toxicology and Environmental Health - Part B: Critical Reviews, (Mar 2008) Vol. 11, No. 3-4, pp. 188-220.
Pressman J	2010	Not applicable	Concentration, Chlorination, and Chemical Analysis of Drinking Water for Disinfection Byproduct Mixtures Health Effects Research: U.S. EPA's Four Lab Study	Environmental Science & Technology (2010), 44 (19), 7184-7192.
Red R	2011	CA 5.9.4	Environmental toxicant exposure during pregnancy.	Obstetrical and Gynecological Survey, (March 2011) Vol. 66, No. 3, pp. 159-169.
Reif D *et al.*	2010	CA 5.8.3	Endocrine profiling and prioritization of environmental chemicals using ToxCast data.	Environmental Health Perspectives (2010), 118(12), 1714-1720.
Rodriguez C *et al.*	2012	CA 5.8.1	Assessing health risks from pesticides in recycled water: a case study of augmentation of drinking water supplies in Perth, Western Australia.	Human and Ecological Risk Assessment (2012), Volume 18, Number 6, pp. 1216-1236

Author(s)	Year	CA data point number	Title	Source
Rosenfeld P *et al.*	2011	CA 5.9.4	Pesticides.	Rosenfeld, PE; Feng, LGH. (2011) pp. 127-154. Risks of Hazardous Wastes.
Rotroff D *et al.*	2010	CA 5.8.2	Xenobiotic-Metabolizing Enzyme and Transporter Gene Expression in Primary Cultures of Human Hepatocytes Modulated by Toxcast Chemicals	Journal of Toxicology and Environmental Health, Part B: Critical Reviews (2010), 13(2-4), 329-346
Rotroff D *et al.*	2014	CA 5.8.3	Predictive Endocrine Testing in the 21st Century Using in Vitro Assays of Estrogen Receptor Signaling Responses.	Environmental Science & Technology (2014), 48 (15), 8706-8716.
Ruder A *et al.*	2004	CA 5.9.4	Gliomas and farm pesticide exposure in men: The upper midwest health study.	Archives of Environmental Health, (Dec 2004) Vol. 59, No. 12, pp. 650-657.
Rusiecki J *et al.*	2005	CA 5.9.4	Cancer incidence among pesticide applicators exposed to metolachlor in the agricultural health study	EPIDEMIOLOGY, (SEP 2005) Vol. 16, No. 5, pp. S98-S98.
Rusiecki J	2006	CA 5.9.4	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	International journal of cancer. Journal international du cancer, (2006 Jun 15) Vol. 118, No. 12, pp. 3118-23.
Sathiakumar N *et al.*	2011	CA 5.9.4	A review of epidemiologic studies of triazine herbicides and cancer.	Critical Reviews in Toxicology, (April 2011) Vol. 41, No. SUPPL. 1, pp. 1-34.
Schummer C. et al.	2012	CP 7.2.1.2, CP 7.2.3.2	Determination of farm workers' exposure to pesticides by hair analysis.	Toxicol. Lett. (2012 Apr) 25;210(2):203-10
Seok S-J *et al.*	2012	CA 5.9.7	Acute oral poisoning due to chloracetanilide herbicides.	Journal of Korean medical science, (2012 Feb) Vol. 27, No. 2, pp. 111-4.
Sinclair C *et al.*	2006	CA 5.8.2	Prioritization of pesticide environmental transformation products in drinking water supplies	ENVIRONMENTAL SCIENCE & TECHNOLOGY, (1 DEC 2006) Vol. 40, No. 23, pp. 7283-7289.
Sipes N *et al.*	2013	CA 5.8.2	Profiling 976 ToxCast Chemicals across 331 Enzymatic and Receptor Signaling Assays	Chemical Research in Toxicology (2013), 26 (6), 878-895.
Slager R	2010	CA 5.9.4	Rhinitis associated with pesticide use among private pesticide applicators in the agricultural health study.	Journal of toxicology and environmental health. Part A, (2010) Vol. 73, No. 20, pp. 1382-93.
Smital T	2011	CA 5.8.2	Assessment of toxicological profiles of the municipal wastewater effluents using chemical analyses and bioassays	Ecotoxicology and Environmental Safety (2011), 74 (4), 844-851.
Swan	2003	CA 5.9.4	Semen Quality in Relation to Biomarkers of Pesticide Exposure	Environmental Health Perspectives, vol 111, 12 September 2003.
Takeuchi S *et al.*	2006	CA 5.8.2	In vitro screening of 200 pesticides for agonistic activity via mouse peroxisome proliferator-activated receptor (PPAR)α and PPARγ and quantitative analysis of in vivo induction pathway	Toxicology and Applied Pharmacology (2006), 217 (3), 235-244

Author(s)	Year	CA data point number	Title	Source
Takeuchi S *et al.*	2008	CA 5.8.2	In vitro screening for aryl hydrocarbon receptor agonistic activity in 200 pesticides using a highly sensitive reporter cell line, DR-EcoScreen cells, and in vivo mouse liver cytochrome P450-1A induction by propanil, diuron and linuron	Chemosphere (2008), 74(1), 155-165
Thorpe N	2005	CA 5.9.4	Herbicides and nitrates in groundwater of Maryland and childhood cancers: a geographic information systems approach.	Journal of environmental science and health. Part C, Environmental carcinogenesis & ecotoxicology reviews, (2005) Vol. 23, No. 2, pp. 261-78.
Toccalino P *et al.*	2012	CA 5.8.2	Chemical mixtures in untreated water from public-supply wells in the U.S. - Occurrence, composition, and potential toxicity	Science of the Total Environment (2012), 431, 262-270.
Val S *et al.*	2011	CA 5.3.3	Role of size and composition of traffic and agricultural aerosols in the molecular responses triggered in airway epithelial cells.	Inhalation Toxicology (2011), 23 (11), 627-640.
Val S *et al.*	2011	CA 5.3.3	Role of size and composition of traffic and agricultural aerosols in the molecular responses triggered in airway epithelial cells [Erratum to document cited in CA156:382398]	Inhalation Toxicology (2011), 23 (14), 957.
Wambaugh J *et al.*	2013	CA 5.8.3	High-Throughput Models for Exposure-Based Chemical Prioritization in the ExpoCast Project.	Environmental Science & Technology (2013), 47 (15), 8479-8488.
Wang N *et al.*	2012	CA 5.9.4	Pollution level and human health risk assessment of some pesticides and polychlorinated biphenyls in Nantong of Southeast China.	Journal of Environmental Sciences (2012), Volume 24, Number 10, pp.1854-1860.
Ward M. et al.	2006	CP 7.2.2.2	Proximity to crops and residential exposure to agricultural herbicides in iowa.	Environ. Health Perspect. 2006 Jun;114(6):893-7
Weichenthal *et al.*	2010	CA 5.9.4	A review of pesticide exposure and cancer incidence in the Agricultural Health Study cohort.	Environmental health perspectives, (2010 Aug) Vol. 118, No. 8, pp. 1117-25.
Wells K et al.	2010	CA 5.9.4	Development of a gis-based model for estimating residential agricultural pesticide exposure and its application to a study of prostate cancer incidence and pesticide exposure.	American Journal of Epidemiology, (JUN 1 2010) Vol. 171, No. Suppl. 11, pp. S84.
Wickerham E et al.	2012	CA 5.9.4	Reduced birth weight in relation to pesticide mixtures detected in cord blood of full-term infants.	Environment International, (OCT 15 2012) Vol. 47, pp. 80-85.
Wofford P et al.	2014	CA 5.9.4	Community air monitoring for pesticides. Part 3: using health-based screening levels to evaluate results collected for a year.	Environmental monitoring and assessment, (2014 Mar) Vol. 186, No. 3, pp. 1355-70.
Yan X *et al.*	2009	CA 5.9.4	Pesticide concentrations in matrices collected in the perinatal period in a population of pregnant women and newborns in New Jersey, USA	Human and Ecological Risk Assessment (2009), 15(5), 948-967

Author(s)	Year	CA data point number	Title	Source
Yoshida M *et al.*	2013	CA 5.8.2	Simulation of acute reference dose (ARfD) settings for pesticides in Japan	Journal of Toxicological Sciences (2013), 38 (2), 205-214.
Zhou B *et al.*	2008	CA 5.6.2	Study on zebrafish embryo-toxicity of four pesticides	Zhejiang Gongye Daxue Xuebao (2008), 36 (2), 136-140.
Zhou M	2009	CA 5.3.2	Observation on toxicity experiment of S-metolachlor	Zhiye Yu Jiankang (2009), 25(24), 2657-2661

A detailed review of the full-text documents identified in Table 9.6-2 resulted in the additional exclusion of the following studies from the dossier.

Table 9.6-4: List of references excluded following detailed review listed by data point number

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
Initial search					
Not applicable	Gordon A	2012	Review of toxicological effects caused by episodic stressor exposure.	Environmental Toxicology and Chemistry, (May 2012) Vol. 31, No. 5, pp. 1169-1174.	On review this is a purely environmental toxicity paper, and not relevant to MCA section 5.
Not applicable	Pressman J	2010	Concentration, Chlorination, and Chemical Analysis of Drinking Water for Disinfection Byproduct Mixtures Health Effects Research: U.S. EPA's Four Lab Study	Environmental Science & Technology (2010), 44 (19), 7184-7192.	This paper looks at water disinfection processes and does not feature any toxicity data.
CA 5.1	Endo S	2011	Serum Albumin Binding of Structurally Diverse Neutral Organic Compounds: Data and Models	Chemical Research in Toxicology (2011), 24(12), 2293-2301.	This paper looks at serum albumin binding potential of a number of chemicals, and a log KBSA/w (BSA-water partition coefficient) of 1.74 is reported for metolachlor. This data does not alter any endpoints.
CA 5.2.6	Gorski J	2012	An in vitro method for detecting chemical sensitization using human reconstructed skin models and its applicability to cosmetic, pharmaceutical, and medical device safety testing.	Cutaneous and Ocular Toxicology, (December 2012) Vol. 31, No. 4, pp. 292-305.	Appears this was flagged in the search as metol, but has erroneously been indexed as metolachlor. There is no metolachlor data in this paper.
CA 5.3.3	Val S *et al.*	2011	Role of size and composition of traffic and agricultural aerosols in the molecular responses triggered in airway epithelial cells.	Inhalation Toxicology (2011), 23 (11), 627-640.	Neither this article, nor the erratum contain data on metolachlor/S-metolachlor. Metolachlor is simply mentioned in the title of one of the references.
CA 5.3.3	Val S *et al.*	2011	Role of size and composition of traffic and agricultural aerosols in the	Inhalation Toxicology (2011), 23 (14), 957.	Neither this erratum, nor the original journal article contain data on

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
			molecular responses triggered in airway epithelial cells [Erratum to document cited in CA156:382398]		metolachlor/S-metolachlor. Metolachlor is simply mentioned in the title of one of the references.
CA 5.4.2	Bokan K *et al.*	2010	Application of the SMART mutagenicity test and an aquatic toxicity biotest on pesticides as environmental stressors.	Noevenytermeles (2010), Volume 59, Number Supplement, pp. 187-190.	This publication looks at ecotoxicity and mutagenicity of specific samples of groundwater that are from a former industrial site and contain a number of pesticides, including very low levels of metolachlor. Given that this is a complex mixture with very little metolachlor content this data is not considered relevant for MCA section 5.
CA 5.5	Kleinstreuer N, *et al.*	2013	In Vitro Perturbations of Targets in Cancer Hallmark Processes Predict Rodent Chemical Carcinogenesis	Toxicological Sciences (2013), 131(1), 40-55	This paper compares Toxcast high-throughput screening output to in vivo rodent carcinogenicity data in the Toxicity Reference Database (ToxRefDB. No new *in vivo* data are presented.
CA 5.6.2	Kleinstreuer N, *et al.*	2011	Environmental impact on vascular development predicted by high-throughput screening.	Environmental Health Perspectives, (November 2011) Vol. 119, No. 11, pp. 1596-1603.	This paper attempts to link profiles from high throughput *in vitro* Toxcast data to developmental toxicity outcomes from the ToxRefDB dataset (i.e. the exiting metolachlor/S-metolachlor studies, which are included in the original EU review). As these *in vivo* data are already available the *in vitro* data reviewed is not considered relevant.
CA 5.6.2	Padilla S *et al.*	2012	Zebrafish developmental screening of the ToxCast Phase I chemical library	Reproductive Toxicology (2012), 33 (2), 174-187.	Paper described screening studies on zebrafish. As part of an evaluation of the model as a screening tool for developmental toxicity. No new *in vivo* mammalian data is presented.
CA 5.6.2	Zhou B *et al.*	2008	Study on zebrafish embryo-toxicity of four pesticides	Zhejiang Gongye Daxue Xuebao (2008), 36 (2), 136-140.	Paper described screening studies on zebrafish. No new *in vivo* mammalian data is presented.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 5.8.1	Kubatova A *et al*.	2006	Genotoxicity of polar fractions from a herbicide-contaminated soil does not correspond to parent contaminants.	Environmental Toxicology and Chemistry, (JUL 2006) Vol. 25, No. 7, pp. 1742-1745.	This study looked at the genotoxicity (by SOS chromotest) of herbicide contaminated soil rinsed with hot pressurised water. Several tested fractions of the contaminant soil extract were considered to be genotoxic in this assay. As the soil samples contained a mixture of herbicide residues any response cannot reliability by attributed to metolachlor.
CA 5.8.1	Rodriguez C *et al.*	2012	Assessing health risks from pesticides in recycled water: a case study of augmentation of drinking water supplies in Perth, Western Australia.	Human and Ecological Risk Assessment (2012), Volume 18, Number 6, pp. 1216-1236	No toxicology information is presented, not relevant for MCA section 5.
CA 5.8.2	Baldwin W *et al.*	2009	A Concentration Addition Model for the Activation of the Constitutive Androstane Receptor by Xenobiotic Mixtures	Toxicological Sciences (2009), 107 (1), 93-105.	This gene reporter assay paper demonstrated that metolachlor is able to active murine CAR, which is consistent with Omiecinski 2014 (MCA Section 5).
CA 5.8.2	Cho H-Y	2008	Study on the biochemical characterization of herbicide detoxification enzyme, glutathione S-transferase	BioFactors, (2007) Vol. 30, No. 4, pp. 281-7.	This paper looks at metolachlor activity towards glutathione-S-transferase (GST) in *E. coli* constructs containing the human pi class GST enzyme. As metolachlor is already known to be metabolised by GST *in vivo* this is not new information.
CA 5.8.2	Crettaz P	2004	In silico methods used in a weight of evidence approach for assessing the human health effects of plant protection products.	Toxicology and Applied Pharmacology, (JUN 15 2004) Vol. 197, No. 3, pp. 284.	This poster analyses DEREK for Windows output on dimethachlor and does not present any new data on metolachlor.
CA 5.8.2	Genter M *et al.*	2009	Comparison of rat olfactory mucosal responses to carcinogenic and non-carcinogenic chloracetanilides.	Food and chemical toxicology: an international journal published for the British Industrial Biological Research Association, (2009 Jun) Vol. 47, No. 6, pp. 1051-7.	This paper looks primarily at alachlor, butachlor and propachlor and does not present new data on metolachlor, which is mentioned as a comparator chloroacetanilide.
CA 5.8.2	Genter M *et al.*	2010	Chloroacetanilide-induced nasal carcinogenesis in rats	Nose and Viral Cancer (2010), 427-434.	This is review and as such does not present any new data.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 5.8.2	Gohill V *et al.*	2010	Nutrient-sensitized screening for drugs that shift energy metabolism from mitochondrial respiration to glycolysis	Nature Biotechnology (2010), 28 (3), 249-255.	Does not present metolachlor/S-metolachlor data in the paper, although it appears to be one of 3500 chemicals tested. The relevance of energy metabolism shift in cultured fibroblasts is considered of low relevance compared to the *in vivo* testing database.
CA 5.8.2	Hu L-L *et al.*	2011	Predicting biological functions of compounds based on chemical-chemical interactions	PLoS One (2011), 6 (12), e29491.	This is a very general paper looking at several thousand chemicals but has no specific information on metolachlor/S-metolachlor.
CA 5.8.2	Judson R *et al*.	2010	In Vitro Screening of Environmental Chemicals for Targeted Testing Prioritization: The ToxCast Project	Environmental Health Perspectives (2010), 118 (4), 485-492.	This is a general EPA approach for prioritisation of testing based on use of ToxCast data. Metolachlor/S-metolachlor are part of the underlying data set but are not discussed in this paper specifically.
CA 5.8.2	Kale V	2007	Mechanistic studies on hepatotoxicity of chloroacetanilide herbicides and hematotoxicity of munitions compound RDX and environmental degradation product MNX.	Dissertation Abstracts International. Vol. 68, no. 12. 2007	This dissertation investigated cytotoxicity of alachlor, acetochlor and metolachlor to rat and human isolated hepatocytes. Metolachlor was less cytotoxic that alachlor and acetochlor to rat hepatocytes, but similarly toxic to human cryopreserved hepatocytes. This is not considered relevant new data as Syngenta have conducted studies on rat and human hepatocytes (Elcombe 2014), and in fact it highlights cytotoxicity at lower concentrations that in Kale's analysis. As the female rat liver tumours have been demonstrated to be due to a CAR activating mode of action rather than resulting

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					from regeneration of frank liver damage these *in vitro* findings are considered incidental.
CA 5.8.2	Kale V *et al.*	2008	Comparative cytotoxicity of alachlor, acetochlor, and metolachlor herbicides in isolated rat and cryopreserved human hepatocytes.	Journal of biochemical and molecular toxicology, (2008 Feb) Vol. 22, No. 1, pp. 41-50.	This investigation is similar to Kale 2007, and looks are alachlor, acetochlor and metolachlor cytotoxicity in rat and human hepatocytes. Metolachlor was less cytotoxic that alachlor and acetochlor to rat hepatocytes, but similarly toxic to human cryopreserved hepatocytes. This is not considered relevant new data as Syngenta have conducted studies on rat and human hepatocytes (Elcombe 2014), and in fact it highlights cytotoxicity at lower concentrations that in Kale's analysis. As the female rat liver tumours have been demonstrated to be due to a CAR activating mode of action rather than resulting from regeneration of frank liver damage these *in vitro* findings are considered incidental.
CA 5.8.2	Leslie E	2005	Multidrug resistance proteins: Role of P-glycoprotein, MRP1, MRP2, and BCRP (ABCG2) in tissue defense.	Toxicology and Applied Pharmacology, (2005) Vol. 204, No. 3, pp. 216-237.	This is a review article that mentions transport by MRP1 of metolachlor conjugates, but does not present new data.
CA 5.8.2	Miranda S *et al.*	2007	Cytotoxicity of chloroacetanilide herbicide alachlor in HepG2 cells independent of CYP3A4 and CYP3A7	Food and Chemical Toxicology (2007), 45 (5), 871-877.	This paper investigated the effects of CYP3A4 and CYP3A7 on alachlor toxicity in HepG2 cells. Metolachlor is used as a comparator and is less cytotoxic (the EC50 for cytotoxicity was approximately 800 µM). This paper does not add meaningful data to the existing metolachlor/S-metolachlor database.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 5.8.2	Sinclair C *et al.*	2006	Prioritization of pesticide environmental transformation products in drinking water supplies	ENVIRONMENTAL SCIENCE & TECHNOLOGY, (1 DEC 2006) Vol. 40, No. 23, pp. 7283-7289.	This paper outlines a general approach for prioritising assessment of transformation products of pesticides – metolachlor is only mentioned in the references – and even then not in a toxicological context.
CA 5.8.2	Smital T	2011	Assessment of toxicological profiles of the municipal wastewater effluents using chemical analyses and bioassays	Ecotoxicology and Environmental Safety (2011), 74 (4), 844-851.	This paper looks at *in vitro* activity (cytotoxicity, Ames mutagenicity, oestrogenicity and CYP induction) of untreated wastewater and secondary effluent from a wastewater treatment plant. Metolachlor was detected in samples of both, however due to the complex nature of the tested mixtures no reliable conclusions can be drawn with regard to metolachlor/S-metolachlor.
CA 5.8.2	Takeuchi S *et al.*	2006	In vitro screening of 200 pesticides for agonistic activity via mouse peroxisome proliferator-activated receptor (PPAR)α and PPARγ and quantitative analysis of in vivo induction pathway	Toxicology and Applied Pharmacology (2006), 217 (3), 235-244	This reporter gene assay paper looks at activation of PPAR by a number of pesticides. Specific data is not shown for metolachlor, but by inference it is negative for PPAR activity
CA 5.8.2	Toccalino P *et al.*	2012	Chemical mixtures in untreated water from public-supply wells in the U.S. - Occurrence, composition, and potential toxicity	Science of the Total Environment (2012), 431, 262-270.	This paper looks at monitoring data, including analysis for metolachlor. No toxicity data are presented.
CA 5.8.2	Yoshida M *et al.*	2013	Simulation of acute reference dose (ARfD) settings for pesticides in Japan	Journal of Toxicological Sciences (2013), 38 (2), 205-214.	This publication outlines the approach taken by Japan's Food Safety Commission to derive acute reference doses from existing data to suit their national requirements. Metolachlor is mentioned as being included in this exercise but no substance specific data are presented – therefore it is not considered of relevance.
CA 5.8.3	Bishop P *et al.*	2014	The Use and Acceptance of Other Scientifically Relevant Information (OSRI) in the U.S. Environmental Protection	Birth Defects Research, Part B: Developmental and Reproductive Toxicology (2014), 101 (1), 3-22.	Generalised EDSP review – doesn't contain data on metolachlor/S-metolachlor.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
			Agency (EPA) Endocrine Disruptor Screening Program		
CA 5.8.3	Hayes T	2006	Chemical mixtures: Hayes responds [4].	Environmental Health Perspectives, (Sep 2006) Vol. 114, No. 9, pp. A518-A519.	On review this is ecotoxicology based so not relevant for MCA Section 5.
CA 5.8.3	Jarosova B *et al.*	2012	Changes in concentrations of hydrophilic organic contaminants and of endocrine-disrupting potential downstream of small communities located adjacent to headwaters	Environment International (2012), 45, 22-31.	This paper primarily focuses on water monitoring. It also features some cell based anti/oestrogenicity and androgenicity assays, however as water samples of varying composition were tested no meaningful conclusions can be made with regard to metolachlor/S-metolachlor.
CA 5.8.3	Mnif W	2011	Effect of endocrine disruptor pesticides: A review.	International Journal of Environmental Research and Public Health, (June 2011) Vol. 8, No. 6, pp. 2265-2303.	Review article – does not present new data. Refers to Lemaire 2006 (discussed above).
CA 5.8.3	Wambaugh J *et al*.	2013	High-Throughput Models for Exposure-Based Chemical Prioritization in the ExpoCast Project.	Environmental Science & Technology (2013), 47 (15), 8479-8488.	No specific reference to metolachlor/S-metoachlor, it is a general ExpoCast analysis.
CA 5.9.2	Beard J *et al.*	2011	Suicide and pesticide use among pesticide applicators and their spouses in the Agricultural Health Study.	Environmental Health Perspectives, (November 2011) Vol. 119, No. 11, pp. 1610-1615.	This paper examines relationships between pesticide use and suicide. Metolachlor appeared to be inversely correlated with suicide. These data do no impact on the endpoints, references values or classifications so are not considered relevant.
CA 5.9.2	Hsu B-G	2009	Late-onset Methemoglobinemia Induced by Metobromuron/metolachlor.	Tzu Chi Medical Journal, (December 2009) Vol. 21, No. 4, pp. 334-338	This paper describes a suicide attempt case report where the patient ingested a litre of Galex (25% metolachlor/2% metobromuron) and was treated for methaemoglobinaemia. It appears highly likely that the methaemoglobinaemia observed was due to metobromuron which is known to cause this effect in animal studies (Conclusion on the peer

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					review of the pesticide risk assessment of the active substance metobromuron, EFSA Journal 2014;12(2):3541)
CA 5.9.4	Alavanja M *et al.*	2004	Pesticides and lung cancer risk in the agricultural health study cohort.	American journal of epidemiology, (2004 Nov 1) Vol. 160, No. 9, pp. 876-85.	On advice on epidemiology review, this paper can be excluded. This study is referenced in Rusiecki et al 2006 and provides no additional findings.
CA 5.9.4	Andreotti G *et al.*	2009	Agricultural pesticide use and pancreatic cancer risk in the Agricultural Health Study Cohort	International Journal of Cancer (2009), 124(10), 2495-2500	On advice on epidemiology review, this paper can be excluded. Well conducted prospective study of pancreatic cancer incidence among pesticide applicators and their spouses. Recall bias is a potential limitation of the exposure data, but the reliability was evaluated. There was no evidence of an increased risk of pancreatic cancer among applicators and spouses exposed to metolachlor, and no evidence of a trend with lifetime days of exposure among applicators.
CA 5.9.4	Barry K *et al.*	2011	Genetic variation in base excision repair pathway genes, pesticide exposure, and prostate cancer risk	Environmental Health Perspectives (2011), 119(12), 1726-1732	On advice on epidemiology review, this paper can be excluded. There were no significant interactions between metolachlor and any of the haplotypes investigated in this study.
CA 5.9.4	Bonner M *et al.*	2005	The Agricultural Health Study biomarker workshop on cancer etiology.	Journal of Biochemical and Molecular Toxicology, (2005) Vol. 19, No. 3, pp. 169-171.	A review paper – does not contain new data. Refers to Alavanja 2004, which was also picked up in this search.
CA 5.9.4	Dayton S *et al.*	2010	Pesticide use and myocardial infarction incidence among farm women in the agricultural health study.	Journal of Occupational and Environmental Medicine, (July 2010) Vol. 52, No. 7, pp. 693-697.	On advice on epidemiology review, this paper can be excluded. Well conducted prospective study of myocardial infarction incidence among women.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					Limitations include self-reported outcome and date of event, and subjects were only asked to report whether they had ever used metolachlor. No evidence of an association between ever use of metolachlor and myocardial infarction incidence.
CA 5.9.4	Dennis L *et al.*	2010	Pesticide use and cutaneous melanoma in pesticide applicators in the agricultural heath study	Environmental Health Perspectives (2010), 118(6), 812-817	On advice on epidemiology review, this paper can be excluded. Not included in dossier as metolachlor was not associated with increased melanoma incidence.
CA 5.9.4	Fantke P *et al.*	2012	Health impact and damage cost assessment of pesticides in Europe	Environment International (2012), 49, 9-17.	This is a very general paper, and the only reference to metolachlor relates to its use pattern – no toxicity data.
CA 5.9.4	Flower K *et al.*	2004	Cancer risk and parental pesticide application in children of agricultural health study participants	Environmental Health Perspectives (2004), 112(5), 631-635.	Looks at the incidence of tumours amongst children of pesticide applicators. Metolachlor is not correlated to an increase in childhood cancer risk. On advice on epidemiology review, this paper can be excluded. Hybrid study design in which incidence of childhood cancer was identified retrospectively before parent enrolled in study and prospectively. Limitations include inability to determine whether prenatal exposure occurred for mothers and prenatal exposure for father could only be determined using information on decade of first use and duration of use. Timing of exposure in relation to pregnancy not known. No evidence of an association between maternal or paternal exposure to metalochlor and childhood cancer.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 5.9.4	Freeman L *et al*.	2011	Atrazine and cancer incidence among pesticide applicators in the agricultural health study (1994-2007)	Environmental Health Perspectives (2011), 119 (9), 1253-1259.	This paper focuses on atrazine-related cancer incidence. Metolachlor is mentioned as a potential confounder (often used alongside atrazine), but is not assessed itself.
CA 5.9.4	Gallois J	2011	DNA adduct variations in non-smoking crop farmers: Potential relationship with occupational exposure to pesticides?	Environmental Toxicology and Pharmacology, (July 2011) Vol. 32, No. 1, pp. 1-9.	This paper looks at seasonal differences in DNA adduct levels in farmers. Metolachlor is one of a number of pesticides for which exposure is reported in the study, however analysis was conducted based on groupings rather than individual pesticides, so no conclusions can be made on the effect of metolachlor.
CA 5.9.4	Huijbregts M *et al.*	2005	Human toxicological effect and damage factors of carcinogenic and noncarcinogenic chemicals for life cycle impact assessment	Integrated Environmental Assessment and Management (2005), 1(3), 181-244.	This paper describes a methodology for deriving human damage and effect factors for over 1100 chemicals including metolachlor. No experimental data is described therefore it is not considered relevant.
CA 5.9.4	Kamel F *et al.*	2012	Pesticide exposure and amyotrophic lateral sclerosis	NeuroToxicology (2012), 33(3), 457-462	On advice on epidemiology review, this paper can be excluded. Well conducted case-control of ALS among pesticide applicators and their spouses. Recall bias is a potential limitation of the exposure data, but the reliability was evaluated. Another limitation is the small number (41) of cases. There was no evidence of an increased risk of ALS among applicators and spouses exposed to metolachlor, and no evidence of a trend with lifetime days of exposure among applicators.
CA 5.9.4	Koutros S *et al.*	2010	Pesticide Use Modifies the Association Between Genetic Variants on Chromosome 8q24 and Prostate Cancer	Cancer Research (2010), 70(22), 9224-9233	On advice on epidemiology review, this paper can be excluded. An interaction between metolachlor and

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					rs12547643, which is telomeric to regions 3 and 1, was not statistically significant after correction for multiple testing. There was no a priori reason to expect an association as prostate cancer risk decreased with increasing metolachlor exposure, and a previous AHS report provided no evidence that a family history of prostate cancer modified prostate cancer risk among those exposed to metolachlor (Alavanja et al, (2003).
CA 5.9.4	Koutros S *et al.*	2011	Xenobiotic-metabolizing gene variants, pesticide use, and the risk of prostate cancer	Pharmacogenetics and Genomics (2011), 21(10), 615-623	On advice on epidemiology review, this paper can be excluded. There were no significant interactions between metolachlor and any of the haplotypes investigated in this study.
CA 5.9.4	Koutros S	2013	Genetic susceptibility loci, pesticide exposure and prostate cancer risk	PLoS One (2013), 8 (4), e58195.	Metolachlor is mentioned briefly in the supplementary table but is not specifically linked with human disease.
CA 5.9.4	Landgren O *et al.*	2009	Pesticide exposure and risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study	Blood (2009), 113(25), 6386-6391	On advice on epidemiology review, this paper can be excluded. Well conducted study of MGUS prevalence in a neurobehavioral study nested within the AHS (a stratified random sample based on lifetime organophosphate use of male pesticide applicators). Comparison between applicators and general population were limited by the lack of a control group from the same states where applicators resided, but comparisons between ever and never users of individual pesticides are more robust. There was no evidence of increased MGUS prevalence among ever users of metolachlor.
CA 5.9.4	Lee W *et al.*	2004	Agricultural pesticide use and adenocarcinomas of the stomach and oesophagus	Occupational and Environmental Medicine (2004), 61(9),	On advice on epidemiology review, this paper can be excluded.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
				743-749	Well conducted case-control study of adenocarcinomas of the stomach and oesophagus and exposure to pesticides including nitrosatiable pesticides. There was no evidence of increased risk for exposure to acetanilide herbicides (alachor, metolachlor, propachlor), but no results were presented for metolachlor because fewer than 5 stomach and 5 oesophageal cancer cases were ever exposed to metolachlor.
CA 5.9.4	Lee W *et al.*	2005	Agricultural pesticide use and risk of glioma in Nebraska, United States	Occupational and Environmental Medicine (2005), 62(11), 786-792	Due to the large number of epidemiology studies that have included metolachlor and apparent complexity of the dataset, Syngenta have commissioned an expert to conduct a review of all of the studies to enable of weight of evidence analysis. This will be submitted at the earliest opportunity. On advice on epidemiology review, this paper can be excluded. Well conducted case-control study of glioma and exposure to pesticides including nitrosatiable pesticides. Among proxy respondents brain cancer risk was significantly increased for male farmers, but the association with farming was inverse among self-respondents. There was no overall association with metolachlor exposure, but the OR was non significantly increased among proxy respondents, and the association with metalochor was inverse among self-respondents. The pattern was unsurprising as non-farmers were the reference group for both analyses of

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					farming and individual pesticides.
CA 5.9.4	Metayer C	2013	Exposure to herbicides in house dust and risk of childhood acute lymphoblastic leukemia	Journal of exposure science & environmental epidemiology, (2013 Jul) Vol. 23, No. 4, pp. 363-70	On advice on epidemiology review, this paper can be excluded. Case-control study examining the association between exposure to herbicides in house dust and childhood acute lymphoblastic leukemia. The quantification of past exposure had numerous major limitations, not least the fact that samples were collected on average 1-2 years after diagnosis. Metolachlor was not detected in the house dust of any cases and only 2 controls (< 1%), and the study had little power to detect an effect of exposure to metolachlor.
CA 5.9.4	Migeot V	2013	Drinking-water exposure to a mixture of nitrate and low-dose atrazine metabolites and small-for-gestational age (SGA) babies: A historic cohort study.	Environmental Research (2013), 122, 58-64.	This paper primarily looks at atrazine. There are mentions of metolachlor as part of the French drinking water monitoring program but there is no toxicity data in this paper.
CA 5.9.4	Pellizzari E	2004	Assessment of data quality for the NHEXAS - Part II: Minnesota children's pesticide exposure study (MNCPES). [Erratum to document cited in CA140:308309]	Journal of Exposure Analysis and Environmental Epidemiology (2004), 14(1), 108	The erratum, and the original paper it belongs to analyse for presence of metolachlor in air, drinking water and beverages, and no toxicity data is presented. Consequently it is not considered relevant for inclusion in MCA Section 5.
CA 5.9.4	Perry M	2008	Effects of environmental and occupational pesticide exposure on human sperm: A systematic review.	Human Reproduction Update, (2008) Vol. 14, No. 3, pp. 233-242.	This is a review article and does not feature new data. It refers to Swan 2003 (Environmental Health Perspectives, Vol 111, 4, April 2003) with reference to metolachlor, but on review of that paper there is no reference to metolachlor.
CA 5.9.4	Phillips K	2008	Human exposure to endocrine disrupters and semen quality.	Journal of Toxicology and Environmental Health - Part B: Critical Reviews, (Mar 2008)	It refers to Swan 2003 (Environmental Health Perspectives, Vol 111, 4, April 2003) with reference

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
				Vol. 11, No. 3-4, pp. 188-220.	to metolachlor, but on review of that paper there is no reference to metolachlor
CA 5.9.4	Red R	2011	Environmental toxicant exposure during pregnancy.	Obstetrical and Gynecological Survey, (March 2011) Vol. 66, No. 3, pp. 159-169.	A review article that does not present new data. .
CA 5.9.4	Rosenfeld P *et al.*	2011	Pesticides.	Rosenfeld, PE; Feng, LGH. (2011) pp. 127-154. Risks of Hazardous Wastes.	This is a book chapter summarising findings on a number of pesticides. Metolachlor is covered but as this a review no novel data is reported.
CA 5.9.4	Ruder A *et al.*	2004	Gliomas and farm pesticide exposure in men: The upper midwest health study.	Archives of Environmental Health, (Dec 2004) Vol. 59, No. 12, pp. 650-657.	On advice on epidemiology review, this paper can be excluded. Well conducted case-control study of glioma and pesticide exposure. There was no association between glioma and exposure to chloroactanilides (including metolachlor and alachlor). Results are not shown for metolachlor but the authors state that there was not a statistically significant association between glioma and metolachlor exposure (either including or excluding proxy respondents).
CA 5.9.4	Rusiecki J *et al.*	2005	Cancer incidence among pesticide applicators exposed to metolachlor in the agricultural health study	EPIDEMIOLOGY, (SEP 2005) Vol. 16, No. 5, pp. S98-S98.	On advice on epidemiology review, this paper can be excluded. This abstract has been superseded by Rusiecki et al 2006) which has an additional year of follow-up and reports more refined and better documented analyses. The conclusion of the abstract is also similar to that of Rusiecki et al (2006).
CA 5.9.4	Sathiakumar N *et al.*	2011	A review of epidemiologic studies of triazine herbicides and cancer.	Critical Reviews in Toxicology, (April 2011) Vol. 41, No. SUPPL. 1, pp. 1-34.	This is review article that does not present new data, but refers to Thorpe 2005, which is reviewed separately.
CA 5.9.4	Slager R	2010	Rhinitis associated with pesticide use among private pesticide applicators in the agricultural health study.	Journal of toxicology and environmental health. Part A, (2010) Vol. 73, No. 20, pp. 1382-93.	On advice on epidemiology review, this paper can be excluded.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					Well conducted cross-sectional study of the prevalence of rhinitis among farmers and commercial pesticide applicators. Limitations include self-reported outcome, and the cross-sectional design resulting in an inability to determine when rhinitis episodes occurred in relation to exposure There was no evidence that current users (used in year before enrolment) of metolachlor were more likely to develop rhinitis or any pattern of association with number of rhinitis episodes. It is stated that metolachlor, was significant in an exposure-response model, but no other information is provided,1 and the analysis is described as an exploratory subgroup analysis. No persuasive evidence is presented that there is an association between rhinitis and metolachlor exposure.
CA 5.9.4	Wang N *et al.*	2012	Pollution level and human health risk assessment of some pesticides and polychlorinated biphenyls in Nantong of Southeast China.	Journal of Environmental Sciences (2012), Volume 24, Number 10, pp.1854-1860.	On review there is no toxicological data in this paper.
CA 5.9.4	Weichenthal *et al.*	2010	A review of pesticide exposure and cancer incidence in the Agricultural Health Study cohort.	Environmental health perspectives, (2010 Aug) Vol. 118, No. 8, pp. 1117-25.	This is a review paper that cites papers by Rusiecki and Alavanja, which are already covered in this literature review. No new primary data is provided therefore this review is not considered of relevance.
CA 5.9.4	Wells K et al.	2010	Development of a gis-based model for estimating residential agricultural pesticide exposure and its application to a study of prostate cancer incidence and pesticide exposure.	American Journal of Epidemiology, (JUN 1 2010) Vol. 171, No. Suppl. 11, pp. S84.	No metolachlor data is presented in this abstract – therefore it is not relevant for this assessment.

[1] The p value is stated to be 0.03 in the NIH Public Access manuscript.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 5.9.4	Wickerham E et al.	2012	Reduced birth weight in relation to pesticide mixtures detected in cord blood of full-term infants.	Environment International, (OCT 15 2012) Vol. 47, pp. 80-85.	This study analyses for a relationship between umbilical cord detects of pesticides and birth weights. Only two subjects had metolachlor detects amongst those measured for in this study, therefore there is insufficient data to make and conclusions.
CA 5.9.4	Yan X *et al.*	2009	Pesticide concentrations in matrices collected in the perinatal period in a population of pregnant women and newborns in New Jersey, USA	Human and Ecological Risk Assessment (2009), 15(5), 948-967	This paper reports potential gestational exposure to pesticides, including metolachlor – showing that metolachlor is detectable in cord serum. No clinical abnormities or aberrant birth outcomes in the newborns were associated with the pesticide exposures.
CA 5.9.7	Seok S-J *et al.*	2012	Acute oral poisoning due to chloracetanilide herbicides.	Journal of Korean medical science, (2012 Feb) Vol. 27, No. 2, pp. 111-4.	This paper summaries the cases of patients admitted to two university hospitals apparently suffering from acute chloroacetanilide poisoning. 5 Of the cases were related to metolachlor. These findings do not alter the AOEL, ADI or classification and labelling as the actual levels of exposure are not defined.
CP 7.2.1.2,	Hayat K. *et al.*	2010	Determination of pesticide residues in blood samples of villagers involved in pesticide application at District Vehari (Punjab), Pakistan	African Journal of Environmental Science and Technology Vol. 4(10), pp. 666-684, October 2010	No residues of metolachlor or s-metolachlor were detected in any of the samples. In addition, there is insufficient detail concerning GAP parameters (e.g. application rates, formulation type, dermal absorption, whether the use was from metolachlor or S-metolachlor) to enable further comparison to the proposed use in the EU. Therefore, the operator assessment provided as part of the re-registration submission dossier (MCP section 7) is

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					considered to be precautionary and appropriate.
CP 7.2.1.2, CP 7.2.3.2	Panuwet P. *et al.*	2008	Concentrations of urinary pesticide metabolites in small-scale farmers in Chiang Mai Province, Thailand.	Sci. Total Environ. (2008 Dec) 15;407(1):655-68	The paper states that metolachlor metabolite was measured in the range from <0.2 to 0.71 µg/L with the 95th percentile being less than the LOD (limit of detection). There are no details given to be able to compare this to an external exposure value. There is insufficient detail concerning GAP parameters (e.g. application rates, formulation type, dermal absorption, whether the use was from metolachlor or S-metolachlor) to enable further comparison to the proposed use in the EU. Therefore, the operator and worker exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be precautionary and appropriate.
CP 7.2.1.2, CP 7.2.2.2, CP 7.2.3.2	Curwin B. et al.	2005	Urinary and hand wipe pesticide levels among farmers and nonfarmers in Iowa	Journal of Exposure Analysis and Environmental Epidemiology (2005) 15, 500–508	With all bio-monitoring studies where urine is sampled, an indication of complete collection is required (including the measurement of creatinine levels), in conjunction with robust pharmacokinetic data to be able to predict either systemic dose, or to back calculate to external exposure. This study only involved spot sampling of urine which is an indicator of exposure, but not of use for quantitative assessment. Additionally, only a relatively small number of hand wipe samples were obtained for operators applying metolachlor and the determinants of exposure (application parameters, timing etc.) were self-reported; again this was

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					essentially an indicator of exposure but not a quantitative measure. However, whilst this study reported that farmers had detectable levels of metolachlor in hand wipe samples, the levels were not significantly higher than for non-farmers. There is nothing in this study, which was intended as a comparison between operators and non-operators, rather than a full exposure study, that suggests that the first tier assessments of exposure for the proposed EU use of S-metolachlor are not sufficiently protective. In addition, there is insufficient detail concerning GAP parameters (e.g. application rates, formulation type, dermal absorption, whether the use was from metolachlor or S-metolachlor) to enable further comparison to the proposed use in the EU. Therefore, the operator and worker exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be precautionary and appropriate.
CP 7.2.1.2, CP 7.2.2.2, CP 7.2.3.2	Curwin B. et al.	2007	Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in iowa.	Ann. Occup. Hyg. (2007 Jan);51(1):53-65	Geometric mean concentrations of metolachlor mercapturate in urine for fathers, mothers and children were typically in the range 0.3 to 0.8 µg/L with the exception of the subgroup ‘fathers who had made an application with metolachlor’ where the geometric mean concentration was 4.5 µg/L. Although this does demonstrate that application of metolachlor results in a systemic dose, it is not possible to compare it to the

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					assessments provided in the current re-registration submission dossier (MCP section 7) as the corresponding external exposure cannot be calculated with the available information and no details of use patterns (GAPs, whether the use was from metolachlor or S-metolachlor, formulation, dermal absorption, use of PPE etc.) are given. The operator and resident exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be precautionary and appropriate.
CP 7.2.1.2, CP 7.2.3.2	Schummer C. et al.	2012	Determination of farm workers' exposure to pesticides by hair analysis.	Toxicol. Lett. (2012 Apr) 25;210(2):203-10	S-metolachlor was determined in hair from farm workers taking part in the study. Positive detections of S-metolachlor were seen in 4 out of 18 workers. The median residue in hair was 14.5 pg/mg, but this cannot be related to external exposure or systemic dose. Exposures to S-metolachlor to farm workers carrying out spraying (operator risk assessment) and other farm activities (worker exposure assessment) have been provided as part of the MCP Section 7 and are considered protective and precautionary. Residues in hair are not required to further refine any exposure assessment already provided.
CP 7.2.1.2, CP 7.2.3.2	Arcury T. et al.	2010	Repeated pesticide exposure among North Carolina migrant and seasonal farmworkers	Am. J. Ind. Med. (2010 Aug);53(8):802-13	Report gives number of detections of urinary metabolite (metolachlor mercapturate) above the LOD (limit of detection) for the farmworkers, but no quantitative residue levels nor an indication of how the measured internal exposures relate to a

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					specific external dose are given. No details of GAPs (e.g. application rates, formulation types) are provided. The operator and worker exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be sufficiently precautionary and appropriate.
CP 7.2.1.2, CP 7.2.3.2	Arcury T. et al.	2009	Seasonal Variation in the Measurement of Urinary Pesticide Metabolites among Latino Farmworkers in Eastern North Carolina	Int. J. Occup. Environ. Health. (2009 Oct–Dec); 15(4): 339–350	The report gives information on the frequency (e.g. number of workers with a detectable level) but does not give the actual level measured and no comparison of internal metabolite dose is made to a potential external dose. Therefore, it is not possible to compare it to the assessments provided in the current re-registration submission dossier (MCP section 7). No details of use patterns (GAPs) are given, or whether the local use was with metolachlor or S-metolachlor. Cultural practices concerning PPE may also lead to differences between levels found in this study from the United States and any expected levels present in the European Union. The operator and worker exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be precautionary and appropriate.
CP 7.2.2.2	Curwin B. et al.	2005	Pesticide contamination inside farm and nonfarm homes.	J. Occup. Environ. Hyg. (2005 Jul);2(7):357-67	The report claims that pesticides, including metolachlor are found in dust from farm and non-farm households implicating contamination from farmer’s shoes and clothing. Although this does represent a potential route of exposure for the resident it is not possible

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					to compare it to the assessments provided in the current submission. No details of use patterns (e.g. application rates, formulation types) are given, or whether the local use was with metolachlor or S-metolachlor. Cultural practices concerning PPE and footwear may also lead to differences between levels found in this study from the United States and any expected levels present in the European Union. The resident exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be sufficiently precautionary and appropriate to account for any additional exposure via this route.
CP 7.2.2.2	Ward M. et al.	2006	Proximity to crops and residential exposure to agricultural herbicides in iowa.	Environ. Health Perspect. 2006 Jun;114(6):893-7	The report claims that metolachlor was found in carpet dust at a median concentration of 129.5 ng/g. Although this does represent a potential, albeit minor route of exposure for the resident it is not possible to compare it to the assessments provided in the current submission. No details of local use patterns (GAPs) are given, or whether the local use was with metolachlor or S-metolachlor. Cultural practices concerning PPE and footwear may also lead to differences between levels found in this study from the United States and any expected levels present in the European Union. The resident exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be sufficiently precautionary and appropriate to account for

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					any additional exposure via this route.
CP 7.2.2.2	Curwin B. et al.	2007	Pesticide dose estimates for children of Iowa farmers and non-farmers	Environmental Research, Volume 105, Issue 3, (November 2007), Pages 307–315	An estimation of metolachlor exposure has been made for children on the basis of their metolachlor mercapturate urine levels and modelling. The modelling requires a value for the amount of metolachlor mercapturate excreted in urine, which was not known, so an estimated conservative figure of 60% was used (based on the fact that the percentage of alachlor mercapturate in human urine has been shown to range from 25% to 62% and they are considered to be structurally similar). Therefore, the modelling itself is not validated to predict exposures of metolachlor. No details of use patterns (GAPs) are given, formulation type including dermal absorption values or whether the local use was with metolachlor or S-metolachlor. The report claims that the highest estimated dose for metolachlor was 3.16 µg/kg/day, equating to 0.0032 mg/kg bw/day, or 2.1% of the AOEL. The resident exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are considered to be precautionary and appropriate.
CP 7.2.2.2	Arcury T. et al.	2007	Pesticide urinary metabolite levels of children in eastern North Carolina farmworker households.	Environ. Health Perspect. (2007 Aug);115(8):1254-60	No details of use patterns (e.g. application rates or other GAP parameters) are given, or whether the local use was with metolachlor or S-metolachlor. The report claims that out of the 14 pesticides that were monitored in urine samples, metolachlor was the only one that had no detects from any of the 60

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					Latino farmworker children. The resident exposure assessments provided as part of the re-registration submission dossier (MCP section 7) are therefore considered to be precautionary and appropriate.
CP 7.2.2.2	Aulagnier F et al.	2008	Pesticides measured in air and precipitation in the Yamaska Basin (Québec): occurrence and concentrations in 2004.	Sci. Total Environ. (2008 May) 15;394 (2-3) 338-48	The report gives an average metolachlor concentration in air of 7713 pg/m^3. No details are provided for the exact distance from an application, or to know the exact use patterns (e.g application rates) that were used in local applications of metolachlor, nor whether metolachlor or S-metolachlor were used and if the same results would be expected from both of these active ingredients. However, the resident exposure assessment submitted in the re-registration submission (MCP section 7) which used a default value of 1 µg/m^3, based on the vapour pressure of S-metolachlor being considered semi-volatile, is considered protective.
CP 7.2.2.2	Peck A. et al.	2005	Gas-Phase Concentrations of Current-Use Pesticides in Iowa	Environ. Sci. Technol. (**2005**), 39, 2952-2959	The report gives an average metolachlor concentration in air of 2.3 ng/m^3. No details are provided for the exact distance from an application, or to know the exact use patterns (e.g application rates, formulation types) that were used in local applications of metolachlor, nor whether metolachlor or S-metolachlor were used and if the same results would be expected from both of these active ingredients. Consequently, the resident exposure assessment submitted in the re-registration submission

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
					(MCP section 7) used a much larger default value of 1 µg/m^3 based on the vapour pressure of S-metolachlor being considered semi-volatile is considered protective in comparison.
CP 7.2.2.2	Wofford P et al.	2014	Community air monitoring for pesticides. Part 3: using health-based screening levels to evaluate results collected for a year.	Environmental monitoring and assessment, (2014 Mar) Vol. 186, No. 3, pp. 1355-70.	The report states that metolachlor was one of seventeen out of forty pesticides and pesticide degradation products monitored but not detected at concentrations above the detection limit. Irrespective of this, no details are provided for the exact distance from an application, or for the exact use patterns (e.g application rates) that were used in local applications of metolachlor, nor whether metolachlor or S-metolachlor were used and if the same results would be expected from both of these active ingredients. Consequently, the resident exposure assessment submitted in the re-registration submission (MCP section 7) which used a default value of 1 µg/m^3, based on the vapour pressure of S-metolachlor being considered semi-volatile, is considered protective.

All documents listed in Table 9.6-2 and not excluded (i.e. not listed in Table 9.6-4) are given below.

Table 9.6-5: List of references which are discussed further (listed by data point number)

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 5.3.2	Zhou M	2009	Observation on toxicity experiment of S-metolachlor	Zhiye Yu Jiankang (2009), 25(24), 2657-2661	EU001
CA 5.4.1	Nikoloff N *et al.*	2013	Comparative study of cytotoxic and genotoxic effects induced by herbicide	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013 Dec) Vol. 62, pp. 777-81.	EU002

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 5.8.2	Ait-Aissa S *et al.*	2010	Anti-androgenic activities of environmental pesticides in the MDA-kb2	Toxicology in Vitro (2010), 24(7), 1979-1985.	EU003
CA 5.8.2	Greenlee E *et al.*	2004	Low-dose agrochemicals and lawn-care pesticides induce developmental	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9.	EU004
CA 5.8.2	Hartnett S *et al.*	2013	Cellular effects of metolachlor exposure on human liver (HepG2) cells.	Chemosphere, (2013 Jan) Vol. 90, No. 3, pp. 1258-66	EU005
CA 5.8.2	Hu J	2009	Immunotoxicity effect of metolachlor on mice	Harbin Yike Daxue Xuebao (2009), 43(1), 53-55	EU006
CA 5.8.2	Takeuchi S *et al.*	2008	In vitro screening for aryl hydrocarbon receptor agonistic activity in 200	Chemosphere (2008), 74(1), 155-165.	EU007
CA 5.8.2	Kojima H *et al.*	2011	Comparative study of human and mouse pregnane X receptor agonistic activity in 200 pesticides using in vitro reporter gene assays	Toxicology (2011), 280(3), 77-87	EU008
CA 5.8.2	Kueblbeck J *et al.*	2011	Use of comprehensive screening methods to detect selective human CAR	Biochemical Pharmacology (2011), 82(12), 1994-2007	EU009
CA 5.8.2	Lemaire G *et al.*	2006	Activation of α- and β-estrogen receptors by persistent pesticides in reporter cell lines	Life Sciences (2006), 79(12), 1160-1169.	EU010
CA 5.8.2	Lemaire G et al.	2006	Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system.	Toxicological sciences : an official journal of the Society of Toxicology,	EU011
CA 5.8.2	Lowry D *et al.*	2013	Mechanism of metolachlor action due to alterations in cell cycle progression	Cell biology and toxicology, (2013 Aug) Vol. 29, No. 4, pp. 283-91.	EU012
CA 5.8.2	Oosterhuis B *at al.*	2008	Specific interactions of chloroacetanilide herbicides with human ABC	Toxicology, (2008 Jun 3) Vol. 248, No. 1, pp. 45-51.	EU013
CA 5.8.2	Pereira S et al.	2009	Toxicity assessment of the herbicide metolachlor comparative effects on	Toxicology in vitro : an international journal published in association	EU014
CA 5.8.2	Rotroff D *et al.*	2010	Xenobiotic-Metabolizing Enzyme and Transporter Gene Expression in Primary	Journal of Toxicology and Environmental Health, Part B: Critical Reviews (2010), 13(2-4), 329-346	EU015
CA 5.8.2	Laville N *et al*.	2006	Modulation of aromatase activity and mRNA by various selected pesticides	Toxicology, (2006 Nov 10) Vol. 228, No. 1, pp. 98-108.	EU016
CA 5.8.2	Cunningham A *et al.*	2009	A structure-activity relationship (SAR) analysis for the identification of	Endocrine Disruption Modeling (2009), 173-198.	EU017
CA 5.8.2	Sipes N *et al.*	2013	Profiling 976 ToxCast Chemicals across 331 Enzymatic and Receptor Signaling Assays	Chemical Research in Toxicology (2013), 26 (6), 878-895.	EU018
CA 5.8.2	Kojima H *et al.*	2004	Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using chinese hamster ovary cells	Environmental Health Perspectives (2004), 112 (5), 524-531.	EU019

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 5.8.3	Mathias *F et al.*	2012	Herbicide Metolachlor Causes Changes in Reproductive Endocrinology of Male Wistar Rats	ISRN Toxicology (2012) 130846.	EU020
CA 5.8.3	Reif D *et al.*	2010	Endocrine profiling and prioritization of environmental chemicals using ToxCast data.	Environmental Health Perspectives (2010), 118(12), 1714-1720.	EU021
CA 5.8.3	Rotroff D *et al.*	2014	Predictive Endocrine Testing in the 21st Century Using in Vitro Assays of Estrogen Receptor Signaling Responses.	Environmental Science & Technology (2014), 48 (15), 8706-8716.	EU022
CA 5.9.4	Alavanja M *et al.*	2003	Use of Agricultural Pesticides and Prostate Cancer Risk in the Agricultural Health Study Cohort	Am J Epidemiol 2003;157:800–814	EU023
CA 5.9.4	Andreotti G *et al.*	2010	Body mass index, agricultural pesticide use, and cancer incidence in the	Cancer causes & control: CCC, (2010 Nov) Vol. 21, No. 11, pp. 1759-75.	EU024
CA 5.9.4	Barr D	2010	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	The Science of the total environment, (2010 Jan 15) Vol. 408, No. 4, pp. 790-5.	EU025
CA 5.9.4	Chevrier Gwendolina	2011	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Environmental health perspectives, (2011 Jul) Vol. 119, No. 7, pp. 1034-41.	EU026
CA 5.9.4	Hoppin J *et al.*	2006	Pesticides and adult respiratory outcomes in the agricultural health study.	Annals of the New York Academy of Sciences, (Sep 2006) Vol. 1076, pp. 343-354.	EU027
CA 5.9.4	Hou L	2013	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Environmental health perspectives, (2013 Aug) Vol. 121, No. 8, pp. 919-24.	EU028
CA 5.9.4	Lee W *et al.*	2007	Pesticide use and colorectal cancer risk in the Agricultural Health Study	International Journal of Cancer (2007), 121(2), 339-346	EU029
CA 5.9.4	Munger	2007	Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies	Environmental Health Perspectives, Volume 105, Number 3, March 1997	EU030
CA 5.9.4	Rusiecki J	2006	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	International journal of cancer. Journal international du cancer, (2006 Jun 15) Vol. 118, No. 12, pp. 3118-23.	EU031
CA 5.9.4	Swan	2003	Semen Quality in Relation to Biomarkers of Pesticide Exposure	Environmental Health Perspectives, vol 111, 12 September 2003.	EU032
CA 5.9.4	Thorpe N	2005	Herbicides and nitrates in groundwater of Maryland and childhood cancers: a	Journal of environmental science and health. Part C, Environmental	EU033

S-Metolachlor

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CA, Section 9

Metabolism and Residues Data

LITERATURE DATA

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

Table of Contents

CA 9 LITERATURE DATA

CA 9.1 Title

This document is a Literature Review Report for S-metolachlor, relevant metabolite(s) and EU representative formulation A9396G (Dual Gold®).

CA 9.2 Author(s) of the review

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CA 9.3 Summary: A brief summary indicating the purpose of the report, the methodology employed and the results obtained

This report summarises the search for "scientific peer-reviewed open literature on S-metolachlor and its relevant metabolites dealing with metabolism and residues data which may impact health, the environment and non-target species and published within the last ten years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

The search strategy is detailed in the tables below. A search was conducted to identify references that included the active substance S-metolachlor, or its major metabolites, or representative formulations, in conjunction with any of the key words set out in Table 9.5-1. The names searched for were:

```
L1      QUE  (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2      QUE  (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3      QUE  (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4      QUE  (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5      QUE  (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6      QUE  (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7      QUE  (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8      QUE  (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9      QUE  (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10     QUE  (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11     QUE  (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12     QUE  (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13     QUE  (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14     QUE  (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15     QUE  (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16     QUE  (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17     QUE  (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18     QUE  (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19     QUE  (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))
L20     QUE  ((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21     QUE  (55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22     QUE  (METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23     QUE  ((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24     QUE  (CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
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L25     QUE  (L1-L20)   METABOLITES
L26     QUE  (L21 OR L22 OR L23 OR L24)   METOLACHLOR
L27     QUE  (L25 OR L26)   METOLACHLOR & METABOLITES
```

An overview of the results is summarised in the table below and further details are provided in Section 9.5.

Data requirement(s) captured in the search	**Number (Initial Search)**
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	1629
Number of *summary records* excluded from the search results after rapid assessment for relevance	1620
Total number of *full-text* documents assessed in detail*	9
Number of *studies* excluded from further consideration after detailed assessment for relevance	9
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	0

*both from bibliographic databases and other sources of peer-reviewed literature

CA 9.4 Protocol

CA 9.4.1 Statement of the objective of the review

The review has the objective of identifying "scientific peer-reviewed open literature on S-metolachlor and its potentially relevant metabolites dealing with metabolism and residue studies which may impact health, the environment and non-target species and published within the last ten years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

CA 9.4.2 Criteria for relevance with which decisions to select studies in the dossier were made

Table 9.4.2-1: List of Criteria for relevance for each data requirement

Data requirements(s) (indicated by the correspondent CA data point(s))	**Criteria for relevance**
Metabolism and residues data (CA 6.1 to 6.10)	
Summary	The relevance criteria applied to determine whether a literature reference was relevant for the residues and metabolism sections of the active substance renewal process are given below. 1. Well defined test material. e.g. are purity and batch data provided? 2. Applicable test species. e.g. is the crop a representative use; were relevant animal commodities used? 3. Study conditions should not differ significantly from guidelines and recommended protocols. e.g. did the study meet the relevant guidelines? 4. Trial site/test system not previously exposed to the test material or other contaminants e.g. was the compound used previously at the trial site; was the animal feed free from the compound? 5. Sufficient experimental information is provided to substantiate and evaluate whether the study conclusions and endpoints are robust.

Data requirements(s) (indicated by the correspondent CA data point(s))	Criteria for relevance
	e.g. were storage intervals recorded; are weather conditions and plot histories available? 6. Validated Analytical methodology employed. e.g. were control samples used, acceptable recoveries obtained, clear example chromatograms given? 7. Study conditions do not interfere with the interpretation of the study results. e.g. starting processing material residue is robust and there is measurable residue in processed products?
6.1 Storage stability **Storage stability studies, plant and animal**	Storage Stability Studies 1. Well defined test material (including purity/content) 2. Applicable test species 3. Study conditions should not differ significantly from guidelines and recommended protocols. 5. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust. 6. Study conditions should not interfere with the interpretation of the study results. 7. Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc.
6.2 Metabolism	Primary Crop Studies Notes for criteria 1. Well defined test material (including purity/content) 2. Applicable test species • N.B. any crop used for food and/or feed could be relevant from a metabolism perspective as results can be extrapolated to other crops 3. Study conditions should not differ significantly from guidelines and recommended protocols. 4. Trial site/test system not previously exposed to the test material or other contaminants. 5. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust. 6. Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc. 7. Study conditions should not interfere with the interpretation of the study results. Metabolism in Rotational Crops Notes for criteria 1. Well defined test material (including purity/content) 2. Applicable test species • N.B. relevant crop groupings are small grain, root and tuber, leafy vegetable (soybean and rice if relevant to product). Bulb vegetable (e.g. onions and garlic) should not be used. 3. Study conditions should not differ significantly from guidelines and recommended protocols. 4. Trial site/test system not previously exposed to the test material or other contaminants. 5. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust. 6. Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc. 7. Study conditions should not interfere with the interpretation of the study results. Livestock Metabolism Studies

<table>
<tr><th>Data requirements(s) (indicated by the correspondent CA data point(s))</th><th>Criteria for relevance</th></tr>
<tr><td></td><td>Notes for criteria

Well defined test material (including purity/content)
Applicable test species
Ruminant, poultry, pig, fish, any edible animal
Study conditions should not differ significantly from guidelines and recommended protocols.
Trial site/test system not previously exposed to the test material or other contaminants.
Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust.
Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc.
Study conditions should not interfere with the interpretation of the study results.
</td></tr>
<tr><td>6.3 Residue studies</td><td>Published monitoring reports were not considered relevant due to the fact that it would not be possible to determine whether or not a misuse scenario had resulted in the residue levels reported.

<u>Crop Studies</u>

Well defined test material (including purity/content)
Applicable test species
Study conditions should not differ significantly from guidelines and recommended protocols.
Trial site/test system not previously exposed to the test material or other contaminants.
Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust.
Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc.
Study conditions should not interfere with the interpretation of the study results.
</td></tr>
<tr><td>6.4 Livestock Feeding studies</td><td>Same criteria as for crop studies, examples could be as above with the following additions.

<u>Livestock Feeding Studies Notes</u>

Well defined test material (including purity/content)
Applicable test species
e.g. Ruminant, poultry, pig, fish, any edible animal.
Study conditions should not differ significantly from recommended protocols.
Trial site/test system not previously exposed to the test material or other contaminants.
Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust.
Study conditions should not interfere with the interpretation of the study results.
Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc.
</td></tr>
<tr><td>6.5 Processing</td><td><u>High Temperature Hydrolysis</u>

Notes for criteria

Well defined test material (including purity/content)
Applicable test system
Study conditions should not differ significantly from guidelines and recommended protocols.
Trial site/test system not previously exposed to the test material or other contaminants.
</td></tr>
</table>

Data requirements(s) (indicated by the correspondent CA data point(s))	Criteria for relevance
	5. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust. 6. Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc. 7. Study conditions should not interfere with the interpretation of the study results. <u>Field Studies</u> 1. Well defined test material (including purity/content) 2. Applicable test species 3. Study conditions should not differ significantly from guidelines and recommended protocols. 4. Trial site not previously exposed to the test material or other contaminants. 5. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust. 6. Study conditions should not interfere with the interpretation of the study results. 7. Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc. <u>Notes for above criteria</u> 1. Well defined test material (including purity/content) 2. Applicable test species 3. Study conditions should not differ significantly from guidelines and recommended protocols. • NB. Processing studies can be conducted at elevated rates and shorter PHI and grown under different conditions to maximize residues. 4. Trial site not previously exposed to the test material or other contaminants. 5. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust. 6. Study conditions should not interfere with the interpretation of the study results. 6. Validated Analytical methodology employed, e.g. control samples used, acceptable recoveries obtained, clear example chromatograms etc.
6.6 Residues in succeeding crops	Same criteria as for crop residue studies, examples could be subtly different, e.g. acceptable PBIs, crop types, again monitoring information should not be considered relevant.
6.7 Proposed residue definition and MRLs	<u>Residue definition</u> Notes for criteria 1. Developed following appropriate EU guidance 2. Any toxicological data relevant to the residue definition are generated following relevant acceptability criteria 3. Metabolism data relevant to the residue definition are generated following relevant acceptability criteria covered in 6.2 <u>Maximum Residue Levels</u> Notes for criteria 1. MRLs are calculated via residues generated following criteria covered in 6.3 2. Correct monitoring residue definition has been used 3. Appropriate MRL calculator utilised
6.8 Proposed PHI, re-entry and withholding periods	Same criteria as for residues generated following criteria covered in 6.3
6.9 Other/special studies	Generic criteria are appropriate as laid out in the summary box above

Data requirements(s) (indicated by the correspondent CA data point(s))	Criteria for relevance
6.10 Risk assessment	Dietary risk assessment conducted using appropriate EU methodology

* Recommended protocols under each data point include but are not limited to those listed in the Commission Communications 2013/C 95/01 and 2013/C 95/02

CA 9.5 Search methods

Date of initial search	20 August 2014
Date of most recent update to search	-
Date span of the search	10 years

For the initial rapid assessment the study titles and abstracts were scanned to identify studies of potential relevance to crop and livestock metabolism and/or residue studies in the context of human exposure through the diet. Studies clearly not within the remit of Regulation (EU) No. 283/2013 and regulation (EU) No. 284/2013 (such as metabolism studies in environmental compartments or microorganisms, other environmental fate studies, toxicological studies, efficacy studies, studies on plants other than crops, and mode of action studies) were eliminated. A second scan checked the full text of 9 records identified as potentially relevant or unclear on the basis of their titles. In-depth review of these papers identified no literature references that were considered to be potentially relevant.

Table 9.5-1: Detailed Search Parameters for Metabolism and Residues data (CA 6.1 to 6.9)

Search Strategy	
L1	QUE (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2	QUE (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3	QUE (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4	QUE (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5	QUE (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6	QUE (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7	QUE (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8	QUE (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9	QUE (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10	QUE (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11	QUE (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12	QUE (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13	QUE (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14	QUE (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15	QUE (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16	QUE (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17	QUE (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18	QUE (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19	QUE (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))
L20	QUE ((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21	QUE (55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22	QUE (METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23	QUE ((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24	QUE (CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
L25	QUE (L1-L20) METABOLITES
L26	QUE (L21 OR L22 OR L23 OR L24) METOLACHLOR
L27	QUE (L25 OR L26) METOLACHLOR & METABOLITES
Plus	
L1	QUE (METABOL? OR RESIDUE# OR TRANSFORM? OR BIOTRANSFORM?)
L2	QUE (DEGRAD? OR BIODEGRAD? OR FATE# OR MRL OR MRLS)
L3	QUE (CONJUGAT? OR EXCRET? OR ELIMINAT?)
L4	QUE (FOOD# OR FEED# OR DIET# OR DIETARY OR CONSUMER? OR HUMAN#)
L5	QUE (CONTAMINAT? OR SAFE? OR EXPOS? OR ANALY? OR ASSES?)
L6	QUE (INTAKE? OR (IN(W)TAKE?) OR SURVEY? OR RISK?)
L7	QUE (TOXIC? OR STUDY? OR STUDIES?)
L8	QUE (L4(10A)(L5 OR L6 OR L7))
L9	QUE (LIVESTOCK# OR COW# OR GOAT# OR CATTLE# OR BULLOCK#)
L10	QUE (BOVINE? OR BOVIDAE? OR BOS OR BULL# OR HEIFER? OR CAPRA#)
L11	QUE (SHEEP# OR EWE OR EWES OR RAM# OR SWINE# OR PIGLET#)
L12	QUE (PIG# OR SUIDAE? OR SUS OR OVIS OR OX OR OXEN)
L13	QUE (RUMINANT? OR HEN# OR CHICKEN# OR FOWL# OR TURKEY?)
L14	QUE (DUCK# OR GOOSE OR GEESE OR CAPON# OR POULTRY?)
L15	QUE (MEAT OR MILK OR EGG# OR TISSUE#)
L16	QUE (((BROKEN? OR BREAK?)(W)(DOWN OR UP)) OR BREAKDOWN?)
L17	QUE (BREAKSDOWN? OR UPTAKE? OR PROCESSING? OR BOUND?)
L18	QUE ((NON(W)EXTRACTAB?) OR (ROTATIONAL(3A)CROP#))
L19	QUE ((L1 OR L2 OR L3) OR L8 OR (L9 OR L10 OR L11 OR L12 OR L13 OR L14) OR (L15 OR L16 OR L17 OR L18))

Table 9.5-2: Detailed Search Parameters for Metabolism and Residues data (CA 6.1 to 6.9)

Provider	Database	Justification	Limits applied	Number*
Host STN	MEDLINE	Contains information on every area of medicine providing comprehensive coverage from 1948 to present. Sources include journals and chapters in books or symposia. The database is updated 5 times each week with an annual reload and therefore stays very current in its cover.	None	247
	EMBASE	The database, covers worldwide literature in the biomedical and pharmaceutical fields, including biological science, biochemistry, human medicine, forensic science, pediatrics, pharmacy, pharmacology and drug therapy, pharmacoeconomics, psychiatry, public health, biomedical engineering and instrumentation, and environmental science. Sources include more than 4,000 journals from approximately 70 countries, monographs, conference proceedings, dissertations, and reports. The databases covers data from 1974-present and is updated daily.		64
	EMBAL	The database provides early access to bibliographic data and the abstracts for references that will appear in EMBASE. Bibliographic information for references is available in EMBAL for the latest 8 weeks of EMBASE data. The database covers the worldwide literature on the biomedical and pharmaceutical fields. Bibliographic information, abstracts, and author keywords are searchable. Sources include over 4,000 journals. The database covers current data and is updated daily.		0
	ESBIOBASE	A database providing comprehensive coverage of the entire spectrum of biological research worldwide. Coverage includes the following areas: applied microbiology, biotechnology, cancer research, cell & developmental biology, clinical chemistry, ecological & environmental sciences, endocrinology, genetics, immunology, infectious diseases, metabolism, molecular biology, neuroscience, plant and crop science, protein biochemistry, and toxicology. Records are selected from over 1,700 international scientific journals, books, and conference proceedings. The database covers the period 1994 - present and is updated weekly.		5
	AGRICOLA	A bibliographic database containing selected worldwide literature of agriculture and related fields. Coverage of the database includes agricultural economics and rural sociology, agricultural production, animal sciences, chemistry, entomology, food and human nutrition, forestry, natural resources, pesticides, plant science, soils and fertilizers, and water resources. Also covered are related areas such as biology and biotechnology, botany, ecology, and natural history. The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. It covers the period 1970-present and is updated monthly.		28
	BIOSIS	A large and comprehensive worldwide life science database covers original research reports, reviews, and selected U.S. patents in biological and biomedical areas, with subject coverage ranging from aerospace biology to zoology. Sources include periodicals, journals, conference proceedings, reviews, reports, patents, and short communications. Nearly 6,000 life source journals, 1,500 international meetings as well as review articles, books, and monographs are reviewed for inclusion. It covers the period 1926 – present and is updated weekly.		74
	CABA	Covers worldwide literature from all areas of agriculture and related sciences including biotechnology, forestry, and veterinary medicine. Sources include journals, books, reports, published theses, conference proceedings, and patents. It covers the period 1973-present and is updated weekly.		287

Provider	Database	Justification	Limits applied	Number*
	CAPLUS	Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences including applied, macromolecular, organic, physical, inorganic, and analytical chemistry. Current sources include over 8,000 journals, patents, technical reports, books, conference proceedings, dissertations, product reviews, bibliographic items, book reviews, and meeting abstracts. Electronic-only journals and Web preprints are also covered. Cited references are included for journals, conference proceedings and basic patents from the U.S., EPO, WIPO, and German patent offices added to the CAS databases from 1999 to the present. Also provides early access to the bibliographic information, abstracts and CAS Registry Numbers for documents in the process of being indexed by CAS. Covers the period 1907 – present and is updated daily		685
	FSTA	The database provides worldwide coverage of all scientific and technological aspects of the processing and manufacture of human food products including basic food sciences, biotechnology, hygiene and toxicology, engineering, packaging, and all individual foods and food products. Sources include more than 2,200 journals, books, reviews, conference proceedings, patents, standards, and legislation. It covers the period 1969 – present and is updated weekly.		3
	FROSTI	The database contains citations to the worldwide literature on food science and technology including food and beverages, analytical methods, quality control, manufacturing, microbiology, food processing, health and nutrition, recipes, and additives. Sources include approximately 800 scientific and technical journals, bulletins, technical reports, conference proceedings, grey literature, and British, European (EP), U.S., Japanese, and international (PCT) patent applications. Covers the period 1972 – present and is updated twice weekly.		0
	GEOREF	Covers international literature on geology and geosciences. Sources include the Bibliography of North American Geology, Bibliography and Index of Geology Exclusive of North America, Geophysical Abstracts, Bibliography of Fossil Vertebrates, selected records from Geoline and from geology sections of PASCAL and state and national geological surveys. Covers the period 1669 – present and is updated twice a month.		43
	TOXCENTER	Covers the pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals. It is composed of the following subfiles: BIOSIS, CAplus, IPA and MEDLINE and sources include abstracts, books and book chapters, bulletins, conference proceedings, journal articles, letters, meetings, monographs, notes, papers, patents, presentations, research and project summaries, reviews, technical reports, theses, translations, unpublished material, web reprints. Covers the period 1907 – present and is updated weekly		0
	PQSCITECH	Is a huge resource in all areas of science and technology from engineering to lifescience. The file is a merge of 25 STN databases formerly known as CSA databases (Cambridge Scientific Abstracts): AEROSPACE, ALUMINIUM, ANTE, AQUALINE, AQUASCI, BIOENG, CERAB, CIVILENG, COMPUAB, CONFSCI, COPPERLIT, CORROSION, ELCOM, EMA, ENVIROENG, HEALSAFE, LIFESCI, LISA, MATBUS, MECHENG, METADEX, OCEAN, POLLUAB, SOLIDSTATE, and WATER. Sources are journals, patents, books, reports, and conference proceedings spanning the period 1962 – present and it is updated monthly.		48
	PASCAL	The database provides access to the world's scientific and technical literature including physics and chemistry, life sciences (biology, medicine, and psychology), applied sciences and technology, earth sciences, and information sciences. French and European literature is particularly well represented. Approximately 5,000 journal titles are indexed. References to theses and to conference proceedings are also included. Spans the period 1977 to present and is updated weekly		5

Provider	Database	Justification	Limits applied	Number*
	SCISEARCH	Is an international index to the literature covering virtually every subject area within the broad fields of science, technology, and biomedicine. SciSearch contains all the records published in Science Citation Index Expanded™ and additional records from the Current Contents series of publications. Bibliographic information and cited references from over 5,600 scientific, technical, and medical journals are contained in the database. Spans the period 1974 to present and is updated weekly.		135
	ANABST	Covers worldwide literature on analytical chemistry. The ANABSTR file contains bibliographic records with abstracts (since 1984) for documents reported in printed Analytical Abstracts. Sources for ANABSTR include journals, books, conference proceedings, reports, and standards. Spans the period 1980 to present and is updated weekly.		5

* Total number of summary records retrieved after removing duplicates

Table 9.5-3: Detailed Search Parameters for Web searches

Website name and service publisher	URL	Justification	Search terms	Limits applied	Number*
A web search has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-4: Detailed Search Parameters for Journal Table of Contents

Journal name	Journal URL or publisher	Dates, volumes and issues searched	Method of searching	Search terms	Number*
A search for journal table of contents has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-5: Detailed Search Parameters for Reference Lists

Bibliographic details of documents whose reference lists were scanned	Number*
A search for reference lists has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.	

* Total number of summary records or full-text documents retrieved after removing duplicates

CA 9.6 Results

Table 9.6-1: Results of study selection process

Data requirement(s) captured in the search	Number (Initial Search)
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	1629
Number of *summary records* excluded from the search results after rapid assessment for relevance	1620
Total number of *full-text* documents assessed in detail*	9
Number of *studies* excluded from further consideration after detailed assessment for relevance	9
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	0

*both from bibliographic databases and other sources of peer-reviewed literature

Table 9.6-2: List of references for all relevant and unclear studies listed by data point number

CA data point number	Author(s)	Year	Title	Source
CA 6.2.1	Pang Sen; Ran Zhaojin; Liu Zhiqian; Song Xiaoyu; Duan Liusheng; Li Xuefeng; Wang Chengju	2012	Enantioselective induction of a glutathione-S-transferase, a glutathione transporter and an ABC transporter in maize by Metolachlor and its (S)-isomer.	PloS one, (2012) Vol. 7, No. 10, pp. e48085
CA 6.2.1	Perez Sandra; Farkas Michael; Barcelo Damia; Aga Diana S	2007	Characterization of glutathione conjugates of chloroacetanilide pesticides using ultra-performance liquid chromatography /quadrupole time-of-flight mass spectrometry and liquid chromatography/ion trap mass spectrometry	Rapid communications in mass spectrometry : RCM, (2007) Vol. 21, No. 24, pp. 4017-22
CA 6.2.1	Berry James O; Aga Diana S	2007	Determination of enzyme kinetics and glutathione conjugates of chlortetracycline and chloroacetanilides using liquid chromatography-mass spectrometry	The Analyst, (2007 Jul) Vol. 132, No. 7, pp. 664-71
CA 6.3	Muhammad Amjad; Tanveer Ahmad; Qumer Iqbal; Aamir Nawaz; Jahangir, M. M.	2013	Herbicide contamination in carrot grown in Punjab, Pakistan	Pakistan Journal of Agricultural Sciences (2013), Volume 50, Number 1, pp. 7-10
CA 6.7	US Environmental Protection Agency	2012	S-Metolachlor; Pesticide Tolerances	[USA] Federal Register (2012), 77 (158), 48902-48907, 15 Aug 2012
CA 6.7	US Environmental Protection Agency	2014	S-Metolachlor; Pesticide Tolerances	Federal Register (2014), 79 (100), 29729-29732, 23 May 2014
CA 6.9	Fantke, Peter; Juraske, Ronnie; Anton, Assumpcio; Friedrich, Rainer; Jolliet, Olivier	2011	Dynamic Multicrop Model to Characterize Impacts of Pesticides in Food	Environmental Science & Technology (2011), 45 (20), 8842-8849
CA 6.9	Nougadere, Alexandre; Reninger, Jean-Cedric; Volatier, Jean-Luc; Leblanc, Jean-Charles	2011	Chronic dietary risk characterization for pesticide residues: A ranking and scoring method integrating agricultural uses and food contamination data	Food and Chemical Toxicology (2011), 49 (7), 1484-1510

CA data point number	Author(s)	Year	Title	Source
CA 6.9	Juraske, Ronnie; Mutel, Christopher L.; Stoessel, Franziska; Hellweg, Stefanie	2009	Life cycle human toxicity assessment of pesticides: Comparing fruit and vegetable diets in Switzerland and the United States	Chemosphere (2009), 77 (7), 939-945

Table 9.6-3: List of references for all relevant and unclear studies listed by Author

Author(s)	Year	CA data point number	Title	Source
Berry James O; Aga Diana S	2007	CA 6.2.1	Determination of enzyme kinetics and glutathione conjugates of chlortetracycline and chloroacetanilides using liquid chromatography-mass spectrometry	The Analyst, (2007 Jul) Vol. 132, No. 7, pp. 664-71
Fantke, Peter; Juraske, Ronnie; Anton, Assumpcio; Friedrich, Rainer; Jolliet, Olivier	2011	CA 6.9	Dynamic Multicrop Model to Characterize Impacts of Pesticides in Food	Environmental Science & Technology (2011), 45 (20), 8842-8849
Juraske, Ronnie; Mutel, Christopher L.; Stoessel, Franziska; Hellweg, Stefanie	2009	CA 6.9	Life cycle human toxicity assessment of pesticides: Comparing fruit and vegetable diets in Switzerland and the United States	Chemosphere (2009), 77 (7), 939-945
Muhammad Amjad; Tanveer Ahmad; Qumer Iqbal; Aamir Nawaz; Jahangir, M. M.	2013	CA 6.3	Herbicide contamination in carrot grown in Punjab, Pakistan	Pakistan Journal of Agricultural Sciences (2013), Volume 50, Number 1, pp. 7-10
Nougadere, Alexandre; Reninger, Jean-Cedric; Volatier, Jean-Luc; Leblanc, Jean-Charles	2011	CA 6.9	Chronic dietary risk characterization for pesticide residues: A ranking and scoring method integrating agricultural uses and food contamination data	Food and Chemical Toxicology (2011), 49 (7), 1484-1510
Pang Sen; Ran Zhaojin; Liu Zhiqian; Song Xiaoyu; Duan Liusheng; Li Xuefeng; Wang Chengju	2012	CA 6.2.1	Enantioselective induction of a glutathione-S-transferase, a glutathione transporter and an ABC transporter in maize by Metolachlor and its (S)-isomer.	PloS one, (2012) Vol. 7, No. 10, pp. e48085
Perez Sandra; Farkas Michael; Barcelo Damia; Aga Diana S	2007	CA 6.2.1	Characterization of glutathione conjugates of chloroacetanilide pesticides using ultra-performance liquid chromatography /quadrupole time-of-flight mass spectrometry and liquid chromatography/ion trap mass spectrometry	Rapid communications in mass spectrometry : RCM, (2007) Vol. 21, No. 24, pp. 4017-22
US Environmental Protection Agency	2012	CA 6.7	S-Metolachlor; Pesticide Tolerances	[USA] Federal Register (2012), 77 (158), 48902-48907, 15 Aug 2012
US Environmental Protection Agency	2014	CA 6.7	S-Metolachlor; Pesticide Tolerances	Federal Register (2014), 79 (100), 29729-29732, 23 May 2014

A detailed review of the full-text documents identified in Table 9.6-2 resulted in the additional exclusion of the following studies from the dossier.

Table 9.6-4: List of references excluded following detailed review listed by data point number

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
Initial search					
CA 6.2.1	Pang Sen; Ran Zhaojin; Liu Zhiqian; Song Xiaoyu; Duan Liusheng; Li Xuefeng; Wang Chengju	2012	Enantioselective induction of a glutathione-S-transferase, a glutathione transporter and an ABC transporter in maize by Metolachlor and its (S)-isomer.	PloS one, (2012) Vol. 7, No. 10, pp. e48085	Discusses differences in metabolism of racemic and S-metolachlor; these differences are well known. No impact on S-metolachlor endpoints
CA 6.2.1	Perez Sandra; Farkas Michael; Barcelo Damia; Aga Diana S	2007	Characterization of glutathione conjugates of chloroacetanilide pesticides using ultra-performance liquid chromatography /quadrupole time-of-flight mass spectrometry and liquid chromatography/ion trap mass spectrometry	Rapid communications in mass spectrometry : RCM, (2007) Vol. 21, No. 24, pp. 4017-22	Study conducted in plant extracts in-vitro; similar conditions will never be encountered in whole plant hence results not relevant to plant metabolism.
CA 6.2.1	Berry James O; Aga Diana S	2007	Determination of enzyme kinetics and glutathione conjugates of chlortetracycline and chloroacetanilides using liquid chromatography-mass spectrometry	The Analyst, (2007 Jul) Vol. 132, No. 7, pp. 664-71	Study conducted in plant extracts in-vitro; similar conditions will never be encountered in whole plant hence results not relevant to plant metabolism.
CA 6.3	Muhammad Amjad; Tanveer Ahmad; Qumer Iqbal; Aamir Nawaz; Jahangir, M. M.	2013	Herbicide contamination in carrot grown in Punjab, Pakistan	Pakistan Journal of Agricultural Sciences (2013), Volume 50, Number 1, pp. 7-10	Relevant only to non-controlled uses of pesticide products in Pakistan.
CA 6.7	US Environmental Protection Agency	2012	S-Metolachlor; Pesticide Tolerances	[USA] Federal Register (2012), 77 (158), 48902-48907, 15 Aug 2012	MRL setting in the US. Not relevant to EU scenario
CA 6.7	US Environmental Protection Agency	2014	S-Metolachlor; Pesticide Tolerances	Federal Register (2014), 79 (100), 29729-29732, 23 May 2014	MRL setting in the US. Not relevant to EU scenario
CA 6.9	Fantke, Peter; Juraske, Ronnie; Anton, Assumpcio; Friedrich, Rainer; Jolliet, Olivier	2011	Dynamic Multicrop Model to Characterize Impacts of Pesticides in Food	Environmental Science & Technology (2011), 45 (20), 8842-8849	Development of generic exposure assessment model. Metolachlor not specifically mentioned in paper.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 6.9	Nougadere, Alexandre; Reninger, Jean-Cedric; Volatier, Jean-Luc; Leblanc, Jean-Charles	2011	Chronic dietary risk characterization for pesticide residues: A ranking and scoring method integrating agricultural uses and food contamination data	Food and Chemical Toxicology (2011), 49 (7), 1484-1510	Describes method to rank pesticides based on levels of concern to stimulate targeted national monitoring programmes. S-metolachlor identified as an active substance that presents no risk for consumers
CA 6.9	Juraske, Ronnie; Mutel, Christopher L.; Stoessel, Franziska; Hellweg, Stefanie	2009	Life cycle human toxicity assessment of pesticides: Comparing fruit and vegetable diets in Switzerland and the United States	Chemosphere (2009), 77 (7), 939-945	Generic exposure assessment of Swiss and US diets. Metolachlor not specifically mentioned in paper.

No literature references were deemed to be relevant to the residue or metabolism endpoints for S-metolachlor.

S-Metolachlor

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CA, Section 9

Ecotoxicological Studies

LITERATURE DATA

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

Table of Contents

CA 9 LITERATURE DATA

CA 9.1 Title

This document is a Literature Review Report for S-metolachlor, relevant metabolite(s) and EU representative formulation A9396G (Dual Gold®).

CA 9.2 Author(s) of the review

Syngenta
Jealott's Hill International Research Centre
Bracknell
Berkshire
RG42 6EY
UK

CA 9.3 Summary: A brief summary indicating the purpose of the report, the methodology employed and the results obtained

This report summarises the search for "scientific peer-reviewed open literature on S-metolachlor and its potentially relevant metabolites dealing with side effects on health and published within the last ten years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

The search strategy is detailed in the tables below. In summary, initially a very broad search was done to look for any references which included the active substance S-metolachlor, or its major metabolites, or its representative formulation, in conjunction with any of the key words set out in Table 9.5-1.

The names searched for were:

```
L1      QUE  (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2      QUE  (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3      QUE  (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4      QUE  (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5      QUE  (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6      QUE  (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7      QUE  (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8      QUE  (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9      QUE  (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10     QUE  (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11     QUE  (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12     QUE  (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13     QUE  (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14     QUE  (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15     QUE  (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16     QUE  (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17     QUE  (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18     QUE  (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19     QUE  (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))
L20     QUE  ((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21     QUE  (55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22     QUE  (METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23     QUE  ((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24     QUE  (CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
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L25     QUE  (L1-L20)   METABOLITES
L26     QUE  (L21 OR L22 OR L23 OR L24)   METOLACHLOR
L27     QUE  (L25 OR L26)   METOLACHLOR & METABOLITES
```

An overview of the results is summarised in the table below and further details are provided in Section 9.5.

Data requirement(s) captured in the search	Number
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	1295
Number of *summary records* excluded from the search results after rapid assessment for relevance	1136
Total number of *full-text* documents assessed in detail*	159
Number of *studies* excluded from further consideration after detailed assessment for relevance	103
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	56

*both from bibliographic databases and other sources of peer-reviewed literature

CA 9.4 Protocol

CA 9.4.1 Statement of the objective of the review

The review has the objective of identifying "scientific peer-reviewed open literature on S-metolachlor and metolachlor and its potentially relevant metabolites dealing with ecotoxicology studies which may impact health, the environment and non-target species and published within the last *ten* years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

CA 9.4.2 Criteria for relevance with which decisions to select studies in the dossier were made

Table 9.4.2-1: List of Criteria for relevance for each data requirement

Data requirements(s) (indicated by the correspondent CA data point (s))	Criteria for relevance
Ecotoxicological studies (CA 8.1 to 8.15)	<u>Laboratory Studies</u> 1. Well defined test material (including purity/content) 2. Number of organisms per group sufficient to establish a statistical significance 3. Applicable test species 4. Test organisms are not previously exposed to the test material or other contaminants 5. Several dose levels tested, at least 3, including a negative control, to establish a dose-response, unless the study design is specifically a limit test. Control must be run concurrently with treatments and mortality to be within test validity criteria. 6. Exposure route is clearly defined, is environmentally relevant and, if appropriate, suitably quantified. 7. If conducted, analytical confirmation of dosing or sufficient information provided to determine concentrations were within acceptable range (e.g. 80-120%) of nominal targets. 8. Effects are related to single test item, and a quantitative relationship exists between the reported endpoint and risk assessment endpoints of growth, mortality, behaviour and/or reproduction. 9. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust.

Data requirements(s) (indicated by the correspondent CA data point (s))	Criteria for relevance
	10. Study conditions should not differ significantly from recommended protocols. 11. Study conditions should not interfere with the interpretation of the study results. Field Studies 12. Appropriate and relevant geoclimatic conditions (setting), appropriate application method and rates (exposure) and observation data (biological relevance) to derive endpoints. 13. Well defined test material (including purity/content) 14. Applicable test species 15. Exposure route is clearly defined, is environmentally relevant and, if appropriate, suitably quantified. 16. Sufficient experimental information provided to substantiate and evaluate whether the study conclusions and endpoints are robust (e.g. pre-treatment details, characterisation of physico-chemical parameters, replication, statistical methods and appropriate sampling regime). 17. Study conditions should not differ significantly from recommended protocols, if available for field study. Study conditions should not interfere with the interpretation of the study results
CA 5.8.3 Endocrine disrupting properties	18. Identified test material 19. All studies considered relevant at this stage – need to be checked for reliability 20. Relevant to ED assessment (LI60, LI 61)

* Recommended protocols under each data point include but are not limited to those listed in the Commission Communications 2013/C 95/01 and 2013/C 95/02

The initial rapid assessment followed the advice given in the EFSA Guidance Document: **Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009; EFSA Journal 2011; 9(2):2092.** Under 'Selecting the relevant studies and reporting the selection process (page 23) the Guidance states:

"If the first iteration results in a large number of studies that are of unclear relevance, refinement of the selection criteria may be considered.

1. *Rapid assessment for relevance based on summary records (e.g. titles and abstracts), to exclude summary records which are obviously irrelevant. Summary records which appear to be relevant and those of unclear relevance go to the next step. If there is insufficient information in the summary record to determine relevance, then assessment of full-text documents (step 2 below) will be required. During this assessment, a summary record may be excluded on the basis of the title alone (e.g. if an abstract is not available), provided that the title provides sufficient information to clearly indicate non-relevance."*

Guidance on setting the relevance criteria are set out in section 5.1. In essence, the relevance criteria are driven by the data requirements for each section, in this case ecotoxicological studies as set out in M-CA Section 8. The Guidance document then gives much more specific criteria to assess relevance (see pages 15 and 16; e.g. well identified test material; sufficient number of doses tested, etc.) which however in practice cannot be identified until a thorough in-depth review of each publication is carried out.

The data requirement criteria were used to define the key words and the search strategies that are presented in Document M-CA Section 9 Supplement Ecotoxicology, in Table 9.5-1.

The rapid assessment for relevance was then carried out by looking at all the published article titles and short abstracts (where available) to identify records which *'are obviously irrelevant'*, as stated in the

Guidance. This followed the general advice given in Appendix C for rapid assessment based on summary records -

"Due to the lack of relevance information in the summary records, the following revised criteria were

Used to classify a summary record as potentially relevant to the [eco-]toxicological risk assessment:

· ***Test material identified in the summary record (regardless the purity/impurity profile).***

· ***Test species relevant to the [ecotoxicological] assessment.***

· *Sufficient number of doses tested (except for OECD code 5.1 and 5.4).*

· ***Relevant route(s) of administration.***

· *Epidemiological studies, medical reports and actual exposure measurements were always considered relevant at this stage.*

· ***Studies which may be helpful for the interpretation of other studies present in the dossier, but do not fit under a specific toxicological endpoint (broadly included in the OECD code referred as "other toxicological studies").***"

In practice only the criteria identified in bold above were used for the ecotoxicological rapid assessment evaluation. In this specific case, the summary records that were identified as obviously not relevant, were not relevant for the ecotoxicological assessment, although they may have been relevant for another data requirement (e.g. environmental fate or (largely) efficacy).

CA 9.5 Search methods

Date of initial search	20 August 2014
Date of most recent update to search	-
Date span of the search	10 years

Table 9.5-1: Detailed Search Parameters for Ecotoxicological studies (CA 8.1 to 8.15)

Search Strategy	
L1	QUE (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2	QUE (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3	QUE (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4	QUE (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5	QUE (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6	QUE (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7	QUE (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8	QUE (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9	QUE (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10	QUE (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11	QUE (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12	QUE (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13	QUE (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14	QUE (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15	QUE (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16	QUE (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17	QUE (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18	QUE (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19	QUE (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))

Search Strategy		
L20	QUE	((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21	QUE	(55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22	QUE	(METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23	QUE	((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24	QUE	(CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
L25	QUE	(L1-L20) METABOLITES
L26	QUE	(L21 OR L22 OR L23 OR L24) METOLACHLOR
L27	QUE	(L25 OR L26) METOLACHLOR & METABOLITES
		Plus
L1	QUE	(RIPARIAN? OR REPTILE? OR SNAKE? OR LIZARD?)
L2	QUE	(TORTOISE? OR TURTLE? OR TERRAPIN? OR CROCODIL?)
L3	QUE	(ALLIGATOR? OR CAIMAN? OR GHARIAL? OR HOVERFLIES)
L4	QUE	((MEADOW#(W)VOLE#) OR PSEUDOKIRSCHNERIELLA)
L5	QUE	(RHAPHIDOCELIS OR NITZSCHIA OR CYCLOTELLA OR MICROCYSTIS)
L6	QUE	(OSCILLATORIA OR APHANIZOMENON OR ANKISTRODESMUS)
L7	QUE	(TEILINGRIA OR MONORAPHIDIUM OR RADIOCOCCACAE OR TETRASPORALES)
L8	QUE	(TETRAEDRON OR TREUBARIA OR WILLEA OR COSMOCLADIUM)
L9	QUE	(HYPOASPIS OR (SOIL(3A)MICROORGAN?) OR ECHINOCHLOA OR SPARTINA)
L10	QUE	(SALVINIA OR NAJAS OR CALLITRICHE OR MYOSOTIS OR STRATIOTES)
L11	QUE	(HIPPURUS OR PERSICARIA OR CLOEON? OR CORBICULA?)
L12	QUE	(NEOCARIDINIA? OR NEOCARIDINA? OR MYSID? OR CICHLIDAE)
L13	QUE	(CICHLID# OR LEPOMIS? OR SERRANIDAE OR PERCIFORMES)
L14	QUE	(ICTALURUS? OR POECILIA? OR ORYZIAS? OR GASTEROSTEUS?)
L15	QUE	(GASTEROSTEIDAE OR SALVELINUS OR BRACHYDANIO? OR CARASSIUS?)
L16	QUE	(MISGUMUS? OR CYPRINODON? OR FUNDULUS? OR MISGURNUS?)
L17	QUE	(BREAM OR ROTIFER# OR GAMMARUS OR GAMMARID? OR MAYFLY?)
L18	QUE	(BIVALVE# OR MUSSEL# OR MOLLUSK# OR MOLLUSC# OR BUFO)
L19	QUE	(NEWT# OR SCALLOP# OR CLAM# OR GAMBUSIA OR OREOCHROMIS)
L20	QUE	(OSTRAC? OR TUBIFEX? OR TURBELLARIA OR COPEPODA)
L21	QUE	(PREDACE? OR PREDACI? OR PARASITOID? OR APIS OR APIDAE)
L22	QUE	(BOMBUS OR BOMBINAE OR WORM# OR LUMBRICIDAE OR LUMBRICUS)
L23	QUE	(ALLOBOPHORA? OR DENDROBAENA? OR APORRECTODEA? OR DENDRODRILUS?)
L24	QUE	(EISENIA? OR OCTOLASION? OR (LACE(W)WING#) OR NEUROPTER?)
L25	QUE	(CARABID? OR CARBUS OR STAPHYLINID? OR COCCINEL? OR ADALIA?)
L26	QUE	(STETHORUS? OR SCYMNUS? OR WASP# OR VESPIDAE OR SPHECOIDEA)
L27	QUE	(SPHECIDAE OR STIZIDAE OR OPIUS OR (ICHNEUMON(W)FL?))
L28	QUE	(ICHNEUMONID? OR BRACONID? OR CHALCID? OR CYNIP? OR APHIDI?)
L29	QUE	(EUCOILID? OR IBALIID? OR FIGITID? OR EURYTOM? OR TORYM?)
L30	QUE	(ORYM? OR EUCHARIT? OR PERILAMP? OR PTEROMAL? OR CHRYSOLAMP?)
L31	QUE	(EUPELM? OR ENCYRT? OR SIGNIPHOR? OR APHELIN? OR ELASMID?)
L32	QUE	(ELASMUS OR TETRACAMP? OR MYMAR? OR HELOR? OR PROCTOTRUP?)
L33	QUE	(DIAPRI? OR SCELION? OR PLATYGASTR? OR PLATYGASTER?)
L34	QUE	(CERAPHRON? OR MEGASPIL? OR ARANE? OR OPILION? OR PHALANG?)
L35	QUE	(ARACHNID? OR HARVESTM? OR DADDYLONGLEG? OR (DADDY(W)LONG (W)LEG?))
L36	QUE	((DADDY(W)LONGLEG?) OR COLLEMB? OR (SPRING(W)TAIL?) OR CYDNODROMUS?)
L37	QUE	(PARDOSA? OR ORIUS? OR TYPHLODROM? OR PHYTOSEIULUS? OR SYRPHID?)
L38	QUE	(METASYRPHUS? OR SYRPHUS? OR EUPEODES? OR EPISYRPHUS? OR SYRPHIAN?)
L39	QUE	(EPISTROPHE? OR AMBLYSEIUS? OR POECILUS? OR TRECHUS? OR BEMBIDION?)
L40	QUE	(NEBRIA? OR PTEROSTICHUS? OR CALOSOMA? OR TACHYPORUS? OR NABIDAE?)
L41	QUE	(GEOCORIS? OR HYMENOPT? OR HAEMATOLOECHA? OR CHRYSOPID? OR SYMPHYTA?)

Search Strategy		
L42	QUE	(OULEMA? OR APHYTIS? OR BATHYPLECTES? OR LINPHIIDAE? OR LYNPHIIDAE?)
L43	QUE	(LINYPHIIDAE? OR ERIGONE? OR BATHYPHANTES? OR MEIONETA? OR OEDOTHORAX?)
L44	QUE	(LEPTHYPHANTES? OR LYCOSID? OR LYCOSA? OR CHRYSOPA? OR DACNUSA?)
L45	QUE	(CYRTORHINUS? OR CRYPTOLAEMUS? OR ZETZELLIA? OR LEPTOMASTIX?)
L46	QUE	(TRICHOGRAMMA? OR ENCARSIA? OR MACROLOPHUS? OR CHRYSOPERLA?)
L47	QUE	(ALEOCHARA? OR CHRYSOPID# OR CHRYSOPIDAE OR DIABROTICA)
L48	QUE	(PALEXORISTA? OR MAMMAL## OR ANIMAL? OR RABBIT? OR RODENT#)
L49	QUE	(BLACKBIRD# OR (BLACK(W)BIRD#) OR ((TURDUS OR T)(W)MERULA))
L50	QUE	(CHAFFINCH? OR ((FRINGILLA OR F)(W)COELEBS) OR GREENFINCH?)
L51	QUE	(((CARDUELIS OR C)(W)CHLORIS) OR SONGTHRUSH?)
L52	QUE	((SONG(W)THRUSH?) OR ((TURDUS OR T)(W)PHILOMELOS) OR WREN#)
L53	QUE	(((TROGLODYTES OR T)(W)TROGLODYTES) OR (WILLOW(W)WARBLER#))
L54	QUE	(((PHYLLOSCOPUS OR P)(W)TROCHILUS) OR (GREAT(W)TIT#))
L55	QUE	(((PARUS OR P)(W)MAJOR) OR ROBIN# OR GOLDFINCH?)
L56	QUE	(((ERITHACUS OR E)(W)RUBECULA) OR DUNNOCK#)
L57	QUE	(((CARDUELIS OR C)(W)CARDUELIS) OR LINNET#)
L58	QUE	(((PRUNELLA OR P)(W)MODULARIS) OR SKYLARK# OR (SKY(W)LARK#))
L59	QUE	((HEDGE(W)(SPARROW# OR ACCENTOR#)))
L60	QUE	(((CARDUELIS OR C)(W)CANNABINA) OR ((ALAUDA OR A)(W)ARVENSIS))
L61	QUE	((RED(W)LEGGED(W)PARTRIDGE#) OR ((ALECTORIS OR A)(W)RUFA))
L62	QUE	((MEADOW(W)PIPIT#) OR MEADOWPIPIT# OR ((ANTHUS OR A)(W) PRATENSIS))
L63	QUE	(LAPWING# OR ((VANELLUS OR V)(W)VANELLUS) OR PEEWIT#)
L64	QUE	(STARLING# OR ((STURNUS OR S)(W)VULGARIS))
L65	QUE	((TURTLE(W)DOVE#) OR ((STREPTOPELIA OR S)(W)TURTUR))
L66	QUE	(YELLOWHAMMER# OR (YELLOW(W)HAMMER#) OR (YELLOW(W)WAGTAIL#))
L67	QUE	(((EMBERIZA OR E)(W)CITRINELLA) OR (YELLOW(W)WAG(W)TAIL#))
L68	QUE	(((MOTACILLA OR M)(W)FLAVA) OR (FAN(W)TAILED(W)WARBLER#))
L69	QUE	((GREY(W)LAG(W)G!!SE) OR ((ANSER OR A)(W)ANSER))
L70	QUE	(REEDBUNTING# OR (REED(W)BUNTING#) OR ((EMBERIZA OR E)(W) SCHOENICLUS))
L71	QUE	(CHAFFINCH? OR BLUETIT? OR (BLUE(W)TIT?))
L72	QUE	(((PARUS OR P)(W)CAERULEUS) OR (SYLVIA(W)COMMUNIS))
L73	QUE	(((GALERIDA OR G)(W)CRISTATA) OR (TREE(W)SPARROW#))
L74	QUE	(((COTURNIX OR C)(W)COTURNIX) OR (GREY(W)PARTRIDGE#))
L75	QUE	(((PERDIX OR P)(W)PERDIX) OR ((PHASIANUS OR P)(W)COLCHICUS))
L76	QUE	(((MILIARIA OR M)(W)CALANDRA?) OR GREYLAGG!!SE)
L77	QUE	((GREYLAG(W)G!!SE) OR ((COLUMBA OR C)(W)PALUMBUS?))
L78	QUE	(((STREPTOPELIA OR S)(W)(ORIENTALIS? OR RISORIA?)))
L79	QUE	(((MOTACILLA OR M)(W)ALBA?) OR (CRESTED(W)LARK#))
L80	QUE	((WHITE(W)WAGTAIL#) OR (WOOD(W)PIGEON#) OR (BIRD(W)LIFE))
L81	QUE	((SONG(W)BIRD#) OR VANELLUS? OR (PEE(W)WIT#))
L82	QUE	(AVIFAUNA? OR (AVI(W)FAUNA?) OR SONGBIRD?)
L83	QUE	(ORNITHOLOG? OR PASSERINE? OR WOODPIGEON#)
L84	QUE	(((PASSER OR P)(W)MONTANUS) OR QUAIL# OR (CALANDRA(W)LARK#))
L85	QUE	(CISTICOLA? OR (Z(W)CISTICOLA?) OR BIRDLIFE)
L86	QUE	(GEESE OR GOOSE OR SPARROWS OR PIGEONS OR LARK#)
L87	QUE	(WARBLER# OR PARTRIDGE# OR BUNTING# OR WAGTAIL#)
L88	QUE	(WHITETHROAT# OR PIED# OR (WHITE(W)THROAT#))
L89	QUE	((FORAGING OR FARMLAND OR GRASSLAND)(3A)BIRD#)
L90	QUE	(BLUEBIRD# OR (ROCK(W)PTARMIGAN#) OR (BLACK(W)REDSTART#))
L91	QUE	((PREDATOR? OR NONTARGET? OR (NON(W)TARGET))(3A)BIRD#)
L92	QUE	((CORN(W)BUNTING#) OR SERINS OR SERINUS)
L93	QUE	(L49 OR L50 OR L51 OR L52 OR L53 OR L54 OR L55 OR L56 OR L57 OR

Search Strategy
L58 OR L59 OR L60 OR L61 OR L62 OR L63 OR L64 OR L65 OR L66 OR L67 OR L68 OR L69 OR L70 OR L71 OR L72 OR L73 OR L74 OR L75 OR L76 OR L77 OR L78 OR L79 OR L80 OR L81 OR L82 OR L83 OR L84 OR L85 OR L86 OR L87 OR L88 OR L89 OR L90 OR L91 OR L92)
L94 QUE L93 NOT (JAPANESE? OR JAPONICA?)
L95 QUE (((SMALL OR WILD)(3A)MAMMAL#) OR (WILD(3A)ANIMAL?))
L96 QUE (VOLE# OR GLIS OR DORMOUSE OR DORMICE OR ELIOMY#)
L97 QUE (LEROT# OR LAGOMORPH# OR LEPORID? OR LEPUS OR ORYCTOLAGUS?)
L98 QUE (HARE# OR SORICIDAE? OR SOREX? OR NEOMY# OR CROCIDURA?)
L99 QUE (SHREW# OR WOODMOUSE OR WOODMICE OR APODEMUS? OR MICROTUS?)
L100 QUE (CLETHRIONOMYS? OR CRICETIDAE? OR MICROTIN?)
L101 QUE (RAPTOR# OR MARMOSET# OR GOPHER# OR GRASSCUTTER#)
L102 QUE ((PREDATOR? OR NONTARGET? OR (NON(W)TARGET?))(3A)MAMMAL#)
L103 QUE ((WOOD(W)(MOUSE OR MICE)) OR ARVICOLA?)
L104 QUE (MEADOW#(W)VOLE#)
L105 QUE (L95 OR L96 OR L97 OR L98 OR L99 OR L100 OR L101 OR L102 OR L103 OR L104)
L106 QUE (ECOTOX? OR LC50 OR ((LC OR EC OR LR)(W)50) OR EC50 OR LR50)
L107 QUE (ECO OR ECOL OR ECOLOG? OR ENV OR ENVIRONM? OR AQUATIC?)
L108 QUE (L107(5A)(TOX? OR RISK? OR IMPACT? OR EFFECT?))
L109 QUE (AQUATIC? OR FRESHWATER? OR (FRESH(W)WATER?))
L110 QUE (FLORA OR FAUNA OR BIOTA OR ORGANISM? OR INSECT?)
L111 QUE (ENVIRONM? OR LIFE OR INVERTEB? OR CRUSTACE? OR SPECIES)
L112 QUE (ENTOMOFAUNA OR (ENTOMO(W)FAUNA))
L113 QUE (L109(5A)(L110 OR L111 OR L112))
L114 QUE (MAGNA? OR (D(W)MAGNA?) OR CHIRONOM? OR BRACHIONUS?)
L115 QUE (LIMNEA? OR CRASSOSTREA? OR ALGA# OR FISH OR FISHES)
L116 QUE (ONCORHYNCHUS? OR SALMONIDAE? OR CYPRINUS? OR CYPRINID?)
L117 QUE (PIMEPHALES? OR PISCES OR TROUT OR SUNFISH? OR CARP)
L118 QUE (MINNOW? OR (F(W)MINNOW?) OR CATFISH? OR ZEBRAFISH?)
L119 QUE (GOLDFISH? OR (ZEBRA(W)DANIO#) OR GUPPY OR GUPPIES)
L120 QUE (KILLFISH? OR FATHEAD? OR BLUEGILL? OR SALMON#)
L121 QUE (THUNDERFISH? OR (WATER(W)(FLY OR FLEA?)) OR WATERFLEA?)
L122 QUE (FROG# OR AMPHIBIA? OR SHRIMP# OR PRAWN# OR CRAB# OR TOAD#)
L123 QUE (TADPOLE# OR CRAYFISH? OR SHELLFISH? OR LOBSTER#)
L124 QUE (OYSTER# OR SNAIL# OR RANA OR RANIDAE? OR PLANKTON?)
L125 QUE L106 OR L108
L126 QUE ((NONTARGET? OR (NON(W)TARGET?))(5A)(PLANT? OR FLORA?))
L127 QUE ((AQUATIC(3A)(PLANT? OR (PHYTO(W)TOX?) OR PHYTOTOX?)))
L128 QUE (SEDIMENT? OR HYDROSOIL? OR DUCKWEED? OR PONDWEED?)
L129 QUE (((DUCK OR POND)(W)WEED#) OR MACROPHYT? OR PERIPHYTON?)
L130 QUE (POTAMOGETON? OR CHAROPHYTA? OR ELODEA? OR HYDROCHARITA?)
L131 QUE (CERATOPHYL? OR CHLAMYDOMON? OR SELENASTRUM? OR CHLORELLA?)
L132 QUE (SCENEDESMUS? OR SKELETONEMA? OR NAVICULA? OR ANABAENA?)
L133 QUE (MYRIOPHYLLUM? OR GLYCERIA?)
L134 QUE (NONTARGET? OR (NON(W)TARGET?) OR BENEFICIAL?)
L135 QUE (EFFECT? OR INVERTEB? OR ORGANISM? OR ARTHROPOD? OR INSECT?)
L136 QUE (FAUNA OR SPECIES OR (ENTOMO(W)FAUNA?) OR ENTOMOFAUNA?)
L137 QUE ((L134(5A)(L135 OR L136)))
L138 QUE (PREDAT? OR (NATURAL(W)ENEM?) OR BEE OR BEES OR HONEYBEE#)
L139 QUE (BUMBLEBEE# OR ((HONEY OR BUMBLE)(W)BEE#) OR EARTHWORM?)
L140 QUE ((EARTH(W)WORM?) OR LADYBUG# OR LADYBEETLE# OR LADYBIRD#)
L141 QUE ((LADY(W)(BUG# OR BEETLE# OR BIRD#)) OR HOVERFLY)
L142 QUE (HOOVERFLIES OR SAWFLY OR SAWFLIES OR DRONEFLY)
L143 QUE (DRONEFLIES OR FLOWERFLY OR FLOWERFLIES OR LACEWING?)
L144 QUE (((HOVER OR DRONE OR FLOWER OR SAW)(W)(FLY OR FLIES)))
L145 QUE (SPIDER# OR SPRINGTAIL? OR (ROOT(W)WORM#) OR ROOTWORM#)

Search Strategy
L146 QUE (L137 OR L138 OR L139 OR L140 OR L141 OR L142 OR L143 OR L144 OR L145) L147 QUE (BIRD? OR AVES OR AVIAN? OR (AVI(W)FAUNA?) OR AVIFAUNA?) L148 QUE (SONGBIRD? OR (SONG(W)BIRD?) OR ORNITHOLOG?) L149 QUE (L147 OR L148) L150 QUE ((WILD(3A)(LIFE OR ANIMAL#)) OR WILDLIFE OR SQUIRREL?) L151 QUE (VOLE# OR SCIURUS OR GLIRID? OR GLIS OR DORMOUSE) L152 QUE (DORMICE OR ELIOMYS OR LEROT# OR MUSTELID? OR MINK#) L153 QUE (MUSTELINE# OR WEASEL? OR STOAT? OR MUSTEL? OR BADGER?) L154 QUE (MELES OR MELINAE OR OTTER# OR LUTRA OR LUTRINAE) L155 QUE (LAGOMORPH# OR LEPORID? OR LEPUS OR ORYCTOLAGUS OR HARE#) L156 QUE (TALPA OR MOLE OR MOLES OR HEDGEHOG? OR (HEDGE(W)HOG?)) L157 QUE (CROCIDURA? OR SHREW# OR WOODMOUSE OR WOODMICE OR APODEMUS) L158 QUE (MICROTUS OR ARVICOLA OR CLETHRIONOMYS? OR CRICETIDAE?) L159 QUE (ERINACEUS OR ERINACEIDAE? OR SORICIDAE? OR SOREX) L160 QUE (ENDOCRIN? OR HORMON?) L161 QUE (DISRUPT? OR MIMIC? OR MODULAT? OR DISORDER? OR DISEASE?) L162 QUE (L160(5A)L161) L163 QUE (DAPHNI? OR CERIODAPHNI? OR HYALELLA? OR ASSELLUS) L164 QUE L113 OR (L114 OR L115 OR L116 OR L117 OR L118 OR L119 OR L120 OR L121 OR L122 OR L123 OR L124) OR L163 L165 QUE (PHYTOPLANKTON? OR AUFWUCH# OR LEMNA? OR ARALES OR CHARA) L166 QUE (L126 OR L127 OR L128 OR L129) OR (L130 OR L131 OR L132 OR L133) OR L165 L167 QUE (NEOMYS OR MICROTINAE?) L168 QUE (L150 OR L151 OR L152 OR L153 OR L154 OR L155 OR L156 OR L157 OR L158 OR L159) OR L167 L169 QUE (LOACH? OR STICKLEBACK? OR MUMMICHOG# OR TILAPIA? OR ASELLUS) L170 QUE L164 OR L169 L171 QUE L125 OR L170 OR L166 OR L146 OR L149 OR L168 OR L162 L172 QUE (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41 OR L42 OR L43 OR L44 OR L45 OR L46 OR L47 OR L48) L173 QUE (L171 OR L172 OR L94 OR L105)

Table 9.5-2: Details of Databases Searched and justification for Selection

Provider	Database	Justification	Limits applied	Number*
Host STN	MEDLINE	Contains information on every area of medicine providing comprehensive coverage from 1948 to present. Sources include journals and chapters in books or symposia. The database is updated 5 times each week with an annual reload and therefore stays very current in its cover.	None	168
	EMBASE	The database, covers worldwide literature in the biomedical and pharmaceutical fields, including biological science, biochemistry, human medicine, forensic science, pediatrics, pharmacy, pharmacology and drug therapy, pharmacoeconomics, psychiatry, public health, biomedical engineering and instrumentation, and environmental science. Sources include more than 4,000 journals from approximately 70 countries, monographs, conference proceedings, dissertations, and reports. The databases covers data from 1974-present and is updated daily.		67
	EMBAL	The database provides early access to bibliographic data and the abstracts for references that will appear in EMBASE. Bibliographic information for references is available in EMBAL for the latest 8 weeks of EMBASE data. The database covers the worldwide literature on the biomedical and pharmaceutical fields. Bibliographic information, abstracts, and author keywords are searchable. Sources include over 4,000 journals. The database covers current data and is updated daily.		0
	ESBIOBASE	A database providing comprehensive coverage of the entire spectrum of biological research worldwide. Coverage includes the following areas: applied microbiology, biotechnology, cancer research, cell & developmental biology, clinical chemistry, ecological & environmental sciences, endocrinology, genetics, immunology, infectious diseases, metabolism, molecular biology, neuroscience, plant and crop science, protein biochemistry, and toxicology. Records are selected from over 1,700 international scientific journals, books, and conference proceedings. The database covers the period 1994 - present and is updated weekly.		32
	AGRICOLA	A bibliographic database containing selected worldwide literature of agriculture and related fields. Coverage of the database includes agricultural economics and rural sociology, agricultural production, animal sciences, chemistry, entomology, food and human nutrition, forestry, natural resources, pesticides, plant science, soils and fertilizers, and water resources. Also covered are related areas such as biology and biotechnology, botany, ecology, and natural history. The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. It covers the period 1970-present and is updated monthly.		25

Provider	Database	Justification	Limits applied	Number*
	BIOSIS	A large and comprehensive worldwide life science database covers original research reports, reviews, and selected U.S. patents in biological and biomedical areas, with subject coverage ranging from aerospace biology to zoology. Sources include periodicals, journals, conference proceedings, reviews, reports, patents, and short communications. Nearly 6,000 life source journals, 1,500 international meetings as well as review articles, books, and monographs are reviewed for inclusion. It covers the period 1926 – present and is updated weekly.		110
	CABA	Covers worldwide literature from all areas of agriculture and related sciences including biotechnology, forestry, and veterinary medicine. Sources include journals, books, reports, published theses, conference proceedings, and patents. It covers the period 1973-present and is updated weekly.		246
	CAPLUS	Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences including applied, macromolecular, organic, physical, inorganic, and analytical chemistry. Current sources include over 8,000 journals, patents, technical reports, books, conference proceedings, dissertations, product reviews, bibliographic items, book reviews, and meeting abstracts. Electronic-only journals and Web preprints are also covered. Cited references are included for journals, conference proceedings and basic patents from the U.S., EPO, WIPO, and German patent offices added to the CAS databases from 1999 to the present. Also provides early access to the bibliographic information, abstracts and CAS Registry Numbers for documents in the process of being indexed by CAS. Covers the period 1907 – present and is updated daily		482
	FSTA	The database provides worldwide coverage of all scientific and technological aspects of the processing and manufacture of human food products including basic food sciences, biotechnology, hygiene and toxicology, engineering, packaging, and all individual foods and food products. Sources include more than 2,200 journals, books, reviews, conference proceedings, patents, standards, and legislation. It covers the period 1969 – present and is updated weekly.		1

Provider	Database	Justification	Limits applied	Number*
	FROSTI	The database contains citations to the worldwide literature on food science and technology including food and beverages, analytical methods, quality control, manufacturing, microbiology, food processing, health and nutrition, recipes, and additives. Sources include approximately 800 scientific and technical journals, bulletins, technical reports, conference proceedings, grey literature, and British, European (EP), U.S., Japanese, and international (PCT) patent applications. Covers the period 1972 – present and is updated twice weekly.		0
	GEOREF	Covers international literature on geology and geosciences. Sources include the Bibliography of North American Geology, Bibliography and Index of Geology Exclusive of North America, Geophysical Abstracts, Bibliography of Fossil Vertebrates, selected records from Geoline and from geology sections of PASCAL and state and national geological surveys. Covers the period 1669 – present and is updated twice a month.		38
	TOXCENTER	Covers the pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals. It is composed of the following subfiles: BIOSIS, CAplus, IPA and MEDLINE and sources include abstracts, books and book chapters, bulletins, conference proceedings, journal articles, letters, meetings, monographs, notes, papers, patents, presentations, research and project summaries, reviews, technical reports, theses, translations, unpublished material, web reprints. Covers the period 1907 – present and is updated weekly		0
	PQSCITECH	Is a huge resource in all areas of science and technology from engineering to lifescience. The file is a merge of 25 STN databases formerly known as CSA databases (Cambridge Scientific Abstracts): AEROSPACE, ALUMINIUM, ANTE, AQUALINE, AQUASCI, BIOENG, CERAB, CIVILENG, COMPUAB, CONFSCI, COPPERLIT, CORROSION, ELCOM, EMA, ENVIROENG, HEALSAFE, LIFESCI, LISA, MATBUS, MECHENG, METADEX, OCEAN, POLLUAB, SOLIDSTATE, and WATER. Sources are journals, patents, books, reports, and conference proceedings spanning the period 1962 – present and it is updated monthly.		45
	PASCAL	The database provides access to the world's scientific and technical literature including physics and chemistry, life sciences (biology, medicine, and psychology), applied sciences and technology, earth sciences, and information sciences. French and European literature is particularly well represented. Approximately 5,000 journal titles are indexed. References to theses and to conference proceedings are also included. Spans the period 1977 to present and is updated weekly		18
	SCISEARCH	Is an international index to the literature covering virtually every subject area within the broad fields of science, technology, and biomedicine. SciSearch contains all the records published in Science Citation Index Expanded™ and additional records from the Current Contents series of publications. Bibliographic information and cited references from over 5,600 scientific, technical, and medical journals are contained in the database. Spans the period 1974 to present and is updated weekly.		74
	ANABST	Covers worldwide literature on analytical chemistry. The ANABSTR file contains bibliographic records with abstracts (since 1984) for documents reported in printed Analytical Abstracts. Sources for ANABSTR include journals, books, conference proceedings, reports, and standards. Spans the period 1980 to present and is updated weekly.		2

* Total number of summary records retrieved after removing duplicates

Table 9.5-3: Detailed Search Parameters for Web searches

Website name and service publisher	URL	Justification	Search terms	Limits applied	Number*
A web search has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-4: Detailed Search Parameters for Journal Table of Contents

Journal name	Journal URL or publisher	Dates, volumes and issues searched	Method of searching	Search terms	Number*
A search for journal table of contents has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-5: Detailed Search Parameters for Reference Lists

Bibliographic details of documents whose reference lists were scanned	Number*
A search for reference lists has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.	

* Total number of summary records or full-text documents retrieved after removing duplicates

CA 9.6 Results

Table 9.6-1: Results of study selection process

Data requirement(s) captured in the search	Number (Top-Up Search)
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	1295
Number of *summary records* excluded from the search results after rapid assessment for relevance	1136
Total number of *full-text* documents assessed in detail*	159
Number of *studies* excluded from further consideration after detailed assessment for relevance	105
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	56

*both from bibliographic databases and other sources of peer-reviewed literature

For the initial rapid assessment, the study titles were scanned to identify whether the studies were indeed relevant to ecotoxicology or not – for example, any studies clearly not in the remit of the European review (such as studies about Brazilian species); or unambiguously belonging to other sections such as environmental fate or efficacy (the majority of the references found), were excluded.

Applicant has additionally reviewed one publication (Jin *et al*., 2011) as outlined in Stop the Clock request 60.

Table 9.6-2: List of references for all relevant and unclear studies listed by data point number

CA data point number	Author(s)	Year	Title	Source
CA 8.0	Ye, J., Liu, J., Liu, W., Zhao, M., Liu, W.	2010	Enantioselectivity in environmental risk assessment of modern chiral pesticides.	Environmental Pollution, (July 2010) Vol. 158, No. 7, pp. 2371-2383. Refs: 69. ISSN: 0269-7491 CODEN: ENPOEK
CA 8.1.1.3	Keseru, M., Juhasz, E., Szabo, R., Tavaszi, J., Varnagy, L.	2007	Study of the individual toxicity of three pesticides in a teratogenicity test on birds. Harom noevenyvedo szer egyedi mereghatasanak vizsgalata madarteratologiai tesztben.	Noevenyvedelem (2007), Vol. 43, Number 3, pp. 113-119, 23 refs. ISSN: 0133-0829
CA 8.1.1.3	Varnagy, L., Budai, P., Fejes, S., Keseru, M., Szabo, R.. Juhasz, E.	2004	Degredation dynamics and toxicity of certain pesticide active ingredients in bird embryos.	Magyar Allatorvosok Lapja (2004), Volume 126, Number 12, pp. 755-760, 21 refs. ISSN: 0025-004X
CA 8.1.2	Greenlee, A.R., Ellis, T.M., Berg, R.L.	2004	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9. Journal code: 0330411. ISSN: 0091-6765. Report No.: NLM-PMC1241965.
CA 8.1.4 CA 8.2.1 CA 8.2.4.1 CA 8.2.4.2	Wan, M. T., Buday, C., Schroeder, G., Kuo, J., Pasternak, J.	2006	Toxicity to *Daphnia magna*, *Hyalella azteca*, *Oncorhynchus kisutch*, *Oncorhynchus mykiss*, *Oncorhynchus tshawytscha* and *Rana catesbeiana* of atrazine, metolachlor, simazine, and their formulated products.	Bulletin of Environmental Contamination and Toxicology (2006) Volume 76, Number 1, pp. 52-58, 9 refs. ISSN: 0007-4861. DOI: 10.1007/s00128-005-0888-4

CA data point number	Author(s)	Year	Title	Source
CA 8.1.4	De Solla, S.R., Palonen K.E., Martin P.A.	2014	Toxicity of pesticides associated with potatoe production, including soil fumigants, to snapping turtle eggs (*Cheludra serpentine*).	Environmental toxicology and chemistry/SETAC (2014 Jan) 33 (1): 102-106.
CA 8.1.4	De Solla, S.R., Martin, P.A	2011	Absorption of current use pesticides by snapping turtle (*Chelydra serpentina*) eggs in treated soil.	Chemosphere, (2011 Oct) Vol. 85, No. 5, pp. 820-5. Electronic Publication Date: 8 Sep 2011. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535
CA 8.1.4	De Solla, S., Martin, P.	2010	Relationship between pesticide properties and absorption in turtles eggs from treated soil.	Canadian Technical Report of Fisheries and Aquatic Sciences, (2010) Vol. 2883, pp. 64. Meeting Info.: 36th Annual Workshop on Aquatic Toxicity. La Malbaie, CANADA. September 27-30, 2009. CODEN: CTRSDR. ISSN: 0706-6457. E-ISSN: 0706-6570.
CA 8.1.4	Papoulias, D.M. , Schwarz, M.S., Mena, L.	2013	Gonadal abnormalities in frogs (*Lithobates* spp.) collected from managed wetlands in an agricultural region of Nebraska, USA.	Environmental Pollution, (January 2013) Vol. 172, pp. 1-8. Refs: 78. ISSN: 0269-7491; E-ISSN: 1873-6424; CODEN: ENPOEK
CA 8.1.4	Spolyarich N., Hyne R.V., Wilson S.P., Palmer C.G., Byrne M.	2011	Morphological abnormalities in frogs from a rice-growing region in NSW, Australia, with investigations into pesticide exposure.	Environmental monitoring and assessment, (2011 Feb) Vol. 173, No. 1-4, pp.397-407. Journal code: 8508350. E-ISSN: 1573-2959. L-ISSN: 0167-6369.
CA 8.1.4	Spolyarich N., Hyne, R., Wilson S., Palmer C., Byrne M.	2010	Growth, development and sex ratios of Spotted Marsh Frog (*Limnodynastes tasmaniensis*) larvae exposed to atrazine and a herbicide mixture.	Chemosphere, (2010 Feb) Vol. 78, No. 7, pp. 807-13. Electronic Publication Date: 30 Dec 2009. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535.
CA 8.1.4	Williams, B.K., Semlitsch, R.D.	2010	Larval responses of three Midwestern anurans to chronic, low-dose exposures of four herbicides.	Arch. Environ. Contam. Toxicol. (2010) 58, 819-827.
CA 8.1.4	Jin, Y., Chen, R., Wang, L., Liu, J., Yang, Y., Zhou, C., Liu, W., Fu, Z	2011	Effects of metolachlor on transcription of thyroid system-related genes in juvenile and adult Japanese medaka (*Oryzias latipes*)	General and Comparative Endocrinology, 170:487-493
CA8.1.4 CA 8.5	Papaefthimiou, C., Cabral, M. de G., Mixailidou, C., Viegas, C.A., Sa-Correia, I., Theophilidis, G.	2004	Comparison of two screening bioassays, based on the frog sciatic nerve and yeast cells, for the assessment of herbicide toxicity.	Environmental toxicology and chemistry / SETAC, (2004 May) Vol. 23, No. 5, pp. 1211-8. Journal code: 8308958. ISSN: 0730-7268. L-ISSN: 0730-7268.
CA 8.2	Caquet Th., Roucaute M; Mazzella N; Delmas F; Madigou C; Farcy E; Burgeot Th; Allenou J-P; Gabellec R	2013	Risk assessment of herbicides and booster biocides along estuarine continuums in the Bay of Vilaine area (Brittany, France).	Environmental science and pollution research international, (2013 Feb) Vol. 20, No. 2, pp. 651-66. Electronic Publication Date: 16 Sep 2012 Journal code: 9441769. E-ISSN: 1614-7499. L-ISSN: 0944-1344.

CA data point number	Author(s)	Year	Title	Source
CA 8.2	Kolpin, D.W., Hubbard, L.E.,. Blazer, V.S., Young, J.A., Iwanowicz, L.R., Gray, J.L., Foreman, W.T., Furlong, E.T., Zaugg, S.D., Sandstrom, M.W., Focazio, M.J., Alvarez, D.A., Speiran, G.K., Meyer, M.T., Barber, L.B.	2013	Chemical contaminants in water and sediment near fish nesting sites in the Potomac River basin: Determining potential exposures to smallmouth bass (*Micropterus dolomieu*).	Science of the Total Environment, (5 Jan 2013) Vol. 443, pp. 700-716. Refs: 85. ISSN: 0048-9697; E-ISSN: 1879-1026 CODEN: STEVA8
CA 8.2	Hayes, T.B., Case, P., Chui, S., Chung D., Haeffele, C., Haston, K., Lee, M., Mai, V.P,., Marjuoa, Y., Parker, J., Tsui, M.	2006	Pesticide mixtures, endocrine disruption, and amphibian declines: are we underestimating the impact?	Environmental health perspectives, (2006 Apr) Vol. 114 Suppl 1, pp. 40-50. Journal code: 0330411. ISSN: 0091-6765. Report No.: NLM-PMC1874187.
CA 8.2	Berube, V.E., Boily, M.H, DeBlois, C., Dassylva, N., Spear, P.A.	2005	Plasma retinoid profile in bullfrogs, *Rana catesbeiana*, in relation to agricultural intensity of sub-watersheds in the Yamaska River drainage basin, Quebec, Canada.	Aquatic toxicology (Amsterdam, Netherlands), (2005 Jan 26) Vol. 71, No. 2, pp. 109-20. Journal code: 8500246. ISSN: 0166-445X. L-ISSN: 0166-445X.
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CA 8.2	McDaniel, T.V., Martin, P.A., Struger, J., Sherry, J., Marvin, C.H., McMaster, M.E., Clarence, S., Tetreault, G.	2008	Potential endocrine disruption of sexual development in free ranging male northern leopard frogs (*Rana pipiens*) and green frogs (*Rana clamitans*) from areas of intensive row crop agriculture. [Erratum to document cited in CA149:301052]	Aquatic Toxicology (2008), 90 (1), 82. CODEN: AQTODG; ISSN: 0166-445X
CA 8.2	Solis, M.E., Liu, C.C., Nam, P., Niyogi, D.K., Bandeff, J.M., Huang, Y.-W.	2007	Occurrence of organic chemicals in two rivers inhabited by Ozark hellbenders (*Cryptobranchus alleganiensis bishopi*)	Archives of Environmental Contamination and Toxicology (2007), 53 (3), 426-434. CODEN: AECTCV; ISSN: 0090-4341
CA 8.2	Gutierrez, M.M.	2007	Evidence of endocrine disruption in amphibians due to agricultural chemical exposure.	Dissertation Abstracts International. Vol. 69, no. 6. 2007. Dissertation Number: AAI3319626. ISSN: 0419-4217 Published by: University Microfilms International, P.O. Box 1764, Ann Arbor, MI, 48106, USA

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CA 8.2.1	Polard T., Jean, S., Gauthier, L., Laplanche, C., Merlina, G., Sanchez-Perez J.M., Pinelli, E.	2011	Mutagenic impact on fish of runoff events in agricultural areas in south-west France.	Aquatic toxicology (Amsterdam, Netherlands), (2011 Jan 17) Vol. 101, No. 1, pp. 126-34. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
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CA 8.2.1	Buckler, D.R., Mayer, F.L., Ellersieck, M.R., Asfaw, A.	2005	Acute Toxicity Value Extrapolation with Fish and Aquatic Invertebrates	Archives of Environmental Contamination and Toxicology (2005), 49 (4), 546-558. CODEN: AECTCV; ISSN: 0090-4341
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CA 8.2.1	Ubachukwu, P.O., Oluah, N.S., Omeje, C.U., Ikele, C.B.	2012	Effect of herbicide (Primextra) on tissue cholesterol level in *Clarias gariepinus* juvenile.	Animal Research International (2012), Volume 9, Number 1, pp. 1524-1528, 16 refs. ISSN: 159-3115

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CA 8.2.4.1 CA 8.2.6.1	Kyriakopoulou, K., Anastasiadou, P., Machera, K.	2009	Comparative Toxicities of Fungicide and Herbicide Formulations on Freshwater and Marine Species	Bulletin of Environmental Contamination and Toxicology (2009), 82 (3), 290-295. CODEN: BECTA6; ISSN: 0007-4861
CA 8.2.5.1	Liu, H., Zhan, X., Ye, W., Liu, W.	2005	Ecotoxicological difference of chiral pesticides: chronic toxicity of metolachlor and S-metolachlor to *Daphnia magna*	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2005), 45 (1), 492-496. CODEN: PEACF2; ISSN: 1524-6434
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CA 8.2.5.2	Liu, H.J.	2006	Ecotoxicological difference of Rac-Metolachlor and S-Metolachlor	Conference: 16th Europe Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC 2006), World Forum Convention Center, Hague (Netherlands (The)), 7 May 2006 - 11 May 2006 Sponsor(s): Society of Environmental Toxicology and Chemistry (SETAC)

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CA 8.2.5.2	Loureiro, S., Perez, J.R., Soares, A.M.V.M.	2010	Effects of atrazine, metolachlor and endosulfan on chlorpyrifos toxicity in *Chironomus riparius*	Conference: 20th Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2010), Palacio de Congresos y Exposiciones - FIBES, Seville, 23-27 May 2010
CA 8.2.5.2	Gerhardt, A., Koster, M., Lang, F., Leib, V.	2012	Active in situ biomonitoring of pesticide pulses using *Gammarus* spp. In small tributaries of lake Constance	Journal of Environmental Protection (2012), 3 (7), 573-583. ISSN: 2152-2197
CA 8.2.5.2	Guy, M., Singh, L., Mineau, P.	2011	Using field data to assess the effects of pesticides on crustacea in freshwater aquatic ecosystems and verifying the level of protection provided by water quality guidelines	Integrated Environmental Assessment and Management (2011), 7 (3), 426-436. CODEN: IEAMCK; ISSN: 1551-3777

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CA 8.2.5.2	Gagnaire, B., Burgeot, T., Geret, F., Thomas-Guyon, H., Renault, T., Editor(s): Feunteun, E., Miramand, P.	2006	Effect of heavy metals and herbicides on immune capacities in Pacific oyster, *Crassostrea gigas*. 599/1308	Cahiers de Biologie Marine (2006) Volume 47, Number 1, pp. 105-107, 7 refs. ISSN: 0007-9723
CA 8.2.5.2	Geret, F., Burgeot T., Haure J., Gagnaire B., Renault T., Communal P.Y., Samain, J.F.	2013	Effects of low-dose exposure to pesticide mixture on physiological responses of the Pacific oyster, *Crassostrea gigas*.	Environmental toxicology, (2013 Dec) Vol. 28, No. 12, pp. 689-99. Journal code: 100885357. E-ISSN: 1522-7278. L-ISSN: 1520-4081.
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CA 8.2.5.2	Mai, H., Gonzalez, P., Pardon, P., Tapie, N., Budzinski, H., Cachot, J., Morin, B.	2014	Comparative responses of sperm cells and embryos of Pacific oyster (*Crassostrea gigas*) to exposure to metolachlor and its degradation products.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Feb) Vol. 147, pp. 48-56. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
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CA 8.2.5.2	Belanger, R.M., Sabhapathy, G.S., Khan, S.	2014	Atrazine and metolachlor exposure affects the chemosensory responses of male crayfish (*Orconectes rusticus*) to female odors.	Integrative and Comparative Biology, (2014) Vol. 54, No. Suppl. 1, pp. E15. http://icb.oxfordjournals.org/. Meeting Info.: Annual Meeting of the Society-for-Integrative-and-Comparative- Biology. Austin, TX, USA. Jan. 03-07, 2014. ISSN: 1540-7063. E-ISSN: 1557-7023.
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CA 8.2.5.2	Smalling, K.L., Morgan, S., Kuivila, K.K.	2010	Accumulation of current-use and organochlorine pesticides in crab embryos from northern California, USA	Environmental Toxicology and Chemistry (2010), 29 (11), 2593-2599. CODEN: ETOCDK; ISSN: 0730-7268
CA 8.2.5.2	Toropov, A.A., Benfenati, E.	2006	QSAR models for *Daphnia* toxicity of pesticides based on combinations of topological parameters of molecular structures 417/559	Bioorganic & Medicinal Chemistry (2006), 14 (8), 2779-2788. CODEN: BMECEP; ISSN: 0968-0896
CA 8.2.5.4	Jin-Clark, Y., Anderson, T.D., Zhu, K.Y.	2008	Effect of alachlor and metolachlor on toxicity of chlorpyrifos and major detoxification enzymes in the aquatic midge, *Chironomus tentans* (Diptera: Chironomidae).	Archives of environmental contamination and toxicology, (2008 May) Vol. 54, No. 4, pp. 645-52. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.
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CA 8.2.6.1	Sbrilli, G., Bimbi, B., Cioni, F., Pagliai, L., Luchi, F., Lanciotti, E.	2005	Surface and ground waters characterization in Tuscany (Italy) by using algal bioassay and pesticide determinations: comparative evaluation of the results and hazard assessment of the pesticides impact on primary productivity	Chemosphere (2005), 58 (5), 571-578. CODEN: CMSHAF; ISSN: 0045-6535
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CA 8.2.6.1	Chalifour, A., Spear, P.A., Boily, M.H., DeBlois, C., Giroux, I., Dassylva, N., Juneau, P.	2009	Assessment of toxic effects of pesticide extracts on different green algal species by using chlorophyll a fluorescence	Toxicological and Environmental Chemistry (2009), 91 (7), 1315-1329. CODEN: TECSDY; ISSN: 0277-2248
CA 8.2.6.1	Vogwill, T., Lagator, M., Colegrave, N., Neve, P.	2012	The experimental evolution of herbicide resistance in *Chlamydomonas reinhardtii* results in a positive correlation between fitness in the presence and absence of herbicides	Journal of Evolutionary Biology (2012), 25 (10), 1955-1964. ISSN: 1010-061X
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CA 8.6	Chindo, P.S., Shebayan, J.A.Y., Marley, P.S.	2010	Effect of pre-emergence herbicides on *Meloidogyne* spp. and *Fusarium* wilt of tomato in Samaru, Zaria, Nigeria.	Journal of Agricultural Research (Lahore) (2010), Volume 48, Number 4, pp. 489-495, 20 refs. ISSN: 0368-1157
CA 8.6	Moore, J.H., Ryder, A., Master, R., Editor(s): Zydenbos, S.M.	2010	Herbicide tolerance of five young perennial grasses.	17th Australasian weeds conference. New frontiers in New Zealand: together we can beat the weeds. Christchurch, New Zealand, 26-30 September, 2010 (2010), pp. 402-405, 3 refs.
CA 8.6	Nagy, L. Editor(s): David, I., Koevics, G.J.	2008	Morphological changes of bird seed (*Phalaris canariensis* L.) by the pre-post herbicides treatments.	13. Tiszantuli Noevenyvedelmi Forum, 15-16 October 2008, Debrecen, Hungary (2008), pp. 175-179, 7 refs.
CA 8.6	Rankova, Z.	2006	Effect of some soil herbicides on the vegetative habits of walnut seedlings (*Juglans regia* L	Acta Agriculturae Serbica (2006), Volume 22, pp. 63-68, 6 refs. ISSN: 0354-9542
CA 8.6	Soltani, N., Bowley, S., Sikkema, P.H.	2005	Responses of black and cranberry beans (Phaseolus vulgaris) to post-emergence herbicides	CROP PROTECTION, (JAN 2005) Vol. 24, No. 1, pp. 15-21. ISSN: 0261-2194.

Table 9.6-3: List of references for all relevant and unclear studies listed by Author

Author(s)	Year	CA data point number	Title	Source
Aly, M.A.S., Schroder, P.	2008	CA 8.4	Effect of herbicides on glutathione S-transferases in the earthworm, *Eisenia fetida*.	Environmental science and pollution research international, (2008 Mar) Vol. 15, No. 2, pp. 143-9. Journal code: 9441769. ISSN: 0944-1344.

Author(s)	Year	CA data point number	Title	Source
Auby, I; Bocquene, G; Quiniou, F; Dreno, J.P.	2007	CA 8.2.5.2	Arcachon basin 's weedkillers and insecticides contamination analysis (2005-2006 period) environmental impact.	Plouzane (France). 2007. Published by: Plouzane (France)
Ayansina, A.D.V., Muhammad, R.G.	2014	CA 8.2	An evaluation of the effect of four herbicides on some aquatic organisms.	International Journal of Biological and Chemical Sciences (2014), Volume 8, Number 1, pp. 304-313, 23 refs. ISSN: 1991-8631
Ayansina, A.D.V., Oso, B.A.	2006	CA 8.5	Effect of two commonly used herbicides on soil microflora at two different concentrations.	African Journal of Biotechnology (2006) Volume 5, Number 2, pp. 129-132, 10 refs. ISSN: 1684-5615
Babatunde, M.M., Balogun, J.K., Auta, J., Balarabe, M.L., Auta, J., Balogun, J.K., Bolorunduro, P.I., Editor(s): Onimisi, H.U.	2009	CA 8.2.1	Acute toxicity of galex to *Oreocromis niloticus* (Trewavas) in Nigeria	Proceedings of the 23rd annual conference of the Fisheries Society of Nigeria. pp. 159-164. 2009. Conference: 23rd annual conference of the fisheries Society of Nigeria (FISON), Kaduna (Nigeria), 26-30 Oct 2008
Belanger, R.M., Sabhapathy, G.S., Khan, S.	2014	CA 8.2.5.2	Atrazine and metolachlor exposure affects the chemosensory responses of male crayfish (*Orconectes rusticus*) to female odors.	Integrative and Comparative Biology, (2014) Vol. 54, No. Suppl. 1, pp. E15. http://icb.oxfordjournals.org/. Meeting Info.: Annual Meeting of the Society-for-Integrative-and-Comparative- Biology. Austin, TX, USA. Jan. 03-07, 2014. ISSN: 1540-7063. E-ISSN: 1557-7023.
Berube, V.E., Boily, M.H, DeBlois, C., Dassylva, N., Spear, P.A.	2005	CA 8.2	Plasma retinoid profile in bullfrogs, *Rana catesbeiana*, in relation to agricultural intensity of sub-watersheds in the Yamaska River drainage basin, Quebec, Canada.	Aquatic toxicology (Amsterdam, Netherlands), (2005 Jan 26) Vol. 71, No. 2, pp. 109-20. Journal code: 8500246. ISSN: 0166-445X. L-ISSN: 0166-445X.
Birchfield, N., Corbin, M., Doelling-Brown, P., Hurley, P.	2006	CA 8.2.5.2	Risk Assessment of Racemic Metolachlor use to 26 Evolutionarily Significant Units of Endangered and Threatened Pacific Salmon and Steelhead	Conference: 27th Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC 2006), Montreal, Quebec (Canada), 3 Nov 2006 - 9 Nov 2006 Sponsor(s): Society of Environmental Toxicology and Chemistry (SETAC)
Bollman, S.L.,; Sprague, . L.	2007	CA 8.6	Response of four commercial sugar beet varieties to s-metolachlor and dimethenamid-P.	Proceedings from the biennial meeting (2007), Number 34, 108 p.
Bollman, S.L., Sprague, C.L.	2008	CA 8.6	Tolerance of 12 Sugarbeet Varieties to Applications of s-Metolachlor and Dimethenamid-P	Weed technology (2008), Volume 22, Number 4, pp. 699-706. ISSN: 0890-037X Source Note: 2008 Oct., v. 22, no. 4
Boutin, C., Elmegaard, N., Kjaer, C.	2004	CA 8.6	Toxicity testing of fifteen non-crop plant species with six herbicides in a greenhouse experiment: Implications for risk assessment.	Ecotoxicology, (May 2004) Vol. 13, No. 4, pp. 349-369. ISSN: 0963-9292.

Author(s)	Year	CA data point number	Title	Source
Brain, R.A., Hoberg, J. Hosmer, A.J., Wall, S.B.	2012	CA 8.2.7	Influence of light intensity on the toxicity of atrazine to the submerged freshwater aquatic macrophyte *Elodea canadensis*	Ecotoxicology and Environmental Safety, (1 May 2012) Vol. 79, pp. 55-61. ISSN: 0147-6513.
Buckler, D.R., Mayer, F.L., Ellersieck, M.R., Asfaw, A.	2005	CA 8.2.1	Acute Toxicity Value Extrapolation with Fish and Aquatic Invertebrates	Archives of Environmental Contamination and Toxicology (2005), 49 (4), 546-558. CODEN: AECTCV; ISSN: 0090-4341
Cai, W,-D., Liu H.-J., Fang Z.-G.	2012	CA 8.2.6.1	Toxicity effects of Rac- and S-metolachlor on two algaes.	Huan jing ke xue= Huanjing kexue / [bian ji, Zhongguo ke xue yuan huan jing ke xue wei yuan hui "Huan jing ke xue" bian ji wei yuan hui.], (2012 Feb) Vol. 33, No. 2, pp. 448-53. Journal code: 8405344. ISSN: 0250-3301. L-ISSN: 0250-3301.
Caquet Th., Roucaute M; Mazzella N; Delmas F; Madigou C; Farcy E; Burgeot Th; Allenou J-P; Gabellec R	2013	CA 8.2	Risk assessment of herbicides and booster biocides along estuarine continuums in the Bay of Vilaine area (Brittany, France).	Environmental science and pollution research international, (2013 Feb) Vol. 20, No. 2, pp. 651-66. Electronic Publication Date: 16 Sep 2012 Journal code: 9441769. E-ISSN: 1614-7499. L-ISSN: 0944-1344.
Carmo, E.L., Bueno, A.F., Bueno, R.C.O.F.	2010	CA 8.3.2	Pesticide selectivity for the insect egg parasitoid *Telenomus remus*.	BioControl (2010) Volume 55, Number 4, pp. 455-464, 38 refs. ISSN: 1386-6141
Cedergreen N., Spliid, N.H., Streibig, J.C.	2004	CA 8.2.7 CA 8.6	Species-specific sensitivity of aquatic macrophytes towards two herbicide	Ecotoxicology and Environmental Safety, (Jul 2004) Vol. 58, No. 3, pp. 314-323. ISSN: 0147-6513.
Chalifour, A., Spear, P.A., Boily, M.H., DeBlois, C., Giroux, I., Dassylva, N., Juneau, P.	2009	CA 8.2.6.1	Assessment of toxic effects of pesticide extracts on different green algal species by using chlorophyll a fluorescence	Toxicological and Environmental Chemistry (2009), 91 (7), 1315-1329. CODEN: TECSDY; ISSN: 0277-2248
Chen, Bo., Xu, D., Wu, J., Liu, G., Liu, W.	2006	CA 8.5	Effect of metolachlor on soil microbial numbers in rhizosphere and its degradation	Nongye Huanjing Kexue Xuebao (2006), 25 (4), 898-902. CODEN: NHKXA7; ISSN: 1672-2043
Chindo, P.S., Shebayan, J.A.Y., Marley, P.S.	2010	CA 8.6	Effect of pre-emergence herbicides on *Meloidogyne* spp. and *Fusarium* wilt of tomato in Samaru, Zaria, Nigeria.	Journal of Agricultural Research (Lahore) (2010), Volume 48, Number 4, pp. 489-495, 20 refs. ISSN: 0368-1157
Collin, H., Meistertzheim, A.-L., David, E., Moraga, D., Boutet, I.	2010	CA 8.2.5.2	Response of the Pacific oyster *Crassostrea gigas*, Thunberg 1793, to pesticide exposure under experimental conditions.	The Journal of experimental biology, (2010 Dec 1) Vol. 213, No. Pt 23, pp. 4010-7. Journal code: 0243705. E-ISSN: 1477-9145. L-ISSN: 0022-0949.
Cook, M.E., Moore, P.A.	2008	CA 8.2.5.2	The effects of the herbicide metolachlor on agonistic behavior in the crayfish, *Orconectes rusticus*.	Archives of environmental contamination and toxicology, (2008 Jul) Vol. 55, No. 1, pp. 94-102. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.

Author(s)	Year	CA data point number	Title	Source
Debenest, T., Pinelli, E., Coste, M., Silvestre, J., Mazzella, N., Madigou, C., Delmas, F.	2009	CA 8.2.6.2	Sensitivity of freshwater periphytic diatoms to agricultural herbicides.	Aquatic toxicology (Amsterdam, Netherlands), (2009 Jun 4) Vol. 93, No. 1, pp. 11-7. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X
De Marez, T., Mechant, E., Goossens, V., Bulcke, R.	2007	CA 8.6	Effect of selected sugar beet herbicides on germination of various *Chenopodium album* populations.	Communications in agricultural and applied biological sciences, (2007) Vol. 72, No. 2, pp. 265-9. Journal code: 101200320. ISSN: 1379-1176. L-ISSN: 1379-1176.
Deng, L., Senseman, S.A., Gentry, T.J., Zuberer, D.A., Weiss, T.L., Devarenne, T.P., Camargo, E.R.	2012	CA 8.2.6.1	Effect of selected herbicides on growth and hydrocarbon content of *Botryococcus braunii* (Race B)	Industrial Crops and Products (2012), 39, 154-161. CODEN: ICRDEW; ISSN: 0926-6690
De Solla, S., Martin, P.	2010	CA 8.1.4	Relationship between pesticide properties and absorption in turtles eggs from treated soil.	Canadian Technical Report of Fisheries and Aquatic Sciences, (2010) Vol. 2883, pp. 64. Meeting Info.: 36th Annual Workshop on Aquatic Toxicity. La Malbaie, CANADA. September 27-30, 2009. CODEN: CTRSDR. ISSN: 0706-6457. E-ISSN: 0706-6570.
De Solla, S.R., Martin, P.A	2011	CA 8.1.4	Absorption of current use pesticides by snapping turtle (*Chelydra serpentina*) eggs in treated soil.	Chemosphere, (2011 Oct) Vol. 85, No. 5, pp. 820-5. Electronic Publication Date: 8 Sep 2011. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535
De Solla, S.R., Palonen K.E., Martin P.A.	2014	CA 8.1.4	Toxicity of pesticides associated with potatoe production, including soil fumigants, to snapping turtle eggs (*Cheludra serpentine*).	Environmental toxicology and chemistry/SETAC (2014 Jan) 33 (1): 102-106.
Dobsikova, R., Blahova, J., Modra, H., Skoric, M., Svobodova, Z.	2011	CA 8.2.1	The effect of acute exposure to herbicide Gardoprim Plus Gold 500 SC on haematological and biochemical indicators and histopathological changes in common carp (*Cyprinus carpio* L.).	Acta Veterinaria Brno (2011) Volume 80, Number 4, pp. 359-363, 14 refs. ISSN: 0001-7213. DOI: 10.2754/avb201180040359
Dussault, S., Fortier, M., Boily, M., Brousseau, P., Fournier, M.	2010	CA 8.2	Immune status of the bullfrog (*Rana catesbeiana*) exposed to agripesticides	Canadian Technical Report of Fisheries and Aquatic Sciences, (2010) Vol. 2883, pp. 66. Meeting Info.: 36th Annual Workshop on Aquatic Toxicity. La Malbaie, CANADA. September 27-30, 2009. CODEN: CTRSDR. ISSN: 0706-6457. E-ISSN: 0706-6570.
Ebenezer, V., Ki, J.-S.	2013	CA 8.2.6.1 CA 8.2.6.2	Quantification of toxic effects of the herbicide metolachlor on marine microalgae *Ditylum brightwellii* (Bacillariophyceae), *Prorocentrum minimum* (Dinophyceae), and *Tetraselmis suecica* (Chlorophyceae).	Journal of microbiology (Seoul, Korea), (2013 Feb) Vol. 51, No. 1, pp. 136-9. Journal code: 9703165. E-ISSN: 1976-3794. L-ISSN: 1225-8873.

Author(s)	Year	CA data point number	Title	Source
Fiori E., Pistocchi R.	2014	CA 8.2.6.2	*Skeletonema marinoi* (Bacillariophyceae) sensitivity to herbicides and effects of temperature increase on cellular responses to terbuthylazine exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Feb) Vol. 147, pp. 112-20. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X
Fischer, B. B.; Roffler, S.; Eggen, R. I. L.	2012	CA 8.2.6.1	Multiple stressor effects of predation by rotifers and herbicide pollution on different *Chlamydomonas* strains and potential impacts on population dynamics.	Environmental Toxicology and Chemistry (2012) Volume 31, Number 12, pp. 2832-2840, 43 refs. ISSN: 0730-7268. DOI: 10.1002/etc.2010
Fulton, B., Brain, R.A., Belden, J.B., Brooks, B.W.	2007	CA 8.2.7	Individual and Combined Effects of Triclosan and Metolachlor on *Lemna Gibba*	Conference: 2007 Summer Speciality Conference of the American Water Resources Association (AWRA 2007), Vail Cascade Resort, Vail, Colorado (USA), 25 Feb 2007 - 27 Feb 2007. Sponsor(s): American Water Resources Association
Fulton, B., Brain, R., Brooks, B.	2007	CA 8.2.7	Responses of *Lemna gibba* Exposed to an Equitoxic Mixture of Triclosan and Metolachlor Across a Range of Nitrogen and Phosphorous Ratios.	Conference: 28th Annual Meeting of the Society of Environmental Toxicology and Chemistry North America, Midwest Express Center, Milwaukee, Wisconsin (USA), 11 Nov 2007- 15 Nov 2007. Sponsor(s): The Society of Environmental Toxicology and Chemistry (SETAC)
Gagnaire, B., Burgeot, T., Geret, F., Thomas-Guyon, H., Renault, T., Editor(s): Feunteun, E., Miramand, P.	2006	CA 8.2.5.2	Effect of heavy metals and herbicides on immune capacities in Pacific oyster, *Crassostrea gigas*. 599/1308	Cahiers de Biologie Marine (2006) Volume 47, Number 1, pp. 105-107, 7 refs. ISSN: 0007-9723
Gagnaire, B., Gay, M., Huvet, A., Daniel, J-Y., Saulnier, D., Renault, T.	2007	CA 8.2.5.2	Combination of a pesticide exposure and a bacterial challenge: in vivo effects on immune response of Pacific oyster, *Crassostrea gigas* (Thunberg).	Aquatic toxicology (Amsterdam, Netherlands), (2007 Aug 15) Vol. 84, No.1, pp. 92-102. Journal code: 8500246. ISSN: 0166-445X. L-ISSN: 0166-445X.
Gagnaire, B., Thomas-Guyon, H., Burgeot, Th., Renault, T.	2006	CA 8.2.5.2	Pollutant effects on Pacific oyster, *Crassostrea gigas* (Thunberg), hemocytes: Screening of 23 molecules using flow cytometry.	Cell Biology and Toxicology (2006), 22 (1), 1-14. CODEN: CBTOE2; ISSN: 0742-2091
Geier, P.W., Stahlman, P.W., Regehr, D.L., Olson, B.L.	2009	CA 8.6	Pre-emergence Herbicide Efficacy and Phytotoxicity in Grain Sorghum	Weed technology (2009), Volume 23, Number 2, pp. 197-201. ISSN: 0890-037X

Author(s)	Year	CA data point number	Title	Source
Genersch, E., von der Ohe, W., Kaatz, H., Schroeder, A., Otten, C., Buechler, R., Berg, S., Ritter, W., Muehlen, W., Gisder, S., Meixner, M., Liebig, G., Rosenkranz, P.	2010	CA 8.3.1	The German bee monitoring project: a long term study to understand periodically high winter losses of honey bee colonies	Apidologie (2010), 41 (3), 332-352. CODEN: APDGB5; ISSN: 0044-8435
Geret, F., Burgeot, T., Haure, J., Gagnaire, B., Renault, T., Communal, P.Y., Samain, J.F.	2011	CA 8.2.5.2	Effects of low-dose exposure to pesticide mixture on physiological responses of the pacific oyster, *Crassostrea gigas*.	Environmental toxicology, (2011 Oct 19). Electronic Publication Date: 19 Oct 2011. Journal code: 100885357. E-ISSN: 1522-7278. L-ISSN: 1520-4081.
Geret, F., Burgeot T., Haure J., Gagnaire B., Renault T., Communal P.Y., Samain, J.F.	2013	CA 8.2.5.2	Effects of low-dose exposure to pesticide mixture on physiological responses of the Pacific oyster, *Crassostrea gigas*.	Environmental toxicology, (2013 Dec) Vol. 28, No. 12, pp. 689-99. Journal code: 100885357. E-ISSN: 1522-7278. L-ISSN: 1520-4081.
Geret, F., Gagnaire, B., Menard, D., Renault, T., Le Roux, A., Haure, J., Bocquene, G., Burgeot, T.	2004	CA 8.2.5.2	Response of the pacific oyster *Crassostrea gigas* to pesticide exposition under experimental conditions.	Marine Environmental Research, (August 2004) Vol. 58, No. 2-5, pp. 312-313. Meeting Info.: 12th International Symposium on Pollutant Responses in Marine Organisms (PRIMO 12). Safety Harbor, FL, USA. May 09-13, 2003. CODEN: MERSDW. ISSN: 0141-1136.
Gerhardt, A., Koster, M., Lang, F., Leib, V.	2012	CA 8.2.5.2	Active in situ biomonitoring of pesticide pulses using *Gammarus* spp. In small tributaries of lake Constance	Journal of Environmental Protection (2012), 3 (7), 573-583. ISSN: 2152-2197
Greenlee, A.R., Ellis, T.M., Berg, R.L.	2004	CA 8.1.2	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9. Journal code: 0330411. ISSN: 0091-6765. Report No.: NLM-PMC1241965.
Griggs, J.L., Belden, L.K.	2005	CA 8.3.2	Decreased survival of trematode cercariae *Echinostoma trivolvis* following atrazine and metolachlor exposure.	Integrative and Comparative Biology, (DEC 2005) Vol. 45, No. 6, pp. 1140. Meeting Info.: Annual Meeting of the Society-for-Integrative-and-Comparative-Biology. Orlando, FL, USA. January 04-08, 2006. ISSN: 1540-7063.

Author(s)	Year	CA data point number	Title	Source
Gutierrez, M.M.	2007	CA 8.2	Evidence of endocrine disruption in amphibians due to agricultural chemical exposure.	Dissertation Abstracts International. Vol. 69, no. 6. 2007. Dissertation Number: AAI3319626. ISSN: 0419-4217 Published by: University Microfilms International, P.O. Box 1764, Ann Arbor, MI, 48106, USA
Guy, M., Singh, L., Mineau, P.	2011	CA 8.2.5.2	Using field data to assess the effects of pesticides on crustacea in freshwater aquatic ecosystems and verifying the level of protection provided by water quality guidelines	Integrated Environmental Assessment and Management (2011), 7 (3), 426-436. CODEN: IEAMCK; ISSN: 1551-3777
Guza, C.J., Stewart, J.F., Hubbell, L.A.	2007	CA 8.6	*Beta vulgaris* response to amide herbicides.	Proceedings from the ... biennial meeting (2007), Number 34, 60 p.
Haluzova, I., Modra, H., Mikula, P., Svobodova, Z.	2009	CA 8.2.1	Subchronic exposure of the common carp (*Cyprinus carpio*) to four herbicide formulations: Effect on the haematological indice.	Toxicology Letters (Shannon), (SEP 13 2009) Vol. 189, No. Sp. Iss. SI, pp. S210. Meeting Info.: 46th Congress of the European-Societies-of-Toxicology. Dresden, GERMANY. September 13 -16, 2009. CODEN: TOLED5. ISSN: 0378-4274. DT Conference; (Meeting)
Hayes, T.B., Case, P., Chui, S., Chung D., Haeffele, C., Haston, K., Lee, M., Mai, V.P,., Marjuoa, Y., Parker, J., Tsui, M.	2006	CA 8.2	Pesticide mixtures, endocrine disruption, and amphibian declines: are we underestimating the impact?	Environmental health perspectives, (2006 Apr) Vol. 114 Suppl 1, pp. 40-50. Journal code: 0330411. ISSN: 0091-6765. Report No.: NLM-PMC1874187.
Helmer, S.H., Kerbaol, A., Aras, P., Jumarie, C., Boily, M.	2014	CA 8.3.1	Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (*Apis mellifera*).	Environmental science and pollution research international, (2014 Apr 15) Journal code: 9441769. E-ISSN: 1614-7499. L-ISSN: 0944-1344.
Hou, Y., Xu, J.-Q., Meng, X.-L., Zhang, K., Yang, G.-F.	2013	CA 8.5	Effects of nine herbicides on mycelial growth of *Rhizoctonia cerealis*	Mailei Zuowu Xuebao (2013), 33 (6), 1289-1293. CODEN: MZXAAG; ISSN: 1009-1041
Hu, X.-N., Zhang, S.-X., Chen, C.-D., Liu, H.-J,.	2014	CA 8.2.6.2	Influence of the coexistence of Zn2+ on the enantioselective toxicity of metolachlor to *Scenedesmus obliquus*.	Huan jing ke xue= Huanjing kexue / [bian ji, Zhongguo ke xue yuan huan jing ke xue wei yuan hui "Huan jing ke xue" bian ji wei yuan hui.], (2014 Jan) Vol. 35, No. 1, pp. 292-8. Journal code: 8405344. ISSN: 0250-3301. L-ISSN: 0250-3301.
Iordache, M., Borza, I.	2011	CA 8.4.1	Study of the acute toxicity of some Pesticides on earthworms *Eisenia fetida* (Savigny, 1826).	Research Journal of agricultural science, 43(4), pp. 95-100, 15 refs. ISSN: 2066-1843.
Ishihara, S., Horio, T., Kobara, Y., Yokoyama, A.	2006	CA 8.2.6.2	Evaluation of herbicide effects on micro algal cells by flow cytometric analysis	Zasso Kenkyu (2006), 51 (4), 239-248. CODEN: ZASKAN; ISSN: 0372-798X

Author(s)	Year	CA data point number	Title	Source
Jin, Y., Chen, R., Wang, L., Liu, J., Yang, Y., Zhou, C., Liu, W., Fu, Z	2011	CA 8.1.4	Effects of metolachlor on transcription of thyroid system-related genes in juvenile and adult Japanese medaka (Oryzias latipes)	General and Comparative Endocrinology, 170:487-493
Jin-Clark, Y., Anderson, T.D., Zhu, K.Y.	2008	CA 8.2.5.4	Effect of alachlor and metolachlor on toxicity of chlorpyrifos and major detoxification enzymes in the aquatic midge, *Chironomus tentans* (Diptera: Chironomidae).	Archives of environmental contamination and toxicology, (2008 May) Vol. 54, No. 4, pp. 645-52. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.
Joly, P., Besse-Hoggan, P., Bonnemoy, F., Batisson, I., Bohatier, J., Mallet, C.	2012	CA 8.5	Impact of maize formulated herbicides Mesotrione and S-metolachlor, applied alone and in mixture, on soil microbial communities	ISRN Ecology, (2012) pp. 329898, 9 pp. CODEN: IESCCC. ISSN: 2090-4614.
Joly, P., Bonnemoy, F., Charvy, J.-C., Bohatier, J., Mallet, C.	2013	CA 8.5	Toxicity assessment of the maize herbicides S-metolachlor, benoxacor, mesotrione and nicosulfuron, and their corresponding commercial formulations, alone and in mixtures, using the Microtox(®) test.	Chemosphere, (2013 Nov) Vol. 93, No. 10, pp. 2444-50. Electronic Publication Date: 26 Sep 2013. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535.
Joly, P., Misson, B., Perriere, F. Bonneymoy, F. Joly, M. Bernard, F., Aguer, J-P., Bohatier, J., Mallet, C., Donnadieu-	2014	CA 8.5	Soil surface colonisation by phototrophic indigenous organisms, in two contrasted soils treated by formulated maize herbicide mixtures	Ecotoxicology (London, England) (2014 Aug 18). Journal code 9885956. E-ISSN:1573-3017. L-ISSN: 0963-9292
Kamionek, M., Jarmul, J., Pezowicz, E.	2005	CA 8.4	Effect of herbicides on *Enchytraeus* sp. (Annelida: Oligochaeta)	Ecological Chemistry and Engineering (2005), 12 (8), 811-816. CODEN: ECECBJ
Kamionek, M., Pezowicz, E., Jarmul, J., Poleszczuk, O.	2005	CA 8.4	Effect of herbicides on earthworms *Lumbricus terrestris* L. (Oligochaeta: Lumbricidae)	Ecological Chemistry and Engineering (2005), 12 (10), 1089-1094. CODEN: ECECBJ
Keseru, M., Juhasz, E., Szabo, R., Tavaszi, J., Varnagy, L.	2007	CA 8.1.1.3	Study of the individual toxicity of three pesticides in a teratogenicity test on birds. Harom noevenyvedo szer egyedi mereghatasanak vizsgalata madarteratologiai tesztben.	Noevenyvedelem (2007), Vol. 43, Number 3, pp. 113-119, 23 refs. ISSN: 0133-0829

Author(s)	Year	CA data point number	Title	Source
Kolpin, D.W., Hubbard, L.E.,. Blazer, V.S., Young, J.A., Iwanowicz, L.R., Gray, J.L., Foreman, W.T., Furlong, E.T., Zaugg, S.D., Sandstrom, M.W., Focazio, M.J., Alvarez, D.A., Speiran, G.K., Meyer, M.T., Barber, L.B.	2013	CA 8.2	Chemical contaminants in water and sediment near fish nesting sites in the Potomac River basin: Determining potential exposures to smallmouth bass (*Micropterus dolomieu*).	Science of the Total Environment, (5 Jan 2013) Vol. 443, pp. 700-716. Refs: 85. ISSN: 0048-9697; E-ISSN: 1879-1026 CODEN: STEVA8
Kondras, M., Czepinska-Kaminska, D., Karczewska, J., Wojewoda, K.	2011	CA 8.5 CA 8.6	The influence of two pesticides in soils on selected plants and earthworms	Roczniki Gleboznawcze (2011), 62 (2), 219-225. CODEN: ROGLAA; ISSN: 0080-3642
Kos, K., Celar, F.A.	2013	CA 8.5	Sensitivity of the entomopathogenic fungus *Beauveria bassiana* (Bals.-Criv.) Vuill. to selected herbicides.	Pest Management Science (2013), Volume 69, Number 6, pp. 717-721, 34 refs. ISSN: 1526-498X
Kyriakopoulou, K., Anastasiadou, P., Machera, K.	2009	CA 8.2.4.1 CA 8.2.6.1	Comparative Toxicities of Fungicide and Herbicide Formulations on Freshwater and Marine Species	Bulletin of Environmental Contamination and Toxicology (2009), 82 (3), 290-295. CODEN: BECTA6; ISSN: 0007-4861
Larras, F., Bouchez, A., Rimet, F., Montuelle, B.	2012	CA 8.2.6.1	Using bioassays and species sensitivity distributions to assess herbicide toxicity towards benthic diatoms.	PloS one, (2012) Vol. 7, No. 8, pp. e44458. Electronic Publication: 2012-08-30.
Larras, F., Montuelle, B., Bouchez, A.	2013	CA 8.2.6.1	Assessment of toxicity thresholds in aquatic environments: does benthic growth of diatoms affect their exposure and sensitivity to herbicides?	The Science of the total environment, (2013 Oct 1) Vol. 463-464, pp. 469-77. Journal code: 0330500. E-ISSN: 1879-1026. L-ISSN: 0048-9697.
Lim, U.T., Mahmoud, A.M.A.	2007	CA 8.3.2	Pesticide susceptibility of *Trissolcus nigripedius* (Hymenoptera:Scelionidae) an egg parasitoid of *Dolycoris baccarum* (Heteroptera:Pentatomidae)	Entomological Research, (AUG 2007) Vol. 37, No. Suppl. 1, pp. A140. Meeting Info.: International Congress of Insect Biotechnology and Industry. Daegu, SOUTH KOREA. August 19-24, 2007. ISSN: 1738-2297.
Lipsa, F.D., Ulea, E., Chiriac, I.P., Coroi, I.G.	2010	CA 8.5	Effect of herbicide S-metolachlor on soil microorganisms.	Lucrari Stiintifice, Universitatea de Stiinte Agricole Si Medicina Veterinara "Ion Ionescu de la Brad" Iasi, Seria Agronomie (2010) Volume 53, Number 2, pp. 110-113, 11 refs. ISSN: 1454-7414

Author(s)	Year	CA data point number	Title	Source
Liu, H.J.	2006	CA 8.2.5.2	Ecotoxicological difference of Rac-Metolachlor and S-Metolachlor	Conference: 16th Europe Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC 2006), World Forum Convention Center, Hague (Netherlands (The)), 7 May 2006 - 11 May 2006 Sponsor(s): Society of Environmental Toxicology and Chemistry (SETAC)
Liu, H.J., Cai, W.D., Huang, R.N., Xia, H.L., Wen, Y.Z.	2012	CA 8.2.6.1	Enantioselective toxicity of metolachlor to *Scenedesmus obliquus* in the presence of cyclodextrins.	Chirality, (2012 Feb) Vol. 24, No. 2, pp. 181-7. Electronic Publication: 2011-12-19. Journal code: 8914261. E-ISSN: 1520-636X. L-ISSN: 0899-0042.
Liu, H., Xiong, M.	2009	CA 8.2.6.1	Comparative toxicity of racemic metolachlor and S-metolachlor to *Chlorella pyrenoidosa*.	Aquatic toxicology (Amsterdam, Netherlands), (2009 Jun 28) Vol. 93, No. 2-3, pp. 100-6. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
Liu, H.J., Ye, W.H., Zhan, X.M., Liu, W.P.	2006	CA 8.2.5.1	A comparative study of rac- and S-metolachlor toxicity to *Daphnia magna*	Ecotoxicology and Environmental Safety (2006) Volume 63, Number 3, pp. 451-455, 25 refs. ISSN: 0147-6513. DOI: 10.1016/j.ecoenv.2005.02.002
Liu, H.-J., Zhan, X.-M., Liu, W.	2005	CA 8.3.2	Ecotoxicological difference of chiral pesticides: effects of metolachlor and S-metolachlor on some enzyme activities of silkworm, *Bombyx mori* L.	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2005), 45 (1), 497-500. CODEN: PEACF2; ISSN: 1524-6434
Liu, H, Zhan, X., Liu, W., Liu, H.J., Zhan, X.M., Liu, W.P.	2006	CA 8.5	Effect of Rac-metolachlor and S-isomer on soil microbial biomass carbon and nitrogen.	Acta Pedologica Sinica (2006) Volume 43, Number 5, pp. 875-878, 11 refs. ISSN: 0564-3929
Liu, H., Zhan, X., Ye, W., Liu, W.	2005	CA 8.2.5.1	Ecotoxicological difference of chiral pesticides: chronic toxicity of metolachlor and S-metolachlor to *Daphnia magna*	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2005), 45 (1), 492-496. CODEN: PEACF2; ISSN: 1524-6434
Liu, W., Fang, Q., Ma, Y.	2005	CA 8.2.4.1 CA 8.2.5.1 CA 8.5	Selectivity in aquatic toxicity and biodegradation of the herbicide Metolachlor	Abstracts of Papers, 230th ACS National Meeting, Washington, DC, United States, Aug. 28-Sept. 1, 2005 (2005), AGRO-060. Publisher: American Chemical Society, Washington, D. C. CODEN: 69HFCL
Liu, W., Xu, D., Liu, H., Liu, G.	2007	CA 8.4.1	Effects of metolachlor on the weight and enzyme activities of earthworms	Huanjing Kexue Xuebao (2007), 27 (12), 2025-2031. CODEN: HKXUDL; ISSN: 0253-2468

Author(s)	Year	CA data point number	Title	Source
Lizotte, R.E., Knight, S.S., Bryant, C.T., Smith, S.	2009	CA 8.2.5.2	Agricultural Pesticides in Mississippi Delta Oxbow Lake Sediments During Autumn and Their Effects on *Hyalella azteca*.	Archives of Environmental Contamination and Toxicology, (OCT 2009) Vol.57, No. 3, pp. 495-503. CODEN: AECTCV. ISSN: 0090-4341.
Lizotte, R.E., Knight, S.S., Shields, F.D., Bryant, C.T.	2009	CA 8.2.5.2	Effects of an atrazine, metolachlor and fipronil mixture on *Hyalella azteca* (Saussure) in a modified backwater wetland.	Bulletin of environmental contamination and toxicology, (2009 Dec) Vol. 83, No. 6, pp. 836-40. Journal code: 0046021. E-ISSN: 1432-0800. L-ISSN: 0007-4861.
Lizotte, R.E., Shields, F.D., Testa, S.	2012	CA 8.2.5.2	Effects of a simulated agricultural runoff event on sediment toxicity in a managed backwater wetland	Water, air, and soil pollution (2012), Volume 223, Number 8, pp. 5375-5389. ISSN: 1573-2932
Lizotte, R., Testa, S., Locke, M., Martin. A, Steinriede, R.W.	2013	CA 8.2.5.2	Responses of phytoplankton and *Hyalella azteca* to agrichemical mixtures in a constructed wetland mesocosm.	Archives of environmental contamination and toxicology, (2013 Oct) Vol. 65, No. 3, pp. 474-85. Electronic Publication Date: 23 Jun 2013. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.
Loureiro, S., Perez, J.R., Soares, A.M.V.M.	2010	CA 8.2.5.2	Effects of atrazine, metolachlor and endosulfan on chlorpyrifos toxicity in *Chironomus riparius*	Conference: 20th Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2010), Palacio de Congresos y Exposiciones - FIBES, Seville, 23-27 May 2010
Mai, H., Cachot, J., Brune, J., Geffard, O., Belles, A., Budzinski, H., Morin, B.	2012	CA 8.2.5.2	Embryotoxic and genotoxic effects of heavy metals and pesticides on early life stages of Pacific oyster (*Crassostrea gigas*).	Marine pollution bulletin, (2012 Dec) Vol. 64, No. 12, pp. 2663-70. Journal code: 0260231. E-ISSN: 1879-3363. L-ISSN: 0025-326X.
Mai, H., Gonzalez, P., Pardon, P., Tapie, N., Budzinski, H., Cachot, J., Morin, B.	2014	CA 8.2.5.2	Comparative responses of sperm cells and embryos of Pacific oyster (*Crassostrea gigas*) to exposure to metolachlor and its degradation products.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Feb) Vol. 147, pp. 48-56. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
Mai, H., Morin, B., Pardon P., Gonzalez P., Budzinski H., Cachot J.	2013	CA 8.2.5.2	Environmental concentrations of irgarol, diuron and S-metolachlor induce deleterious effects on gametes and embryos of the Pacific oyster, *Crassostrea gigas*.	Marine environmental research, (2013 Aug) Vol. 89, pp. 1-8. Journal code: 9882895. E-ISSN: 1879-0291. L-ISSN: 0141-1136.
Ma, J., Wang, S., Wang, P., Ma, L., Chen, X., Xu, R.	2006	CA 8.2.6.1	Toxicity assessment of 40 herbicides to the green alga *Raphidocelis subcapitata*	Ecotoxicology and Environmental Safety (2006), 63 (3), 456-462. CODEN: EESADV; ISSN: 0147-6513

Author(s)	Year	CA data point number	Title	Source
Martins, P.F., Carvalho, G., Gratao, P.L., Dourado, M.N., Pileggi, M., Araujo, W.L., Azevedo, R.A.	2011	CA 8.5	Effects of the herbicides acetochlor and metolachlor on antioxidant enzymes in soil bacteria	Process Biochemistry, Vol. 46, no. 5, pp. 1186-1195, May 2011. ISSN: 1359-5113.
Martins, P.F., Martinez, C.O., Carvalho, G.de., Carneiro, P.I.B., Azevedo, R.A., Pileggi, S.A.V., Melo, I.S.de., Pileggi, M., de Carvalho, G., de Melo, I.S.	2007	CA 8.5	Selection of microorganisms degrading S-metolachlor herbicide.	Brazilian Archives of Biology and Technology (2007) Volume 50, Number 1, pp. 153-159, 27 refs. ISSN: 1516-8913
McDaniel, T.V., Martin, P.A., Struger, J., Sherry, J., Marvin, C.H., McMaster, M.E., Clarence, S., Tetreault, G.	2008	CA 8.2	Potential endocrine disruption of sexual development in free ranging male northern leopard frogs (*Rana pipiens*) and green frogs (*Rana clamitans*) from areas of intensive row crop agriculture. [Erratum to document cited in CA149:301052]	Aquatic Toxicology (2008), 90 (1), 82. CODEN: AQTODG; ISSN: 0166-445X
Moore, J.H., Ryder, A., Master, R., Editor(s): Zydenbos, S.M.	2010	CA 8.6	Herbicide tolerance of five young perennial grasses.	17th Australasian weeds conference. New frontiers in New Zealand: together we can beat the weeds. Christchurch, New Zealand, 26-30 September, 2010 (2010), pp. 402-405, 3 refs.
Moore, M. T., Krger, R.	2010	CA 8.6	Effect of three insecticides and two herbicides on rice (*Oryza sativa*) seedling germination and growth.	Archives of Environmental Contamination and Toxicology (2010) Volume 59, Number 4, pp. 574-581, 53 refs. ISSN: 0090-4341
Moore, M.T. (Reprint Author), Lizotte, R.E., Cooper, C.M., Smith, S., Knight, S.S.	2004	CA 8.2.5.2	Survival and growth of *Hyalella azteca* exposed to three Mississippi Oxbow lake Sediments.	Bulletin of Environmental Contamination and Toxicology, (April 2004) Vol. 72, No. 4, pp. 777-783. ISSN: 0007-4861.
Nagy, L. Editor(s): David, I., Koevics, G.J.	2008	CA 8.6	Morphological changes of bird seed (*Phalaris canariensis* L.) by the pre-post herbicides treatments.	13. Tiszantuli Noevenyvedelmi Forum, 15-16 October 2008, Debrecen, Hungary (2008), pp. 175-179, 7 refs.
Neugebauerova, J., Petrikova, K.	2004	CA 8.6	Possibilities of pre-emergence and post-emergence herbicide applications in *Prunella vulgaris* L. growth.	Zahradnictvi (Horticultural Science) (2004), Volume 31, Number 3, pp. 115-118, 13 refs. ISSN: 0862-867X
Norsworthy, J.K., Smith, J.P., Meister, C.	2007	CA 8.6	Tolerance of direct-seeded green onions to herbicides applied before or after crop emergence.	Weed Technology (2007), Volume 21, Number 1, pp. 119-123. ISSN: 0890-037X

Author(s)	Year	CA data point number	Title	Source
Padilla, S., Corum, D., Padnos, B., Hunter, D. L., Beam, A.; Houck, K.A., Sipes, N., Kleinstreuer, N., Knudsen, T., Dix, D.J., Reif, D.M.	2012	CA 8.2.1	Zebrafish developmental screening of the ToxCast Phase I chemical library	Reproductive Toxicology (2012), 33 (2), 174-187. CODEN: REPTED; ISSN: 0890-6238
Papaefthimiou, C., Cabral, M. de G., Mixailidou, C., Viegas, C.A., Sa-Correia, I., Theophilidis, G.	2004	CA8.1.4 CA 8.5	Comparison of two screening bioassays, based on the frog sciatic nerve and yeast cells, for the assessment of herbicide toxicity.	Environmental toxicology and chemistry / SETAC, (2004 May) Vol. 23, No. 5, pp. 1211-8. Journal code: 8308958. ISSN: 0730-7268. L-ISSN: 0730-7268.
Papoulias, D.M. , Schwarz, M.S., Mena, L.	2013	CA 8.1.4	Gonadal abnormalities in frogs (*Lithobates* spp.) collected from managed wetlands in an agricultural region of Nebraska, USA.	Environmental Pollution, (January 2013) Vol. 172, pp. 1-8. Refs: 78. ISSN: 0269-7491; E-ISSN: 1873-6424; CODEN: ENPOEK
Park, E.-K., Lees, E.M.	2005	CA 8.3.2	Application of an artificial sea salt solution to determine acute toxicity of herbicides to *Proisotoma minuta* (Collembola).	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, (2005) Vol. 40, No. 4, pp. 595-604. Journal code: 7607167. ISSN: 0360-1234. L-ISSN: 0360-1234.
Passy, S.I., Bode, R.W., Carlson, D. M., Novak, M. A.	2004	CA 8.2.1 CA 8.2.4 CA 8.2.6	Comparative environmental assessment in the studies of benthic diatom, macroinvertebrate, and fish communities	International Review of Hydrobiology (2004), 89 (2), 121-138. ISSN: 1434-2944
Perez, J.R.	2011	CA 8.2.1	Effects of s-triazines and metolachlor on chlorpyrifos toxicity in Zebrafish (*Danio rerio*) early life-stages	Conference: 21st Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2011), Milano Convention Centre, Milan, 15 May 2011 - 19 May 2011
Perez, J., Domingues, I., Soares, A.M.V.M., Loureiro, S.	2011	CA 8.2.6.1	Growth rate of *Pseudokirchneriella subcapitata* exposed to herbicides found in surface waters in the Alqueva reservoir (Portugal): a bottom-up approach using binary mixtures.	Ecotoxicology (London, England), (2011 Aug) Vol. 20, No. 6, pp. 1167-75. Journal code: 9885956. E-ISSN: 1573-3017. L-ISSN: 0963-9292.
Perez, J.R., Loureiro, S.M., Soares, A.M.V.M.	2010	CA 8.2.5.2	Effects of atrazine and metolachlor on chlorpyrifos toxicity in *Chironomus riparius*	Conference: 20th Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2010), Palacio de Congresos y Exposiciones - FIBES, Seville, 23 May 2010-27 May 2010

Author(s)	Year	CA data point number	Title	Source
Perez, J., Monteiro, M.S., Quintaneiro C., Soares, A.M.V.M., Loureiro, S.	2013	CA 8.2.5.4	Characterization of cholinesterases in *Chironomus riparius* and the effects of three herbicides on chlorpyrifos toxicity.	Aquatic toxicology (Amsterdam, Netherlands), (2013 Nov 15) Vol. 144-145, pp. 296-302. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
Polard T., Jean, S., Gauthier, L., Laplanche, C., Merlina, G., Sanchez-Perez J.M., Pinelli, E.	2011	CA 8.2.1	Mutagenic impact on fish of runoff events in agricultural areas in south-west France.	Aquatic toxicology (Amsterdam, Netherlands), (2011 Jan 17) Vol. 101, No. 1, pp. 126-34. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
Praet, N. van; Bruyn, L. de; Jonge, M. de; Vanhaecke, L.; Stoks, R.; Bervoets, L.; van Praet, N.; de Bruyn, L.; de Jonge, M.	2014	CA 8.2.5.2	Can damsel fly larvae (*Ischnura elegans*) be used as bioindicators of sublethal effects of environmental contamination?	Aquatic Toxicology (2014), Volume 154, pp. 270-277. ISSN: 0166-445X
Rankova, Z.	2006	CA 8.6	Effect of some soil herbicides on the vegetative habits of walnut seedlings (*Juglans regia* L	Acta Agriculturae Serbica (2006), Volume 22, pp. 63-68, 6 refs. ISSN: 0354-9542
Rea, G., Polticelli, F., Antonacci, A., Scognamiglio, V., Katiyar, P., Kulkarni, S.A., Johanningmeier, U., Giardi, M.T.	2009	CA 8.2.6.2	Structure-based design of novel *Chlamydomonas reinhardtii* D1-D2 photosynthetic proteins for herbicide monitoring	Protein Science (2009), 18 (10), 2139-2151. CODEN: PRCIEI; ISSN: 1469-896X
Roubeix, V., Fauvelle, V., Tison-Rosebery, J., Mazzella, N., Coste M., Delmas F.	2012	CA 8.2.6.2	Assessing the impact of chloroacetanilide herbicides and their metabolites on periphyton in the Leyre River (SW France) via short term growth inhibition tests on autochthonous diatoms.	Journal of environmental monitoring : JEM, (2012 May) Vol. 14, No. 6, pp. 1655-63. Journal code: 100968688. E-ISSN: 1464-0333. L-ISSN: 1464-0325.
Roubeix, V., Mazzella, N., Mechin, B., Coste, M., Delmas, F.	2011	CA 8.2.6.2	Impact of the herbicide metolachlor on river periphytic diatoms: experimental comparison of descriptors at different biological organization levels.	Annales de Limnologie - International Journal of Limnology (2011) Volume 47, Number 3, pp. 239-249, 46 refs. ISSN: 0003-4088. DOI: 10.1051/limn/2011009
Samtani, J.B., Masiunas, J.B., Appleby, J.E.	2008	CA 8.6	Injury on white oak seedlings from herbicide exposure simulating drift.	HortScience (2008), Vol. 43, Number 7, pp. 2076-2080, 27 refs. ISSN: 0018-5345
Samtani, J.B., Masiunas, J.B., Applyby, J.E.	2010	CA 8.6	White Oak and Northern Red Oak Leaf Injury from Exposure to Chloroacetanilide Herbicides.	HortScience : a publication of the American Society for Horticultural Science (2010), Volume 45, Number 4, pp. 696-700. ISSN: 0018-5345
Sanchez-Bayo, F.	2006	CA 8.2.5.2	Comparative acute toxicity of organic pollutants and reference values for crustaceans. I. Branchiopoda, Copepoda and Ostracoda	Environmental Pollution (Amsterdam, Netherlands) (2006), 139 (3), 385-420 CODEN: ENPOEK; ISSN: 0269-7491

Author(s)	Year	CA data point number	Title	Source
Sangwan, M., Wei, L.	2008	CA 8.2.6.2	Effect of herbicide metolachlor on brown tide alga *Aureococcus anophagefferens* growth and detoxification.	Abstracts of Papers American Chemical Society, (AUG 17 2008) Vol. 236, pp. 122-ENVR. Meeting Info.: 236th National Meeting of the American-Chemical-Society. Philadelphia, PA, USA. August 17 -21, 2008. CODEN: ACSRAL. ISSN: 0065-7727.
Sbrilli, G., Bimbi, B., Cioni, F., Pagliai, L., Luchi, F., Lanciotti, E.	2005	CA 8.2.6.2	Surface and ground waters characterization in Tuscany (Italy) by using algal bioassay and pesticide determinations: comparative evaluation of the results and hazard assessment of the pesticides impact on primary productivity	Chemosphere (2005), 58 (5), 571-578. CODEN: CMSHAF; ISSN: 0045-6535
Shutler, D., Marcogliese, D.J.	2011	CA 8.2	Leukocyte profiles of Northern Leopard Frogs, *Lithobates pipiens*, exposed to pesticides and hematozoa in agricultural wetlands.	Copeia (2011), Number 2, pp. 301-307. ISSN: 0045-8511
Sikkema, P.H., Shropshire, C., Soltani, N.	2009	CA 8.6	Response of dry bean to pre-plant incorporated and pre-emergence applications of S-metolachlor and fomesafen	Crop protection (2009), Volume 28, Number 9, pp. 744-748. ISSN: 0261-2194
Sikkema, P.H., Soltani, N., Shropshire, C., Robinson, D.E.	2006	CA 8.6	Response of adzuki bean to pre-emergence herbicides.	Canadian journal of plant science = Revue Canadienne de phytotechnie (2006), Volume 86, Number 2, pp. 601-604. ISSN: 0008-4220
Smalling, K.L., Morgan, S., Kuivila, K.K.	2010	CA 8.2.5.2	Accumulation of current-use and organochlorine pesticides in crab embryos from northern California, USA	Environmental Toxicology and Chemistry (2010), 29 (11), 2593-2599. CODEN: ETOCDK; ISSN: 0730-7268
Solis, M.E., Liu, C.C., Nam, P., Niyogi, D.K., Bandeff, J.M., Huang, Y.-W.	2007	CA 8.2	Occurrence of organic chemicals in two rivers inhabited by Ozark hellbenders (*Cryptobranchus alleganiensis bishopi*)	Archives of Environmental Contamination and Toxicology (2007), 53 (3), 426-434. CODEN: AECTCV; ISSN: 0090-4341
Soltani, N., Bowley, S., Sikkema, P.H.	2005	CA 8.6	Responses of black and cranberry beans (Phaseolus vulgaris) to post-emergence herbicides	CROP PROTECTION, (JAN 2005) Vol. 24, No. 1, pp. 15-21. ISSN: 0261-2194.
Soltani, N., Shropshire, C., Cowan, T., Sikkema, P.	2004	CA 8.6	White bean sensitivity to preemergence herbicides.	Weed Technology (2004), Vol. 18, Number 3, pp. 675-679, 15 refs. ISSN: 0890-037X
Soltani, N., Shropshire, C., Cowan, T., Sikkema, P.	2004	CA 8.6	Tolerance of black beans (*Phaseolus vulgaris*) to soil applications of S-metolachlor and imazethapyr.	Weed Technology (2004), Volume 18, Number 1, pp. 111-118, 25 refs. ISSN: 0890-037X
Souissi Y., Bouchonnet, S; Bourcier, S; Kusk K. O.; Sablier M., Andersen H. R.	2013	CA 8.2.4.1	Identification and ecotoxicity of degradation products of chloroacetamide herbicides from UV-treatment of water.	The Science of the total environment, (2013 Aug 1) Vol. 458-460, pp. 527-34. Journal code: 0330500. E-ISSN: 1879-1026. L-ISSN: 0048-9697

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Spoljaric, D., Cipak, A., Horvatic, J., Andrisic, L., Waeg, G., Zarkovic, N., Jaganjac, M.	2011	CA8.2.6.2.	Endogenous 4-hydroxy-2-nonenal in microalga *Chlorella kessleri* acts as a bioactive indicator of pollution with common herbicides and growth regulating factor of hormesis.	Aquatic toxicology (Amsterdam, Netherlands), (2011 Oct) Vol. 105, No. 3-4, pp. 552-8. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
Spolyarich N., Hyne, R., Wilson S., Palmer C., Byrne M.	2010	CA 8.1.4	Growth, development and sex ratios of Spotted Marsh Frog (*Limnodynastes tasmaniensis*) larvae exposed to atrazine and a herbicide mixture.	Chemosphere, (2010 Feb) Vol. 78, No. 7, pp. 807-13. Electronic Publication Date: 30 Dec 2009. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535.
Spolyarich N., Hyne R.V., Wilson S.P., Palmer C.G., Byrne M.	2011	CA 8.1.4	Morphological abnormalities in frogs from a rice-growing region in NSW, Australia, with investigations into pesticide exposure.	Environmental monitoring and assessment, (2011 Feb) Vol. 173, No. 1-4, pp.397-407. Journal code: 8508350. E-ISSN: 1573-2959. L-ISSN: 0167-6369.
Stepic, S., Hackenberger, B.K., Velki, M., Hackenberger, D.K., Loncaric, Z.	2013	CA 8.4	Potentiation effect of metolachlor on toxicity of organochlorine and organophosphate insecticides in earthworm *Eisenia andrei*.	Bulletin of environmental contamination and toxicology, (2013 Jul) Vol. 91, No. 1, pp. 55-61. Journal code: 0046021. E-ISSN: 1432-0800. L-ISSN: 0007-4861.
Swanton, C.J., Gulden, R.H., Chandler, K.	2007	CA 8.6	A Rationale for Atrazine Stewardship in Corn	Weed science (2007), Volume 55, Number 1, pp. 75-81. ISSN: 0043-1745
Thakkar, M., Randhawa, V., Wei, L.	2013	CA 8.2.6.1	Comparative responses of two species of marine phytoplankton to metolachlor exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2013 Jan 15) Vol. 126, pp. 198-206. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.
Tierney, K.B., Sampson, J.L., Kennedy, C.J., Ross, P.S., Sekela, M.A., Kennedy, C. J.	2008	CA 8.2.1	Salmon olfaction is impaired by an environmentally realistic pesticide mixture.	Environmental Science and Technology, (1 Jul 2008) Vol. 42, No. 13, pp. 4996-5001. Refs: 26. ISSN: 0013-936X; CODEN: ESTHAG
Toropov, A.A., Benfenati, E.	2006	CA 8.2.5.2	QSAR models for *Daphnia* toxicity of pesticides based on combinations of topological parameters of molecular structures 417/559	Bioorganic & Medicinal Chemistry (2006), 14 (8), 2779-2788. CODEN: BMECEP; ISSN: 0968-0896
Ubachukwu, P.O., Oluah, N.S., Omeje, C.U., Ikele, C.B.	2012	CA 8.2.1	Effect of herbicide (Primextra) on tissue cholesterol level in *Clarias gariepinus* juvenile.	Animal Research International (2012), Volume 9, Number 1, pp. 1524-1528, 16 refs. ISSN: 159-3115
Vallotton, N., Moser, D., Eggen R.I.L., Junghans, M., Chevre, N.	2008	CA 8.2.6.1	S-metolachlor pulse exposure on the alga *Scenedesmus vacuolatus*: effects during exposure and the subsequent recovery.	Chemosphere, (2008 Sep) Vol. 73, No. 3, pp. 395-400. Electronic Publication: 2008-07-07. Journal code: 0320657. ISSN: 0045-6535. L-ISSN: 0045-6535.

Author(s)	Year	CA data point number	Title	Source
Varnagy, L., Budai, P., Fejes, S., Keseru, M., Szabo, R.. Juhasz, E.	2004	CA 8.1.1.3	Degredation dynamics and toxicity of certain pesticide active ingredients in bird embryos.	Magyar Allatorvosok Lapja (2004), Volume 126, Number 12, pp. 755-760, 21 refs. ISSN: 0025-004X
Vodovnik, M., Bistan, M., Zorec, M., Marinsek-Logar, R.	2012	CA 8.5	Membrane Changes Associated with Exposure of *Pseudomonas putida* to Selected Environmental Pollutants and their Possible Roles in Toxicity.	Acta chimica Slovenica, (2012 Mar) Vol. 59, No. 1, pp. 83-8. Journal code: 101247110. ISSN: 1318-0207. L-ISSN: 1318-0207.
Vogwill, T., Lagator, M., Colegrave, N., Neve, P.	2012	CA 8.2.6.1	The experimental evolution of herbicide resistance in *Chlamydomonas reinhardtii* results in a positive correlation between fitness in the presence and absence of herbicides	Journal of Evolutionary Biology (2012), 25 (10), 1955-1964. ISSN: 1010-061X
Wan, M. T., Buday, C., Schroeder, G., Kuo, J., Pasternak, J.	2006	CA 8.1.4 CA 8.2.1 CA 8.2.4.1 CA 8.2.4.2	Toxicity to *Daphnia magna*, *Hyalella azteca*, *Oncorhynchus kisutch*, *Oncorhynchus mykiss*, *Oncorhynchus tshawytscha* and *Rana catesbeiana* of atrazine, metolachlor, simazine, and their formulated products.	Bulletin of Environmental Contamination and Toxicology (2006) Volume 76, Number 1, pp. 52-58, 9 refs. ISSN: 0007-4861. DOI: 10.1007/s00128-005-0888-4
Wang, Y., Wu, S., Chen, L., Wu, C., Yu, R., Wang, Q., Zhao, X.	2012	CA 8.4	Toxicity assessment of 45 pesticides to the epigeic earthworm *Eisenia fetida*.	Chemosphere, (July 2012) Vol. 88, No. 4, pp. 484-491. Refs: 63. ISSN: 0045-6535; E-ISSN: 1879-1298. CODEN: CMSHAF
Wang, Y., Yu, W., Yang, L., Cang, T., Yu R., Wang, Q., Zhao, X.	2012	CA 8.4.1	Acute Toxicity of Twenty-Two Commonly Used Herbicides to Earthworm (*Eisenia fetida*).	Asian Journal of Ecotoxicology, (JUN 2012) Vol. 7, No. 3, pp. 317-325. ISSN: 1673-5897.
Whaley, C.M., Armel, G.R., Wilson, H.P., Hines, T.E.	2009	CA 8.6	Evaluation of S-Metolachlor and S-Metolachlor Plus Atrazine Mixtures with Mesotrione for Broadleaf Weed Control in Corn	Weed technology (2009), Volume 23, Number 2, pp. 193-196. ISSN: 0890-037X
Williams, B.K., Semlitsch, R.D.	2010	CA 8.1.4	Larval responses of three Midwestern anurans to chronic, low-dose exposures of four herbicides.	Arch. Environ. Contam. Toxicol. (2010) 58, 819-827.
Xie, F., Liu, H.J., Cai, W.D., Xie, F.	2010	CA 8.6	Enantioselectivity of racemic metolachlor and S-metolachlor in maize seedlings	Journal of Environmental Science and Health. Part B, Pesticides, Food Contaminants, and Agricultural Wastes (2010), Volume 45, Number 8, pp. 774-782, 33 refs. ISSN: 0360-1234
Xu, D., Wen, Y., Wang, K.	2010	CA 8.4	Effect of chiral differences of metolachlor and its (S)-isomer on their toxicity to earthworms.	Ecotoxicology and environmental safety, (2010 Nov) Vol. 73, No. 8, pp. 1925-31. Journal code: 7805381. E-ISSN: 1090-2414. L-ISSN: 0147-6513.
Xu, D.-M., Xu, X.-L., Liu, W.-L., Liu, W.-P.	2009	CA 8.4.1	Acute toxicity difference of metolachlor and its S-isomer on earthworms	Zhongguo Huanjing Kexue (2009), 29 (9), 1000-1004. CODEN: ZHKEEI; ISSN: 1000-6923

Author(s)	Year	CA data point number	Title	Source
Xu H., Xue, M., Zhao, H., Ma, X., Liu, Y., Xu, H.Q., Xue, M., Zhao, H.P., Ma, X.D., Liu, Y.Y.	2013	CA 8.3.2	Analysis and evaluation of eight herbicides toxicity and sensitivity against two *Trichogramma* spp.	Journal of Food, Agriculture & Environment (2013), Volume 11, Number 3/4, pp. 855-858, 19 refs. ISSN: 1459-0255
Yadav, P.K., Khan, A.H., Murti, R., Upadhyay, R.K.	2006	CA 8.6	Effect of herbicides on germination, growth and nodulation in chickpea (*Cicer arietinum*)	Indian Journal of Agricultural Sciences (2006), 76 (11), 682-684
Yadav, P.K., Khan, A.H., Amar, N., Yadav, S.K.S., Nath, A.	2007	CA 8.6	Effect of herbicides on biochemical and growth parameters of chickpea (*Cicer arietinum* L.).	Research on Crops (2007), Vol. 8, Number 2, pp. 388-390, 8 refs. ISSN: 0972-
Ye, J., Liu, J., Liu, W., Zhao, M., Liu, W.	2010	CA 8.0	Enantioselectivity in environmental risk assessment of modern chiral pesticides.	Environmental Pollution, (July 2010) Vol. 158, No. 7, pp. 2371-2383. Refs: 69. ISSN: 0269-7491 CODEN: ENPOEK
You, W.-Y., Chen, X.-F., Song, M., Wang, C.-J.	2010	CA 8.3.2	Toxicity Evaluation of Sixteen Herbicides to *Bombyx mori*.	Asian Journal of Ecotoxicology, (FEB 2010) Vol. 5, No. 1, pp. 91-94. ISSN: 1673-5897.
Zablotowicz, R.M., Locke, M.A., Lerch, R.N., Knight, S.S.	2004	CA 8.2.6.2	Dynamics of herbicide concentrations in Mississippi Delta Oxbow Lakes and the role of planktonic microorganisms in herbicide metabolism	ACS Symposium Series (2004), 877 (Water Quality Assessments in the Mississippi Delta), 134-149. CODEN: ACSMC8; ISSN: 0097-6156
Zhan, X., Liu, H., Miao, Y., Liu, W., Zhan, X.M., Liu, H.J., Miao, Y.G., Liu, W.P.	2006	CA 8.3.1	A comparative study of rac- and S-metolachlor on some activities and metabolism of silkworm, *Bombyx mori* L.	Pesticide Biochemistry and Physiology (2006) Volume 85, Number 3, pp. 133-138, 33 refs. ISSN: 0048-3575. DOI: 10.1016/j.pestbp.2005.12.003
Zhao , S., Arthur, E.L., Moorman, T.B., Coats, J.R.	2005	CA 8.5	Evaluation of microbial inoculation and vegetation to enhance the dissipation of atrazine and metolachlor in soil.	Environmental toxicology and chemistry / SETAC, (2005 Oct) Vol. 24, No. 10, pp. 2428-34. Journal code: 8308958. ISSN: 0730-7268. L-ISSN: 0730-7268.
Zhou, B., Zhao, M.-R., Huang, H.-F.	2008	CA 8.2.1	Study on zebrafish embryo-toxicity of four pesticides	Zhejiang Gongye Daxue Xuebao (2008), 36 (2), 136-140. ISSN: 1006-4303
Zhou, Y., Liu, W., Wang, T.	2005	CA 8.5	Effects of pesticides metolachlor and S-metolachlor on soil microorganisms in aquisols of Southern China. I. Catalase activity.	Ying yong sheng tai xue bao = The journal of applied ecology / Zhongguo sheng tai xue xue hui, Zhongguo ke xue yuan Shenyang ying yong sheng tai yan jiu suo zhu ban, (2005 May) Vol. 16, No. 5, pp. 895-8. Journal code: 9425159. ISSN: 1001-9332. L-ISSN: 1001-9332.

Author(s)	Year	CA data point number	Title	Source
Zhou, Y., Liu, W., Ye, H.	2006	CA 8.5	Effects of pesticides metolachlor and S-metolachlor on soil microorganisms in aquisols. II. Soil respiration.	Ying yong sheng tai xue bao = The journal of applied ecology / Zhongguo sheng tai xue xue hui, Zhongguo ke xue yuan Shenyang ying yong sheng tai yan jiu suo zhu ban, (2006 Jul) Vol. 17, No. 7, pp. 1305-9. Journal code: 9425159. ISSN: 1001-9332. L-ISSN: 1001-9332.

A detailed review of the full-text documents identified in Table 9.6-2 resulted in the additional exclusion of the following studies from the dossier.

Table 9.6-4: List of references excluded following detailed review listed by data point number

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.0	Ye, J., Liu, J., Liu, W., Zhao, M., Liu, W.	2010	Enantioselectivity in environmental risk assessment of modern chiral pesticides.	Environmental Pollution, (July 2010) Vol. 158, No. 7, pp. 2371-2383. Refs: 69. ISSN: 0269-7491 CODEN: ENPOEK	Not relevant. Review paper. No new data presented.
CA 8.1.1.3	Keseru, M., Juhasz, E., Szabo, R., Tavaszi, J., Varnagy, L.	2007	Study of the individual toxicity of three pesticides in a teratogenicity test on birds. Harom noevenyvedo szer egyedi mereghatasanak vizsgalata madarteratologiai tesztben.	Noevenyvedelem (2007), Vol. 43, Number 3, pp. 113-119, 23 refs. ISSN: 0133-0829	Does not fulfil criteria 6 (exposure route is clearly defined, is environmentally relevant and, if appropriate, suitably quantified). Embryos were either injected or immersed in Dual Gold. Not appropriate route of exposure.
CA 8.1.1.3	Varnagy, L., Budai, P., Fejes, S., Keseru, M., Szabo, R.. Juhasz, E.	2004	Degredation dynamics and toxicity of certain pesticide active ingredients in bird embryos.	Magyar Allatorvosok Lapja (2004), Volume 126, Number 12, pp. 755-760, 21 refs. ISSN: 0025-004X	Does not fulfil criteria 6 (exposure route is clearly defined, is environmentally relevant and, if appropriate, suitably quantified). Embryos were either injected or immersed in Dual Gold. Not appropriate route of exposure.
CA 8.1.2	Greenlee, A.R., Ellis, T.M., Berg, R.L.	2004	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9. Journal code: 0330411. ISSN: 0091-6765. Report No.: NLM-PMC1241965.	Does not fulfil criteria 6 (exposure route is clearly defined, is environmentally relevant and, if appropriate, suitably quantified). Embryos were incubated in vitro for 96 hrs. This is not a plausible route of exposure for wild mammals.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.1.4	De Solla, S.R., Palonen K.E., Martin P.A.	2014	Toxicity of pesticides associated with potatoe production, including soil fumigants, to snapping turtle eggs (*Cheludra serpentine*).	Environmental toxicology and chemistry/SETAC (2014 Jan) 33 (1): 102-106.	Does not fulfil criteria 8 (effects are not related to a single test item). Soil was treated with a mixture of chlorothalonil, S-metolachlor, metribuzin, and chlorpyrifos applied at typical and higher field application rates. Turtle eggs were incubated in soil in outdoor plots. The mixture did not affect survivorship, deformities, or body size at applications up to 10 times the typical field application rates. Hatching success ranged between 87% and 100% for these treatments.
CA 8.1.4	De Solla, S.R., Martin, P.A	2011	Absorption of current use pesticides by snapping turtle (*Chelydra serpentina*) eggs in treated soil.	Chemosphere, (2011 Oct) Vol. 85, No. 5, pp. 820-5. Electronic Publication Date: 8 Sep 2011. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535	Does not fulfil criteria 8 (effects are not related to a single test item). Snapping turtle (Chelydra serpentina) eggs were incubated in soil that was treated with 10 pesticides (atrazine, simazine, metolachlor, azinphos-methyl, dimethoate, chlorpyrifos, carbaryl, endosulfan (I and II), captan, and chlorothalonil).
CA 8.1.4	De Solla, S., Martin, P.	2010	Relationship between pesticide properties and absorption in turtles eggs from treated soil.	Canadian Technical Report of Fisheries and Aquatic Sciences, (2010) Vol. 2883, pp. 64. Meeting Info.: 36th Annual Workshop on Aquatic Toxicity. La Malbaie, CANADA. September 27-30, 2009. CODEN: CTRSDR. ISSN: 0706-6457. E-ISSN: 0706-6570.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.1.4	Papoulias, D.M. , Schwarz, M.S., Mena, L.	2013	Gonadal abnormalities in frogs (*Lithobates* spp.) collected from managed wetlands in an agricultural region of Nebraska, USA.	Environmental Pollution, (January 2013) Vol. 172, pp. 1-8. Refs: 78. ISSN: 0269-7491; E-ISSN: 1873-6424; CODEN: ENPOEK	Does not fulfil criteria 4 (test organisms are not previously exposed to the test material or other contaminants) and criteria 8 (effects are not related to a single test item). Wild caught froglets from river water basins where agriculture is conducted and atrazine, glyphosate an metolachlor are used. The paper tries to relate morphological observations in frogs to the original source location. Not clear what else the frogs may have been exposed to as only these 3 compounds were examined analytically.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.1.4	Spolyarich N., Hyne R.V., Wilson S.P., Palmer C.G., Byrne M.	2011	Morphological abnormalities in frogs from a rice-growing region in NSW, Australia, with investigations into pesticide exposure.	Environmental monitoring and assessment, (2011 Feb) Vol. 173, No. 1-4, pp.397-407. Journal code: 8508350. E-ISSN: 1573-2959. L-ISSN: 0167-6369.	Text relates to chemical sampling of watercourses that contain a mixture of pesticides and does not include exposure of test organisms. So there are no effects to relate to the risk assessment from this paper.
CA 8.2.1	Zhou, B., Zhao, M.-R., Huang, H.-F.	2008	Study on zebrafish embryo-toxicity of four pesticides	Zhejiang Gongye Daxue Xuebao (2008), 36 (2), 136-140. ISSN: 1006-4303	English version of publication unavailable; English abstract available The effects on zebrafish embryos on morphological development, survival and percent hatching at 2.8, 28, 283 and 2838 mg/L. Effects on survival, abnormality and reduced feeding were observed at the 2838 mg/L concentration only. This relevant information indicating an effect on zebrafish embryos. The result is in line with the current regulatory EU fish acute and chronic endpoints of 1.23 mg/L and 0.78 mg/L. The effects seen were at concentrations much in exceedance of expected PEC_{sw} therefore tis reference is not relevant for this review.
CA 8.2	Caquet Th., Roucaute M; Mazzella N; Delmas F; Madigou C; Farcy E; Burgeot Th; Allenou J-P; Gabellec R	2013	Risk assessment of herbicides and booster biocides along estuarine continuums in the Bay of Vilaine area (Brittany, France).	Environmental science and pollution research international, (2013 Feb) Vol. 20, No. 2, pp. 651-66. Electronic Publication Date: 16 Sep 2012 Journal code: 9441769. E-ISSN: 1614-7499. L-ISSN: 0944-1344.	Text relates to chemical sampling only and does not include exposure of test organisms. So there are no effects to relate to the risk assessment from this paper.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2	Kolpin, D.W., Hubbard, L.E.,. Blazer, V.S., Young, J.A., Iwanowicz, L.R., Gray, J.L., Foreman, W.T., Furlong, E.T., Zaugg, S.D., Sandstrom, M.W., Focazio, M.J., Alvarez, D.A., Speiran, G.K., Meyer, M.T., Barber, L.B.	2013	Chemical contaminants in water and sediment near fish nesting sites in the Potomac River basin: Determining potential exposures to smallmouth bass (*Micropterus dolomieu*).	Science of the Total Environment, (5 Jan 2013) Vol. 443, pp. 700-716. Refs: 85. ISSN: 0048-9697; E-ISSN: 1879-1026 CODEN: STEVA8	Text relates to chemical sampling only and does not include exposure of test organisms. So there are no effects to relate to the risk assessment from this paper.
CA 8.2	Berube, V.E., Boily, M.H, DeBlois, C., Dassylva, N., Spear, P.A.	2005	Plasma retinoid profile in bullfrogs, *Rana catesbeiana*, in relation to agricultural intensity of sub-watersheds in the Yamaska River drainage basin, Quebec, Canada.	Aquatic toxicology (Amsterdam, Netherlands), (2005 Jan 26) Vol. 71, No. 2, pp. 109-20. Journal code: 8500246. ISSN: 0166-445X. L-ISSN: 0166-445X.	Does not fulfil criteria 8 (effects are not related to a single test item). This research is not relevant as bullfrogs were collected from various watersheds which contained mixtures of up to nine pesticides. So the contribution of metolachlor to the retinoid profile of bullfrogs could not be quantified
CA 8.2	Dussault, S., Fortier, M., Boily, M., Brousseau, P., Fournier, M.	2010	Immune status of the bullfrog (*Rana catesbeiana*) exposed to agripesticides	Canadian Technical Report of Fisheries and Aquatic Sciences, (2010) Vol. 2883, pp. 66. Meeting Info.: 36th Annual Workshop on Aquatic Toxicity. La Malbaie, CANADA. September 27-30, 2009. CODEN: CTRSDR. ISSN: 0706-6457. E-ISSN: 0706-6570.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2	Shutler, D., Marcogliese , D.J.	2011	Leukocyte profiles of Northern Leopard Frogs, *Lithobates pipiens*, exposed to pesticides and hematozoa in agricultural wetlands.	Copeia (2011), Number 2, pp. 301-307. ISSN: 0045-8511	Does not fulfil criteria 8 (effects are not related to a single test item). A mixture of atrazine and metolachlor was used.
CA 8.2	McDaniel, T.V., Martin, P.A., Struger, J., Sherry, J., Marvin, C.H., McMaster, M.E., Clarence, S., Tetreault, G.	2008	Potential endocrine disruption of sexual development in free ranging male northern leopard frogs (*Rana pipiens*) and green frogs (*Rana clamitans*) from areas of intensive row crop agriculture. [Erratum to document cited in CA149:301052]	Aquatic Toxicology (2008), 90 (1), 82. CODEN: AQTODG; ISSN: 0166-445X	Does not fulfil criteria 8 (effects are not related to a single test item). Assessed in the endocrine review CGA077102_11322. Blood samples were taken from wild caught frogs from agricultural sites and examined for endocrine markers of endocrine disruption. Therefore the frogs were likely to have been exposed to more than one compound. This is therefore not relevant to this review.
CA 8.2	Solis, M.E., Liu, C.C., Nam, P., Niyogi, D.K., Bandeff, J.M., Huang, Y.-W.	2007	Occurrence of organic chemicals in two rivers inhabited by Ozark hellbenders (*Cryptobranchus alleganiensis bishopi*)	Archives of Environmental Contamination and Toxicology (2007), 53 (3), 426-434. CODEN: AECTCV; ISSN: 0090-4341	Not relevant as water monitoring study only. No ecotoxicological testing of hellbenders was conducted.
CA 8.2	Gutierrez, M.M.	2007	Evidence of endocrine disruption in amphibians due to agricultural chemical exposure.	Dissertation Abstracts International. Vol. 69, no. 6. 2007. Dissertation Number: AAI3319626. ISSN: 0419-4217 Published by: University Microfilms International, P.O. Box 1764, Ann Arbor, MI, 48106, USA	Atrazine focused paper. No data generated on S-metolachlor or metolachlor or their metabolites.
CA 8.2.1	Polard T., Jean, S., Gauthier, L., Laplanche, C., Merlina, G., Sanchez-Perez J.M., Pinelli, E.	2011	Mutagenic impact on fish of runoff events in agricultural areas in south-west France.	Aquatic toxicology (Amsterdam, Netherlands), (2011 Jan 17) Vol. 101, No. 1, pp. 126-34. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.	Does not fulfil criteria 8 (effects are not related to a single test item).

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.1	Tierney, K.B., Sampson, J.L., Kennedy, C.J., Ross, P.S., Sekela, M.A., Kennedy, C. J.	2008	Salmon olfaction is impaired by an environmentally realistic pesticide mixture.	Environmental Science and Technology, (1 Jul 2008) Vol. 42, No. 13, pp. 4996-5001. Refs: 26. ISSN: 0013-936X; CODEN: ESTHAG	Does not fulfil criteria 8 (effects are not related to a single test item).
CA 8.2.1	Haluzova, I., Modra, H., Mikula, P., Svobodova, Z.	2009	Subchronic exposure of the common carp (*Cyprinus carpio*) to four herbicide formulations: Effect on the haematological indice.	Toxicology Letters (Shannon), (SEP 13 2009) Vol. 189, No. Sp. Iss. SI, pp. S210. Meeting Info.: 46th Congress of the European-Societies-of-Toxicology. Dresden, GERMANY. September 13 -16, 2009. CODEN: TOLED5. ISSN: 0378-4274. DT Conference; (Meeting)	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.1	Dobsikova, R., Blahova, J., Modra, H., Skoric, M., Svobodova, Z.	2011	The effect of acute exposure to herbicide Gardoprim Plus Gold 500 SC on haematological and biochemical indicators and histopathological changes in common carp (*Cyprinus carpio* L.).	Acta Veterinaria Brno (2011) Volume 80, Number 4, pp. 359-363, 14 refs. ISSN: 0001-7213. DOI: 10.2754/avb201180040359	Does not fulfil criteria 8 (effects are not related to a single test item). Gardoprim Plus Gold 500 SC formulation was tested which contains both terbuthylazine and S-metolachlor.
CA 8.2.1	Buckler, D.R., Mayer, F.L., Ellersieck, M.R., Asfaw, A.	2005	Acute Toxicity Value Extrapolation with Fish and Aquatic Invertebrates	Archives of Environmental Contamination and Toxicology (2005), 49 (4), 546-558. CODEN: AECTCV; ISSN: 0090-4341	Reference evaluated data from other sources. No new data presented.
CA 8.2.1 CA 8.2.4 CA 8.2.6	Passy, S.I., Bode, R.W., Carlson, D. M., Novak, M. A.	2004	Comparative environmental assessment in the studies of benthic diatom, macroinvertebrate, and fish communities	International Review of Hydrobiology (2004), 89 (2), 121-138. ISSN: 1434-2944	Does not fulfil criteria 8 (effects are not related to a single test item).

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2	Ayansina, A.D.V., Muhammad, R.G.	2014	An evaluation of the effect of four herbicides on some aquatic organisms.	International Journal of Biological and Chemical Sciences (2014), Volume 8, Number 1, pp. 304-313, 23 refs. ISSN: 1991-8631	Requested in September 2014. Our Library staff tried until 19 November 2014 to obtain this reference without success. They were not able to provide the article/ copyright permission of the publication requested. The requested article/ permission was not available through our primary source at the present. Our Advanced Referencing specialist contacted the publisher of International journal of biological and chemical sciences (http://www.ajol.info/index.php/ijbcs/about/contact) via ijbcs@yahoo.fr, ijbcs.ifg@gmail.com, ijbcs_ifg@yahoo.fr and fax +237 33 45 11 02 (failed) but despite numerous efforts at contact with the publisher our attempts remain unanswered. In addition the author was contacted (Victor Ayansina) via ayandvt@yahoo.com who replied that the publisher is the rights holder in this case. It has not therefore been possible to review this article. This is not considered to be an issue given the wealth of data available on aquatic organisms for S-metolachlor and metolachlor.
CA 8.2.1	Perez, J.R.	2011	Effects of s-triazines and metolachlor on chlorpyrifos toxicity in Zebrafish (*Danio rerio*) early life-stages	Conference: 21st Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2011), Milano Convention Centre, Milan, 15 May 2011 - 19 May 2011	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.1	Babatunde, M.M., Balogun, J.K., Auta, J., Balarabe, M.L., Auta, J., Balogun, J.K., Bolorundur o, P.I., Editor(s): Onimisi, H.U.	2009	Acute toxicity of galex to *Oreocromis niloticus* (Trewavas) in Nigeria	Proceedings of the 23rd annual conference of the Fisheries Society of Nigeria. pp. 159-164. 2009. Conference: 23rd annual conference of the fisheries Society of Nigeria (FISON), Kaduna (Nigeria), 26-30 Oct 2008	Does not fulfil criteria 8 (effects are not related to a single test item). Galex is not the relevant formulation for the EU. Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.1	Ubachukwu, P.O., Oluah, N.S., Omeje, C.U., Ikele, C.B.	2012	Effect of herbicide (Primextra) on tissue cholesterol level in *Clarias gariepinus* juvenile.	Animal Research International (2012), Volume 9, Number 1, pp. 1524-1528, 16 refs. ISSN: 159-3115	Does not fulfil criteria 8 (effects are not related to a single test item).
CA 8.2.4.1	Souissi Y., Bouchonnet, S; Bourcier, S; Kusk K. O.; Sablier M., Andersen H. R.	2013	Identification and ecotoxicity of degradation products of chloroacetamide herbicides from UV-treatment of water.	The Science of the total environment, (2013 Aug 1) Vol. 458-460, pp. 527-34. Journal code: 0330500. E-ISSN: 1879-1026. L-ISSN: 0048-9697	Does not fulfil criteria 6. The treated water from waste water treatment plants is unlikely to go back into the environment. In addition to this the length of time the water has been irradiated for (90 mins) is vastly in excess of UV water treatment procedures where the flow rates are more L/s, therefore exposure time is seconds.
CA 8.2.5.1	Liu, H., Zhan, X., Ye, W., Liu, W.	2005	Ecotoxicological difference of chiral pesticides: chronic toxicity of metolachlor and S-metolachlor to *Daphnia magna*	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2005), 45 (1), 492-496. CODEN: PEACF2; ISSN: 1524-6434	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.4.1 CA 8.2.5.1 CA 8.5	Liu, W., Fang, Q., Ma, Y.	2005	Selectivity in aquatic toxicity and biodegradation of the herbicide Metolachlor	Abstracts of Papers, 230th ACS National Meeting, Washington, DC, United States, Aug. 28-Sept. 1, 2005 (2005), AGRO-060. Publisher: American Chemical Society, Washington, D. C. CODEN: 69HFCL	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.5.2	Liu, H.J.	2006	Ecotoxicological difference of Rac-Metolachlor and S-Metolachlor	Conference: 16th Europe Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC 2006), World Forum Convention Center, Hague (Netherlands (The)), 7 May 2006 - 11 May 2006 Sponsor(s): Society of Environmental Toxicology and Chemistry (SETAC)	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Praet, N. van; Bruyn, L. de; Jonge, M. de; Vanhaecke, L.; Stoks, R.; Bervoets, L.; van Praet, N.; de Bruyn, L.; de Jonge, M.	2014	Can damsel fly larvae (*Ischnura elegans*) be used as bioindicators of sublethal effects of environmental contamination?	Aquatic Toxicology (2014), Volume 154, pp. 270-277. ISSN: 0166-445X	Does not fulfil criteria 4 (test organisms are not previously exposed to the test material or other contaminants) or criteria 8 (effects are not related to a single test item);
CA 8.2.5.2	Lizotte, R., Testa, S., Locke, M., Martin. A, Steinriede, R.W.	2013	Responses of phytoplankton and *Hyalella azteca* to agrichemical mixtures in a constructed wetland mesocosm.	Archives of environmental contamination and toxicology, (2013 Oct) Vol. 65, No. 3, pp. 474-85. Electronic Publication Date: 23 Jun 2013. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.	Does not fulfil criteria 8 (effects are not related to a single test item). A mixture of S-metolachlor was tested together with atrazine and permethrin. Therefore the effects of S-metolachlor are difficult to distinguish. This is therefore not relevant to his review.
CA 8.2.5.2	Lizotte, R.E., Shields, F.D., Testa, S.	2012	Effects of a simulated agricultural runoff event on sediment toxicity in a managed backwater wetland	Water, air, and soil pollution (2012), Volume 223, Number 8, pp. 5375-5389. ISSN: 1573-2932	Does not fulfil criteria 8 (effects are not related to a single test item). A pesticide mixture of atrazine, metolachlor and permethrin was pumped into hydrologically managed floodplain wetland to mimic a run-off event. The effects of this mixture on *Hyalella azteca* were assessed in acute 48h laboratory tests. So there is no solo metolachlor data which is relevant to this review in this paper.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Lizotte, R.E., Knight, S.S., Bryant, C.T., Smith, S.	2009	Agricultural Pesticides in Mississippi Delta Oxbow Lake Sediments During Autumn and Their Effects on *Hyalella azteca*.	Archives of Environmental Contamination and Toxicology, (OCT 2009) Vol.57, No. 3, pp. 495-503. CODEN: AECTCV. ISSN: 0090-4341.	Does not fulfil criteria 8 (effects are not related to a single test item). Sediment was collected from Mississippi Delta oxbow lakes and their effects and bioavailability to *Hyalella azteca* were assessed. Each sediment was analyzed for 17 current and historic-use pesticides and metabolites. Chronic 28-day *H. azteca* sediment bioassays and pesticide body residue analyses were conducted. The compound p,p0-DDE [1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene] was ubiquitous. 7/15 samples contained metolachlor and the maximum concentration was 0.15 µg/g. No significant (p[0.05) differences in *H. azteca* survival. So there is no solo metolachlor data which is relevant to this review in this paper.
CA 8.2.5.2	Lizotte, R.E., Knight, S.S., Shields, F.D., Bryant, C.T.	2009	Effects of an atrazine, metolachlor and fipronil mixture on *Hyalella azteca* (Saussure) in a modified backwater wetland.	Bulletin of environmental contamination and toxicology, (2009 Dec) Vol. 83, No. 6, pp. 836-40. Journal code: 0046021. E-ISSN: 1432-0800. L-ISSN: 0007-4861.	Does not fulfil criteria 8 (effects are not related to a single test item). A pesticide mixture of atrazine and metolachlor (as Bicep II Magnum) was injected into the wetland. Effects of this mixture on *Hyalella azteca* were assessed. Acute 96h tests were also conducted with fipronil. So there is no solo metolachlor data which is relevant to this review in this paper.
CA 8.2.5.2	Moore, M.T. (Reprint Author), Lizotte, R.E., Cooper, C.M., Smith, S., Knight, S.S.	2004	Survival and growth of *Hyalella azteca* exposed to three Mississippi Oxbow lake Sediments.	Bulletin of Environmental Contamination and Toxicology, (April 2004) Vol. 72, No. 4, pp. 777-783. ISSN: 0007-4861.	Does not fulfil criteria 8 (effects are not related to a single test item). A pesticide mixture of atrazine, metolachlor and permethrin was pumped into hydrologically managed floodplain wetland to mimic a run-off event. The effects of this mixture on *Hyalella azteca* were assessed in acute 48h laboratory tests. So there is no solo metolachlor data which is relevant to this review in this paper. (Same comment as above for reference 334).

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Perez, J.R., Loureiro, S.M., Soares, A.M.V.M.	2010	Effects of atrazine and metolachlor on chlorpyrifos toxicity in *Chironomus riparius*	Conference: 20th Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2010), Palacio de Congresos y Exposiciones - FIBES, Seville, 23 May 2010-27 May 2010	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.5.2	Loureiro, S., Perez, J.R., Soares, A.M.V.M.	2010	Effects of atrazine, metolachlor and endosulfan on chlorpyrifos toxicity in *Chironomus riparius*	Conference: 20th Annual Meeting of the Europe branch of the Society of Environmental Toxicology and Chemistry (SETAC 2010), Palacio de Congresos y Exposiciones - FIBES, Seville, 23-27 May 2010	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.5.2	Gerhardt, A., Koster, M., Lang, F., Leib, V.	2012	Active in situ biomonitoring of pesticide pulses using *Gammarus* spp. In small tributaries of lake Constance	Journal of Environmental Protection (2012), 3 (7), 573-583. ISSN: 2152-2197	Does not fulfil criteria 8 (effects are not related to a single test item). The survival and feeding behavior of caged gammarids were investigated small streams in the catchment of Lake Constance. Metolachlor was found at 0.01 to 2.7 µg/L alongside >16 other crop protection compounds. The effects of metolachlor are not discernable as a mixture was examined.
CA 8.2.5.2	Guy, M., Singh, L., Mineau, P.	2011	Using field data to assess the effects of pesticides on crustacea in freshwater aquatic ecosystems and verifying the level of protection provided by water quality guidelines	Integrated Environmental Assessment and Management (2011), 7 (3), 426-436. CODEN: IEAMCK; ISSN: 1551-3777	Not relevant. Paper covers the modelling of existing data.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Collin, H., Meistertzheim, A.-L., David, E., Moraga, D., Boutet, I.	2010	Response of the Pacific oyster *Crassostrea gigas*, Thunberg 1793, to pesticide exposure under experimental conditions.	The Journal of experimental biology, (2010 Dec 1) Vol. 213, No. Pt 23, pp. 4010-7. Journal code: 0243705. E-ISSN: 1477-9145. L-ISSN: 0022-0949.	Does not fulfil criteria 4 (test organisms are not previously exposed to the test item or other contaminants. Oysters were collected from two polluted sites. In the ‘low’ pollution area 2 and 4.7 µg/kg lindane and DDT were found in bivalve tissues. In the ‘high’ pollution area 6 and 11 µg/kg lindane and DDT were found in bivalve tissues. No mention of S-metolachlor or metolachlor so not relevant.
CA 8.2.5.2	Gagnaire, B., Gay, M., Huvet, A., Daniel, J-Y., Saulnier, D., Renault, T.	2007	Combination of a pesticide exposure and a bacterial challenge: in vivo effects on immune response of Pacific oyster, *Crassostrea gigas* (Thunberg).	Aquatic toxicology (Amsterdam, Netherlands), (2007 Aug 15) Vol. 84, No.1, pp. 92-102. Journal code: 8500246. ISSN: 0166-445X. L-ISSN: 0166-445X.	Does not fulfil criteria 8 (effects are not related to a single test item). Not relevant as a mixture of 8 pesticides (atrazine, glyphosate, alachlor, metolachlor, fosetyl-alumimium, terbuthylazine, diuron and carbaryl) was used. Haemocyte parameters (cell mortality, enzyme activities and phagocytosis) were monitored using flow cytometry and gene expression was evaluated by real-time PCR (RT-PCR). The effects of metolachlor are not discernable as a mixture was examined.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Gagnaire, B., Burgeot, T., Geret, F., Thomas-Guyon, H., Renault, T., Editor(s): Feunteun, E., Miramand, P.	2006	Effect of heavy metals and herbicides on immune capacities in Pacific oyster, *Crassostrea gigas*. 599/1308	Cahiers de Biologie Marine (2006) Volume 47, Number 1, pp. 105-107, 7 refs. ISSN: 0007-9723	Does not fulfil criteria 8 (effects are not related to a single test item). In vitro and in vitro experiments to determine the effects of heavy metals and herbicides on immune capacities in Pacific oyster, *C. gigas*. The in vitro experiments focused on the direct contact between pollutants and cells of the immune system, the haemocytes. A mixture of 8 pesticides: carbaryl (10 pM-1 µM), diuron (179 pM-17 µM), atrazine (300-30 µM), terbuthylazine (260 pM-26 µM), alachlor (70 pM-7 µM), metolachlor (70 pM-7 µM), glyphosate (120 pM-12 µM) and foseryl-aluminium [fosetyl] (7 pM-0.7 µM). The in vivo experiments consisted of a contact between oysters and contaminated water. A mixture of 8 pesticides: carbaryl (0.25 nM), diuron (2 nM), atrazine (3 nM), terbuthylazine (2.5 nM), alachlor (3 nM), metolachlor (2 nM), glyphosate (4 nM) and fosetyl-aluminium (2 nM). The in vitro experiments showed that the pesticide mixture at high concentrations induced an increase of phagocytosis activity. The pesticide mixture also modulated phagocytosis in vivo by inducing a decrease after a 7-day contamination period. The effects of metolachlor are not discernable as a mixture was examined.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Geret, F., Burgeot T., Haure J., Gagnaire B., Renault T., Communal P.Y., Samain, J.F.	2013	Effects of low-dose exposure to pesticide mixture on physiological responses of the Pacific oyster, *Crassostrea gigas*.	Environmental toxicology, (2013 Dec) Vol. 28, No. 12, pp. 689-99. Journal code: 100885357. E-ISSN: 1522-7278. L-ISSN: 1520-4081.	Does not fulfil criteria 8 (effects are not related to a single test item). Effects on the physiology of Pacific oyster, *Crassostrea gigas*, of a mixture of pesticides containing 0.8 µg/L alachlor, 0.6 µg/L metolachlor, 0.7 µg/L atrazine, 0.6 µg/L terbuthylazine, 0.5 µg/L diuron, 0.6 µg/L fosetyl aluminum, 0.05 µg/L carbaryl, and 0.7 µg/L glyphosate for a total concentration of 4.55 µg/L. The total nominal concentration of pesticides mixture corresponds to the pesticide concentrations in the shellfish culture area of the Marennes-Oleron basin. Two varieties of *C. gigas* were tested for 7d under controlled conditions. The effects were assessed using enzyme biomarkers of nitrogen metabolism (GS, glutamine synthetase), detoxification metabolism (GST, glutathione S-transferase), and oxidative stress (CAT, catalase). Sublethal effects on hemocyte parameters (phagocytosis and esterase activity) and DNA damages (DNA adducts) were also measured. Changes in metabolic activities were characterized by increases in GS, GST, and CAT levels on the first day of exposure for the "resistant" oysters and after 3-7 days of exposure for the "susceptible" oysters. The formation of DNA adducts was detected after 7 days of exposure. The percentage of hemocyte esterase-positive cells was reduced in the resistant oysters, as was the hemocyte phagocytic capacity in both oyster varieties after 7 days of exposure to the pesticide mixture. The effects of metolachlor are not discernable as a mixture was examined.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Geret, F., Burgeot, T., Haure, J., Gagnaire, B., Renault, T., Communal, P.Y., Samain, J.F.	2011	Effects of low-dose exposure to pesticide mixture on physiological responses of the pacific oyster, *Crassostrea gigas*.	Environmental toxicology, (2011 Oct 19). Electronic Publication Date: 19 Oct 2011. Journal code: 100885357. E-ISSN: 1522-7278. L-ISSN: 1520-4081.	Does not fulfil criteria 8 (effects are not related to a single test item). Effects on the physiology of Pacific oyster, *Crassostrea gigas*, of a mixture of pesticides containing 0.8 l µg/L alachlor, 0.6 µg/L metolachlor, 0.7 µg/L atrazine, 0.6 µg/L terbuthylazine, 0.5 µg/L diuron, 0.6 µg/L fosetyl aluminum, 0.05 µg/L carbaryl, and 0.7 µg/L glyphosate. The early effects of the mixture were assessed using enzyme biomarkers of nitrogen metabolism, detoxification metabolism, and oxidative stress. Sublethal effects on haemocyte parameters (phagocytosis and esterase activity) and DNA damages (DNA adducts) were also measured. The effects of metolachlor are not discernable as a mixture was examined.
CA 8.2.5.2	Geret, F., Gagnaire, B., Menard, D., Renault, T., Le Roux, A., Haure, J., Bocquene, G., Burgeot, T.	2004	Response of the pacific oyster *Crassostrea gigas* to pesticide exposition under experimental conditions.	Marine Environmental Research, (August 2004) Vol. 58, No. 2-5, pp. 312-313. Meeting Info.: 12th International Symposium on Pollutant Responses in Marine Organisms (PRIMO 12). Safety Harbor, FL, USA. May 09-13, 2003. CODEN: MERSDW. ISSN: 0141-1136.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.5.2	Mai, H., Gonzalez, P., Pardon, P., Tapie, N., Budzinski, H., Cachot, J., Morin, B.	2014	Comparative responses of sperm cells and embryos of Pacific oyster (*Crassostrea gigas*) to exposure to metolachlor and its degradation products.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Feb) Vol. 147, pp. 48-56. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.	Does not fulfil criteria 8 (effects are not related to a single test item).

CA 8.2.5.2	Mai, H., Morin, B., Pardon P., Gonzalez P., Budzinski H., Cachot J.	2013	Environmental concentrations of irgarol, diuron and S-metolachlor induce deleterious effects on gametes and embryos of the Pacific oyster, *Crassostrea gigas*.	Marine environmental research, (2013 Aug) Vol. 89, pp. 1-8. Journal code: 9882895. E-ISSN: 1879-0291. L-ISSN: 0141-1136.	Does not fulfil criteria 8 (effects are not related to a single test item). Toxicity of S-metolachlor was evaluated in Pacific oyster (*Crassostrea gigas*) gametes or embryos exposed to concentrations of 0.0001× to 1.0 µg/L. Tests were performed on (1) spermatozoa (2) oocytes and (3) both spermatozoa and oocytes; gametes were exposed for 30 mins and for 1 to 3, examined over subsequent 24h for fertilization success and offspring development. After exposure of 1.0 µg/L to sperm, oocytes or both, fertilisation success was 85% (96% in controls). There was 25%, 30% and 33% of abnormal larvae for sperm, oocytes or both exposed to 1.0 µg/L (control 4-5%). The results were considered to be a dose response. This test type can be difficult to fulfil the test criteria. The validity criteria for the control is to have <40% abnormal larvae. When tests have such a large allowance for the control, this is indicative that this parameter is very variable and that abnormal D-larvae prevalence is a common occurrence for the test species. Therefore there should be some caution before the results of this test are considered of critical significance as no effects >33% were found. The NOECs have been presented in the paper, however the results of this test are usually expressed as a 24h EC_{50}. The values would be >1.0 µg/L for the endpoints measured. The filtered seawater (FSW) used for test solutions came from Arcachon Bay. Table 1 shows up to 40 ng/L diuron, 22 ng/L irgarol and 5 ng/L metolachlor have been found. Samples analysed of the FSW used for the test contained 1-2ng/L of these 3 compounds. However, no screening was conducted for other compounds. Mai *et al*. 2012 (Ref. ID 35) found copper (700 to 810 ng/L), cadmium (9 ng/L) and Irgarol (2 to 22 ng/L) are also present in the Arachon Bay. Mai *et al* (2012) also found that the NOEC for copper toxicity to *C. gigas* gametes from a very similar test design was <1 µg/L. As the FSW was not analysed the presence of other pollutants cannot be confirmed. There was no analytical confirmation of test concentrations and the study is not GLP. The GLP regulatory study found an EC_{50} of 9.8 mg/L. Therefore this paper has not been considered relevant for this review.
CA 8.2.5.2	Mai, H., Cachot, J., Brune, J.,	2012	Embryotoxic and genotoxic effects of heavy metals and	Marine pollution bulletin, (2012 Dec) Vol. 64, No. 12, pp.	Does not fulfil criteria 8 (effects are not related to a single test item).

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
	Geffard, O., Belles, A., Budzinski, H., Morin, B.		pesticides on early life stages of Pacific oyster (*Crassostrea gigas*).	2663-70. Journal code: 0260231. E-ISSN: 1879-3363. L-ISSN: 0025-326X.	After 24 h exposure, significant increases of the percentage of abnormal D-larvae and the DNA strand breaks were observed from l.0 µg/L metolachlor in comparison with the controls. The EC_{50} was >10 µg/L. The amount of abnormal D-larvae in the control was 20%. Filtered seawater (FSW) used for test solutions came from Arcachon Bay. As discussed for Ref ID 29/1308 other compounds which are toxic to oysters have been found in those waters and no screening for other toxicants was conducted prior to use. Therefore it is not certain whether the effects noted all result from metolachlor exposure.
CA 8.2.5.2	Auby, I; Bocquene, G; Quiniou, F; Dreno, J.P.	2007	Arcachon basin 's weedkillers and insecticides contamination analysis (2005-2006 period) environmental impact.	Plouzane (France). 2007. Published by: Plouzane (France)	Text relates to chemical sampling only and does not include exposure of test organisms. So there are no effects to relate to the risk assessment from this paper.
CA 8.2.5.2	Birchfield, N., Corbin, M., Doelling-Brown, P., Hurley, P.	2006	Risk Assessment of Racemic Metolachlor use to 26 Evolutionarily Significant Units of Endangered and Threatened Pacific Salmon and Steelhead	Conference: 27th Annual Meeting of the Society of Environmental Toxicology and Chemistry (SETAC 2006), Montreal, Quebec (Canada), 3 Nov 2006 - 9 Nov 2006 Sponsor(s): Society of Environmental Toxicology and Chemistry (SETAC)	Reference evaluated data from other sources. No new data presented.
CA 8.2.5.2	Belanger, R.M., Sabhapathy, G.S., Khan, S.	2014	Atrazine and metolachlor exposure affects the chemosensory responses of male crayfish (*Orconectes rusticus*) to female odors.	Integrative and Comparative Biology, (2014) Vol. 54, No. Suppl. 1, pp. E15. http://icb.oxfordjournals.org/. Meeting Info.: Annual Meeting of the Society-for-Integrative-and-Comparative-Biology. Austin, TX, USA. Jan. 03-07, 2014. ISSN: 1540-7063. E-ISSN: 1557-7023.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.5.2	Sanchez-Bayo, F.	2006	Comparative acute toxicity of organic pollutants and reference values for crustaceans. I. Branchiopoda, Copepoda and Ostracoda	Environmental Pollution (Amsterdam, Netherlands) (2006), 139 (3), 385-420 CODEN: ENPOEK; ISSN: 0269-7491	No new data presented in this reference. Pre-existing data was compared. Hence it is not relevant for this literature search.
CA 8.2.5.2	Smalling, K.L., Morgan, S., Kuivila, K.K.	2010	Accumulation of current-use and organochlorine pesticides in crab embryos from northern California, USA	Environmental Toxicology and Chemistry (2010), 29 (11), 2593-2599. CODEN: ETOCDK; ISSN: 0730-7268	Crabs were collected from a rocky intertidal area downstream of a suburban golf course (S-metolachlor is not a golf-course herbicide), and a saltmarsh surrounded by an urban area. Crab embryos were screened for metolachlor, none was detected. Not relevant to the risk assessment.
CA 8.2.5.2	Toropov, A.A., Benfenati, E.	2006	QSAR models for *Daphnia* toxicity of pesticides based on combinations of topological parameters of molecular structures 417/559	Bioorganic & Medicinal Chemistry (2006), 14 (8), 2779-2788. CODEN: BMECEP; ISSN: 0968-0896	Irrelevant as this paper deals with predictive toxicity not actual measured values, therefore no new data provided.
CA 8.2.6.1	Chalifour, A., Spear, P.A., Boily, M.H., DeBlois, C., Giroux, I., Dassylva, N., Juneau, P.	2009	Assessment of toxic effects of pesticide extracts on different green algal species by using chlorophyll a fluorescence	Toxicological and Environmental Chemistry (2009), 91 (7), 1315-1329. CODEN: TECSDY; ISSN: 0277-2248	Does not fulfil criteria 8 (effects are not related to a single test item). *Chlorella vulgaris*, *Scenedesmus obliquus* and *Pseudokirchneriella subcapitata* (green algae) were tested to metolachlor at a maximum of 1.7 µg/L in a mixture together with Desisopropyl-atrazine; Deethyl-atrazine, Simazine, Atrazine, Dimethenamid. It is therefore not possible to define the effects of metolachlor on these algal species from this study.
CA 8.2.6.1	Vogwill, T., Lagator, M., Colegrave, N., Neve, P.	2012	The experimental evolution of herbicide resistance in *Chlamydomonas reinhardtii* results in a positive correlation between fitness in the presence and absence of herbicides	Journal of Evolutionary Biology (2012), 25 (10), 1955-1964. ISSN: 1010-061X	Not relevant as 'fitness' of algae exposed to S-metolachlor for several generations was compared to 'fitness' of algae which had no previous exposure. Also, there was no mention of concentrations of S-metolachlor used

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.6.2	Hu, X.-N., Zhang, S.-X., Chen, C.-D., Liu, H.-J,.	2014	Influence of the coexistence of Zn2+ on the enantioselective toxicity of metolachlor to *Scenedesmus obliquus*.	Huan jing ke xue= Huanjing kexue / [bian ji, Zhongguo ke xue yuan huan jing ke xue wei yuan hui "Huan jing ke xue" bian ji wei yuan hui.], (2014 Jan) Vol. 35, No. 1, pp. 292-8. Journal code: 8405344. ISSN: 0250-3301. L-ISSN: 0250-3301.	English version of publication unavailable; English abstract provided enough information to confirm relevance. Does not fulfil criteria 5 (several doses tested, at least 3, including a negative control, to establish a dose response. The enantioselective toxicity of Rac-, S-metolachlor alone was included in a test *Scenedesmus obliquus*. Only one rate was tested at 0.30 mg/L Rac- and S-metolachlor, resulting in 24 h inhibition rates of 49.6% and 59.7%, respectively.
CA 8.2.4.1 & algae CA 8.2.6.1	Kyriakopoulou, K., Anastasiadou, P., Machera, K.	2009	Comparative Toxicities of Fungicide and Herbicide Formulations on Freshwater and Marine Species	Bulletin of Environmental Contamination and Toxicology (2009), 82 (3), 290-295. CODEN: BECTA6; ISSN: 0007-4861	Does not fulfil criteria 8 (effects are not related to a single test item). Not relevant as S-metolachlor was tested in a mixture with terbuthylazine.
CA 8.2.6.2	Roubeix, V., Fauvelle, V., Tison-Rosebery, J., Mazzella, N., Coste M., Delmas F.	2012	Assessing the impact of chloroacetanilide herbicides and their metabolites on periphyton in the Leyre River (SW France) via short term growth inhibition tests on autochthonous diatoms.	Journal of environmental monitoring : JEM, (2012 May) Vol. 14, No. 6, pp. 1655-63. Journal code: 100968688. E-ISSN: 1464-0333. L-ISSN: 1464-0325.	Does not fulfil criteria 4 (test organisms are not previously exposed to the test item or other contaminants. The algae in the test were taken from rocks at sites in the Leyre River is the major tributary to the Bassin d'Arcachon (lagoon, SW French Atlantic coast). Area of maize cultivation and metolachlor and acetochlor have been found in the river. The 96 h EC_{50}s from this study were 18 to 21 mg/L for the standard laboratory test with *Nitzschia nana*. Therefore the test organisms are likely to be previously exposed to these or other contaminants; therefore it was not considered to be relevant for this review.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.6.2	Roubeix, V., Mazzella, N., Mechin, B., Coste, M., Delmas, F.	2011	Impact of the herbicide metolachlor on river periphytic diatoms: experimental comparison of descriptors at different biological organization levels.	Annales de Limnologie - International Journal of Limnology (2011) Volume 47, Number 3, pp. 239-249, 46 refs. ISSN: 0003-4088. DOI: 10.1051/limn/2011009	Does not fulfil criteria 4 (test organisms are not previously exposed to the test item or other contaminants. Two week microcosm test in which naturally derived diatom communities were exposed to two concentrations of metolachlor. Monospecific tests were also conducted. For these two species of diatom were exposed to different concs of metolachlor. EC_{50} values were 2.96 and 1.88 mg/L for *Surirella angusta* and *Achnathidium minutissimum*, respectively. The diatoms from 3 rivers in SW France (the Ge`ze, Sousson and Save, “Coteaux de Gascogne”) with different exposures to agricultural pollution. Therefore the test organisms are likely to be previously exposed to these or other contaminants; therefore it was not considered to be relevant for this review.
CA 8.2.6.2	Debenest, T., Pinelli, E., Coste, M., Silvestre, J., Mazzella, N., Madigou, C., Delmas, F.	2009	Sensitivity of freshwater periphytic diatoms to agricultural herbicides.	Aquatic toxicology (Amsterdam, Netherlands), (2009 Jun 4) Vol. 93, No. 1, pp. 11-7. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X	Does not fulfil criteria 4 (test organisms are not previously exposed to the test item or other contaminants. Diatoms were collected from the river Save. This site reportedly contained low concentrations of herbicides (≈0.2 µg/L). These herbicides were not quantified and therefore pre-exposure to S-metolachlor cannot be excluded.
CA 8.2.6.2	Sangwan, M., Wei, L.	2008	Effect of herbicide metolachlor on brown tide alga *Aureococcus anophagefferens* growth and detoxification.	Abstracts of Papers American Chemical Society, (AUG 17 2008) Vol. 236, pp. 122-ENVR. Meeting Info.: 236th National Meeting of the American-Chemical-Society. Philadelphia, PA, USA. August 17 - 21, 2008. CODEN: ACSRAL. ISSN: 0065-7727.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.6.2	Rea, G., Polticelli, F., Antonacci, A., Scognamiglio, V., Katiyar, P., Kulkarni, S.A., Johanningmeier, U., Giardi, M.T.	2009	Structure-based design of novel *Chlamydomonas reinhardtii* D1-D2 photosynthetic proteins for herbicide monitoring	Protein Science (2009), 18 (10), 2139-2151. CODEN: PRCIEI; ISSN: 1469-896X	Not relevant as atrazine is the subject of the research plus an in-silico evaluation of protein binding is the subject matter.
CA 8.2.6.2	Ishihara, S., Horio, T., Kobara, Y., Yokoyama, A.	2006	Evaluation of herbicide effects on micro algal cells by flow cytometric analysis	Zasso Kenkyu (2006), 51 (4), 239-248. CODEN: ZASKAN; ISSN: 0372-798X	English version of publication unavailable; end; English abstract only available. Translation acquired. Does not fulfil criteria 5 (several doses tested, at least 3, including a negative control, to establish a dose response. Metolachlor was tested with *Pseudokirchneriella subcapitata*, *Achnanthidium minutissimum* (diatom) and *Merismopedia tenuissima* (blue green alga). 72h growth inhibition rate at 10 mg/L is *P. subcapitata*; = 80%; *M. tenuissima*; = <19%; *A. minutissimum*; = 60-70% As the test was conducted only at 10 mg/L no EC_{50} endpoints could be calculated. Therefore this reference is not relevant for this review.
CA 8.2.6.2	Zablotowicz, R.M., Locke, M.A., Lerch, R.N., Knight, S.S.	2004	Dynamics of herbicide concentrations in Mississippi Delta Oxbow Lakes and the role of planktonic microorganisms in herbicide metabolism	ACS Symposium Series (2004), 877 (Water Quality Assessments in the Mississippi Delta), 134-149. CODEN: ACSMC8; ISSN: 0097-6156	Does not fulfil criteria 8 (effects are not related to a single test item). Effects of watershed management and cropping practices were evaluated on the dynamics of herbicide concentrations and planktonic populations. Cotton is cultivated in this area (approx.50% of the area of 3 watersheds). Concentrations of fluometuron, the metabolite desmethyl fluometuron, atrazine and metolachlor were observed. Differences in planktonic populations and activity were observed among the lakes. Therefore the effects relating to metolachlor are not clear, so this reference is not relevant for this review.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.2.7	Brain, R.A., Hoberg, J. Hosmer, A.J., Wall, S.B.	2012	Influence of light intensity on the toxicity of atrazine to the submerged freshwater aquatic macrophyte *Elodea canadensis*	Ecotoxicology and Environmental Safety, (1 May 2012) Vol. 79, pp. 55-61. ISSN: 0147-6513.	Paper focused on atrazine. No data generated on S-metolachlor or metolachlor.
CA 8.2.7	Fulton, B., Brain, R., Brooks, B.	2007	Responses of *Lemna gibba* Exposed to an Equitoxic Mixture of Triclosan and Metolachlor Across a Range of Nitrogen and Phosphorous Ratios.	Conference: 28th Annual Meeting of the Society of Environmental Toxicology and Chemistry North America, Midwest Express Center, Milwaukee, Wisconsin (USA), 11 Nov 2007- 15 Nov 2007. Sponsor(s): The Society of Environmental Toxicology and Chemistry (SETAC)	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.7	Fulton, B., Brain, R.A., Belden, J.B., Brooks, B.W.	2007	Individual and Combined Effects of Triclosan and Metolachlor on *Lemna Gibba*	Conference: 2007 Summer Speciality Conference of the American Water Resources Association (AWRA 2007), Vail Cascade Resort, Vail, Colorado (USA), 25 Feb 2007 - 27 Feb 2007. Sponsor(s): American Water Resources Association	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.2.7 CA 8.6	Cedergreen N., Spliid, N.H., Streibig, J.C.	2004	Species-specific sensitivity of aquatic macrophytes towards two herbicide	Ecotoxicology and Environmental Safety, (Jul 2004) Vol. 58, No. 3, pp. 314-323. ISSN: 0147-6513.	No data generated on S-metolachlor or metolachlor.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.3.1	Genersch, E., von der Ohe, W., Kaatz, H., Schroeder, A., Otten, C., Buechler, R., Berg, S., Ritter, W., Muehlen, W., Gisder, S., Meixner, M., Liebig, G., Rosenkranz, P.	2010	The German bee monitoring project: a long term study to understand periodically high winter losses of honey bee colonies	Apidologie (2010), 41 (3), 332-352. CODEN: APDGB5; ISSN: 0044-8435	Does not fulfil criteria 8 (effects are not related to a single test item). This research involved monitoring bee colonies over a four-year period. Disease, pest and pesticide residues were measured. Metolachlor was found in a small number of pollen samples. As it is difficult to isolate the effects relating solely to metolachlor this reference is not relevant for this review.
CA 8.3.2	Lim, U.T., Mahmoud, A.M.A.	2007	Pesticide susceptibility of *Trissolcus nigripedius* (Hymenoptera:Scelionidae) an egg parasitoid of *Dolycoris baccarum* (Heteroptera:Pentatomidae)	Entomological Research, (AUG 2007) Vol. 37, No. Suppl. 1, pp. A140. Meeting Info.: International Congress of Insect Biotechnology and Industry. Daegu, SOUTH KOREA. August 19-24, 2007. ISSN: 1738-2297.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.3.2	Griggs, J.L., Belden, L.K.	2005	Decreased survival of trematode cercariae *Echinostoma trivolvis* following atrazine and metolachlor exposure.	Integrative and Comparative Biology, (DEC 2005) Vol. 45, No. 6, pp. 1140. Meeting Info.: Annual Meeting of the Society-for-Integrative-and-Comparative-Biology. Orlando, FL, USA. January 04-08, 2006. ISSN: 1540-7063.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.3.2	You, W.-Y., Chen, X.-F., Song, M., Wang, C.-J.	2010	Toxicity Evaluation of Sixteen Herbicides to *Bombyx mori*.	Asian Journal of Ecotoxicology, (FEB 2010) Vol. 5, No. 1, pp. 91-94. ISSN: 1673-5897.	English version of publication unavailable; English abstract available. The acute toxicity of sixteen herbicides to silkworm (*Bombyx mori*) was evaluated in laboratory using food intake method. Results indicated that the 96h LC_{50} of the other thirteen herbicides (*including metolachlor (720 g/L EC formulation)* was higher than 200 mg/kg (mulberry leaf) (i.e. low toxicity substance). The results are difficult to put into context as units are expressed in mg/kg of mulberry leaf. As the silkworm does not appear sensitive; this reference provides nothing to contradict the current regulatory data in terms of toxicity it would be a relevant category of ‘c’ or ‘b’ at the best. It has been considered to be none relevant as the units presented cannot be directly compared to the regulatory data or used in the risk assessment.
CA 8.3.2	Liu, H.-J., Zhan, X.-M., Liu, W.	2005	Ecotoxicological difference of chiral pesticides: effects of metolachlor and S-metolachlor on some enzyme activities of silkworm, *Bombyx mori* L.	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2005), 45 (1), 497-500. CODEN: PEACF2; ISSN: 1524-6434	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.4.1	Iordache, M., Borza, I.	2011	Study of the acute toxicity of some Pesticides on earthworms *Eisenia fetida* (Savigny, 1826).	Research Journal of agricultural science, 43(4), pp. 95-100, 15 refs. ISSN: 2066-1843.	Acute exposure and therefore is no longer a data point of relevance. Does not fulfil criteria 8 (effects are not related to a single test item). Gardoprim Plus Gold 500 SC formulation was tested which contains both terbuthylazine and S-metolachlor.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.4	Kamionek, M., Jarmul, J., Pezowicz, E.	2005	Effect of herbicides on *Enchytraeus* sp. (Annelida: Oligochaeta)	Ecological Chemistry and Engineering (2005), 12 (8), 811-816. CODEN: ECECBJ	Does not fulfil criteria 5 (several doses tested, at least 3, including a negative control, to establish a dose response, unless the study design is specifically a limit test. Control must be run concurrently with treatments and mortality to be within the test validity criteria). *Enchytraeus sp.* were sprayed with an unspecified amount of a metolachlor formulation. As there was only 1 test dose and the actual amount used is not clear the data in this paper are considered to be not relevant.
CA 8.4	Kamionek, M., Pezowicz, E., Jarmul, J., Poleszczuk, O.	2005	Effect of herbicides on earthworms *Lumbricus terrestris* L. (Oligochaeta: Lumbricidae)	Ecological Chemistry and Engineering (2005), 12 (10), 1089-1094. CODEN: ECECBJ	Not obtainable at time of submission due to copyright delays. Cannot ascertain if this is relevant.
CA 8.4.1	Xu, D.-M., Xu, X.-L., Liu, W.-L., Liu, W.-P.	2009	Acute toxicity difference of metolachlor and its S-isomer on earthworms	Zhongguo Huanjing Kexue (2009), 29 (9), 1000-1004. CODEN: ZHKEEI; ISSN: 1000-6923	English version of publication unavailable; an English abstract is available. The acute lethal effect of metolachlor and its S-isomer on earthworms with the chiral difference was analysed by using the methods of standard OECD filter paper test, artificial soil test and natural soil test. The acute toxicity of Rac-metolachlor and S-isomer on earthworms in the natural soil test was larger than that in the artificial soil test. There were little differences in LC_{50} of Rac-metolachlor and S-isomer on earthworms, therefore the chiral differences on acute toxicity of earthworms were insignificant. This same group published a similarly named paper 2010 (see Ref ID 75 in Table 9.6-2). It is therefore not considered necessary to translate this paper.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.4.1	Wang, Y., Yu, W., Yang, L., Cang, T., Yu R., Wang, Q., Zhao, X.	2012	Acute Toxicity of Twenty-Two Commonly Used Herbicides to Earthworm (*Eisenia fetida*).	Asian Journal of Ecotoxicology, (JUN 2012) Vol. 7, No. 3, pp. 317-325. ISSN: 1673-5897.	English version of publication unavailable. Abstract only available. The 48-h filter paper contact test for S-metolachlor was moderately toxic to *E. fetida* with an LC_{50} value within the range of 10 (8.3-12) to 35 (29-44) µg/cm^2. The 14-d LC_{50} value (artificial soil) for S-metolachlor was within the range of 107 (84-123) to 5162 (367-1015) mg/kg ~ range for 16 herbicides (all categorised a low toxicity). The latter range in the study from the 14d test is comparable with SYN data where the S-metolachlor EU endpoint is 570 mg/kg. This is in the middle of the stated results range. So the result is either 5 fold below or 2 fold above the SYN endpoint. Either way it is close and indicates low toxicity to earthworms. As acute toxicity to earthworms is not part of the risk assessment framework a closer examination is not considered necessary, and it has been regarded as non-relevant for this review.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.4.1	Liu, W., Xu, D., Liu, H., Liu, G.	2007	Effects of metolachlor on the weight and enzyme activities of earthworms	Huanjing Kexue Xuebao (2007), 27 (12), 2025-2031. CODEN: HKXUDL; ISSN: 0253-2468	English version of publication unavailable; English abstract available. The natural soil test method was used to study the effects of metolachlor on the weight and enzyme activities of earthworms (*Eisenia foetida*). The activities of cellulase, superoxide dismutase (SOD), catalase (CAT), and peroxidase (POD) were measured. The weight and cellulase activity of earthworms were inhibited after exposure to metolachlor. The activities of SOD, CAT, and POD of the earthworm showed different responses to metolachlor, in the sensitivity order CAT > POD > SOD. The weight, cellulase activity, and CAT activity were significantly affected by metolachlor concentration, and all parameters were significantly affected by the duration of exposure. The interaction exposure concentration and duration had significant effects on the activities of CAT and POD but had little effect on the weight and the activities of cellulase and SOD. As the doses cannot be confirmed from the abstract, this has been considered as not relevant for this review. There is ample regulatory and other literary references for this species, none of which indicate that worms would drive the risk assessment.
CA 8.5	Ayansina, A.D.V., Oso, B.A.	2006	Effect of two commonly used herbicides on soil microflora at two different concentrations.	African Journal of Biotechnology (2006) Volume 5, Number 2, pp. 129-132, 10 refs. ISSN: 1684-5615	Does not fulfil criteria 8 (effects are not related to a single test item). Field collected soil was treated with atrazine solo and Primextra (metolachlor + atrazine). Bacterial and fungal counts were conducted for 8 weeks. Effects were related to a mixture of atrazine and metolachlor so therefore this research is not relevant.
CA 8.5	Zhao , S., Arthur, E.L., Moorman, T.B., Coats, J.R.	2005	Evaluation of microbial inoculation and vegetation to enhance the dissipation of atrazine and metolachlor in soil.	Environmental toxicology and chemistry / SETAC, (2005 Oct) Vol. 24, No. 10, pp. 2428-34. Journal code: 8308958. ISSN: 0730-7268. L-ISSN: 0730-7268.	Reference focus is on bioremediation. Not relevant to the risk assessment.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.5	Chen, Bo., Xu, D., Wu, J., Liu, G., Liu, W.	2006	Effect of metolachlor on soil microbial numbers in rhizosphere and its degradation	Nongye Huanjing Kexue Xuebao (2006), 25 (4), 898-902. CODEN: NHKXA7; ISSN: 1672-2043	English version of publication unavailable; English abstract available. The effect of metolachlor on microbial nos. and its degradation in celery rhizosphere and non-rhizosphere soil were studied with rhizobag technique. The results showed that bacterial nos. were inhibited by metolachlor initially, but increased after 7 d. Fungi nos. were stimulated by metolachlor, and the higher the metolachlor concentration the greater the influence, which indicated that fungi could utilize metolachlor as carbon and energy sources. The results indicated that degradation of metolachlor was stimulated by plant roots in rhizosphere. Plants and their associated rhizosphere microorganisms could be a good method for bioremediation of soils contaminated with organic pollutants. This is not relevant as the focus is on bioremediation.
CA 8.5	Liu, H, Zhan, X., Liu, W., Liu, H.J., Zhan, X.M., Liu, W.P.	2006	Effect of Rac-metolachlor and S-isomer on soil microbial biomass carbon and nitrogen.	Acta Pedologica Sinica (2006) Volume 43, Number 5, pp. 875-878, 11 refs. ISSN: 0564-3929	English version of publication unavailable; English abstract available which contains no detail. Not an area which drives the risk assessment position therefore this reference has not yet been considered.
CA 8.5	Martins, P.F., Carvalho, G., Gratao, P.L., Dourado, M.N., Pileggi, M., Araujo, W.L., Azevedo, R.A.	2011	Effects of the herbicides acetochlor and metolachlor on antioxidant enzymes in soil bacteria	Process Biochemistry, Vol. 46, no. 5, pp. 1186-1195, May 2011. ISSN: 1359-5113.	Does not fulfil criteria 4 (test organisms are not previously exposed to the test material or other contaminants). Microorganisms were isolated from soil which had been collected from a farm with known history over the previous two years of acetochlor and metolachlor use. This is therefore not relevant for this review.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.5	Martins, P.F., Martinez, C.O., Carvalho, G.de., Carneiro, P.I.B., Azevedo, R.A., Pileggi, S.A.V., Melo, I.S.de., Pileggi, M., de Carvalho, G., de Melo, I.S.	2007	Selection of microorganisms degrading S-metolachlor herbicide.	Brazilian Archives of Biology and Technology (2007) Volume 50, Number 1, pp. 153-159, 27 refs. ISSN: 1516-8913	Focus is on bioremediation hence not relevant.
CA 8.5	Zhou, Y., Liu, W., Wang, T.	2005	Effects of pesticides metolachlor and S-metolachlor on soil microorganisms in aquisols of Southern China. I. Catalase activity.	Ying yong sheng tai xue bao = The journal of applied ecology / Zhongguo sheng tai xue xue hui, Zhongguo ke xue yuan Shenyang ying yong sheng tai yan jiu suo zhu ban, (2005 May) Vol. 16, No. 5, pp. 895-8. Journal code: 9425159. ISSN: 1001-9332. L-ISSN: 1001-9332.	English version of publication unavailable; English abstract available. The effects of 0, 5, 20, and 100 mg/kg metolachlor and S-metolachlor (Dual Gold) were conducted on soil catalase activity. The results showed that 20 mg/kg metolachlor had the most successive stimulating effect; 5 mg/kg metolachlor had an inhibitory effect in the early period, while 100 mg/kg metolachlor had a stimulating effect in the late period. Different concentrations Dual Gold displayed a tendency stimulation-inhibition-stimulation. 5 and 100 mg/kg metolachlor might have more damage on soil ecosystem than different concentrations Dual Gold. The PECs of interest in the dossier are 2.22 mg/kg for the formulation A9396G and 1.92 mg/kg for S-metolachlor. Therefore this study is looking at PECs values much higher than this therefore the results are not relevant for application rates of 1.44 g a.s. /ha.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.5	Zhou, Y., Liu, W., Ye, H.	2006	Effects of pesticides metolachlor and S-metolachlor on soil microorganisms in aquisols. II. Soil respiration.	Ying yong sheng tai xue bao = The journal of applied ecology / Zhongguo sheng tai xue xue hui, Zhongguo ke xue yuan Shenyang ying yong sheng tai yan jiu suo zhu ban, (2006 Jul) Vol. 17, No. 7, pp. 1305-9. Journal code: 9425159. ISSN: 1001-9332. L-ISSN: 1001-9332.	English version of publication unavailable; English abstract available. Soil microbial respiration was tested at 0, 5, 20, and 100 mg/kg of metolachlor and S-metolachlor (Dual Gold). There was a significant difference in soil microbial respiration between treated and blank soil at the beginning of incubation, but no significant difference was observed during the later period. The PECs of interest in the dossier are 2.22 mg/kg for the formulation A9396G and 1.92 mg/kg for S-metolachlor. Therefore this study is looking at PECs values much higher than this therefore the results are not relevant for application rates of 1.44 g a.s./ha.
CA 8.5	Hou, Y., Xu, J.-Q., Meng, X.-L., Zhang, K., Yang, G.-F.	2013	Effects of nine herbicides on mycelial growth of *Rhizoctonia cerealis*	Mailei Zuowu Xuebao (2013), 33 (6), 1289-1293. CODEN: MZXAAG; ISSN: 1009-1041	English version of publication unavailable; English abstract available. The effects of metolachlor on the mycelial growth of *Rhizoctonia cerealis* were studied. The results showed that metolachlor inhibited mycelial growth and the EC_{50} was 56 mg/L. The amides herbicides changed the colony characteristics. *Rhizoctonia cerealis* is a fungal pathogen of turf so it relevance to corn is not known. The units of inhibition in mg/L are not easily applicable to the risk assessment which would require mg/kg, therefore it has been considered not relevant as there is much data on metolachlor (regulatory and literature which confirms that this area does not drive the risk assessment position.
CA 8.6	Moore, M. T., Krger, R.	2010	Effect of three insecticides and two herbicides on rice (*Oryza sativa*) seedling germination and growth.	Archives of Environmental Contamination and Toxicology (2010) Volume 59, Number 4, pp. 574-581, 53 refs. ISSN: 0090-4341	Does not fulfil criteria 8 (effects are not related to a single test item). Bicep tested (mixture of metolachlor and atrazine).
CA 8.6	Geier, P.W., Stahlman, P.W., Regehr, D.L., Olson, B.L.	2009	Pre-emergence Herbicide Efficacy and Phytotoxicity in Grain Sorghum	Weed technology (2009), Volume 23, Number 2, pp. 197-201. ISSN: 0890-037X	Reference is not relevant as refers to efficacy,

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.6	Whaley, C.M., Armel, G.R., Wilson, H.P., Hines, T.E.	2009	Evaluation of S-Metolachlor and S-Metolachlor Plus Atrazine Mixtures with Mesotrione for Broadleaf Weed Control in Corn	Weed technology (2009), Volume 23, Number 2, pp. 193-196. ISSN: 0890-037X	Does not fulfil criteria 8 (effects are not related to a single test item). Paper evaluates mesotrione efficacy so it is not relevant as have been mixtures tested.
CA 8.6	Bollman, S.L.,; Sprague, . L.	2007	Response of four commercial sugar beet varieties to s-metolachlor and dimethenamid-P.	Proceedings from the biennial meeting (2007), Number 34, 108 p.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.6	Swanton, C.J., Gulden, R.H., Chandler, K.	2007	A Rationale for Atrazine Stewardship in Corn	Weed science (2007), Volume 55, Number 1, pp. 75-81. ISSN: 0043-1745	Reference is not relevant as refers to efficacy.
CA 8.6	Guza, C.J., Stewart, J.F., Hubbell, L.A.	2007	*Beta vulgaris* response to amide herbicides.	Proceedings from the ... biennial meeting (2007), Number 34, 60 p.	Reference is not relevant as refers to efficacy. Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.6	Chindo, P.S., Shebayan, J.A.Y., Marley, P.S.	2010	Effect of pre-emergence herbicides on *Meloidogyne* spp. and *Fusarium* wilt of tomato in Samaru, Zaria, Nigeria.	Journal of Agricultural Research (Lahore) (2010), Volume 48, Number 4, pp. 489-495, 20 refs. ISSN: 0368-1157	Does not fulfil criteria 8 (effects are not related to a single test item). Codal (metolachlor and prometryne) was tested.
CA 8.6	Moore, J.H., Ryder, A., Master, R., Editor(s): Zydenbos, S.M.	2010	Herbicide tolerance of five young perennial grasses.	17th Australasian weeds conference. New frontiers in New Zealand: together we can beat the weeds. Christchurch, New Zealand, 26-30 September, 2010 (2010), pp. 402-405, 3 refs.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.6	Nagy, L. Editor(s): David, I., Koevics, G.J.	2008	Morphological changes of bird seed (*Phalaris canariensis* L.) by the pre-post herbicides treatments.	13. Tiszantuli Noevenyvedelmi Forum, 15-16 October 2008, Debrecen, Hungary (2008), pp. 175-179, 7 refs.	Only an abstract published from a conference; therefore, not peer reviewed and not significantly detailed for assessment.
CA 8.6	Rankova, Z.	2006	Effect of some soil herbicides on the vegetative habits of walnut seedlings (*Juglans regia* L	Acta Agriculturae Serbica (2006), Volume 22, pp. 63-68, 6 refs. ISSN: 0354-9542	Dosing is unclear (150mL/da) and one treatment rate was used. Results therefore cannot be interpreted or compared with Syngenta data.

CA data point number	Author(s)	Year	Title	Source	Reason(s) for not including the study in the dossier
CA 8.6	Soltani, N., Bowley, S., Sikkema, P.H.	2005	Responses of black and cranberry beans (Phaseolus vulgaris) to post-emergence herbicides	CROP PROTECTION, (JAN 2005) Vol. 24, No. 1, pp. 15-21. ISSN: 0261-2194.	Not relevant as metolachlor and S-metolachlor were not evaluated.

All documents listed in Table 9.6-2 and not excluded (i.e. not listed in Table 9.6-4) are given below.

Table 9.6-5: List of references which are discussed further (listed by data point number)

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 8.1.4 CA 8.2.1 CA 8.2.4.1 CA 8.2.4.2	Wan, M. T., Buday, C., Schroeder, G., Kuo, J., Pasternak, J.	2006	Toxicity to *Daphnia magna*, *Hyalella azteca*, *Oncorhynchus kisutch*, *Oncorhynchus mykiss*, *Oncorhynchus tshawytscha* and *Rana catesbeiana* of atrazine, metolachlor, simazine, and their formulated products.	Bulletin of Environmental Contamination and Toxicology (2006) Volume 76, Number 1, pp. 52-58, 9 refs. ISSN: 0007-4861. DOI: 10.1007/s00128-005-0888-4	EU038
CA 8.1.4	Spolyarich N., Hyne, R., Wilson S., Palmer C., Byrne M.	2010	Growth, development and sex ratios of Spotted Marsh Frog (*Limnodynastes tasmaniensis*) larvae exposed to atrazine and a herbicide mixture.	Chemosphere, (2010 Feb) Vol. 78, No. 7, pp. 807-13. Electronic Publication Date: 30 Dec 2009. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535.	EU035
CA 8.1.4	Williams, B.K., Semlitsch, R.D.	2010	Larval responses of three Midwestern anurans to chronic, low-dose exposures of four herbicides.	Arch. Environ. Contam. Toxicol. (2010) 58, 819-827.	EU036
CA 8.1.4	Jin, Y., Chen, R., Wang, L., Liu, J., Yang, Y., Zhou, C., Liu, W., Fu, Z	2011	Effects of metolachlor on transcription of thyroid system-related genes in juvenile and adult Japanese medaka (*Oryzias latipes*)	General and Comparative Endocrinology, 170:487-493	EU037
CA8.1.4 CA 8.5	Papaefthimiou, C., Cabral, M. de G., Mixailidou, C., Viegas, C.A., Sa-Correia, I., Theophilidis, G.	2004	Comparison of two screening bioassays, based on the frog sciatic nerve and yeast cells, for the assessment of herbicide toxicity.	Environmental toxicology and chemistry / SETAC, (2004 May) Vol. 23, No. 5, pp. 1211-8. Journal code: 8308958. ISSN: 0730-7268. L-ISSN: 0730-7268.	EU091
CA 8.2	Hayes, T.B., Case, P., Chui, S., Chung D., Haeffele, C., Haston, K., Lee, M., Mai, V.P,., Marjuoa, Y., Parker, J., Tsui, M.	2006	Pesticide mixtures, endocrine disruption, and amphibian declines: are we underestimating the impact?	Environmental health perspectives, (2006 Apr) Vol. 114 Suppl 1, pp. 40-50. Journal code: 0330411. ISSN: 0091-6765. Report No.: NLM-PMC1874187.	EU039
CA 8.2.2.1	Padilla, S., Corum, D., Padnos, B., Hunter, D. L., Beam, A.; Houck, K.A., Sipes, N., Kleinstreuer, N., Knudsen, T., Dix, D.J., Reif, D.M.	2012	Zebrafish developmental screening of the ToxCast Phase I chemical library	Reproductive Toxicology (2012), 33 (2), 174-187. CODEN: REPTED; ISSN: 0890-6238	EU040

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 8.2.5.1	Liu, H.J., Ye, W.H., Zhan, X.M., Liu, W.P.	2006	A comparative study of rac- and S-metolachlor toxicity to *Daphnia magna*	Ecotoxicology and Environmental Safety (2006) Volume 63, Number 3, pp. 451-455, 25 refs. ISSN: 0147-6513. DOI: 10.1016/j.ecoenv.2005.02.002	EU041
CA 8.2.5.2	Cook, M.E., Moore, P.A.	2008	The effects of the herbicide metolachlor on agonistic behavior in the crayfish, *Orconectes rusticus*.	Archives of environmental contamination and toxicology, (2008 Jul) Vol. 55, No. 1, pp. 94-102. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.	EU042
CA 8.2.5.2	Gagnaire, B., Thomas-Guyon, H., Burgeot, Th., Renault, T.	2006	Pollutant effects on Pacific oyster, *Crassostrea gigas* (Thunberg), hemocytes: Screening of 23 molecules using flow cytometry.	Cell Biology and Toxicology (2006), 22 (1), 1-14. CODEN: CBTOE2; ISSN: 0742-2091	EU043
CA 8.2.5.4	Jin-Clark, Y., Anderson, T.D., Zhu, K.Y.	2008	Effect of alachlor and metolachlor on toxicity of chlorpyrifos and major detoxification enzymes in the aquatic midge, *Chironomus tentans* (Diptera: Chironomidae).	Archives of environmental contamination and toxicology, (2008 May) Vol. 54, No. 4, pp. 645-52. Journal code: 0357245. E-ISSN: 1432-0703. L-ISSN: 0090-4341.	EU044
CA 8.2.5.4	Perez, J., Monteiro, M.S., Quintaneiro C., Soares, A.M.V.M., Loureiro, S.	2013	Characterization of cholinesterases in *Chironomus riparius* and the effects of three herbicides on chlorpyrifos toxicity.	Aquatic toxicology (Amsterdam, Netherlands), (2013 Nov 15) Vol. 144-145, pp. 296-302. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.	EU045
CA 8.2.6.1	Fischer, B. B.; Roffler, S.; Eggen, R. I. L.	2012	Multiple stressor effects of predation by rotifers and herbicide pollution on different *Chlamydomonas* strains and potential impacts on population dynamics.	Environmental Toxicology and Chemistry (2012) Volume 31, Number 12, pp. 2832-2840, 43 refs. ISSN: 0730-7268. DOI: 10.1002/etc.2010	EU046
CA 8.2.6.1	Cai, W,-D., Liu H.-J., Fang Z.-G.	2012	Toxicity effects of Rac- and S-metolachlor on two algaes.	Huan jing ke xue= Huanjing kexue / [bian ji, Zhongguo ke xue yuan huan jing ke xue wei yuan hui "Huan jing ke xue" bian ji wei yuan hui.], (2012 Feb) Vol. 33, No. 2, pp. 448-53. Journal code: 8405344. ISSN: 0250-3301. L-ISSN: 0250-3301.	EU047
CA 8.2.6.1	Liu, H.J., Cai, W.D., Huang, R.N., Xia, H.L., Wen, Y.Z.	2012	Enantioselective toxicity of metolachlor to *Scenedesmus obliquus* in the presence of cyclodextrins.	Chirality, (2012 Feb) Vol. 24, No. 2, pp. 181-7. Electronic Publication: 2011-12-19. Journal code: 8914261. E-ISSN: 1520-636X. L-ISSN: 0899-0042.	EU048
CA 8.2.6.1	Liu, H., Xiong, M.	2009	Comparative toxicity of racemic metolachlor and S-metolachlor to *Chlorella pyrenoidosa*.	Aquatic toxicology (Amsterdam, Netherlands), (2009 Jun 28) Vol. 93, No. 2-3, pp. 100-6. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.	EU049

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 8.2.6.2	Spoljaric, D., Cipak, A., Horvatic, J., Andrisic, L., Waeg, G., Zarkovic, N., Jaganjac, M.	2011	Endogenous 4-hydroxy-2-nonenal in microalga *Chlorella kessleri* acts as a bioactive indicator of pollution with common herbicides and growth regulating factor of hormesis.	Aquatic toxicology (Amsterdam, Netherlands), (2011 Oct) Vol. 105, No. 3-4, pp. 552-8. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.	EU057
CA 8.2.6.1	Vallotton, N., Moser, D., Eggen R.I.L., Junghans, M., Chevre, N.	2008	S-metolachlor pulse exposure on the alga *Scenedesmus vacuolatus*: effects during exposure and the subsequent recovery.	Chemosphere, (2008 Sep) Vol. 73, No. 3, pp. 395-400. Electronic Publication: 2008-07-07. Journal code: 0320657. ISSN: 0045-6535. L-ISSN: 0045-6535.	EU050
CA 8.2.6.1	Deng, L., Senseman, S.A., Gentry, T.J., Zuberer, D.A., Weiss, T.L., Devarenne, T.P., Camargo, E.R.	2012	Effect of selected herbicides on growth and hydrocarbon content of *Botryococcus braunii* (Race B)	Industrial Crops and Products (2012), 39, 154-161. CODEN: ICRDEW; ISSN: 0926-6690	EU051
CA 8.2.6.1	Sbrilli, G., Bimbi, B., Cioni, F., Pagliai, L., Luchi, F., Lanciotti, E.	2005	Surface and ground waters characterization in Tuscany (Italy) by using algal bioassay and pesticide determinations: comparative evaluation of the results and hazard assessment of the pesticides impact on primary productivity	Chemosphere (2005), 58 (5), 571-578. CODEN: CMSHAF; ISSN: 0045-6535	EU052
CA 8.2.6.1	Perez, J., Domingues, I., Soares, A.M.V.M., Loureiro, S.	2011	Growth rate of *Pseudokirchneriella subcapitata* exposed to herbicides found in surface waters in the Alqueva reservoir (Portugal): a bottom-up approach using binary mixtures.	Ecotoxicology (London, England), (2011 Aug) Vol. 20, No. 6, pp. 1167-75. Journal code: 9885956. E-ISSN: 1573-3017. L-ISSN: 0963-9292.	EU053
CA 8.2.6.1	Ma, J., Wang, S., Wang, P., Ma, L., Chen, X., Xu, R.	2006	Toxicity assessment of 40 herbicides to the green alga *Raphidocelis subcapitata*	Ecotoxicology and Environmental Safety (2006), 63 (3), 456-462. CODEN: EESADV; ISSN: 0147-6513	EU054
CA 8.2.6.1 CA 8.2.6.2	Ebenezer, V., Ki, J.-S.	2013	Quantification of toxic effects of the herbicide metolachlor on marine microalgae *Ditylum brightwellii* (Bacillariophyceae), *Prorocentrum minimum* (Dinophyceae), and *Tetraselmis suecica* (Chlorophyceae).	Journal of microbiology (Seoul, Korea), (2013 Feb) Vol. 51, No. 1, pp. 136-9. Journal code: 9703165. E-ISSN: 1976-3794. L-ISSN: 1225-8873.	EU055
CA 8.2.6.1 CA 8.2.6.2	Thakkar, M., Randhawa, V., Wei, L.	2013	Comparative responses of two species of marine phytoplankton to metolachlor exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2013 Jan 15) Vol. 126, pp. 198-206. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X.	EU056
CA 8.2.6.2	Fiori E., Pistocchi R.	2014	*Skeletonema marinoi* (Bacillariophyceae) sensitivity to herbicides and effects of temperature increase on cellular responses to terbuthylazine exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Feb) Vol. 147, pp. 112-20. Journal code: 8500246. E-ISSN: 1879-1514. L-ISSN: 0166-445X	EU058

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 8.2.6.2	Larras, F., Bouchez, A., Rimet, F., Montuelle, B.	2012	Using bioassays and species sensitivity distributions to assess herbicide toxicity towards benthic diatoms.	PloS one, (2012) Vol. 7, No. 8, pp. e44458. Electronic Publication: 2012-08-30.	EU059
CA 8.2.6.2	Larras, F., Montuelle, B., Bouchez, A.	2013	Assessment of toxicity thresholds in aquatic environments: does benthic growth of diatoms affect their exposure and sensitivity to herbicides?	The Science of the total environment, (2013 Oct 1) Vol. 463-464, pp. 469-77. Journal code: 0330500. E-ISSN: 1879-1026. L-ISSN: 0048-9697.	EU060
CA 8.3.1	Helmer, S.H., Kerbaol, A., Aras, P., Jumarie, C., Boily, M.	2014	Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (*Apis mellifera*).	Environmental science and pollution research international, (2014 Apr 15) Journal code: 9441769. E-ISSN: 1614-7499. L-ISSN: 0944-1344.	EU061
CA 8.3.1	Zhan, X., Liu, H., Miao, Y., Liu, W., Zhan, X.M., Liu, H.J., Miao, Y.G., Liu, W.P.	2006	A comparative study of rac- and S-metolachlor on some activities and metabolism of silkworm, *Bombyx mori* L.	Pesticide Biochemistry and Physiology (2006) Volume 85, Number 3, pp. 133-138, 33 refs. ISSN: 0048-3575. DOI: 10.1016/j.pestbp.2005.12.003	EU062
CA 8.3.2	Carmo, E.L., Bueno, A.F., Bueno, R.C.O.F.	2010	Pesticide selectivity for the insect egg parasitoid *Telenomus remus*.	BioControl (2010) Volume 55, Number 4, pp. 455-464, 38 refs. ISSN: 1386-6141	EU063
CA 8.3.2	Xu H., Xue, M., Zhao, H., Ma, X., Liu, Y., Xu, H.Q., Xue, M., Zhao, H.P., Ma, X.D., Liu, Y.Y.	2013	Analysis and evaluation of eight herbicides toxicity and sensitivity against two *Trichogramma* spp.	Journal of Food, Agriculture & Environment (2013), Volume 11, Number 3/4, pp. 855-858, 19 refs. ISSN: 1459-0255	EU064
CA 8.4	Park, E.-K., Lees, E.M.	2005	Application of an artificial sea salt solution to determine acute toxicity of herbicides to *Proisotoma minuta* (Collembola).	Journal of environmental science and health. Part. B, Pesticides, food contaminants, and agricultural wastes, (2005) Vol. 40, No. 4, pp. 595-604. Journal code: 7607167. ISSN: 0360-1234. L-ISSN: 0360-1234.	EU065
CA 8.4	Wang, Y., Wu, S., Chen, L., Wu, C., Yu, R., Wang, Q., Zhao, X.	2012	Toxicity assessment of 45 pesticides to the epigeic earthworm *Eisenia fetida*.	Chemosphere, (July 2012) Vol. 88, No. 4, pp. 484-491. Refs: 63. ISSN: 0045-6535; E-ISSN: 1879-1298. CODEN: CMSHAF	EU066
CA 8.4	Xu, D., Wen, Y., Wang, K.	2010	Effect of chiral differences of metolachlor and its (S)-isomer on their toxicity to earthworms.	Ecotoxicology and environmental safety, (2010 Nov) Vol. 73, No. 8, pp. 1925-31. Journal code: 7805381. E-ISSN: 1090-2414. L-ISSN: 0147-6513.	EU067
CA 8.4	Stepic, S., Hackenberger, B.K., Velki, M., Hackenberger, D.K., Loncaric, Z.	2013	Potentiation effect of metolachlor on toxicity of organochlorine and organophosphate insecticides in earthworm *Eisenia andrei*.	Bulletin of environmental contamination and toxicology, (2013 Jul) Vol. 91, No. 1, pp. 55-61. Journal code: 0046021. E-ISSN: 1432-0800. L-ISSN: 0007-4861.	EU068

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 8.4 CA 8.6	Kondras, M., Czepinska-Kaminska, D., Karczewska, J., Wojewoda, K.	2011	The influence of two pesticides in soils on selected plants and earthworms	Roczniki Gleboznawcze (2011), 62 (2), 219-225. CODEN: ROGLAA; ISSN: 0080-3642	EU070
CA 8.4	Aly, M.A.S., Schroder, P.	2008	Effect of herbicides on glutathione S-transferases in the earthworm, *Eisenia fetida*.	Environmental science and pollution research international, (2008 Mar) Vol. 15, No. 2, pp. 143-9. Journal code: 9441769. ISSN: 0944-1344.	EU069
CA 8.5	Joly, P., Besse-Hoggan, P., Bonnemoy, F., Batisson, I., Bohatier, J., Mallet, C.	2012	Impact of maize formulated herbicides Mesotrione and S-metolachlor, applied alone and in mixture, on soil microbial communities	ISRN Ecology, (2012) pp. 329898, 9 pp. CODEN: IESCCC. ISSN: 2090-4614.	EU071
CA 8.5	Joly, P., Bonnemoy, F., Charvy, J.-C., Bohatier, J., Mallet, C.	2013	Toxicity assessment of the maize herbicides S-metolachlor, benoxacor, mesotrione and nicosulfuron, and their corresponding commercial formulations, alone and in mixtures, using the Microtox(®) test.	Chemosphere, (2013 Nov) Vol. 93, No. 10, pp. 2444-50. Electronic Publication Date: 26 Sep 2013. Journal code: 0320657. E-ISSN: 1879-1298. L-ISSN: 0045-6535.	EU072
CA 8.5	Joly, P., Misson, B., Perriere, F. Bonneymoy, F. Joly, M. Bernard, F., Aguer, J-P., Bohatier, J., Mallet, C., Donnadieu-	2014	Soil surface colonisation by phototrophic indigenous organisms, in two contrasted soils treated by formulated maize herbicide mixtures	Ecotoxicology (London, England) (2014 Aug 18). Journal code 9885956. E-ISSN:1573-3017. L-ISSN: 0963-9292	EU073
CA 8.5	Lipsa, F.D., Ulea, E., Chiriac, I.P., Coroi, I.G.	2010	Effect of herbicide S-metolachlor on soil microorganisms.	Lucrari Stiintifice, Universitatea de Stiinte Agricole Si Medicina Veterinara "Ion Ionescu de la Brad" Iasi, Seria Agronomie (2010) Volume 53, Number 2, pp. 110-113, 11 refs. ISSN: 1454-7414	EU074
CA 8.5	Vodovnik, M., Bistan, M., Zorec, M., Marinsek-Logar, R.	2012	Membrane Changes Associated with Exposure of *Pseudomonas putida* to Selected Environmental Pollutants and their Possible Roles in Toxicity.	Acta chimica Slovenica, (2012 Mar) Vol. 59, No. 1, pp. 83-8. Journal code: 101247110. ISSN: 1318-0207. L-ISSN: 1318-0207.	EU075
CA 8.5	Kos, K., Celar, F.A.	2013	Sensitivity of the entomopathogenic fungus *Beauveria bassiana* (Bals.-Criv.) Vuill. to selected herbicides.	Pest Management Science (2013), Volume 69, Number 6, pp. 717-721, 34 refs. ISSN: 1526-498X	EU076
CA 8.6	Sikkema, P.H., Shropshire, C., Soltani, N.	2009	Response of dry bean to pre-plant incorporated and pre-emergence applications of S-metolachlor and fomesafen	Crop protection (2009), Volume 28, Number 9, pp. 744-748. ISSN: 0261-2194	EU077
CA 8.6	Samtani, J.B., Masiunas, J.B., Applyby, J.E.	2010	White Oak and Northern Red Oak Leaf Injury from Exposure to Chloroacetanilide Herbicides.	HortScience : a publication of the American Society for Horticultural Science (2010), Volume 45, Number 4, pp. 696-700. ISSN: 0018-5345	EU078

CA data point number	Author(s)	Year	Title	Source	Ref. ID
CA 8.6	Sikkema, P.H., Soltani, N., Shropshire, C., Robinson, D.E.	2006	Response of adzuki bean to pre-emergence herbicides.	Canadian journal of plant science = Revue Canadienne de phytotechnie (2006), Volume 86, Number 2, pp. 601-604. ISSN: 0008-4220	EU079
CA 8.6	Boutin, C., Elmegaard, N., Kjaer, C.	2004	Toxicity testing of fifteen non-crop plant species with six herbicides in a greenhouse experiment: Implications for risk assessment.	Ecotoxicology, (May 2004) Vol. 13, No. 4, pp. 349-369. ISSN: 0963-9292.	EU080
CA 8.6	Bollman, S.L., Sprague, C.L.	2008	Tolerance of 12 Sugarbeet Varieties to Applications of S-metolachlor and Dimethenamid-P	Weed technology (2008), Volume 22, Number 4, pp. 699-706. ISSN: 0890-037X Source Note: 2008 Oct., v. 22, no. 4	EU081
CA 8.6	Xie, F., Liu, H.J., Cai, W.D., Xie, F.	2010	Enantioselectivity of racemic metolachlor and S-metolachlor in maize seedlings	Journal of Environmental Science and Health. Part B, Pesticides, Food Contaminants, and Agricultural Wastes (2010), Volume 45, Number 8, pp. 774-782, 33 refs. ISSN: 0360-1234	EU082
CA 8.6	Samtani, J.B., Masiunas, J.B., Appleby, J.E.	2008	Injury on white oak seedlings from herbicide exposure simulating drift.	HortScience (2008), Vol. 43, Number 7, pp. 2076-2080, 27 refs. ISSN: 0018-5345	EU083
CA 8.6	Yadav, P.K., Khan, A.H., Amar, N., Yadav, S.K.S., Nath, A.	2007	Effect of herbicides on biochemical and growth parameters of chickpea (*Cicer arietinum* L.).	Research on Crops (2007), Vol. 8, Number 2, pp. 388-390, 8 refs. ISSN: 0972-3226	EU084
CA 8.6	Yadav, P.K., Khan, A.H., Murti, R., Upadhyay, R.K.	2006	Effect of herbicides on germination, growth and nodulation in chickpea (*Cicer arietinum*)	Indian Journal of Agricultural Sciences (2006), 76 (11), 682-684	EU085
CA 8.6	Norsworthy, J.K., Smith, J.P., Meister, C.	2007	Tolerance of direct-seeded green onions to herbicides applied before or after crop emergence.	Weed Technology (2007), Volume 21, Number 1, pp. 119-123. ISSN: 0890-037X	EU086
CA 8.6	Soltani, N., Shropshire, C., Cowan, T., Sikkema, P.	2004	White bean sensitivity to preemergence herbicides.	Weed Technology (2004), Vol. 18, Number 3, pp. 675-679, 15 refs. ISSN: 0890-037X	EU087
CA 8.6	Neugebauerova, J., Petrikova, K.	2004	Possibilities of pre-emergence and post-emergence herbicide applications in *Prunella vulgaris* L. growth.	Zahradnictvi (Horticultural Science) (2004), Volume 31, Number 3, pp. 115-118, 13 refs. ISSN: 0862-867X	EU088
CA 8.6	Soltani, N., Shropshire, C., Cowan, T., Sikkema, P.	2004	Tolerance of black beans (*Phaseolus vulgaris*) to soil applications of S-metolachlor and imazethapyr.	Weed Technology (2004), Volume 18, Number 1, pp. 111-118, 25 refs. ISSN: 0890-037X	EU089
CA 8.6	De Marez, T., Mechant, E., Goossens, V., Bulcke, R.	2007	Effect of selected sugar beet herbicides on germination of various *Chenopodium album* populations.	Communications in agricultural and applied biological sciences, (2007) Vol. 72, No. 2, pp. 265-9. Journal code: 101200320. ISSN: 1379-1176. L-ISSN: 1379-1176.	EU090

S-Metolachlor

NOTIFICATION OF AN ACTIVE SUBSTANCE UNDER COMMISSION REGULATION (EU) 844/2012

DOCUMENT M-CA, Section 9

Fate and Behaviour in the Environment

LITERATURE DATA

Version history[1]

Date	Data points containing amendments or additions and brief description	Document identifier and version number

Table of Contents

CA 9 LITERATURE DATA

CA 9.1 Title

This document is a Literature Review Report for S-metolachlor, relevant metabolite(s) and EU representative formulation A9396G (Dual Gold®).

CA 9.2 Author(s) of the review

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CA 9.3 UK Summary: A brief summary indicating the purpose of the report, the methodology employed and the results obtained

This report summarises the search for scientific peer-reviewed open literature on physical and chemical properties "on the active substance S-metolachlor and its relevant metabolites(s) dealing with side-effects on health, the environment and non-target species and published within the last ten years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

The search strategy is detailed in the tables below. In summary, initially a very broad search was done to look for any references which included the active substance S-metolachlor, or its major metabolites, or its representative formulation, in conjunction with any of the key words set out in Table 9.5-1. The names searched for were:

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L1      QUE  (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2      QUE  (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3      QUE  (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4      QUE  (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5      QUE  (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6      QUE  (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7      QUE  (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8      QUE  (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9      QUE  (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10     QUE  (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11     QUE  (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12     QUE  (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13     QUE  (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14     QUE  (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15     QUE  (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16     QUE  (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17     QUE  (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18     QUE  (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19     QUE  (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))
L20     QUE  ((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21     QUE  (55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22     QUE  (METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23     QUE  ((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24     QUE  (CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
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L25      QUE  (L1-L20)   METABOLITES
L26      QUE  (L21 OR L22 OR L23 OR L24)   METOLACHLOR
L27      QUE  (L25 OR L26)   METOLACHLOR & METABOLITES
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An overview of the results is summarised in the table below and further details are provided in Section 9.5.

Data requirement(s) captured in the search	**Number (Initial Search)**
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	4281
Number of *summary records* excluded from the search results after rapid assessment for relevance	4230
Total number of *full-text* documents assessed in detail*	51
Number of *studies* excluded from further consideration after detailed assessment for relevance	50
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	1

*both from bibliographic databases and other sources of peer-reviewed literature

CA 9.4 Protocol

CA 9.4.1 Statement of the objective of the review

The review has the objective of identifying "scientific peer-reviewed open literature on S-metolachlor and its potentially relevant metabolites dealing with metabolism and residue studies which may impact health, the environment and non-target species and published within the last ten years before the date of submission of the dossier" in accordance with Article 8(5) of Regulation (EC) No. 1107/2009.

CA 9.4.2 Criteria for relevance with which decisions to select studies in the dossier were made

Table 9.4.2-1: List of Criteria for relevance for each data requirement

Data requirements(s) (indicated by the correspondent CA data point (s))	**Criteria for relevance**
Route and rate of degradation in soil – Laboratory Studies – aerobic and anaerobic, parent and metabolites CA 7.1.1 CA 7.1.1.1 CA 7.1.1.2	1. Well defined test material (including purity/content) 2. Soil(s) must be agricultural and relevant for the EU e.g. from temperate zone, no extreme characteristics (e.g. meets the criteria in OECD 307) 3. Soil collection, preparation and storage did not differ significantly from recommended protocols 4. Test soils had not previously been exposed to the test material or structural analogues. 5. Experimental conditions did not differ significantly from recommended protocols e.g. temperature and moisture 6. Application rate is within the range of the proposed use and can be verified from the data (time zero samples) 7. Sufficient number of samples taken to determine kinetics (minimum 5) 8. Extraction system was appropriate e.g. avoidance of excessive or inadequate methods 9. Analytical method well described, LOD/LOQ at appropriate level 10. Mass balance or recovery for radiolabelled and unlabelled studies respectively is adequate to support the conclusions, e.g. >90%.

	11. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. for unlabelled studies are suitable blank controls included 12. Identification of 'new' metabolites is robust with appropriate details of method used 13. Anaerobic conditions are verified by measurement
Route and rate of degradation in soil – Field Studies CA 7.1.2.2	1. In addition to criteria under laboratory route and rate: 2. Field site(s) must be geoclimatically relevant for the EU 3. Adequate weather data available to verify relevance of study 4. Application technique relevant to proposed use (foliar, ST granule etc) 5. Sufficient sampling detail and description of sample handling prior to analysis 6. Initial and procedural recoveries are adequate to support the conclusions, e.g. 70-120%.
Soil photolysis CA 7.1.1.3	In addition to criteria under laboratory route and rate: 1. Light source was suitable with details of spectrum and intensity available 2. Dark control included and reported
Mobility studies Adsorption, desorption – parent and metabolites CA 7.1.3 Column or TLC leaching CA 7.1.4.1.1, CA 7.1.4.1.2	1. Well defined test material (including purity/content) 2. Soil(s) must be agricultural and relevant for EU e.g. from temperate zone, no extreme characteristics (e.g. meets the criteria in OECD 106) 3. Soil collection, preparation and storage did not differ significantly from recommended protocols 4. Test soils had not previously been exposed to the test material or structural analogues. 5. Experimental conditions did not differ significantly from recommended protocols 6. Application rate is appropriate to the proposed use and can be verified from the data 7. Sufficient number of samples taken to determine isotherm (if done) 8. Stability of the test item in the system was demonstrated 9. Extraction system was appropriate e.g. avoidance of excessive or inadequate methods 10. Mass balance or recovery for radiolabelled and unlabelled studies respectively is adequate to support the conclusions, e.g. >90% 11. Analytical method well described, LOD/LOQ at appropriate level 12. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. for unlabelled studies are suitable blank controls included
Lysimeter studies CA 7.1.4.2	In addition to criteria under laboratory route and rate: 1. Field site(s) must be geoclimatically relevant for the EU 2. Adequate weather data available to verify relevance of study. Combined rainfall/irrigation sufficient to meet guideline requirements 3. Minimum 1 m depth soil monolith 4. Study continued for sufficient years to support the conclusions
Field leaching CA 7.1.4.3.	In addition to criteria under laboratory route and rate: 1. Field site(s) must be geoclimatically relevant for the EU 2. Adequate weather data and groundwater data (depth, direction) available to verify the validity of study 3. Installation and operation of lysimeters and/or wells and samplers follows recommended protocols 4. Study continued for sufficient years to support the conclusions

Hydrolysis CA 7.2.1	1. Well defined test material (including purity/content) 2. Experimental conditions should not differ significantly from recommended protocols 3. Application rate is within an acceptable the range (e.g. consider solubility) and can be verified from the data (time zero samples) 4. Sufficient number of samples taken to determine kinetics (minimum 5) 5. Analytical method well described, LOD/LOQ at appropriate level 6. Mass balance or recovery for radiolabelled and unlabelled studies respectively is adequate to support the conclusions, e.g. >90%. 7. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. for unlabelled studies are suitable blank controls included 8. Identification of ‘new’ metabolites is robust with appropriate details of method used
Aqueous photolysis CA 7.2.1.2	In addition to criteria under hydrolysis: 1. Light source was suitable with details of spectrum and intensity available 2. Dark control included and reported
Degradation in aquatic systems CA 7.2.2	1. Well defined test material (including purity/content) 2. Water(s) and sediment(s) must be from an agricultural area and relevant for the EU e.g. from temperate zone, no extreme characteristics (e.g. meets the criteria in OECD 308) 3. Water/sediment collection, preparation and storage do not differ significantly from recommended protocols 4. Experimental conditions do not differ significantly from recommended protocols e.g. temperature and aeration 5. Application rate is within the range of the proposed use and can be verified from the data (time zero samples) 6. Sufficient number of samples taken to determine kinetics (minimum 5) 7. Extraction system was appropriate e.g. avoidance of excessive or inadequate methods 8. Analytical method well described, LOD/LOQ at appropriate level 9. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. for unlabelled studies are suitable blank controls included 10. Mass balance or recovery for radiolabelled and unlabelled studies respectively is adequate to support the conclusions, e.g. >90% 11. Identification of ‘new’ metabolites is robust with appropriate details of method used 12. Anaerobic conditions are verified by measurement
Degradation in the saturated zone CA 7.2.3	1. For laboratory studies refer to criteria under laboratory route and rate 2. Field site(s) must be geoclimatically relevant for the EU 3. Adequate site characterisation data available e.g. soils, geology, hydrology 4. Installation of samplers e.g. wells, lysimeters follows recommended protocols 5. Analytical method well described, LOD/LOQ at appropriate level 6. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. for unlabelled studies are suitable blank controls included
Route and rate of degradation in air CA 7.3.1	1. Experimental conditions or calculations differ significantly from recommended protocols 2. Analytical method well described, LOD/LOQ at appropriate level 3. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. for unlabelled studies are suitable blank controls included

Monitoring CA 7.5	1. Site(s) or areas must be geoclimatically relevant for the EU 2. Adequate site characterisation data available e.g. soils, geology, hydrology 3. Installation of samplers e.g. wells, lysimeters follows recommended protocols OR adequate description of wells is available (depth of well, length of screen, depth of screen opening, depth of groundwater) 4. Appropriate sampling methodology. 5. Analytical method well described, LOD/LOQ at appropriate level 6. Analytical method appears robust with suitable reproducibility and supports the conclusions made e.g. suitable blank controls included 7. For surface water: description of sampling methodology and handling of detects (peaks, interpolated time-step?), linked to rainfall intensity and volume). Discharge volumes, catchment drained area.

* Recommended protocols under each data point include but are not limited to those listed in the Commission Communications 2013/C 95/01 and 2013/C 95/02

CA 9.5 Search methods

Date of initial search	22.08.2014
Date of most recent update to search	-
Date span of the search	10 years

Table 9.5-1: Detailed Search Parameters for Fate and behaviour in the environment (CA 7.1 to 7.12)

Search Strategy

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L1      QUE  (693288-41-4 OR 131068-72-9 OR 1217465-10-5 OR 244270-80-2)
L2      QUE  (244270-82-4 OR 887649-86-7 OR 244270-79-9 OR 244270-81-3)
L3      QUE  (887649-85-6 OR 947601-85-6 OR 446027-17-4 OR 1173021-76-5)
L4      QUE  (1418095-19-8 OR 126605-22-9 OR 153516-68-8 OR 61520-53-4)
L5      QUE  (82508-08-5 OR 82508-09-6 OR 61520-54-5 OR 97055-05-5)
L6      QUE  (32428-71-0 OR 97055-06-6 OR 52559-52-1 OR 51219-00-2)
L7      QUE  (96394-97-7 OR 121073-75-4 OR 170379-74-5 OR 152019-73-3)
L8      QUE  (120375-14-6 OR 65513-61-3 OR 159956-64-6 OR 171118-09-5)
L9      QUE  (CGA098847 OR CGA98847 OR CGA46129 OR CGA138868)
L10     QUE  (CGA354743 OR CGA41507 OR CGA51202 OR CGA40172)
L11     QUE  (CGA40919 OR CGA37735 OR CGA49751 OR CGA37913)
L12     QUE  (CGA351915 OR CGA133275 OR CGA046129 OR CGA13656)
L13     QUE  (CGA(2W)(098847 OR 98847 OR 46129 OR 138868))
L14     QUE  (CGA(2W)(354743 OR 41507 OR 51202 OR 40172))
L15     QUE  (CGA(2W)(40919 OR 37735 OR 49751 OR 37913))
L16     QUE  (CGA(2W)(351915 OR 133275 OR 046129 OR 13656))
L17     QUE  (SYN542491 OR SYN542489 OR SYN542492 OR SYN547969)
L18     QUE  (SYN542488 OR SYN542490 OR SYN542607 OR NOA436611)
L19     QUE  (SYN(2W)(542491 OR 542489 OR 542492 OR 547969))
L20     QUE  ((SYN(2W)(542488 OR 542490 OR 542607)) OR (NOA(2W)436611))
L21     QUE  (55762-76-0 OR 63150-68-5 OR 94449-58-8 OR (CGA(W)77102))
L22     QUE  (METETILACHLOR OR METOLACHLOR OR (CGA(W)24705) OR CGA24705)
L23     QUE  ((S OR ALPHA)(2W)(METOLACHLOR OR METHOLACHLOR))
L24     QUE  (CGA77102 OR 51218-45-2 OR 87392-12-9 OR METHOLACHLOR)
L25     QUE  (L1-L20)   METABOLITES
L26     QUE  (L21 OR L22 OR L23 OR L24)   METOLACHLOR
L27     QUE  (L25 OR L26)   METOLACHLOR & METABOLITES
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Plus

Search Strategy	
L1	QUE (FATE# OR DEGRAD? OR PERSIST? OR DECOMP? OR DECAY?)
L2	QUE (TRANSFORM? OR DETERIORAT? OR METAB? OR DEGENERAT?)
L3	QUE (BIODEGRAD? OR BIOTRANSFORM? OR BIODETERIORAT?)
L4	QUE (BIODEGENERAT? OR BREAKDOWN? OR BREAKSDOWN?)
L5	QUE (((BROKEN? OR BREAK?)(W)(UP OR DOWN)) OR HALFLIFE#)
L6	QUE (HALFLIVES OR HALF(W)(LIFE OR LIVES) OR DEGRDN# OR DECOMPN#)
L7	QUE (BIODEGRDN# OR DEGN# OR BIODEGN# OR DISSIP? OR RESIDUE?)
L8	QUE (LEACH? OR TRANSPORT? OR MOBIL? OR MOVEMENT? OR HYDROLY?)
L9	QUE (ADSORP? OR ADSORB? OR SORP? OR SORB? OR DESORP?)
L10	QUE (DESORB? OR RUNOFF OR (RUN#(W)OFF) OR DRAIN? OR PERCOLAT?)
L11	QUE (WASHOFF? OR WASHOUT? OR (WASH?(W)(OUT OR OFF)))
L12	QUE ((((OFF(W)TARGET) OR LATERAL OR HORIZONTAL)(3W)MOVE?))
L13	QUE (PHOTOLY? OR PHOTODEGRAD? OR PHOTODECOMP?)
L14	QUE (PHOTOTRANSFORM? OR PHOTOSTAB? OR PHOTODEGRDN# OR PHOTODEGN#)
L15	QUE ((PHOTO(W)(DECOMP? OR DEGRAD? OR TRANSFORM? OR STAB? OR CHEM?)))
L16	QUE (PHOTOCHEM? OR VOLATIL? OR VAPOUR? OR VAPOR? OR DT50 OR DT90)
L17	QUE ((DT(W)50) OR (DT(W)90) OR KDOC OR (K(W)DOC) OR KD OR KOC)
L18	QUE ((K(W)OC) OR (PARTITION?(3W)COEFF?) OR FREUNDLICH)
L19	QUE (SEDIMENT? OR SOIL OR SOILS OR PODZOL? OR CLAY? OR SAND?)
L20	QUE (SILT? OR CHERNOZEM? OR PODSOL? OR LOAM? OR PEAT?)
L21	QUE ((ORGANIC(2W)MATTER?) OR MONTMORIL? OR LATOSOL? OR HUMIC?)
L22	QUE (HUMUS? OR SUBSOIL? OR AIR OR WATER? OR ATMOSPHER?)
L23	QUE (RAIN### OR RAINWATER? OR RAINFALL? OR LEACH?)
L24	QUE (GROUNDWATER? OR ENVIRONMENT? OR PRECIPITAT? OR POND#)
L25	QUE (STREAM# OR RIVER# OR DELTA# OR ESTUAR? OR SEDIMENT?)
L26	QUE (AQUATIC? OR MARINE? OR TIDAL? OR BENTHIC? OR LAKE#)
L27	QUE (BENTHOS? OR LIMNO? OR FRESHWATER? OR SEAWATER?)
L28	QUE (SALTWATER? OR ((GROUND? OR FRESH OR SEA OR SALT)(W)WATER?))
L29	QUE (LACUSTRINE? OR MIRE OR MIRES OR RESERVOIR# OR CANAL#)
L30	QUE (LOCH# OR SEA OR OCEAN OR OCEANS OR LAGOON? OR SEAS)
L31	QUE (SEABED OR SEAFLOOR OR INTERTIDAL? OR SHORE? OR COAST?)
L32	QUE (BRACKISH OR LITTORAL? OR SEASHORE? OR MEIOBENTH?)
L33	QUE (MICROBENTH? OR MACROBENTH? OR HARBOUR# OR FLUVIAL?)
L34	QUE (MARSH? OR BOG OR BOGS OR SWAMP? OR FEN OR FENS OR ALLUVI?)
L35	QUE (MUDFLAT? OR (MUD(W)FLAT?) OR BAY OR BAYS OR CREEK#)
L36	QUE (HYDROSOIL# OR (HYDRO(W)SOIL#) OR MESOCOSM? OR MICROCOSM?)
L37	QUE (WETLAND? OR FENLAND? OR ((WET OR FEN)(W)LAND?))
L38	QUE (WATERWAY? OR WATERSHED? OR (WATER(W)(WAY? OR SHED?)))
L39	QUE (CATCHMENT? OR DITCH? OR DRAIN# OR DRAINAG?)
L40	QUE (((FOLIAGE OR FOLIAR OR LEAF OR LEAVES)(5A)EVAPORAT？））
L41	QUE ((SPRAY? OR DUST?)(3A)DRIFT)
L42	QUE (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8 OR L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR L17 OR L18 OR L19 OR L20 OR L21 OR L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31 OR L32 OR L33 OR L34 OR L35 OR L36 OR L37 OR L38 OR L39 OR L40 OR L41)

Table 9.5-2: Detailed Search Parameters for Fate and behaviour in the environment (CA 7.1 to 7.12)

Provider	Database	Justification	Limits applied	Number*
Host STN	MEDLINE	Contains information on every area of medicine providing comprehensive coverage from 1948 to present. Sources include journals and chapters in books or symposia. The database is updated 5 times each week with an annual reload and therefore stays very current in its cover.	None	604
	EMBASE	The database, covers worldwide literature in the biomedical and pharmaceutical fields, including biological science, biochemistry, human medicine, forensic science, pediatrics, pharmacy, pharmacology and drug therapy, pharmacoeconomics, psychiatry, public health, biomedical engineering and instrumentation, and environmental science. Sources include more than 4,000 journals from approximately 70 countries, monographs, conference proceedings, dissertations, and reports. The databases covers data from 1974-present and is updated daily.		165
	EMBAL	The database provides early access to bibliographic data and the abstracts for references that will appear in EMBASE. Bibliographic information for references is available in EMBAL for the latest 8 weeks of EMBASE data. The database covers the worldwide literature on the biomedical and pharmaceutical fields. Bibliographic information, abstracts, and author keywords are searchable. Sources include over 4,000 journals. The database covers current data and is updated daily.		
	ESBIOBASE	A database providing comprehensive coverage of the entire spectrum of biological research worldwide. Coverage includes the following areas: applied microbiology, biotechnology, cancer research, cell & developmental biology, clinical chemistry, ecological & environmental sciences, endocrinology, genetics, immunology, infectious diseases, metabolism, molecular biology, neuroscience, plant and crop science, protein biochemistry, and toxicology. Records are selected from over 1,700 international scientific journals, books, and conference proceedings. The database covers the period 1994 - present and is updated weekly.		16
	AGRICOLA	A bibliographic database containing selected worldwide literature of agriculture and related fields. Coverage of the database includes agricultural economics and rural sociology, agricultural production, animal sciences, chemistry, entomology, food and human nutrition, forestry, natural resources, pesticides, plant science, soils and fertilizers, and water resources. Also covered are related areas such as biology and biotechnology, botany, ecology, and natural history. The database draws on bibliographies, serial articles, book chapters, monographs, computer files, serials, maps, audiovisuals, and reports. It covers the period 1970-present and is updated monthly.		59
	BIOSIS	A large and comprehensive worldwide life science database covers original research reports, reviews, and selected U.S. patents in biological and biomedical areas, with subject coverage ranging from aerospace biology to zoology. Sources include periodicals, journals, conference proceedings, reviews, reports, patents, and short communications. Nearly 6,000 life source journals, 1,500 international meetings as well as review articles, books, and monographs are reviewed for inclusion. It covers the period 1926 – present and is updated weekly.		246
	CABA	Covers worldwide literature from all areas of agriculture and related sciences including biotechnology, forestry, and veterinary medicine. Sources include journals, books, reports, published theses, conference proceedings, and patents. It covers the period 1973-present and is updated weekly.		834

Provider	Database	Justification	Limits applied	Number*
	CAPLUS	Covers worldwide literature from all areas of chemistry, biochemistry, chemical engineering, and related sciences including applied, macromolecular, organic, physical, inorganic, and analytical chemistry. Current sources include over 8,000 journals, patents, technical reports, books, conference proceedings, dissertations, product reviews, bibliographic items, book reviews, and meeting abstracts. Electronic-only journals and Web preprints are also covered. Cited references are included for journals, conference proceedings and basic patents from the U.S., EPO, WIPO, and German patent offices added to the CAS databases from 1999 to the present. Also provides early access to the bibliographic information, abstracts and CAS Registry Numbers for documents in the process of being indexed by CAS. Covers the period 1907 – present and is updated daily		1779
	FSTA	The database provides worldwide coverage of all scientific and technological aspects of the processing and manufacture of human food products including basic food sciences, biotechnology, hygiene and toxicology, engineering, packaging, and all individual foods and food products. Sources include more than 2,200 journals, books, reviews, conference proceedings, patents, standards, and legislation. It covers the period 1969 – present and is updated weekly.		9
	FROSTI	The database contains citations to the worldwide literature on food science and technology including food and beverages, analytical methods, quality control, manufacturing, microbiology, food processing, health and nutrition, recipes, and additives. Sources include approximately 800 scientific and technical journals, bulletins, technical reports, conference proceedings, grey literature, and British, European (EP), U.S., Japanese, and international (PCT) patent applications. Covers the period 1972 – present and is updated twice weekly.		
	GEOREF	Covers international literature on geology and geosciences. Sources include the Bibliography of North American Geology, Bibliography and Index of Geology Exclusive of North America, Geophysical Abstracts, Bibliography of Fossil Vertebrates, selected records from Geoline and from geology sections of PASCAL and state and national geological surveys. Covers the period 1669 – present and is updated twice a month.		119
	TOXCENTER	Covers the pharmacological, biochemical, physiological, and toxicological effects of drugs and other chemicals. It is composed of the following subfiles: BIOSIS, CAplus, IPA and MEDLINE and sources include abstracts, books and book chapters, bulletins, conference proceedings, journal articles, letters, meetings, monographs, notes, papers, patents, presentations, research and project summaries, reviews, technical reports, theses, translations, unpublished material, web reprints. Covers the period 1907 – present and is updated weekly		
	PQSCITECH	Is a huge resource in all areas of science and technology from engineering to lifescience. The file is a merge of 25 STN databases formerly known as CSA databases (Cambridge Scientific Abstracts): AEROSPACE, ALUMINIUM, ANTE, AQUALINE, AQUASCI, BIOENG, CERAB, CIVILENG, COMPUAB, CONFSCI, COPPERLIT, CORROSION, ELCOM, EMA, ENVIROENG, HEALSAFE, LIFESCI, LISA, MATBUS, MECHENG, METADEX, OCEAN, POLLUAB, SOLIDSTATE, and WATER. Sources are journals, patents, books, reports, and conference proceedings spanning the period 1962 – present and it is updated monthly.		181
	PASCAL	The database provides access to the world's scientific and technical literature including physics and chemistry, life sciences (biology, medicine, and psychology), applied sciences and technology, earth sciences, and information sciences. French and European literature is particularly well represented. Approximately 5,000 journal titles are indexed. References to theses and to conference proceedings are also included. Spans the period 1977 to present and is updated weekly		28

Provider	Database	Justification	Limits applied	Number*
	SCISEARCH	Is an international index to the literature covering virtually every subject area within the broad fields of science, technology, and biomedicine. SciSearch contains all the records published in Science Citation Index Expanded™ and additional records from the Current Contents series of publications. Bibliographic information and cited references from over 5,600 scientific, technical, and medical journals are contained in the database. Spans the period 1974 to present and is updated weekly.		332
	ANABST	Covers worldwide literature on analytical chemistry. The ANABSTR file contains bibliographic records with abstracts (since 1984) for documents reported in printed Analytical Abstracts. Sources for ANABSTR include journals, books, conference proceedings, reports, and standards. Spans the period 1980 to present and is updated weekly.		16

* Total number of summary records retrieved after removing duplicates

Table 9.5-3: Detailed Search Parameters for Web searches

Website name and service publisher	URL	Justification	Search terms	Limits applied	Number*
A web search has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-4: Detailed Search Parameters for Journal Table of Contents

Journal name	Journal URL or publisher	Dates, volumes and issues searched	Method of searching	Search terms	Number*
A search for journal table of contents has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.					

* Total number of summary records or full-text documents retrieved after removing duplicates

Table 9.5-5: Detailed Search Parameters for Reference Lists

Bibliographic details of documents whose reference lists were scanned	Number*
A search for reference lists has not been conducted as the database search reported above is considered to provide an adequately comprehensive search of the quality peer reviewed literature.	

* Total number of summary records or full-text documents retrieved after removing duplicates

CA 9.6 Results

Table 9.6-1: Results of study selection process

Data requirement(s) captured in the search	Number (Initial Search)
Total number of *summary records* retrieved after *all** searches of peer-reviewed literature (excluding duplicates)	4281
Number of *summary records* excluded from the search results after rapid assessment for relevance	4230
Total number of *full-text* documents assessed in detail	51
Number of *studies* excluded from further consideration after detailed assessment for relevance	50
Number of *studies* not excluded for relevance after detailed assessment (i.e. relevant studies and studies of unclear relevance)	1

*both from bibliographic databases and other sources of peer-reviewed literature

Applicant has additionally reviewed two publications on the degradation of S-metolachlor in water/sediment systems (Rice *et al*., 2004 and Mersie *et al*., 2004) as outlined in Stop the Clock request 60.

Table 9.6-2: List of references for all relevant and unclear studies listed by data point number

CA data point number	Author(s)	Year	Title	Source
Initial search				
7.1.1.1	Klein, C, Schneider, RJ, Meter, MT & Aga, DS	2006	Enantiomeric separation of metolachlor and its metabolites using LC-MS and CZE	Chemosphere, 62, 1591-1599
7.1.1.1	Polcaro CM, Berti A; Mannina, L; Marra C; Sinibaldi M; Viel S	2007	Chiral HPLC resolution of neutral pesticides	Journal of Liquid Chromatography & Related Technologies, 27:1,49-61
7.1.1.1	Accinelli, C.; Dinelli, G.; Vicari, A.	2004	Metolachlor and linuron soil degradation after repeated applications under laboratory conditions.	Agrochimica (2004), Vol. 48, Number 3/4, pp. 132-140
7.1.1.1	Capel, Paul D.; Webb, Richard M. T.	2007	Multi-compartment analysis of the behavior and fate of metolachlor in the environment	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2007), 47(2), 593-595
7.1.1.1	Vryzas Zisis	2012	Biotransformation of atrazine and metolachlor within soil profile and changes in microbial communities.	Chemosphere, (2012 Nov) Vol. 89, No. 11, pp. 1330-8
7.1.1.1	Cao P, Wang X, Liu F, Zhao E & Han L	2008	Dissipation and Residue of S-Metolachlor in Maize and Soil	Bull Environ Contam Toxicol, Vol 80, pp. 391-394
7.1.1.1	Shaner, D L; Brunk, G; Belles, D; Westra, P; Nissen, S	2006	Soil dissipation and biological activity of metolachlor and S-metolachlor in five soils	Pest management science (2006), Volume 62, Number 7, pp. 617-623
7.1.4	Vryzas Z; Papadakis EN; Papadopoulou-Mourkidou E	2012	Leaching of Br-, metolachlor, alachlor, atrazine, deethylatrazine and deisopropylatrazine in clayey vadoze zone: a field scale experiment in north-east Greece.	Water research, (2012 Apr 15) Vol. 46, No. 6, pp. 1979-89

CA data point number	Author(s)	Year	Title	Source
7.1.4	Barra CA; Giuliano G; Grenni P; Guzzella L; Pozzoni F; Bottoni P; Fava L; Crobe A; Orru M; Funari E	2005	Degradation and leaching of the herbicides metolachlor and diuron: a case study in an area of Northern Italy.	Environmental pollution (Barking, Essex : 1987), (2005 Apr) Vol. 134, No.3, pp. 525-34.
7.1.4	Doppler, T.; Camenzuli, L.; Hirzel, G.; Krauss, M.; Luck, A.; Stamm, C.	2012	Spatial variability of herbicide mobilization and transport at catchment scale: insights from a field experiment	Hydrology and Earth System Sciences (2012), 16 (7), 1947-1967
7.2.1.2	Coffinet, S.; Rifai, A.; Genty, C.; Souissi, Y.; Bourcier, S.; Sablier, M.; Bouchonnet, S.	2012	Characterization of the photodegradation products of metolachlor: structural elucidation, potential toxicity and persistence	Journal of Mass Spectrometry , Volume 47, Number 12, pp. 1582-1593
7.2.1.2	Souissi Y, Bouchonnet S, Bourcier S, Kusk KO, Sbalier M & Andersen HR	2013	Identification and ecotoxicity of degradation products of chloroacetamide herbicides from UV-treatment of water	Science of the Total Environment 458-460, 527-534
7.2.2	Kurt-Karakus PH, Bidleman, TF, Muir, DCG, Struger J, Sverko E, Cagampan SJ, Small JM and Jantunen LM	2010	Comparison of concentrations and stereoisomer ratios of mecoprop, dichlorprop and metolachlor in Ontario streams, 2006-2007 vs. 2003-2004	Environmental Pollution, 158, 1842-1849
7.2.2	Aboul Eish, MYZ; Wells, MJM	2008	Monitoring stereoselective degradation of metolachlor in a constructed wetland: use of statistically valid enantiomeric and diastereomeric fractions as opposed to ratios.	Journal of chromatographic science, (2008 Mar) Vol. 46, No. 3, pp. 269-75.
7.2.2	Rice PJ, Anderson TA & Coats JR	2004	Effect of sediment on the fate of metolachlor and atrazine in surface water	Environ. Toxicol. Chem 23(5); 1145-55
7.2.2.	Mersie W, McNamee C, Seybold C & Tierney D	2004	Degradation of metolachlor in bare and vegetated soils and in simulated water-sediment systems	Environ Toxicol Chem 23(11), 2627-2632
7.3.2	Gish, TJ; Prueger, JH; Daughtry, CST; Kustas, WP; McKee, LG; Russ, AL; Hatfield, JL	2011	Comparison of field-scale herbicide runoff and volatilization losses: an eight-year field investigation. Journal of environmental quality	Journal of environmental quality, Vol. 40, No. 5, pp.1432-42
7.5	Amalric L, Baran N, Coureau C, Maingot L, Buron F & Routier S	2013	Analytical developments for 47 pesticides: first identification of neutral chloroacetanilide derivatives in French groundwater	Inter. J. Environ. Anal. Chem. 93(15), 1660-1675
7.5	Baran N & Gourcy L	2013	Soprtion and mineralisation of S-metolachlor and its ionic metabolites in soils and vadose zone solids: Consequences on groundwater quality in an alluvial aquifer (Ain Plain, France)	Journal of Contaminant Hydrology, 154, 20-28
7.5	Hildebrandt A, Guillamón M, Lacorte S, Tauler R & Barceló D	2008	Impact of pesticides used in agriculture and vineyards to surface and groundwater quality (North Spain)	Water Research 42, 3315-3326
7.5	Silva E, Mendes MP, Ribeiro L & Cerejeira MJ	2012	Exposure assessment of pesticides in a shallow groundwater of the Tagus vulnerable zone (Portugal): a multivariate statistical approach (JCA)	Environ. Sci. Pollut. Res. 19: 2667-2680
7.5	Reemtsma T, Alder L & Banasiak U	2013	Emerging pesticide metabolites in groundwater and surface water as determined by the application of a multimethod for 150 pesticide metabolites	Water Research 47, 5535-5545

CA data point number	Author(s)	Year	Title	Source
7.5	Vryzas Z, Alexoudis C, Vassiliou G, Galanis K, Papadopoulou-Mourkidou E	2011	Determination and aquatic risk assessment of pesticide residues in riparian drainage canals in northeastern Greece	Ecotoxicology and Environmental Safety 74, 174-181
7.5	Antić N, Radišić M, Radović T, Vasiljević T, Grujić S, Petković A, Dimkić M, Laušević M	2014	Pesticide residues in the Danube river basin in Serbia – a survey during 2009-2011	Clean – Soil, Air, Water 00(0), 1-8
7.5	Boithias L, Sauvage S, Taghavi L, Merlina G, Probst J-L & Pérez LMS	2011	Occurrence of metolachlor and trifluralin losses in the Save river agricultural catchment during floods	Journal of Hazardous Materials 196, 210-219
7.5	Claver, A.; Ormad, P.; Rodriguez, L.; Ovelleiro, J.L	2006	Study of the presence of pesticides in surface waters in the Ebro river basin (Spain)	Chemosphere 8, 1437-1443
7.5	Hladik ML, Bouwer EJ & Roberts AL	2008	Neutral degradates of chloroacetamide herbicides: Occurrence in drinking water and removal during conventional water treatment	Water Research 42, 4905-4914
7.5	Schipper PNM, Vissers MJM & van der Linden AMA	2008	Pesticides in groundwater and drinking water wells: overview of the situation in the Netherlands	Water Science & Technology 57(8), 1277-1286
7.5	Papadopoulou-Mourkidou E, Karpouzas DG, Patsias J, Kotopoulou A, Milothridou A, Kintzikoglou K & Vlachou P	2004	The potential of pesticides to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece. Part II. Monitoring study in the south part of the basin.	Science of the Total Environment 321, 147-164
7.5	Freitas, L. G.; Singer, H.; Mueller, S. R.; Schwarzenbach, R. P.; Stamm, C.	2008	Source area effects on herbicide losses to surface waters - a case study in the Swiss Plateau.	Agriculture, Ecosystems & Environment (2008), Vol. 128, Number 3, pp. 177-184
7.5	Reemtsma T, Alder L & Banasiak U	2013	A multimethod for the determination of 150 pesticide metabolites in surface water and groundwater using direct injection liquid chromatography-mass spectrometry	Journal of Chromatography A 1271, 95-104
7.5	Silva E, Pereira AC, Estalagem SP, Moreira-Santos M, Ribeiro R & Cerejeira MJ	2012	Assessing the quality of freshwaters in a protected area within the Tagus river basin district (Central Portugal)	Journal of Environmental Quality 41, 1413-1426
7.5	Hildebrandt A, Lacorte S & Barceló D	2007	Assessment of priority pesticides, degradation products, and pesticide adjuvants in groundwater and top soils from agricultural areas of the Ebro river basin	Anal Bioanal Chem 387, 1459-1468
7.5	Papadopoulou-Mourkidou E, Karpouzas DG, Patsias J, Kotopoulou A, Milothridou A, Kintzikoglou K & Vlachou P	2004	The potential of pesticides to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece. Part I. Monitoring study in the north part of the basin.	Science of the Total Environment 321, 127-146
7.5	Köck-Schulmeyer M, Ginebreda A, Postigo C, Garrido T, Fraile J, López de Alda M & Barceló D	2014	Four-year advanced monitoring program of polar pesticides in groundwater of Catalonia (NE-Spain)	Science of the Total Environment 470-471, 1087-1098

CA data point number	Author(s)	Year	Title	Source
7.5	Loos R, Locoro G, Comero S, Contini S, Schwesig D, Werres F, Balsaa P, Gans O, Weiss S, Blaha L, Bolchi M, Gawlik B	2010	Pan-European survey on the occurrence of selected polar organic persistent pollutants in groundwater	Water Research 44, 4115-4126
7.5	Sagratini, G.; Ametisti, M.; Canella, M.; Cristalli, G.; Francoletti, E.; Giardina, D; Luminari, M. C; Paparelli, G; Pico, Y; Volpini, R; Vittori, S.	2007	Well water in central Italy: analysis of herbicide residues as potential pollutants of untreated crops.	Fresenius Environmental Bulletin (2007), Volume 16, Number 8, pp. 973-979
7.5	Rossi, C.; Menegus, L.; Mion, F.	2004	Pesticide products and their metabolism in water bodies and groundwater in Veneto.	Rapporti ISTISAN - Istituto Superiore di Sanita (2004), Number 04/35, pp. 121-130
7.5	Sanchez-Gonzalez, S; Pose-Juan, E; Herrero-Hernandez, E; Alvarez-Martin, A; Sanchez-Martin, MJ; Rodriguez-Cruz, S	2013	Pesticide residues in groundwaters and soils of agricultural areas in the Agueda River Basin from Spain and Portugal	International Journal of Environmental Analytical Chemistry (2013), 93 (15), 1585-1601.
7.5	Masia, Ana; Campo, Julian; Vazquez-Roig, Pablo; Blasco, Cristina; Pico, Yolanda	2012	Screening of currently used pesticides in water, sediments and biota of the Guadalquivir River Basin (Spain)	Journal of Hazardous Materials (2013), 263 (P1), 95-104
7.5	Herrero-Hernandez, Eliseo; Pose-Juan, Eva; Alvarez-Martin, Alba; Andrades, Maria Soledad; Rodriguez-Cruz, Maria Sonia; Sanchez-Martin, Maria J.	2012	Pesticides and degradation products in groundwaters from a vineyard region: Optimization of a multiresidue method based on SPE and GC-MS	Journal of Separation Science (2012), 35 (24), 3492-3500
7.5	Rocha, MJ; Ribeiro, MFT.; Cruzeiro, C; Figueiredo, F; Rocha, E	2012	Development and validation of a GC-MS method for determination of 39 common pesticides in estuarine water - targeting hazardous amounts in the Douro River estuary	International Journal of Environmental Analytical Chemistry (2012), 92 (14), 1587-1608
7.5	Rice, Clifford P.; Bialek-Kalinski, Krystyna; McCarty, Gregory W	2012	Chiral separation of metolachlor ethane sulfonic acid as a groundwater dating tool	SO Abstracts of Papers, 244th ACS National Meeting & Exposition, Philadelphia, PA, United States, August 19-23, 2012 (2012), AGRO-35
7.5	Koeck-Schulmeyer, M; Ginebreda, A; Gonzalez, S; Cortina, JL; de Alda, ML; Barcelo, D	2012	Analysis of the occurrence and risk assessment of polar pesticides in the Llobregat River Basin (NE Spain)	Chemosphere (2012), 86 (1), 8-16
7.5	Mansilha, C.; Melo, A.; Ferreira, I. M. P. L. V. O.; Pinho, O.; Domingues, V.; Pinho, C.; Gameiro, P.	2012	Groundwater from Infiltration Galleries Used for Small Public Water Supply Systems- Contamination with Pesticides and Endocrine Disruptors	Bulletin of Environmental Contamination and Toxicology (2011), 87 (3), 312-318
7.5	Finizio, Antonio; Azimonti, Giovanna; Villa, Sara	2011	Occurrence of pesticides in surface water bodies: A critical analysis of the Italian national pesticide survey programs	Journal of Environmental Monitoring (2011), 13 (1), 49-57

CA data point number	Author(s)	Year	Title	Source
7.5	Hamer, Kay; Freudenberger, Uta	2011	Plant protection legal irrelevant metabolites in groundwater	Wasser und Abfall (Wiesbaden, Germany) (2011), 13 (9), 42-45
7.5	Fava, L; Orru, MA; Scardala, S; Alonzo, E;Fardella, M; Strumia, C; Martinelli, A; Finocchiaro,S; Previtera, M; Franchi, A; Cala, P; Dovis,M; Bartoli, D; Sartori, G; Broglia, L; Funari, E	2010	Pesticides and their metabolites in selected Italian groundwater and surface water used for drinking	Annali dell'Istituto Superiore di Sanita (2010), 46 (3), 309-316
7.5	Vryzas, Z.; Vassiliou, G.; Alexoudis, C.; Papadopoulou-Mourkidou, E.	2009	Spatial and temporal distribution of pesticide residues in surface waters in northeastern Greece	Water Research (2009), 43 (1), 1-10.
7.5	Villaverde, J; Hildebrandt, A; Martinez, E; Lacorte, S;Morillo, E; Maqueda, C; Viana, P; Barcelo, D	2008	Priority pesticides and their degradation products in river sediments from Portugal	Science of the Total Environment (2008), 390 (2-3), 507-513
7.5	Wuelser, R	2005	Herbicide and pesticide studies in the Lange Erlen groundwater works	SO GWA (Zurich, Switzerland) (2005), 85 (1), 48-52
7.5	Kolpin, DW.; Schnoebelen, DJ.; Thurman, EM	2004	Degradates provide insight to spatial and temporal trends of herbicides in ground water	Ground Water (2004), 42 (4), 601-608
7.5	Karoly, G; Schremm, A; Boronkai, A	2004	Monitoring the pesticide contamination of the Lake Balaton and its inflows	Novenyvedelem (Budapest, Hungary) (2004), 40 (4), 185-192

Table 9.6-3: List of references for all relevant and unclear studies listed by Author

Author(s)	Year	OECD data point number	Title	Source
Initial Search				
Aboul Eish, MYZ; Wells, MJM	2008	7.2.2	Monitoring stereoselective degradation of metolachlor in a constructed wetland: use of statistically valid enantiomeric and diastereomeric fractions as opposed to ratios.	Journal of chromatographic science, (2008 Mar) Vol. 46, No. 3, pp. 269-75.
Accinelli, C.; Dinelli, G.; Vicari, A.	2004	7.1.1.1	Metolachlor and linuron soil degradation after repeated applications under laboratory conditions.	Agrochimica (2004), Vol. 48, Number 3/4, pp. 132-140
Amalric L, Baran N, Coureau C, Maingot L, Buron F & Routier S	2013	7.5	Analytical developments for 47 pesticides: first identification of neutral chloroacetanilide derivatives in French groundwater	Inter. J. Environ. Anal. Chem. 93(15), 1660-1675
Antić N, Radišić M, Radović T, Vasiljević T, Grujić S, Petković A, Dimkić M, Laušević M	2014	7.5	Pesticide residues in the Danube river basin in Serbia – a survey during 2009-2011	Clean – Soil, Air, Water 00(0), 1-8

Author(s)	Year	OECD data point number	Title	Source
Baran N & Gourcy L	2013	7.5	Soprtion and mineralisation of S-metolachlor and its ionic metabolites in soils and vadose zone solids: Consequences on groundwater quality in an alluvial aquifer (Ain Plain, France)	Journal of Contaminant Hydrology, 154, 20-28
Barra CA; Giuliano G; Grenni P; Guzzella L; Pozzoni F; Bottoni P; Fava L; Crobe A; Orru M; Funari E	2005	7.1.4	Degradation and leaching of the herbicides metolachlor and diuron: a case study in an area of Northern Italy.	Environmental pollution (Barking, Essex : 1987), (2005 Apr) Vol. 134, No.3, pp. 525-34.
Boithias L, Sauvage S, Taghavi L, Merlina G, Probst J-L & Pérez LMS	2011	7.5	Occurrence of metolachlor and trifluralin losses in the Save river agricultural catchment during floods	Journal of Hazardous Materials 196, 210-219
Cao P, Wang X, Liu F, Zhao E & Han L	2008	7.1.1.1	Dissipation and Residue of S-Metolachlor in Maize and Soil	Bull Environ Contam Toxicol, Vol 80, pp. 391-394
Capel, Paul D.; Webb, Richard M. T.	2007	7.1.1.1	Multi-compartment analysis of the behavior and fate of metolachlor in the environment	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2007), 47(2), 593-595
Claver, A.; Ormad, P.; Rodriguez, L.; Ovelleiro, J.L	2006	7.5	Study of the presence of pesticides in surface waters in the Ebro river basin (Spain)	Chemosphere 8, 1437-1443
Coffinet, S.; Rifai, A.; Genty, C.; Souissi, Y.; Bourcier, S.; Sablier, M.; Bouchonnet, S.	2012	7.2.1.2	Characterization of the photodegradation products of metolachlor: structural elucidation, potential toxicity and persistence	Journal of Mass Spectrometry , Volume 47, Number 12, pp. 1582-1593
Doppler, T.; Camenzuli, L.; Hirzel, G.; Krauss, M.; Luck, A.; Stamm, C.	2012	7.1.4	Spatial variability of herbicide mobilization and transport at catchment scale: insights from a field experiment	Hydrology and Earth System Sciences (2012), 16 (7), 1947-1967
Fava, L; Orru, MA; Scardala, S; Alonzo, E;Fardella, M; Strumia, C; Martinelli, A; Finocchiaro,S; Previtera, M; Franchi, A; Cala, P; Dovis,M; Bartoli, D; Sartori, G; Broglia, L; Funari, E	2010	7.5	Pesticides and their metabolites in selected Italian groundwater and surface water used for drinking	Annali dell'Istituto Superiore di Sanita (2010), 46 (3), 309-316
Finizio, Antonio; Azimonti, Giovanna; Villa, Sara	2011	7.5	Occurrence of pesticides in surface water bodies: A critical analysis of the Italian national pesticide survey programs	Journal of Environmental Monitoring (2011), 13 (1), 49-57
Freitas, L. G.; Singer, H.; Mueller, S. R.; Schwarzenbach, R. P.; Stamm, C.	2008	7.5	Source area effects on herbicide losses to surface waters - a case study in the Swiss Plateau.	Agriculture, Ecosystems & Environment (2008), Vol. 128, Number 3, pp. 177-184
Gish, TJ; Prueger, JH; Daughtry, CST; Kustas, WP; McKee, LG; Russ, AL; Hatfield, JL	2011	7.3.2	Comparison of field-scale herbicide runoff and volatilization losses: an eight-year field investigation. Journal of environmental quality	Journal of environmental quality, Vol. 40, No. 5, pp.1432-42

Author(s)	Year	OECD data point number	Title	Source
Hamer, Kay; Freudenberger, Uta	2011	7.5	Plant protection legal irrelevant metabolites in groundwater	Wasser und Abfall (Wiesbaden, Germany) (2011), 13 (9), 42-45
Herrero-Hernandez, Eliseo; Pose-Juan, Eva; Alvarez-Martin, Alba; Andrades, Maria Soledad; Rodriguez-Cruz, Maria Sonia; Sanchez-Martin, Maria J.	2012	7.5	Pesticides and degradation products in groundwaters from a vineyard region: Optimization of a multiresidue method based on SPE and GC-MS	Journal of Separation Science (2012), 35 (24), 3492-3500
Hildebrandt A, Guillamón M, Lacorte S, Tauler R & Barceló D	2008	7.5	Impact of pesticides used in agriculture and vineyards to surface and groundwater quality (North Spain)	Water Research 42, 3315-3326
Hildebrandt A, Lacorte S & Barceló D	2007	7.5	Assessment of priority pesticides, degradation products, and pesticide adjuvants in groundwater and top soils from agricultural areas of the Ebro river basin	Anal Bioanal Chem 387, 1459-1468
Hladik ML, Bouwer EJ & Roberts AL	2008	7.5	Neutral degradates of chloroacetamide herbicides: Occurrence in drinking water and removal during conventional water treatment	Water Research 42, 4905-4914
Karoly, G; Schremm, A; Boronkai, A	2004	7.5	Monitoring the pesticide contamination of the Lake Balaton and its inflows	Novenyvedelem (Budapest, Hungary) (2004), 40 (4), 185-192
Klein, C, Schneider, RJ, Meter, MT & Aga, DS	2006	7.1.1.1	Enantiomeric separation of metolachlor and its metabolites using LC-MS and CZE	Chemosphere, 62, 1591-1599
Köck-Schulmeyer M, Ginebreda A, Postigo C, Garrido T, Fraile J, López de Alda M & Barceló D	2014	7.5	Four-year advanced monitoring program of polar pesticides in groundwater of Catalonia (NE-Spain)	Science of the Total Environment 470-471, 1087-1098
Koeck-Schulmeyer, M; Ginebreda, A; Gonzalez, S; Cortina, JL; de Alda, ML; Barcelo, D	2012	7.5	Analysis of the occurrence and risk assessment of polar pesticides in the Llobregat River Basin (NE Spain)	Chemosphere (2012), 86 (1), 8-16
Kolpin, DW.; Schnoebelen, DJ.; Thurman, EM	2004	7.5	Degradates provide insight to spatial and temporal trends of herbicides in ground water	Ground Water (2004), 42 (4), 601-608
Kurt-Karakus PH, Bidleman, TF, Muir, DCG, Struger J, Sverko E, Cagampan SJ, Small JM and Jantunen LM	2010	7.2.2	Comparison of concentrations and stereoisomer ratios of mecoprop, dichlorprop and metolachlor in Ontario streams, 2006-2007 vs. 2003-2004	Environmental Pollution, 158, 1842-1849
Loos R, Locoro G, Comero S, Contini S, Schwesig D, Werres F, Balsaa P, Gans O, Weiss S, Blaha L, Bolchi M, Gawlik B	2010	7.5	Pan-European survey on the occurrence of selected polar organic persistent pollutants in groundwater	Water Research 44, 4115-4126
Mansilha, C.; Melo, A.; Ferreira, I. M. P. L. V. O.; Pinho, O.; Domingues, V.; Pinho, C.; Gameiro, P.	2012	7.5	Groundwater from Infiltration Galleries Used for Small Public Water Supply Systems-Contamination with Pesticides and Endocrine Disruptors	Bulletin of Environmental Contamination and Toxicology (2011), 87 (3), 312-318
Masia, Ana; Campo, Julian; Vazquez-Roig, Pablo; Blasco, Cristina; Pico, Yolanda	2012	7.5	Screening of currently used pesticides in water, sediments and	Journal of Hazardous Materials (2013), 263 (P1), 95-104

Author(s)	Year	OECD data point number	Title	Source
			biota of the Guadalquivir River Basin (Spain)	
Mersie W, McNamee C, Seybold C & Tierney D	2004	7.2.2.	Degradation of metolachlor in bare and vegetated soils and in simulated water-sediment systems	Environ Toxicol Chem 23(11), 2627-2632
Papadopoulou-Mourkidou E, Karpouzas DG, Patsias J, Kotopoulou A, Milothridou A, Kintzikoglou K & Vlachou P	2004	7.5	The potential of pesticides to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece. Part II. Monitoring study in the south part of the basin.	Science of the Total Environment 321, 147-164
Papadopoulou-Mourkidou E, Karpouzas DG, Patsias J, Kotopoulou A, Milothridou A, Kintzikoglou K & Vlachou P	2004	7.5	The potential of pesticides to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece. Part I. Monitoring study in the north part of the basin.	Science of the Total Environment 321, 127-146
Polcaro CM, Berti A; Mannina, L; Marra C; Sinibaldi M; Viel S	2007	7.1.1.1	Chiral HPLC resolution of neutral pesticides	Journal of Liquid Chromatography & Related Technologies, 27:1,49-61
Reemtsma T, Alder L & Banasiak U	2013	7.5	Emerging pesticide metabolites in groundwater and surface water as determined by the application of a multimethod for 150 pesticide metabolites	Water Research 47, 5535-5545
Reemtsma T, Alder L & Banasiak U	2013	7.5	A multimethod for the determination of 150 pesticide metabolites in surface water and groundwater using direct injection liquid chromatography-mass spectrometry	Journal of Chromatography A 1271, 95-104
Rice, Clifford P.; Bialek-Kalinski, Krystyna; McCarty, Gregory W	2012	7.5	Chiral separation of metolachlor ethane sulfonic acid as a groundwater dating tool	SO Abstracts of Papers, 244th ACS National Meeting & Exposition, Philadelphia, PA, United States, August 19-23, 2012 (2012), AGRO-35
Rice PJ, Anderson TA & Coats JR	2004	7.2.2	Effect of sediment on the fate of metolachlor and atrazine in surface water	Environ. Toxicol. Chem 23(5); 1145-55
Rocha, MJ; Ribeiro, MFT.; Cruzeiro, C; Figueiredo, F; Rocha, E	2012	7.5	Development and validation of a GC-MS method for determination of 39 common pesticides in estuarine water - targeting hazardous amounts in the Douro River estuary	International Journal of Environmental Analytical Chemistry (2012), 92 (14), 1587-1608
Rossi, C.; Menegus, L.; Mion, F.	2004	7.5	Pesticide products and their metabolism in water bodies and groundwater in Veneto.	Rapporti ISTISAN - Istituto Superiore di Sanita (2004), Number 04/35, pp. 121-130
Sagratini, G.; Ametisti, M.; Canella, M.; Cristalli, G.; Francoletti, E.; Giardina, D; Luminari, M. C; Paparelli, G; Pico, Y; Volpini, R; Vittori, S.	2007	7.5	Well water in central Italy: analysis of herbicide residues as potential pollutants of untreated crops.	Fresenius Environmental Bulletin (2007), Volume 16, Number 8, pp. 973-979

Author(s)	Year	OECD data point number	Title	Source
Sanchez-Gonzalez, S; Pose-Juan, E; Herrero-Hernandez, E; Alvarez-Martin, A; Sanchez-Martin, MJ; Rodriguez-Cruz, S	2013	7.5	Pesticide residues in groundwaters and soils of agricultural areas in the Agueda River Basin from Spain and Portugal	International Journal of Environmental Analytical Chemistry (2013), 93 (15), 1585-1601.
Schipper PNM, Vissers MJM & van der Linden AMA	2008	7.5	Pesticides in groundwater and drinking water wells: overview of the situation in the Netherlands	Water Science & Technology 57(8), 1277-1286
Shaner, D L; Brunk, G; Belles, D; Westra, P; Nissen, S	2006	7.1.1.1	Soil dissipation and biological activity of metolachlor and S-metolachlor in five soils	Pest management science (2006), Volume 62, Number 7, pp. 617-623
Silva E, Mendes MP, Ribeiro L & Cerejeira MJ	2012	7.5	Exposure assessment of pesticides in a shallow groundwater of the Tagus vulnerable zone (Portugal): a multivariate statistical approach (JCA)	Environ. Sci. Pollut. Res. 19: 2667-2680
Silva E, Pereira AC, Estalagem SP, Moreira-Santos M, Ribeiro R & Cerejeira MJ	2012	7.5	Assessing the quality of freshwaters in a protected area within the Tagus river basin district (Central Portugal)	Journal of Environmental Quality 41, 1413-1426
Souissi Y, Bouchonnet S, Bourcier S, Kusk KO, Sbalier M & Andersen HR	2013	7.2.1.2	Identification and ecotoxicity of degradation products of chloroacetamide herbicides from UV-treatment of water	Science of the Total Environment 458-460, 527-534
Villaverde, J; Hildebrandt, A; Martinez, E; Lacorte, S;Morillo, E; Maqueda, C; Viana, P; Barcelo, D	2008	7.5	Priority pesticides and their degradation products in river sediments from Portugal	Science of the Total Environment (2008), 390 (2-3), 507-513
Vryzas Z, Alexoudis C, Vassiliou G, Galanis K, Papadopoulou-Mourkidou E	2011	7.5	Determination and aquatic risk assessment of pesticide residues in riparian drainage canals in northeastern Greece	Ecotoxicology and Environmental Safety 74, 174-181
Vryzas Z; Papadakis EN; Papadopoulou-Mourkidou E	2012	7.1.4	Leaching of Br-, metolachlor, alachlor, atrazine, deethylatrazine and deisopropylatrazine in clayey vadoze zone: a field scale experiment in north-east Greece.	Water research, (2012 Apr 15) Vol. 46, No. 6, pp. 1979-89
Vryzas Zisis	2012	7.1.1.1	Biotransformation of atrazine and metolachlor within soil profile and changes in microbial communities.	Chemosphere, (2012 Nov) Vol. 89, No. 11, pp. 1330-8
Vryzas, Z.; Vassiliou, G.; Alexoudis, C.; Papadopoulou-Mourkidou, E.	2009	7.5	Spatial and temporal distribution of pesticide residues in surface waters in northeastern Greece	Water Research (2009), 43 (1), 1-10.
Wuelser, R	2005	7.5	Herbicide and pesticide studies in the Lange Erlen groundwater works	SO GWA (Zurich, Switzerland) (2005), 85 (1), 48-52

A detailed review of the full-text of documents identified in Table 9.6-2 resulted in the additional exclusion of the following studies from the dossier.

Table 9.6-4: List of references excluded following detailed review listed by data point number

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.1.1.1	Accinelli, C.; Dinelli, G.; Vicari, A.	2004	Metolachlor and linuron soil degradation after repeated applications under laboratory conditions.	Agrochimica (2004), Vol. 48, Number 3/4, pp. 132-140	Does not meet relevance criteria – endpoint not relevant as soils exposed multiple times to test compounds (non-guideline compliant)
7.1.1.1	Capel, Paul D.; Webb, Richard M. T.	2007	Multi-compartment analysis of the behavior and fate of metolachlor in the environment	Preprints of Extended Abstracts presented at the ACS National Meeting, American Chemical Society, Division of Environmental Chemistry (2007), 47(2), 593-595	Insufficient data to assess – abstract only
7.1.1.1	Polcaro CM, Berti A; Mannina, L; Marra C; Sinibaldi M; Viel S	2007	Chiral HPLC resolution of neutral pesticides	Journal of Liquid Chromatography & Related Technologies, 27:1,49-61	Does not meet relevance criteria: No details of the test material e.g. purity; No complete soil characterisation; No details on the biomass measurements or microbial activity; No verification of the exact amount applied and detected in soil; No details regarding the sample storage stability; No details on analytics: repeatability, linearity, accuracy and precision of the analytical method; No details of control samples.
7.1.1.1	Klein, C, Schneider, RJ, Meter, MT & Aga, DS	2006	Enantiomeric separation of metolachlor and its metabolites using LC-MS and CZE	Chemosphere, 62, 1591-1599	Does not meet relevance criteria – no information provided regarding sampling, storage or preparation of soil & sludge samples, no physicochemical characteristics of soil/sludge samples provided, no history of potential exposure of sludge/soil to metolachlor provided, insufficient samples for kinetics.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.1.1.1	Vryzas Zisis	2012	Biotransformation of atrazine and metolachlor within soil profile and changes in microbial communities.	Chemosphere, (2012 Nov) Vol. 89, No. 11, pp. 1330-8	Does not meet relevance criteria: soils analysed have a history of agrochemical application and are therefore non-guideline compliant. Further, no information is provided on the sampling, storage and reparation of soils for use in the experiment, and where subsoils are investigated, no discussion of preservation of anoxic/microaerophilic conditions is described despite this being clearly relevant for anaerobic microbes.
7.1.1.1	Cao P, Wang X, Liu F, Zhao E & Han L	2008	Dissipation and Residue of S-Metolachlor in Maize and Soil	Bull Environ Contam Toxicol, Vol 80, pp. 391-394	Does not meet relevance criteria – field sites have not been demonstrated to be geoclimitically relevant for EU
7.1.1.1	Shaner, D L; Brunk, G; Belles, D; Westra, P; Nissen, S	2006	Soil dissipation and biological activity of metolachlor and S-metolachlor in five soils	Pest management science (2006), Volume 62, Number 7, pp. 617-623	Does not meet relevance criteria – field sites have not been demonstrated to be geoclimitically relevant for EU, soil sampling, preparation and handling of soils is poorly described, field sites have likely received significant inputs of agrochemicals proceeding use in study and are thus non guideline compliant for rate evaluation.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.1.4	Vryzas Z; Papadakis EN; Papadopoulou-Mourkidou E	2012	Leaching of Br-, metolachlor, alachlor, atrazine, deethylatrazine and deisopropylatrazine in clayey vadoze zone: a field scale experiment in north-east Greece.	Water research, (2012 Apr 15) Vol. 46, No. 6, pp. 1979-89	Does not meet relevance criteria: no soil characterisation data provided for field sites, no historical product use history provided for sampling sites, no description of installation of suction lysimeters (in particular, no discussion of how this did not disrupt the soil profile and adversely impact the residue profile), no description of the groundwater monitoring well construction or installation….
7.1.4	Barra CA; Giuliano G; Grenni P; Guzzella L; Pozzoni F; Bottoni P; Fava L; Crobe A; Orru M; Funari E	2005	Degradation and leaching of the herbicides metolachlor and diuron: a case study in an area of Northern Italy.	Environmental pollution (Barking, Essex : 1987), (2005 Apr) Vol. 134, No.3, pp. 525-34.	Does not meet relevance criteria: No discussion of groundwater sample locations with specific absence of demonstrating that wells are not under point source influence (wells located on farmyards), no description of well construction or depths, no description of historical product use, no description of lysimeter installation protocols or depths.
7.1.4	Doppler, T.; Camenzuli, L.; Hirzel, G.; Krauss, M.; Luck, A.; Stamm, C.	2012	Spatial variability of herbicide mobilization and transport at catchment scale: insights from a field experiment	Hydrology and Earth System Sciences (2012), 16 (7), 1947-1967	Does not meet relevance criteria: LOQ not defined, no verification of spray application through spray card or other relevant device, soil extraction efficiency not reported; no details of soil analysis performance such as LOQ, repeatability or accuracy.
7.2.1.2	Coffinet, S.; Rifai, A.; Genty, C.; Souissi, Y.; Bourcier, S.; Sablier, M.; Bouchonnet, S.	2012	Characterization of the photodegradation products of metolachlor: structural elucidation, potential toxicity and persistence	Journal of Mass Spectrometry , Volume 47, Number 12, pp. 1582-1593	Does not meet relevance criteria: Not environmentally relevant as UV source is a mercury lamp emitting a spectrum irrelevant to sunlight (specifically wavelengths <290 nm)

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.2.1.2	Souissi Y, Bouchonnet S, Bourcier S, Kusk KO, Sbalier M & Andersen HR	2013	Identification and ecotoxicity of degradation products of chloroacetamide herbicides from UV-treatment of water	Science of the Total Environment 458-460, 527-534	Does not meet relevance criteria: Not environmentally relevant as UV source is a mercury lamp emitting a spectrum irrelevant to sunlight (specifically wavelengths <290 nm)
7.2.2	Aboul Eish, MYZ; Wells, MJM	2008	Monitoring stereoselective degradation of metolachlor in a constructed wetland: use of statistically valid enantiomeric and diastereomeric fractions as opposed to ratios.	Journal of chromatographic science, (2008 Mar) Vol. 46, No. 3, pp. 269-75.	Does not meet relevance criteria: No details on water characterisation No verification of the exact amount applied; No details of the recovery rate nor LOQ reported; No details on the sample storage stability; No details on analytics: repeatability, linearity, accuracy and precision of the analytical method; No replicates and control samples.
7.2.2	Kurt-Karakus PH, Bidleman, TF, Muir, DCG, Struger J, Sverko E, Cagampan SJ, Small JM and Jantunen LM	2010	Comparison of concentrations and stereoisomer ratios of mecoprop, dichlorprop and metolachlor in Ontario streams, 2006-2007 vs. 2003-2004	Environmental Pollution, 158, 1842-1849	Does not meet relevance criteria: Study conducted in Canada and as such not geoclimatically relevant for EU28, use rates historically higher than EU, no description of sampling points and catchment areas.
7.2.2	Rice PJ, Anderson TA & Coats JR	2004	Effect of sediment on the fate of metolachlor and atrazine in surface water	Environ. Toxicol. Chem 23(5); 1145-55	Does not meet relevance criteria: Only 3 sampling points and thus cannot be used to estimate DT50
7.2.2	Mersie W, McNamee C, Seybold C & Tierney D	2004	Degradation of metolachlor in bare and vegetated soils and in simulated water-sediment systems	Environ Toxicol Chem 23(11), 2627-2632	Does not meet relevance criteria: Study protocol differs radically from OECD308 study design.
7.5	Baran N & Gourcy L	2013	Soprtion and mineralisation of S-metolachlor and its ionic metabolites in soils and vadose zone solids: Consequences on groundwater quality in an alluvial aquifer (Ain Plain, France)	Journal of Contaminant Hydrology, 154, 20-28	Insufficient description of sampling location, catchments, hydrology, weather analysis or cropping. No details on analytics: repeatability, linearity, accuracy and precision of the analytical method

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Hildebrandt A, Guillamón M, Lacorte S, Tauler R & Barceló D	2008	Impact of pesticides used in agriculture and vineyards to surface and groundwater quality (North Spain)	Water Research 42, 3315-3326	Does not meet relevance criteria: Insufficient information provided regarding the construction, integrity and design of the groundwater sampling wells. Specifically, table 2 does not provide an indication of the screened interval. Further, description of groundwater sampling protocols is insufficient (potential contamination route). For surface water, no detailed description of sampling area and agrochemical use in the catchment area is provided, and no analysis of catchment hydrology and potential routes of transfer from fields to surface water.
7.5	Silva E, Mendes MP, Ribeiro L & Cerejeira MJ	2012	Exposure assessment of pesticides in a shallow groundwater of the Tagus vulnerable zone (Portugal): a multivariate statistical approach (JCA)	Environ. Sci. Pollut. Res. 19: 2667-2680	Does not meet relevance criteria: Insufficient description of the groundwater monitoring wells with regards to design, construction (in particular the integrity of the well and susceptibility to point source influences) and screen. Further, there is no interpretation of local groundwater flow direction nor an analysis of up-gradient agrochemical use (including potential point sources).
7.5	Reemtsma T, Alder L & Banasiak U	2013	Emerging pesticide metabolites in groundwater and surface water as determined by the application of a multimethod for 150 pesticide metabolites	Water Research 47, 5535-5545	Does not meet relevance criteria: The report describes a new multi-residue analytical method. No details are provided regarding the sampling points for either groundwater or surface water.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Vryzas Z, Alexoudis C, Vassiliou G, Galanis K, Papadopoulou-Mourkidou E	2011	Determination and aquatic risk assessment of pesticide residues in riparian drainage canals in northeastern Greece	Ecotoxicology and Environmental Safety 74, 174-181	Does not meet relevance criteria: No details of the recovery rate nor LOQ reported; No details on the sample storage stability; No details on analytics: repeatability, linearity, accuracy and precision of the analytical method; No replicates and control samples. Insufficient description of sampling location, catchments, hydrology, weather analysis or cropping.
7.5	Antić N, Radišić M, Radović T, Vasiljević T, Grujić S, Petković A, Dimkić M, Laušević M	2014	Pesticide residues in the Danube river basin in Serbia – a survey during 2009-2011	Clean – Soil, Air, Water 00(0), 1-8	Does not meet relevance criteria: Insufficient description of the sampling location and local hydrology of soils relevant to the local fields. No understanding of local cropping practices; no weather data supplied despite an indication that the monitored year was extremely unusual.
7.5	Boithias L, Sauvage S, Taghavi L, Merlina G, Probst J-L & Pérez LMS	2011	Occurrence of metolachlor and trifluralin losses in the Save river agricultural catchment during floods	Journal of Hazardous Materials 196, 210-219	Does not meet relevance criteria: No details of the recovery rate nor LOQ reported; No details on the sample storage stability; No details on analytics: repeatability, linearity, accuracy and precision of the analytical method; No replicates and control samples.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Claver, A.; Ormad, P.; Rodriguez, L.; Ovelleiro, J.L	2006	Study of the presence of pesticides in surface waters in the Ebro river basin (Spain)	Chemosphere 8, 1437-1443	Does not meet relevance criteria: Insufficient description of the sampling location and local hydrology of soils relevant to the local fields. No understanding of local cropping practices; no weather data supplied; analytical methodology is not described, no LOD/LOQ, no evidence of control blanks, method performance questionable (recovery 65-135% is not compliant with method validation requirements) NB – metolachlor is not registered for use on wheat.
7.5	Papadopoulou-Mourkidou E, Karpouzas DG, Patsias J, Kotopoulou A, Milothridou A, Kintzikoglou K & Vlachou P	2004	The potential of pesticides to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece. Part II. Monitoring study in the south part of the basin.	Science of the Total Environment 321, 147-164	Does not meet relevance criteria: no description of the appropriate installation of lysimeter or groundwater monitoring equipment in the test fields, no documentation of product use in the vicinity of the test fields, no information provided on geology or hydrogeology of the test sites, no information provided about the estuarine sampling location and consideration of their catchment and product use therein.
7.5	Freitas, L. G.; Singer, H.; Mueller, S. R.; Schwarzenbach, R. P.; Stamm, C.	2008	Source area effects on herbicide losses to surface waters - a case study in the Swiss Plateau.	Agriculture, Ecosystems & Environment (2008), Vol. 128, Number 3, pp. 177-184	Metolachlor was not the main targets of the monitoring, just used as a tracer.
7.5	Reemtsma T, Alder L & Banasiak U	2013	A multimethod for the determination of 150 pesticide metabolites in surface water and groundwater using direct injection liquid chromatography-mass spectrometry	Journal of Chromatography A 1271, 95-104	Does not meet relevance criteria; Predominantly a method development paper.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Hladik ML, Bouwer EJ & Roberts AL	2008	Neutral degradates of chloroacetamide herbicides: Occurrence in drinking water and removal during conventional water treatment	Water Research 42, 4905-4914	Does not meet relevance criteria: insufficient description of groundwater sample points and their relevant construction features and proximity to agronomic regions. No description of potential recharge zones for monitored areas and use of key herbicides in said recharge areas. No evidence that regions are geoclimitically relevant to EU28. No description of surface water bodies and potential influences on quality of surface water.
7.5	Silva E, Pereira AC, Estalagem SP, Moreira-Santos M, Ribeiro R & Cerejeira MJ	2012	Assessing the quality of freshwaters in a protected area within the Tagus river basin district (Central Portugal)	Journal of Environmental Quality 41, 1413-1426	Does not meet relevance criteria: Insufficient (no) description of groundwater sampling well construction, design and intake, specifically integrity of well and protection from point sources. Further, the location of the monitoring well considering regional groundwater flow and upstream cropping is not reported. With RE: Surface water, there is no description of sampling points, catchments, hydrology, weather analysis or cropping.
7.5	Hildebrandt A, Lacorte S & Barceló D	2007	Assessment of priority pesticides, degradation products, and pesticide adjuvants in groundwater and top soils from agricultural areas of the Ebro river basin	Anal Bioanal Chem 387, 1459-1468	Does not meet relevance criteria: Insufficient description of groundwater sampling well construction, design and intake, specifically integrity of well and protection from point sources. Further, the location of the monitoring well considering regional groundwater flow and upstream cropping is not reported.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Papadopoulou-Mourkidou E, Karpouzas DG, Patsias J, Kotopoulou A, Milothridou A, Kintzikoglou K & Vlachou P	2004	The potential of pesticides to contaminate the groundwater resources of the Axios river basin in Macedonia, Northern Greece. Part I. Monitoring study in the north part of the basin.	Science of the Total Environment 321, 127-146	Does not meet relevance criteria: no description of the appropriate installation of lysimeter or groundwater monitoring equipment in the test fields (in particular how potential preferential flow pathways were avoided), no documentation of product use in the vicinity of the test fields, no information provided on geology or hydrogeology of the test sites,
7.5	Köck-Schulmeyer M, Ginebreda A, Postigo C, Garrido T, Fraile J, López de Alda M & Barceló D	2014	Four-year advanced monitoring program of polar pesticides in groundwater of Catalonia (NE-Spain)	Science of the Total Environment 470-471, 1087-1098	Does not meet relevance criteria: Insufficient description of groundwater sampling wells and sampling methodology. A number of the wells appear to be constructed with very long screens in deep groundwater bodies. Unknown impact of point source on well integrity.
7.5	Loos R, Locoro G, Comero S, Contini S, Schwesig D, Werres F, Balsaa P, Gans O, Weiss S, Blaha L, Bolchi M, Gawlik B	2010	Pan-European survey on the occurrence of selected polar organic persistent pollutants in groundwater	Water Research 44, 4115-4126	Does not meet relevance criteria: insufficient description of groundwater sample points and their relevant construction features and proximity to agronomic regions. No description of potential recharge zones for monitored areas and use of key herbicides in said recharge areas.
7.5	Sagratini, G.; Ametisti, M.; Canella, M.; Cristalli, G.; Francoletti, E.; Giardina, D; Luminari, M. C; Paparelli, G; Pico, Y; Volpini, R; Vittori, S.	2007	Well water in central Italy: analysis of herbicide residues as potential pollutants of untreated crops.	Fresenius Environmental Bulletin (2007), Volume 16, Number 8, pp. 973-979	Does not meet relevance criteria: Irrigation wells are subject to contamination and as such are not appropriate for use to derive groundwater quality. No description of well construction or design, no description of sampling protocol.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Rossi, C.; Menegus, L.; Mion, F.	2004	Pesticide products and their metabolism in water bodies and groundwater in Veneto.	Rapporti ISTISAN - Istituto Superiore di Sanita (2004), Number 04/35, pp. 121-130	Does not meet relevance criteria: No description of sampling locations with respect to potential point source (location on farmyards?) or agronomic applications, no description of well construction or design, no description of sampling protocol.
7.5	Sanchez-Gonzalez, S; Pose-Juan, E; Herrero-Hernandez, E; Alvarez-Martin, A; Sanchez-Martin, MJ; Rodriguez-Cruz, S	2013	Pesticide residues in groundwaters and soils of agricultural areas in the Agueda River Basin from Spain and Portugal	International Journal of Environmental Analytical Chemistry (2013), 93 (15), 1585-1601.	Does not meet relevance criteria: No description of sampling locations with respect to potential point source (location on farmyards?) or agronomic applications, no description of well construction or design, no description of sampling protocol.
7.5	Masia, Ana; Campo, Julian; Vazquez-Roig, Pablo; Blasco, Cristina; Pico, Yolanda	2012	Screening of currently used pesticides in water, sediments and biota of the Guadalquivir River Basin (Spain)	Journal of Hazardous Materials (2013), 263 (P1), 95-104	Does not meet relevance criteria: no description of the sampling points with relation to catchment area and potential agronomic uses in said catchments, no information on hydrology, no assessment of potential point source contamination.
7.5	Herrero-Hernandez, Eliseo; Pose-Juan, Eva; Alvarez-Martin, Alba; Andrades, Maria Soledad; Rodriguez-Cruz, Maria Sonia; Sanchez-Martin, Maria J.	2012	Pesticides and degradation products in groundwaters from a vineyard region: Optimization of a multiresidue method based on SPE and GC-MS	Journal of Separation Science (2012), 35 (24), 3492-3500	Does not meet relevance criteria: a method validation report mostly, no details provided with regards to the nature or construction of the groundwater sampling wells and potential agrochemical use in the recharge zone.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Rocha, MJ; Ribeiro, MFT.; Cruzeiro, C; Figueiredo, F; Rocha, E	2012	Development and validation of a GC-MS method for determination of 39 common pesticides in estuarine water - targeting hazardous amounts in the Douro River estuary	International Journal of Environmental Analytical Chemistry (2012), 92 (14), 1587-1608	Does not meet relevance criteria: no description of the sampling points with relation to catchment area and potential agronomic uses in said catchments, no information on hydrology, no assessment of potential point source contamination.
7.5	Rice, Clifford P.; Bialek-Kalinski, Krystyna; McCarty, Gregory W	2012	Chiral separation of metolachlor ethane sulfonic acid as a groundwater dating tool	SO Abstracts of Papers, 244th ACS National Meeting & Exposition, Philadelphia, PA, United States, August 19-23, 2012 (2012), AGRO-35	Abstract – insufficient data to assess
7.5	Koeck-Schulmeyer, M; Ginebreda, A; Gonzalez, S; Cortina, JL; de Alda, ML; Barcelo, D	2012	Analysis of the occurrence and risk assessment of polar pesticides in the Llobregat River Basin (NE Spain)	Chemosphere (2012), 86 (1), 8-16	Does not meet relevance criteria: No site characterisation data, no catchment data provided, no correlation with rainfall events, no product use survey in proximity of sampling locations to demonstrate potential pathways, no surface water flow rates or discharge volumes…
7.5	Mansilha, C.; Melo, A.; Ferreira, I. M. P. L. V. O.; Pinho, O.; Domingues, V.; Pinho, C.; Gameiro, P.	2012	Groundwater from Infiltration Galleries Used for Small Public Water Supply Systems-Contamination with Pesticides and Endocrine Disruptors	Bulletin of Environmental Contamination and Toxicology (2011), 87 (3), 312-318	Does not meet relevance criteria: Study describes groundwater collected in infiltration galleries which are a unique and irregular GW collection structure. Such data cannot be interpreted to provide an indication of potential leaching and overall groundwater health.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Finizio, Antonio; Azimonti, Giovanna; Villa, Sara	2011	Occurrence of pesticides in surface water bodies: A critical analysis of the Italian national pesticide survey programs	Journal of Environmental Monitoring (2011), 13 (1), 49-57	Does not meet relevance criteria: No site characterisation data, no catchment data provided, no correlation with rainfall events, no product use survey in proximity of sampling locations to demonstrate potential pathways, no surface water flow rates or discharge volumes, no description of groundwater sampling well locations, groundwater well construction or the potential for point source exposure in SW and GW samples. Further, the authors also questions the principles and approaches of the monitoring campaign.
7.5	Hamer, Kay; Freudenberger, Uta	2011	Plant protection legal irrelevant metabolites in groundwater	Wasser und Abfall (Wiesbaden, Germany) (2011), 13 (9), 42-45	Does not meet relevance criteria: no description of well design and construction, no details of pesticide use history in the recharge zone of the monitoring well, no discussion of well
7.5	Fava, L; Orru, MA; Scardala, S; Alonzo, E;Fardella, M; Strumia, C; Martinelli, A; Finocchiaro,S; Previtera, M; Franchi, A; Cala, P; Dovis,M; Bartoli, D; Sartori, G; Broglia, L; Funari, E	2010	Pesticides and their metabolites in selected Italian groundwater and surface water used for drinking	Annali dell'Istituto Superiore di Sanita (2010), 46 (3), 309-316	Does not meet relevance criteria: No description of sampling locations with respect to potential point source (location on farmyards?) or agronomic applications, no description of well construction or design, no description of sampling protocol.

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Vryzas, Z.; Vassiliou, G.; Alexoudis, C.; Papadopoulou-Mourkidou, E.	2009	Spatial and temporal distribution of pesticide residues in surface waters in northeastern Greece	Water Research (2009), 43 (1), 1-10.	Does not meet relevance criteria: No site characterisation data, no catchment data provided, no correlation with rainfall events, no product use survey in proximity of sampling locations to demonstrate potential pathways, no surface water flow rates or discharge volumes…
7.5	Villaverde, J; Hildebrandt, A; Martinez, E; Lacorte, S;Morillo, E; Maqueda, C; Viana, P; Barcelo, D	2008	Priority pesticides and their degradation products in river sediments from Portugal	Science of the Total Environment (2008), 390 (2-3), 507-513	Does not meet relevance criteria: no information provided about the sampling locations for the sediment samples, no attempt to relate site location to relevant agronomic practices in the region.
7.5	Wuelser, R	2005	Herbicide and pesticide studies in the Lange Erlen groundwater works	GWA (Zurich, Switzerland) (2005), 85 (1), 48-52	Does not meet relevance criteria; Insufficient information provided on sampling wells (construction, depths, screened intervals), no review of local cropping, analytical method poorly described
7.5	Kolpin, DW.; Schnoebelen, DJ.; Thurman, EM	2004	Degradates provide insight to spatial and temporal trends of herbicides in ground water	Ground Water (2004), 42 (4), 601-608	Does not meet relevance criteria: no description of well design and construction, no details of pesticide use history in the recharge zone of the monitoring well, no discussion of well screened interval, regions not necessarily geoclimatically relevant, use rates in USA much higher than EU28.
7.5	Karoly, G; Schremm, A; Boronkai, A	2004	Monitoring the pesticide contamination of the Lake Balaton and its inflows	Novenyvedelem (Budapest, Hungary) (2004), 40 (4), 185-192	Does not meet relevance criteria: not available to review

CA data point number	Author(s)	Year	Title	Source	Reason for exclusion
7.5	Schipper, PNM.; Vissers, MJM.; van der Linden, AMA.	2008	Pesticides in groundwater and drinking water wells; overview of the situation in the Netherlands	Water Science and Technology (2008), Volume 57, Number 8, pp. 1277-1286	Does not meet relevance criteria: Insufficient information provided on sampling wells (construction, depths, screened intervals), no review of local cropping, analytical method poorly described. Document is a simplistic overview of monitoring in Netherlands and Is not suitable for assessing leaching processes.
7.5	Amalric L, Baran N, Coureau C, Maingot L, Buron F & Routier S	2013	Analytical developments for 47 pesticides: first identification of neutral chloroacetanilide derivatives in French groundwater	Inter. J. Environ. Anal. Chem. 93(15), 1660-1675	Does not meet relevance criteria: Insufficient data has been provided on the groundwater sampling locations including the structure and design of the monitoring equipment. In particular, no data is provided regarding linking monitoring location to applications of agrochemicals in the recharge areas. Further, the report appears to be punctuated by errors (see Figure 1 where structures XI and XV are the same).

All documents listed in Table 9.6-2 and not excluded (i.e. not listed in Table 9.6-4) are given below.

Table 9.6-5: List of references which are discussed further

CA data point/ reference number	Authors	Year	Title	Source	Ref. ID
7.3.2	Gish, TJ; Prueger, JH; Daughtry, CST; Kustas, WP; McKee, LG; Russ, AL; Hatfield, JL.	2011	Comparison of Field-scale Herbicide Runoff and Volatilization Losses: An Eight-Year Field Investigation	Journal of Environmental Quality, (2011) 40, pp.1432-42	EU034

EU 提出の公表文献調査結果の再評価報告書

有効成分名：S-メトラクロール

シンジェンタジャパン株式会社 提出

提出日：令和 5 年 9 月 26 日

EU提出の公表文献調査結果の再評価報告書

有効成分名： S-メトラクロール

目次

1. 目的

本報告書は、S-メトラクロールについてシンジェンタ社がEUに提出した公表文献調査結果（2004年8月22日～2014年8月22日までの英文文献検索結果）を「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日農薬資材審議会農薬分科会決定、令和5年7月27日一部改正)」(以下、「ガイドライン」という）に基づき再評価したものである。

オリジナルの報告書で適合性ありと判断された文献に対して、ガイドラインに基づいた評価目的との適合性評価を行い、適合性の判断並びに適合性の区分分け、信頼性評価を実施した。また、毒性分野で適合性ありと判断した文献については、別途食品安全委員会フォーマットでその内容をまとめた。

2. 評価目的との適合性評価及び信頼性評価で設定した判断基準

文献全文の内容に基づいて、以下の手順に従って評価目的との適合性を検証し、その結果により分類した。

（ア）評価の目的と適合しない文献の除外

① 当該農薬と関係しない論文（当該農薬の代替剤等）
② 政策、社会、経済分析に関する論文
③ 農産物等の生産、流通に関する論文
④ 薬効、薬害、物理的化学的性状に関する論文
⑤ 分析法やその開発に関する論文
⑥ 新規合成法や基礎化学の観点で記載された論文
⑦ 特許関連文献
⑧ リスク評価をする上で十分なデータや情報を含まない学会発表等の概要や総説、成書
⑨ リスク評価に使用できる新規のデータが提示されていない意見書
⑩ 科学論文や規制についての総説を含む二次情報において、当該文献が参照する一次資料（原著）の確認ができないもの
⑪ 一般的な農薬の暴露に関する論文（当該農薬に限定せず、広範囲の農薬について記載されたもの）
⑫ 異なる有効成分に由来する混合製剤の毒性に関する論文
⑬ ヒトに対する毒性、農作物及び畜産物への残留、生活環境動植物及び家畜に対する毒性及び環境動態の4分野に関係しない論文
⑭ 日本で登録されている処方以外の製剤に関する論文
⑮ コンピュータシミュレーション等を用いたドライラボのみの論文
⑯ 試験設計、試験系、試験種、被験物質、暴露経路等が評価に活用する観点で妥当でないもの
  a）試験方法が記載されていないもの
  b）適切に評価できる試験種で実施されていないもの
  c）適切な経路で投与／処理されていないもの
  d）投与又は処理した被験物質量が明記されていないもの

e）被験物質の添加に用いた媒体が確認できないもの

f）分析法が記載されていないもの

⑰ 日本の代表的な使用方法／使用条件における評価に活用できない文献（ほ場条件、土性等）

⑱ 日本語もしくは英語以外で書かれた論文

（イ）評価の目的と適合した文献の分類

（ア）で除外した以外の文献については適合性があると判断し、下記の分類基準に従って、全文をレビューし３つの区分に分類した。

＜分類基準＞

1. 実施している試験環境がテストガイドライン（TG）で定める条件と合っていること
2. 投与又は処理した被験物質の純度が明記されていること
3. 統計解析が可能な動物数／例数が確保されていること
4. 複数の用量で実施されていること（最低 3 用量で実施）
5. 無処理区（コントロール区）が設定されており、TG に照らしその結果が適正であること
6. 解析方法及び結果が報告されていること

ヒトに対する毒性に関して、区分 a に該当するかどうかについては、食品安全委員会で示された「定量的データ」として分類される下記基準を参考とした。

1. 公表文献で用いられた用量が、研究内容と同等である安全性試験で用いられた最低用量よりも低いこと
2. 公表文献の研究結果が、他の試験結果と比較できる単位を用いて報告されていること
3. 研究の結論、エンドポイント及び用量が正確で、信頼でき、妥当であることを実証するための十分な情報が公表文献中に提供されており、研究結果が再現される可能性があると判断できること

表 2-1-1 評価目的への適合性がある文献の分類

区分	該当する文献
a	リスク評価パラメーター(ADI、ARfD、AOEL、残留基準、生活環境動植物の登録基準、水産 PEC 等)を設定又は見直すために利用可能と判断される文献
b	リスク評価パラメーターを設定する際の補足データとして利用が可能と想定される文献
c	a 又は b に分類されない文献

3. 評価目的との適合性評価の結果

3.1. 評価目的との適合性評価の結果のまとめ

表 3-1-1 評価目的との適合性評価の結果のまとめ

分野	評価対象文献数	適合性評価	
		適合性なし	適合性あり
ヒトに対する毒性	33	4	29
農作物及び畜産物への残留	0	0	0
生活環境動植物及び家畜に対する毒性	46	3	43
環境動態	1	0	1
上記以外	11	11	0
合計	91	18	73

3.2. 適合性評価で適合性ありとされた文献と分類結果

表 3-2-1 適合性評価で適合性ありとされた文献と分類結果

分野	該当する論文数		
	区分 a	区分 b	区分 c
ヒトに対する毒性	0	14	15
農作物及び畜産物への残留	0	0	0
生活環境動植物及び家畜に対する毒性	0	16	27
環境動態	0	1	0
合計	0	31	42

3.3. 適合性評価で「適合しない」と判断した論文とその理由

表 3-3-1 適合性評価で「適合しない」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU001		Zhou, M., et al.	2009	Observation on toxicity experiment of S-metolachlor	Zhiye Yu Jiankang (2009), 25(24), 2657-2661	中国語文献。
EU006		Hu, J.	2009	Immunotoxicity effect of metolachlor on mice	Harbin Yike Daxue Xuebao (2009), 43(1), 53-55	中国語文献。
EU009		Kublbeck, J. et al.	2011	Use of comprehensive screening methods to detect selective human CAR activators	Biochemical Pharmacology (2011), 82(12), 1994-2007	当該農薬に関する情報を含まない。
EU017		Cunningham, A. et al.	2009	A structure-activity relationship (SAR) analysis for the identification of environmental estrogens: the categorical-SAR (cat-SAR) approach	Endocrine Disruption Modeling (2009), 173-198.	環境中のエストロゲンに関する in silico 研究。

表 3-3-2 適合性評価で「適合しない」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU047		Cai, W. et al.	2012	Toxicity effects of Rac- and S-metolachlor on two algaes.	Huan jing ke xue= Huanjing kexue / [bian ji, Zhongguo ke xue yuan huan jing ke xue wei yuan hui "Huan jing ke xue" bian ji wei yuan hui.], (2012 Feb) Vol. 33, No. 2, pp. 448-53.	中国語文献。
EU053		Pérez, J. et al.	2011	Growth rate of Pseudokirchneriella subcapitata exposed to herbicides found in surface waters in the Alqueva reservoir (Portugal): a bottom-up approach using binary mixtures.	Ecotoxicology (London, England), (2011 Aug) Vol. 20, No. 6, pp. 1167-75.	複数の農薬の混合製剤がムレミカヅキモに与える影響に関する研究。
EU071		Joly, P. et al.	2012	Impact of maize formulated herbicides Mesotrione and S-metolachlor, applied alone and in mixture, on soil microbial communities	ISRN Ecology, (2012) pp. 329898, 9 pp.	2種の農薬が土壌中の微生物群衆に与える影響に関する研究(混合製剤)。

表 3-3-3 適合性評価で「適合しない」と判断した論文とその理由(4 分野以外)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU077		Sikkema, P. et al.	2009	Response of dry bean to pre-plant incorporated and pre-emergence applications of S-metolachlor and fomesafen	Crop protection (2009), Volume 28, Number 9, pp. 744-748. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	当該物質による豆類の薬害に関する研究。
EU079		Sikkema, P. et al.	2006	Response of adzuki bean to pre-emergence herbicides.	Canadian journal of plant science = Revue Canadienne de phytotechnie (2006), Volume 86, Number 2, pp. 601-604.	当該物質によるアズキの薬害に関する研究。
EU081		Bollman, S. et al.	2008	Tolerance of 12 Sugarbeet Varieties to Applications of S-metolachlor and Dimethenamid-P	Weed technology (2008), Volume 22, Number 4, pp. 699-706. ISSN: 0890-037X Source Note: 2008 Oct., v. 22, no. 4	当該物質によるてん菜類の薬害に関する研究。

表 3-3-3 適合性評価で「適合しない」と判断した論文とその理由(4 分野以外)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU082		Xie, F. et al.	2010	Enantioselectivity of racemic metolachlor and S-metolachlor in maize seedlings	Journal of Environmental Science and Health. Part B, Pesticides, Food Contaminants, and Agricultural Wastes (2010), Volume 45, Number 8, pp. 774-782, 33 refs.	トウモロコシの実生に対するラセミ体メトラクロール S-メトラクロールの薬害に関する比較研究。
EU084		Yadav, P. et al.	2007	Effect of herbicides on biochemical and growth parameters of chickpea (Cicer arietinum L.).	Research on Crops (2007), Vol. 8, Number 2, pp. 388-390, 8 refs.	当該物質によるひよこ豆の薬害に関する研究。
EU085		Yadav, P. et al.	2006	Effect of herbicides on germination, growth and nodulation in chickpea (Cicer arietinum)	Indian Journal of Agricultural Sciences (2006), 76 (11), 682-684	当該物質によるひよこ豆の薬害に関する研究。
EU086		Norsworthy, J. et al.	2007	Tolerance of direct-seeded green onions to herbicides applied before or after crop emergence.	Weed Technology (2007), Volume 21, Number 1, pp. 119-123.	当該物質によるネギの薬害に関する研究。
EU087		Soltani, N. et al.	2004	White bean sensitivity to preemergence herbicides.	Weed Technology (2004), Vol. 18, Number 3, pp. 675-679, 15 refs.	当該物質による white beans の薬害に関する研究。

表 3-3-3 適合性評価で「適合しない」と判断した論文とその理由(4 分野以外)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU088		Neugebauerova, J. et al.	2004	Possibilities of pre-emergence and post-emergence herbicide applications in Prunella vulgaris L. growth.	Zahradnictvi (Horticultural Science) (2004), Volume 31, Number 3, pp. 115-118	当該物質の薬効に関する研究。
EU089		Soltani, N. et al.	2004	Tolerance of black beans (Phaseolus vulgaris) to soil applications of S-metolachlor and imazethapyr.	Weed Technology (2004), Volume 18, Number 1, pp. 111-118, 25 refs.	当該物質に対するインゲン豆の薬害に関する研究。
EU090		De Marez, T. et al.	2007	Effect of selected sugar beet herbicides on germination of various Chenopodium album populations.	Communications in agricultural and applied biological sciences, (2007) Vol. 72, No. 2, pp. 265-9.	当該物質のシロザに対する薬効に関する研究。

3.4. 適合性評価で「区分 b」と判断した論文とその理由

表 3-4-1 適合性評価で「区分 b」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU002	IIA 5	Nikoloff, N. et al.	2013	Comparative study of cytotoxic and genotoxic effects induced by herbicide S-metolachlor and its commercial formulation Twin Pack Gold® in human hepatoma (HepG2) cells.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013 Dec) Vol. 62, pp. 777-81. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	S-メトラクロール原体及びS-メトラクロール製剤のヒト肝細胞に対する毒性に関する研究。 原体の毒性と製剤の毒性の間で異なる結果が示され、製剤に含まれる原体以外の物質による毒性が示唆されている。
EU005	IIA 5	Hartnett, S. et al.	2013	Cellular effects of metolachlor exposure on human liver (HepG2) cells.	Chemosphere, (2013 Jan) Vol. 90, No. 3, pp. 1258-66 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	HepG2（ヒト肝腫瘍細胞）に対する毒性研究。 メトラクロールがサイクリン A の転写発現を阻害することによりS期が遅滞し、その結果として細胞増殖速度の低下を招くことが示された。

表 3-4-1 適合性評価で「区分 b」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU014	IIA 5	Pereira, S. et al.	2009	Toxicity assessment of the herbicide metolachlor comparative effects on bacterial and mitochondrial model systems.	Toxicology in vitro : an international journal published in association 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	当該物質の毒性に関する細菌（*Bacillus stearothermophilus*）とラット肝ミトコンドリアを用いた *in vitro* 研究。他の多くの農薬と比べて毒性が大幅に低いことが示された。
EU020	IIA 5.4.6	Mathias, F. et al.	2012	Herbicide Metolachlor Causes Changes in Reproductive Endocrinology of Male Wistar Rats	ISRN Toxicology (2012) 130846. https://doi.org/10.5402/2012/130846 《海外評価書引用：USEPA (2014) EPA-HQ-OPP-2014-0772-0033 Comment submitted by Olga Naidenko, Vice President, Science Investigations, Environmental Working Group (EWG)》	ラット雄の生殖内分泌に与える影響。思春期前の暴露がラット雄の生殖内分泌に影響することを明らかにしている。
EU023	IIA 5.5	Alavanja, M. et al.	2003	Use of Agricultural Pesticides and Prostate Cancer Risk in the Agricultural Health Study Cohort	Am J Epidemiol 2003;157:800-814 https://doi.org/10.1093/aje/kwg040 《海外評価書引用：USEPA (2014) EPA-HQ-OPP-2014-0772-0004 Metolachlor: Tier I Review of Human Incidents.》	農薬と前立腺がんの関係に関する疫学的研究。

表 3-4-1 適合性評価で「区分 b」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU024	IIA 5.5	Andoreotti, G. et al.	2010	Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort.	Cancer causes & control: CCC, (2010 Nov) Vol. 21, No. 11, pp. 1759-75. 《海外評価書引用：USEPA (2014) EPA-HQ-OPP-2014-0772-0004 Metolachlor: Tier I Review of Human Incidents.》	農薬及び体重指数と発がん性に関する疫学的研究。 メトラクロール使用歴があり、肥満度が高いと、結腸がんのリスクが高まることが認められた。
EU025	IIA 5	Barr, D. et al.	2010	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	The Science of the total environment, (2010 Jan 15) Vol. 408, No. 4, pp. 790-5. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	母体及び胎児への農薬濃縮と出生時の健康状態に関する疫学的研究。臍帯血中のメトラクロール濃度と出生時体重との間の高い相関が示された。
EU026	IIA 5	Chevrier, C. et al.	2011	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Environmental health perspectives, (2011 Jul) Vol. 119, No. 7, pp. 1034-41. https://doi.org/10.1289/ehp.1002775 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	農薬と出生時異常の関係に関する疫学的研究。 新生児の頭囲長と尿中のメトラクロール濃度との間に相関が認められた。

表 3-4-1 適合性評価で「区分 b」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU027	IIA 5	Hoppin, J. et al.	2006	Pesticides and adult respiratory outcomes in the agricultural health study.	Annals of the New York Academy of Sciences, Vol. 1076, pp. 343-354. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	農薬と呼吸器疾患の関係に関する疫学的研究。
EU028	IIA 5	Hou, L. et al.	2013	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Environmental health perspectives, (2013 Aug) Vol. 121, No. 8, pp. 919-24. https://doi.org/10.1289/ehp.1206432 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	生涯の農薬使用履歴とテロメア短縮との関係に関する疫学的研究。
EU029	IIA 5.5	Lee, W. et al.	2007	Pesticide use and colorectal cancer risk in the Agricultural Health Study	International Journal of Cancer (2007), 121(2), 339-346 https://doi.org/10.1002/ijc.22635 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	農薬と結腸がん/直腸がんの関係に関する疫学的研究。 メトラクロールと結腸がん/直腸がんとの相関は見られなかった。

表 3-4-1 適合性評価で「区分 b」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU031	IIA 5.5	Rusiecki, J. et al.	2006	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	International journal of cancer. Journal international du cancer, (2006 Jun 15) Vol. 118, No. 12, pp. 3118-23. https://doi.org/10.1002/ijc.21758 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	メトラクロール暴露と6種類のがんの発がんとの関係に関する疫学的研究。 いずれのがんについても明白な相関は認められなかった。
EU032	IIA 5.6.8	Swan, S. et al.	2003	Semen Quality in Relation to Biomarkers of Pesticide Exposure	Environmental Health Perspectives, vol 111, 12 September 2003. https://doi.org/10.1289/ehp.6417 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》 https://doi.org/10.1289/ehp.6417 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	農薬と精子の質の間の関係に関する疫学的研究。
EU033	IIA 5.5	Thorpe, N. et al.	2005	Herbicides and nitrates in groundwater of Maryland and childhood cancers: a geographic information systems approach.	Journal of environmental science and health. Part C, Environmental 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	農薬と小児がんの間の関係に関する疫学的研究。 当該物質を含む農薬と白血病及び骨がんとの関連性が示唆された。

表 3-4-2 適合性評価で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU037	IIA 8.2.2	Jin, Y. et al.	2011	Effects of metolachlor on transcription of thyroid system-related genes in juvenile and adult Japanese medaka (Oryzias latipes)	General and Comparative Endocrinology, 170:487-493 《海外評価書引用：USEPA (2015) EPA-HQ-OPP-2014-0772-0022 Metolachlor Weight of Evidence Analysis》	メトラクロールが、メダカ（幼魚／成魚）の甲状腺システムに関連する遺伝子の転写に及ぼす影響についての研究。 当該物質がメダカの視床下部 - 下垂体-甲状腺の恒常性に影響する可能性が示された。
EU038	IIA 8.2.1 IIA 8.3.1	Wan, M. et al.	2006	Toxicity to Daphnia magna, Hyalella azteca, Oncorhynchus kisutch, Oncorhynchus mykiss, Oncorhynchus tshawytscha and Rana catesbeiana of atrazine, metolachlor, simazine, and their formulated products.	Bulletin of Environmental Contamination and Toxicology (2006) Volume 76, Number 1, pp. 52-58, 9 refs. DOI: 10.1007/s00128-005-0888-4 《海外評価書引用：USEPA (2015) EPA-HQ-OPP-2014-0772-0002 Registration Review Problem Formulation for Metolachlor and S-Metolachlor.	水生動物（オオミジンコ、魚類を含む）に対する 3 種類の農薬の急性毒性に関する研究。いずれの動物に対しても毒性は低いことが示された。

表 3-4-2 適合性評価で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU041	IIA 8.3.1.1	Liu, H. et al.	2006	A comparative study of rac- and S-metolachlor toxicity to Daphnia magna	Ecotoxicology and Environmental Safety (2006) Volume 63, Number 3, pp. 451-455, 25 refs. DOI: 10.1016/j.ecoenv.2005.02.002 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ラセミ体メトラクロールと S-メトラクロールの間の、オオミジンコに対する毒性の比較研究。相対的に S-メトラクロールの毒性が大幅に低いことが示された。
EU048	IIA 8.4	Hui, J. et al.	2012	Enantioselective toxicity of metolachlor to Scenedesmus obliquus in the presence of cyclodextrins.	Chirality, (2012 Feb) Vol. 24, No. 2, pp. 181-7.	緑藻(イカダモ) に対する毒性。シクロデキストリン存在下では、イカダモに対する毒性に差異が存在することが示された。
EU049	IIA 8.4	Liu, H. et al.	2009	Comparative toxicity of racemic metolachlor and S-metolachlor to Chlorella pyrenoidosa.	Aquatic toxicology (Amsterdam, Netherlands), (2009 Jun 28) Vol. 93, No. 2-3, pp. 100-6.	クロレラ・ピレノイドサに対するメトラクロール (ラセミ体) と S-メトラクロールの毒性の比較。両者の毒性には差異が見られ、S-メトラクロールの毒性がラセミ体の毒性よりも高かった。

表 3-4-2 適合性評価で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU050	IIA 8.4	Vallotton, N. et al.	2008	S-metolachlor pulse exposure on the alga Scenedesmus vacuolatus: effects during exposure and the subsequent recovery.	Chemosphere, (2008 Sep) Vol. 73, No. 3, pp. 395-400.	緑藻（イカダモ）に対する当該物質の短時間（6h）暴露が与える影響に関する研究。
EU051	IIA 8.4	Deng, L. et al.	2012	Effect of selected herbicides on growth and hydrocarbon content of Botryococcus braunii (Race B)	Industrial Crops and Products (2012), 39, 154-161.	緑藻(ボツリオコッカス）に対する毒性研究。S-メトラクロールによる強度の発生阻害が見られた。
EU052	IIA 8.4	Sbrilli, G. et al.	2005	Surface and ground waters characterization in Tuscany (Italy) by using algal bioassay and pesticide determinations: comparative evaluation of the results and hazard assessment of the pesticides impact on primary productivity	Chemosphere (2005), 58 (5), 571-578.	河川水及び地下水が藻類に与える影響の調査、及び 15 種類の農薬の藻類に対する毒性の研究。
EU054	IIA 8.4	Ma, J. et al.	2006	Toxicity assessment of 40 herbicides to the green alga Raphidocelis subcapitata	Ecotoxicology and Environmental Safety (2006), 63 (3), 456-462.	緑藻（ムレミカヅキモ）に対する 40 種類の農薬のスクリーニング調査。
EU057	IIA 8.4	Spoljaric, D. et al.	2011	Endogenous 4-hydroxy-2-nonenal in microalga Chlorella kessleri acts as a bioactive indicator of pollution with common herbicides and growth regulating factor of hormesis.	Aquatic toxicology (Amsterdam, Netherlands), (2011 Oct) Vol. 105, No.-3-4, pp. 552-8.	メトラクロールが緑藻（Chlorella kessleri）の過酸化水素産生への関与に関する研究。

表 3-4-2 適合性評価で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU059	IIA 8.4	Larras, F. et al.	2012	Using bioassays and species sensitivity distributions to assess herbicide toxicity towards benthic diatoms.	PloS one, (2012) Vol. 7, No. 8, pp. e44458. https://doi.org/10.1371/journal.pone.0044458	8 種類の農薬の淡水底生珪藻類 11 種に対する毒性の研究。
EU060	IIA 8.4	Larras, F. et al.	2013	Assessment of toxicity thresholds in aquatic environments: does benthic growth of diatoms affect their exposure and sensitivity to herbicides?	The Science of the total environment, (2013 Oct 1) Vol. 463-464, pp. 469-77.	珪藻類の浮遊状態と底生状態での農薬の吸収効率の違いに関する研究。底生時の農薬の吸着及び農薬からの隔離にバイオフィルムが関与する可能性について考察。
EU061	IIA 8.7	Helmer, H. et al.	2014	Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (Apis mellifera).	Environmental science and pollution research international, (2014 Apr 15)	BARS（チオバルビツール酸反応性物質）試験により、微量の農薬がミツバチの代謝に与える影響を調査。
EU072	IIA 8.10	Joly, P. et al.	2013	Toxicity assessment of the maize herbicides S-metolachlor, benoxacor, mesotrione and nicosulfuron, and their corresponding commercial formulations, alone and in mixtures, using the Microtox(®) test.	Chemosphere, (2013 Nov) Vol. 93, No. 10, pp. 2444-50. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	発光細菌（V. fischeri）を用いたマイクロトックス法による、4 種類の農薬の環境毒性に関する研究。

表 3-4-2 適合性評価で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU073	IIA 8.10	Joly, P. et al.	2014	Soil surface colonisation by phototrophic indigenous organisms, in two contrasted soils treated by formulated maize herbicide mixtures	Ecotoxicology (London, England) (2014 Aug 18).	農薬製剤が土壌表面の光合成微生物群衆に与える影響に関する研究。
EU074	IIA 8.10	Lipsa, F. et al.	2010	Effect of herbicide S-metolachlor on soil microorganisms.	Lucrari Stiintifice, Universitatea de Stiinte Agricole Si Medicina Veterinara "Ion Ionescu de la Brad" Iasi, Seria Agronomie (2010) Volume 53, Number 2, pp. 110-113 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	S-メトラクロールが土壌中の微生物群衆に与える影響に関する研究。

表 3-4-3 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU034	IIA 7.3.2	Gish, T. et al.	2011	Comparison of Field-scale Herbicide Runoff and Volatilization Losses: An Eight-Year Field Investigation	Journal of Environmental Quality, (2011) 40, pp.1432-42	メトラクロールの 2 種類の喪失（蒸発と流出）に関するフィールド研究。 蒸発による喪失が流出による喪失を大きく上回ることが示された。

3.5. 適合性評価で「区分 c」と判断した論文とその理由

表 3-5-1 適合性評価で「区分 c」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU003	IIA 5	Aït-Aïssa, S. et al.	2010	Anti-androgenic activities of environmental pesticides in the MDA-kb2 reporter cell line	Toxicology in Vitro (2010), 24(7), 1979-1985.	当該物質を含む 15 種類の農薬の、ジヒドロテストステロン存在下/非存在下でのヒト上皮由来細胞に対する毒性研究。
EU004	IIA 5	Greenlee, 1 A. et al.	2004	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9. https://doi.org/10.1289/ehp.6774 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ネズミの着床前胚に対する 26 種類の農薬/肥料の発生毒性研究。
EU007	IIA 5	Takeuchi, S. et al.	2008	In vitro screening for aryl hydrocarbon receptor agonistic activity in 200 pesticides using a highly sensitive reporter cell line, DR-EcoScreen cells, and in vivo mouse liver cytochrome P450-1A induction by propanil, diuron and linuron	Chemosphere (2008), 74(1), 155-165.	アリル炭化水素受容体アゴニスト同定のための新しい測定法の開発。

表 3-5-1 適合性評価で「区分 c」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU008	IIA 5	Kojima, S. et al.	2011	Comparative study of human and mouse pregnane X receptor agonistic activity in 200 pesticides using in vitro reporter gene assays	Toxicology (2011), 280(3), 77-87	200 種類の農薬におけるヒト及びマウスのプレグナン X 受容体アゴニスト活性の比較研究。
EU010	IIA 5	Lemaire, G. et al.	2006	Activation of a- and b-estrogen receptors by persistent pesticides in reporter cell lines	Life Sciences (2006), 79(12), 1160-1169.	49 種類の農薬が HELN 細胞エストロゲン受容体活性に与える影響に関する研究。
EU011	IIA 5	Lemaire, G. et al.	2006	Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system.	Toxicological sciences : an official journal of the Society of Toxicology https://doi.org/10.1093/toxsci/kfj173 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	HeLa 細胞より新たに作成した細胞株 (HGPXR) を用いた、プレグナン X 受容体リガンズの新しい同定法の開発。

表 3-5-1 適合性評価で「区分 c」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU012	IIA 5	Lowry, M. et al.	2013	Mechanism of metolachlor action due to alterations in cell cycle progression	Cell biology and toxicology, (2013 Aug) Vol. 29, No. 4, pp. 283-91.《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	HepG2（ヒト肝腫瘍細胞）内でのメトラクロールの作用機序の研究。メトラクロールの細胞毒性は、細胞のネクローシス/アポトーシスの誘発ではなく、細胞分裂の阻害によることが示唆された。
EU013	IIA 5	Oosterhuis, B. et al.	2008	Specific interactions of chloroacetanilide herbicides with human ABC transporter proteins.	Toxicology, (2008 Jun 3) Vol. 248, No. 1, pp. 45-51.《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	当該物質を含むクロロアセトアニリド系農薬と ABC トランスポータータンパク質の相互作用に関する研究。クロロアセトアニリド系農薬は、ABC トランスポーテーションの基質として、MDR1 に作用していることが示唆された。
EU015		Rotroff, D. et al.	2010	Xenobiotic-Metabolizing Enzyme and Transporter Gene Expression in Primary Cultures of Human Hepatocytes Modulated by Toxcast Chemicals	Journal of Toxicology and Environmental Health, Part B: Critical Reviews (2010), 13(2-4), 329-346	ToxCast に登録されている 320 種類の化学物質の、ヒト肝細胞の遺伝子発現への影響に関する研究。

表 3-5-1 適合性評価で「区分 c」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU016	IIA 5	Laville, N. et al.	2006	Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line.	Toxicology, (2006 Nov 10) Vol. 228, No. 1, pp. 98-108. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	当該物質を含む 30 種類の農薬の、アロマターゼ酵素活性に対する影響について、ヒト絨毛がん JEG-3 細胞株を用いて調査。
EU018	IIA 5	Sipes, N. et al.	2013	Profiling 976 ToxCast Chemicals across 331 Enzymatic and Receptor Signaling Assays	Chemical Research in Toxicology (2013), 26 (6), 878-895. https://doi.org/10.1021/tx400021f 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ToxCast に登録されている 976 種類の化学物質を、331 種類の試験により分類。

表 3-5-1 適合性評価で「区分 c」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU019	IIA 5	Kojima, H. et al.	2004	Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using chinese hamster ovary cells	Environmental Health Perspectives (2004), 112 (5), 524-531. https://doi.org/10.1289/ehp.6649 《海外評価書引用：USEPA (2016) EPA-HQ-OPP-2014-0772-0022 Metolachlor Weight of Evidence Analysis》	200 種類の農薬（及び代謝物）に対する、レポーター遺伝子試験によるエストロゲン/アンドロゲン活性のスクリーニング調査。
EU021	IIA 5.5	Reif, D. et al.	2010	Endocrine profiling and prioritization of environmental chemicals using ToxCast data.	Environmental Health Perspectives (2010), 118(12), 1714-1720. https://doi.org/10.1289/ehp.1002180	ToxCast のデータに基づき、309 種類の環境内物質が内分泌経路に与える影響を順位付けしている。
EU022	IIA 5.5	Rotroff, D. et al.	2014	Predictive Endocrine Testing in the 21st Century Using in Vitro Assays of Estrogen Receptor Signaling Responses.	Environmental Science & Technology (2014), 48 (15), 8706-8716. https://doi.org/10.1021/es502676e	化学物質の内分泌かく乱性に関する新しい in vitro スクリーニング試験の開発。

表 3-5-1 適合性評価で「区分 c」と判断した論文とその理由(ヒトに対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU030	IIA 5	Munger, R. et al.	2007	Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies	Environmental Health Perspectives, Volume 105, Number 3, March 1997 https://doi.org/10.1289/ehp.97105308 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	飲料水内の4種類の農薬と子宮内発育遅延の関係に関する疫学的研究。 各農薬ごとの影響については調査されていない。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU035	IIA 8.3	Spolyarich, N. et al.	2010	Growth, development and sex ratios of Spotted Marsh Frog (Limnodynastes tasmaniensis) larvae exposed to atrazine and a herbicide mixture.	Chemosphere, (2010 Feb) Vol. 78, No. 7, pp. 807-13.	Spotted Marsh Frog の成長に与える影響の研究(適切に評価できる試験種ではない)。
EU036	IIA 8.3	Williams, B. et al.	2010	Larval responses of three Midwestern anurans to chronic, low-dose exposures of four herbicides.	Arch. Environ. Contam. Toxicol. (2010) 58, 819-827.	3種類のカエルに対する慢性毒性の研究（適切に評価できる試験種ではない）。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU039	IIA 8.3	Hayes, T. et al.	2006	Pesticide mixtures, endocrine disruption, and amphibian declines: are we underestimating the impact?	Environmental health perspectives, (2006 Apr) Vol. 114 Suppl 1, pp. 40-50. https://doi.org/10.1289/ehp.8051	leopard frogs に対する毒性研究（適切に評価できる試験種ではない）。
EU040	IIA 8.2.1	Padilla, S. et al.	2012	Zebrafish developmental screening of the ToxCast Phase I chemical library	Reproductive Toxicology (2012), 33 (2), 174-187.	ゼブラフィッシュに対する ToxCast 物質の毒性スクリーン試験。
EU042	IIA 8.5.1	Cook, M. et al.	2008	The effects of the herbicide metolachlor on agonistic behavior in the crayfish, Orconectes rusticus.	Archives of environmental contamination and toxicology, (2008 Jul) Vol. 55, No. 1, pp. 94-102. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ザリガニに対する毒性研究(適切に評価できる試験種ではない)。
EU043	IIA 8.5.1	Gagnaire, B. et al.	2006	Pollutant effects on Pacific oyster, Crassostrea gigas (Thunberg), hemocytes: Screening of 23 molecules using flow cytometry.	Cell Biology and Toxicology (2006), 22 (1),-1-14. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	マガキに対する毒性研究（適切に評価できる試験種ではない）。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU044	IIA 8.3.1.2	Jin-Clark, Y. et al.	2008	Effect of alachlor and metolachlor on toxicity of chlorpyrifos and major detoxification enzymes in the aquatic midge, Chironomus tentans (Diptera: Chironomidae).	Archives of environmental contamination and toxicology, (2008 May) Vol. 54, No. 4, pp. 645-52. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ユスリカ幼生に対する毒性研究(主に他剤との混在時の毒性)。メトラクロールと殺虫剤クロルピリホスの混在時にクロルピリホスの毒性が上昇する。
EU045	IIA 8.3.1.2	Pérez, J. et al.	2013	Characterization of cholinesterases in Chironomus riparius and the effects of three herbicides on chlorpyrifos toxicity.	Aquatic toxicology (Amsterdam, Netherlands), (2013 Nov 15) Vol. 144-145, pp. 296-302. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ユスリカ幼生に対する毒性研究(主に他剤との混在時の毒性)。他の試験対象除草剤と異なり、メトラクロールは殺虫剤クロルピリホスのアセチルコリンエステラーゼ活性阻害を助長しなかった。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU046	IIA 8.4	Fischer, B. et al.	2012	Multiple stressor effects of predation by rotifers and herbicide pollution on different Chlamydomonas strains and potential impacts on population dynamics.	Environmental Toxicology and Chemistry (2012) Volume 31, Number 12, pp. 2832-2840, 43 refs. DOI: 10.1002/etc.2010 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	緑藻（クラミドモナス）に対して捕食と農薬の２つのストレスを与えた場合の動態の研究。 明らかな傾向が見られなかった。
EU055	IIA 8.4	Ebenezer, V. et al.	2013	Quantification of toxic effects of the herbicide metolachlor on marine microalgae Ditylum brightwellii (Bacillariophyceae), Prorocentrum minimum (Dinophyceae), and Tetraselmis suecica (Chlorophyceae).	Journal of microbiology (Seoul, Korea), (2013 Feb) Vol. 51, No. 1, pp. 136-9.	メトラクロールの海生藻類に対する毒性の研究（適切に評価できる試験種ではない）。
EU056	IIA 8.4	Thakkar, M. et al.	2013	Comparative responses of two species of marine phytoplankton to metolachlor exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2013 Jan 15) Vol. 126, pp. 198-206.	メトラクロールの海生藻類に対する毒性の研究（適切に評価できる試験種ではない）。
EU058	IIA 8.4	Fiori, E. et al.	2014	Skeletonema marinoi (Bacillariophyceae) sensitivity to herbicides and effects of temperature increase on cellular responses to terbuthylazine exposure.	Aquatic toxicology (Amsterdam, Netherlands), (2014 Feb) Vol. 147, pp. 112-20.	メトラクロールの海生藻類（珪藻）に対する毒性の研究（適切に評価できる試験種ではない）。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU062	IIA 8.8	Zhan, X. et al.	2006	A comparative study of rac- and S-metolachlor on some activities and metabolism of silkworm, Bombyx mori L.	Pesticide Biochemistry and Physiology (2006) Volume 85, Number 3, pp. 133-138, 33 refs. DOI: 10.1016/j.pestbp.2005.12.003 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	カイコに対するメトラクロール（ラセミ体）とS-メトラクロールの毒性の比較研究（適切に評価できる試験種ではない）。
EU063	IIA 8.8.1.1	Carmo, E. et al.	2010	Pesticide selectivity for the insect egg parasitoid Telenomus remus.	BioControl (2010) Volume 55, Number 4, pp. 455-464, 38 refs.	寄生性のハエ（Telenomus remus）に対する農薬の影響に関する研究（適切に評価できる試験種ではない）。
EU064	IIA 8.8.1.1	Xu, H. et al.	2013	Analysis and evaluation of eight herbicides toxicity and sensitivity against two Trichogramma spp.	Journal of Food, Agriculture & Environment (2013), Volume 11, Number 3/4, pp. 855-858, 19 refs. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	寄生性のハチ（Trichogramma spp.）2種に対する農薬の影響に関する研究（適切に評価できる試験種ではない）。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU065	IIA 8.8	PARK, E. et al.	2005	Application of an artificial sea salt solution to determine acute toxicity of herbicides to Proisotoma minuta (Collembola).	Journal of environmental science and health. Part.B, (2005) Vol.40, No. 4, pp. 595-604. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	トビムシの一種 (Proisotoma minuta) に対する農薬の影響に関する研究 (適切に評価できる試験種ではない) 。
EU066	IIA 8.9	Wang, Y. et al.	2012	Toxicity assessment of 45 pesticides to the epigeic earthworm Eisenia fetida.	Chemosphere, (July 2012) Vol. 88, No. 4, pp. 484-491. Refs: 63.	シマミミズに対する農薬の影響に関する研究 (適切に評価できる試験種ではない) 。
EU067	IIA 8.9	Xu, D. et al.	2010	Effect of chiral differences of metolachlor and its (S)-isomer on their toxicity to earthworms.	Ecotoxicology and environmental safety, (2010 Nov) Vol. 73, No. 8, pp. 1925-31.	ミミズに対するメトラクロール (ラセミ体) と S-メトラクロールの毒性の比較研究 (適切に評価できる試験種ではない) 。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU068	IIA 8.9	Stepic, S. et al.	2013	Potentiation effect of metolachlor on toxicity of organochlorine and organophosphate insecticides in earthworm Eisenia andrei.	Bulletin of environmental contamination and toxicology, (2013 Jul) Vol. 91, No. 1, pp. 55-61. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ミミズに対するメトラクロールと殺虫剤の相乗作用に関する研究（適切に評価できる試験種ではない）。
EU069	IIA 8.9	Aly, M. et al.	2008	Effect of herbicides on glutathione S-transferases in the earthworm, Eisenia fetida.	Environmental science and pollution research international, (2008 Mar) Vol. 15, No. 2, pp. 143-9. https://doi.org/10.1065/espr2007.02.385	シマミミズに対する農薬の影響に関する研究（適切に評価できる試験種ではない）。
EU070	IIA 8.9	Kondras, M. et al.	2011	The influence of two pesticides in soils on selected plants and earthworms	Roczniki Gleboznawcze (2011), 62 (2), 219-225. http://ssa.ptg.sggw.pl/en/artykul/2784/the-influence-of-two-pesticides-in-soils-on-selected-plants-and-earthworms	土壌中の農薬の植物及びミミズへの影響に関する研究（適切に評価できる試験種ではない）。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU075	IIA 8.10	Vodovnik, M. et al.	2012	Membrane Changes Associated with Exposure of Pseudomonas putida to Selected Environmental Pollutants and their Possible Roles in Toxicity.	Acta chimica Slovenica, (2012 Mar) Vol. 59, No. 1, pp. 83-8. https://www.researchgate.net/publication/256984314_Membrane_Changes_Associated_with_Exposure_of_Pseudomonas_putida_to_Selected_Environmental_Pollutants_and_their_Possible_Roles_in_Toxicity 《海外評価書引用:EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	Pseudomonas putida (グラム陰性菌) に対する環境内毒物の影響に関する研究 (適切に評価できる試験種ではない) 。
EU076	IIA 8.10	Kos, K. et al.	2013	Sensitivity of the entomopathogenic fungus Beauveria bassiana (Bals.-Criv.) Vuill. to selected herbicides.	Pest Management Science (2013), Volume 69, Number 6, pp. 717-721, 34 refs. 《海外評価書引用:EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	6 種類の農薬が糸状菌に与える影響に関する研究 (適切に評価できる試験種ではない) 。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU078	IIA 8.6	Samtani, J. et al.	2010	White Oak and Northern Red Oak Leaf Injury from Exposure to Chloroacetanilide Herbicides.	HortScience : a publication of the American Society for Horticultural Science (2010), Volume 45, Number 4, pp. 696-700. https://doi.org/10.21273/HORTSCI.45.4.696 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	カシ類 2 種に対する影響に関する研究（適切に評価できる試験種ではない）。
EU080	IIA 8.6	Boutin, C. et al.	2004	Toxicity testing of fifteen non-crop plant species with six herbicides in a greenhouse experiment: Implications for risk assessment.	Ecotoxicology, (May 2004) Vol. 13, No. 4, pp. 349-369.	温室内での園芸花弁に対する農薬の毒性研究（適切に評価できる試験種ではない）。
EU083	IIA 8.6	Samtani, J. et al.	2008	Injury on white oak seedlings from herbicide exposure simulating drift.	HortScience (2008), Vol. 43, Number 7, pp. 2076-2080, 27 refs. 《海外評価書引用：EFSA (2018) Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	ホワイトオークに対する農薬の影響に関する研究（適切に評価できる試験種ではない）。

表 3-5-2 適合性評価で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
EU091	IIA 8.5	Papaefthimiou, C. et al.	2004	Comparison of two screening bioassays, based on the frog sciatic nerve and yeast cells, for the assessment of herbicide toxicity.	Environmental toxicology and chemistry / SETAC, (2004 May) Vol. 23, No. 5, pp. 1211-8.	カエルの坐骨神経と酵母菌に対する６種類の農薬の毒性に関する研究（適切に評価できる試験種ではない）。

4. 結果および結論

S-メトラクロールについてシンジェンタ社がEUに提出した公表文献調査結果（2004年8月22日～2014年8月22日までの英文文献検索結果）において適合性ありと判断された文献91件を、「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日農薬資材審議会農薬分科会決定、令和5年7月27日一部改正)」に基づき「適合性なし」：ヒトに対する毒性4件、生活環境動植物及び家畜に対する毒性3件、評価対象の4分野のいずれにも関係しない論文11件、「区分 b」：ヒトに対する毒性14件、生活環境動植物及び家畜に対する毒性16件、環境動態1件「区分 c」：ヒトに対する毒性15件、生活環境動植物及び家畜に対する毒性27件に分類した。「区分 a」に該当する文献はなかった。

ヒトに対する毒性に関する文献で、疫学研究に関するもの以外は18件を検討対象として選抜し、また疫学に関する文献は11件を検討対象として選抜し、合わせて「食品安全委員会フォーマット表」として別添した。

No.	文献名	ジャーナル名等	公表年	著者	著者の所属機関	書誌情報	研究分野	原著/総説	海外評価書での引用の有無	ドシエでの引用の有無	*in vivo* （動物種）/ *in vitro*	用量 (mg/kg体重又はg/kg体重/日)	NOAEL /NOEL	LOEAL /LOEL	Klimisch コード	評価の目的との適合性に関する情報	備考
EU002	Comparative study of cytotoxic and genotoxic effects induced by herbicide S-metolachlor and its commercial formulation Twin Pack Gold® in human hepatoma (HepG2) cells.	Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, (2013 Dec) Vol. 62, pp. 777-81.	2013	Nikoloff, N. et al.	Univ. Nacional de La Plata, Argentina	http://dx.doi.org/10.1016/j.fct.2013.10.015	遺伝／発がん性	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	肝がんの発症メカニズムに関する研究。 試験ガイドラインに準拠していないin vitro 試験。	S-メトラクロール原体及びS-メトラクロール製剤のヒト肝細胞に対する毒性に関する研究。 原体の毒性と製剤の毒性の間で異なる結果が示され、製剤に含まれる原体以外の物質による毒性が示唆されている。
EU003	Anti-androgenic activities of environmental pesticides in the MDA-kb2 reporter cell line	Toxicology in Vitro (2010), 24(7), 1979-1985.	2010	Aït-Aïssa, S. et al.	Institut National de l’Environnement Industriel et des Risques, France	http://dx.doi.org/10.1016/j.tiv.2010.08.014	代謝	原著	－	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。 試験ガイドラインに準拠していないin vitro 試験。	当該物質を含む15種類の農薬の、ジヒドロテストステロン存在下/非存在下でのヒト上皮由来細胞に対する毒性研究。
EU004	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental health perspectives, (2004 May) Vol. 112, No. 6, pp. 703-9. https://doi.org/10.1289/ehp.6774	2004	Greenlee, 1 A. et al.	Marshfield Clinic Research Foundation, USA	https://doi.org/10.1289/ehp.6774	生殖毒性	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。 試験ガイドラインに準拠していないin vitro 試験。	マウスの着床前胚に対する26種類の農薬/肥料の発生毒性研究。
EU005	Cellular effects of metolachlor exposure on human liver (HepG2) cells.	Chemosphere, (2013 Jan) Vol. 90, No. 3, pp. 1258-66	2013	Hartnett, S. et al.	Univ. of Northern Iowa, USA	http://dx.doi.org/10.1016/j.chemosphere.2012.09.077	代謝	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	肝がんの発症メカニズムに関する研究。 試験ガイドラインに準拠していないin vitro 試験。	HepG2（ヒト肝腫瘍細胞）に対する毒性研究。 メトラクロールがサイクリンAの転写発現を阻害することによりS期が遅滞し、その結果として細胞増殖速度の低下を招くことが示された。
EU007	In vitro screening for aryl hydrocarbon receptor agonistic activity in 200 pesticides using a highly sensitive reporter cell line, DR-EcoScreen cells, and in vivo mouse liver cytochrome P450-1A induction by propanil, diuron and linuron	Chemosphere (2008), 74(1), 155-165.	2008	Takeuchi, S. et al.	北海道立衛生研究所	http://dx.doi.org/10.1016/j.chemosphere.2008.08.015	代謝	原著	－	－	in vitro	－	－	－	－	細胞活性の新規測定法の評価試験。 メトラクロールの毒性を評価していない。	アリル炭化水素受容体アゴニスト同定のための新しい測定法の開発。
EU008	Comparative study of human and mouse pregnane X receptor agonistic activity in 200 pesticides using in vitro reporter gene assays	Toxicology (2011), 280(3), 77-87	2011	Kojima, S. et al.	北海道立衛生研究所	http://dx.doi.org/10.1016/j.tox.2010.11.008	代謝	原著	－	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。 試験ガイドラインに準拠していないin vitro 試験。	200種類の農薬におけるヒト及びマウスのプレグナンX受容体アゴニスト活性の比較研究。
EU010	Activation of a- and b-estrogen receptors by persistent pesticides in reporter cell lines	Life Sciences (2006), 79(12), 1160-1169.	2006	Lemaire, G. et al.	Institut national de la recherche agronomique, France	http://dx.doi.org/10.1016/j.lfs.2006.03.023	代謝	原著	－	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。 試験ガイドラインに準拠していないin vitro 試験。	49種類の農薬がHELN細胞エストロゲン受容体活性に与える影響に関する研究。
EU011	Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system.	Toxicological sciences : an official journal of the Society of Toxicology, https://doi.org/10.1093/toxsci/kfj173	2006	Lemaire, G. et al.	L’Institut national de la santé et de la recherche médicale, France	https://doi.org/10.1093/toxsci/kfj173	代謝	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	リガンド同定の新しい手法の紹介。 メトラクロールの毒性を評価していない。	HeLa細胞より新たに作成した細胞株（HGPXR）を用いた、プレグナンX受容体リガンドの新しい同定法の開発。
EU012	Mechanism of metolachlor action due to alterations in cell cycle progression	Cell biology and toxicology, (2013 Aug) Vol. 29, No. 4, pp. 283-91.	2013	Lowry, M. et al.	University of Northern Iowa, USA	http://dx.doi.org/10.1007/s10565-013-9256-z	代謝	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	毒性作用の機序に関する研究。	HepG2（ヒト肝腫瘍細胞）内でのメトラクロールの作用機序の研究。メトラクロールの細胞毒性は、細胞のネクローシス/アポトーシスの誘発ではなく、細胞分裂の阻害によることが示唆された。
EU013	Specific interactions of chloroacetanilide herbicides with human ABC transporter proteins.	Toxicology, (2008 Jun 3) Vol. 248, No. 1, pp. 45-51.	2008	Oosterhuis, B. et al.	SOLVO Biotechnology, Hungary	http://dx.doi.org/10.1016/j.tox.2008.03.003	代謝	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	毒性作用の機序に関する研究。	メトラクロールを含むクロロアセトアニリド系農薬とABCトランスポータータンパク質の相互作用に関する研究。クロロアセトアニリド系農薬は、ABCトランスポーテーションの基質として、MDR1に作用していることが示唆された。
EU014	Toxicity assessment of the herbicide metolachlor comparative effects on bacterial and mitochondrial model systems.	Toxicology in vitro : an international journal published in association	2009	Pereira, S. et al.	Coimbra University, Portugal	http://dx.doi.org/10.1016/j.tiv.2009.06.032	一般毒性	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	肝がんの発症メカニズムに関する研究。 試験ガイドラインに準拠していないin vitro 試験。	当該物質の毒性に関する細菌（*Bacillus stearothermophilus*）とラット肝ミトコンドリアを用いた*in vitro*研究。他の多くの農薬と比べて毒性が大幅に低いことが示された。
EU015	Xenobiotic-Metabolizing Enzyme and Transporter Gene Expression in Primary Cultures of Human Hepatocytes Modulated by Toxcast Chemicals	Journal of Toxicology and Environmental Health, Part B: Critical Reviews (2010), 13(2-4), 329-346	2010	Rotroff, D. et al.	Environmental Protection Agency, USA	http://dx.doi.org/10.1080/10937404.2010.483949	代謝	原著	－	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。試験ガイドラインに準拠していないin vitro 試験。	ToxCastに登録されている320種類の化学物質の、ヒト肝細胞の遺伝子発現への影響に関する研究。
EU016	Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line.	Toxicology, (2006 Nov 10) Vol. 228, No. 1, pp. 98-108.	2006	Laville, N. et al.	Institut national de l’environnement industriel et des risques, France	http://dx.doi.org/10.1016/j.tox.2006.08.021	代謝	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。試験ガイドラインに準拠していないin vitro 試験。	当該物質を含む30種類の農薬の、アロマターゼ酵素活性に対する影響について、ヒト絨毛がんJEG-3細胞株を用いて調査。
EU018	Profiling 976 ToxCast Chemicals across 331 Enzymatic and Receptor Signaling Assays	Chemical Research in Toxicology (2013), 26 (6), 878-895. https://doi.org/10.1021/tx400021f	2013	Sipes, N. et al.	U.S. Environmental Protection Agency	http://dx.doi.org/10.1021/tx400021f	一般毒性	原著	〇 EFSA 2018年	－	in vitro	－	－	－	－	新規のデータが提示されない文献調査。	ToxCastに登録されている976種類の化学物質を、331種類の試験により分類（文献調査）。
EU019	Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using chinese hamster ovary cells	Environmental Health Perspectives (2004), 112 (5), 524-531. https://doi.org/10.1289/ehp.6649	2004	Kojima, H. et al.	北海道立衛生研究所	https://doi.org/10.1289/ehp.6649	代謝	原著	〇 EPA 2016年	－	in vitro	－	－	－	－	多種類の農薬に関するスクリーニング研究。試験ガイドラインに準拠していないin vitro 試験。	200種類の農薬（及び代謝物）に対する、レポーター遺伝子試験によるエストロゲン/アンドロゲン活性のスクリーニング調査。
EU020	Herbicide Metolachlor Causes Changes in Reproductive Endocrinology of Male Wistar Rats	ISRN Toxicology (2012) 130846. https://doi.org/10.5402/2012/130846	2012	Mathias, F. et al.	State University of Centro-Oeste, Brazil	https://doi.org/10.5402/2012/130846	生殖毒性	原著	〇 EPA 2014年	－	in vivo （ラット）	5 mg/kg/日 50 mg/kg/日	－	－	－	生殖毒性のメカニズムに関する研究。 試験ガイドラインに準拠していないin vitro 試験。	ラット雄の生殖内分泌に与える影響に関する研究。 思春期前の暴露がラット雄の生殖内分泌に影響することを明らかにしている。
EU021	Endocrine Profiling and Prioritization of Environmental Chemicals Using ToxCast Data	Environmental Health Perspectives (2010), 118(12), 1714-1720. https://doi.org/10.1289/ehp.1002180	2010	Reif, D. et al.	U.S. Environmental Protection Agency	https://doi.org/10.1289/ehp.1002180	代謝	原著	－	－	in vitro	－	－	－	－	新規のデータが提示されない文献調査。	ToxCastのデータに基づき、309種類の環境内物質が内分泌経路に与える影響を順位付けしている（文献調査）。
EU022	Predictive Endocrine Testing in the 21st Century Using in Vitro Assays of Estrogen Receptor Signaling Responses.	Environmental Science & Technology (2014), 48 (15), 8706-8716. https://doi.org/10.1021/es502676e	2014	Rotroff, D. et al.	University of North Carolina, Chapel Hill, USA	https://doi.org/10.1021/es502676e	代謝	原著	－	－	in vitro	－	－	－	－	スクリーニング試験の評価研究。 メトラクロールの毒性を評価していない。	化学物質の内分泌かく乱性に関する新しいin vitroスクリーニング試験の開発。

No.	文献名	ジャーナル名等	公表年	著者名	著者の所属機関	書誌情報	原著	海外評価書での引用の有無	ドシエでの引用の有無	備考
EU023	Use of Agricultural Pesticides and Prostate Cancer Risk in the Agricultural Health Study Cohort	Am J Epidemiol 2003;157:800-814 https://doi.org/10.1093/aje/kwg040	2003	Alavanja, M. et al.	National Cancer Institute, USA	https://doi.org/10.1093/aje/kwg040	原著	○ EPA 2014年	－	農薬と前立腺がんの関係に関する疫学的研究。
EU024	Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort.	Cancer causes & control: CCC, (2010 Nov) Vol. 21, No. 11, pp. 1759-75.	2010	Andoreotti, G. et al.	National Institutes of Health, USA	http://dx.doi.org/10.1007/s10552-010-9603-9	原著	○ EPA 2014年	－	農薬及び体重指数と発がん性に関する疫学的研究。 メトラクロール使用歴があり、肥満度が高いと、結腸がんのリスクが高まることが認められた。
EU025	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	The Science of the total environment, (2010 Jan 15) Vol. 408, No. 4, pp. 790-5.	2010	Barr, D. et al.	Centers for Disease Control and Prevention, USA	http://dx.doi.org/10.1016/j.scitotenv.2009.10.007	原著	○ EFSA 2018年	－	母体及び胎児への農薬濃縮と出生時の健康状態に関する疫学的研究。臍帯血中のメトラクロール濃度と出生時体重との間の高い相関が示された。
EU026	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Environmental health perspectives, (2011 Jul) Vol. 119, No. 7, pp. 1034-41. https://doi.org/10.1289/ehp.1002775	2011	Chevrier, C. et al.	L'Institut national de la santé et de la recherche médicale, France	https://doi.org/10.1289/ehp.1002775	原著	○ EFSA 2018年	－	農薬と出生時異常の関係に関する疫学的研究。 新生児の頭囲長と尿中のメトラクロール濃度との間に相関が認められた。
EU027	Pesticides and adult respiratory outcomes in the agricultural health study.	Annals of the New York Academy of Sciences, (Sep 2006) Vol. 1076, pp. 343-354.	2006	Hoppin, J. et al.	National Institutes of Health, USA	http://dx.doi.org/10.1196/annals.1371.044	原著	○ EFSA 2018年	－	農薬と呼吸器疾患の関係に関する疫学的研究。
EU028	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Environmental health perspectives, (2013 Aug) Vol. 121, No. 8, pp. 919-24. https://doi.org/10.1289/ehp.1206432	2013	Hou, L. et al.	Northwestern Univ., USA	https://doi.org/10.1289/ehp.1206432	原著	○ EFSA 2018年	－	生涯の農薬使用履歴とテロメア短縮との関係に関する疫学的研究。
EU029	Pesticide use and colorectal cancer risk in the Agricultural Health Study	International Journal of Cancer (2007), 121(2), 339-346 https://doi.org/10.1002/ijc.22635	2007	Lee, W. et al.	Korea University, Korea	https://doi.org/10.1002/ijc.22635	原著	○ EFSA 2018年	－	農薬と結腸がん/直腸がんの関係に関する疫学的研究。 メトラクロールと結腸がん/直腸がんとの相関は見られなかった。

EU030	Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies	Environmental Health Perspectives, Volume 105, Number 3, March 1997 https://doi.org/10.1289/ehp.97105308	2007	Munger, R. et al.	University of Iowa, USA	https://doi.org/10.1289/ehp.97105308	原著	○ EFSA 2018年	－	飲料水内の4種類の農薬と子宮内発育遅延の関係に関する疫学的研究。 各農薬ごとの影響については調査されていない。
EU031	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	International journal of cancer. Journal international du cancer, (2006 Jun 15) Vol. 118, No. 12, pp. 3118-23. https://doi.org/10.1002/ijc.21758	2006	Rusiecki, J. et al.	National Institutes of Health, USA	https://doi.org/10.1002/ijc.21758	原著	○ EFSA 2018年	－	メトラクロール暴露と6種類のがんの発がんとの関係に関する疫学的研究。 いずれのがんについても明白な相関は認められなかった。
EU032	Semen Quality in Relation to Biomarkers of Pesticide Exposure	Environmental Health Perspectives, vol 111, 12 September 2003. https://doi.org/10.1289/ehp.6417	2003	Swan, S. et al.	University of Missouri-Columbia, USA	https://doi.org/10.1289/ehp.6417	原著	○ EFSA 2018年	－	農薬と精子の質の間の関係に関する疫学的研究。
EU033	Herbicides and nitrates in groundwater of Maryland and childhood cancers: a geographic information systems approach.	Journal of environmental science and health. Part C, Environmental	2005	Thorpe, N. et al.	Hagerstown Community College, USA	http://dx.doi.org/10.1080/10590500500235001	原著	○ EFSA 2018年	－	農薬と小児がんの間の関係に関する疫学的研究。 メトラクロールを含む農薬と、白血病及び骨がんとの関連性が示唆された。

			研究デザイン								健康関連の事象の情報								
No.	文献名	著者名	国名（地域名、研究名）	試験設計	調査時期	対象者、年齢	アウトカムの定義	アウトカムの確認方法	暴露指標の定義	暴露の確認方法	試験全体のN数（症例/対照）	アウトカムのN数	分析カテゴリー	暴露に係るN数	相対リスク/オッズ比等	95%信頼区間	p値	交絡因子の考慮	備考
EU023	Use of Agricultural Pesticides and Prostate Cancer Risk in the Agricultural Health Study Cohort	Alavanja, M. et al.	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1999	男性農薬散布免許取得者	前立腺がん発症	アンケート及びインタビュー	当該農薬の使用実態	アンケート	89658（他農薬含む）	-	-	-	-	-	-	-	メトラクロール単体のデータは示されていない。
EU024	Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort.	Andoreotti, G. et al.	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2005	農薬散布免許取得者とその配偶者	結腸がん	アンケート及びインタビュー	当該農薬の使用実態	アンケート	67947（他農薬含む）	4432（調査対象の全農薬に対するN）	散布経験及び肥満度（BMI）	48730（調査対象の全農薬に対するN）	-	-	-	人種、喫煙状況、野菜摂取、運動、家族の発がん履歴、高血圧、ビタミン剤摂取、果物摂取、州、糖尿、アルコール摂取、教育、肉摂取、日焼け止め使用の有無、出産歴	農薬使用及び肥満度の発がん性との関連性の調査。米国農業健康調査（AHS）コホートによる研究。
EU025	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	Barr, D. et al.	米国（ニュージャージー州）	コホート研究	2003-2004	妊婦及び新生児	血液内の農薬濃度	妊婦と臍帯からの採血	–	–	150	–	–	–	–	–	–	–	妊婦及び新生児における農薬含有量の調査。
EU026	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Chevrier, C. et al.	フランス	コホート内症例対照研究	2002-2006	妊娠19週未満の妊婦	異常出生	医師による診断	水道水中のアトラジン含有量（推測値）	全国農業統計のとうもろこし農地の比率から、水道水中のアトラジン含有量を推測	579	–	暴露履歴	–	メトラクロール オッズ比 0.8,1.2,1.0	0.4-1.4,0.8-1.9,0.6-1.7	–	–	フランス農業地帯の妊婦の血中農薬濃度と異常出生の関係を調査。
EU027	Pesticides and adult respiratory outcomes in the agricultural health study.	Hoppin, J. et al.	米国（アイオワ州及びノースカロライナ州）	横断研究	1993-1997	農薬散布免許取得者	成人呼吸器疾患	アンケートによる自己申告（呼吸音の異常）	当該農薬の使用実態	アンケート	20175（他農薬含む）	–	散布経験	–	オッズ比 農業従事者1.09 散布業者1.01	0.97-1.21 0.71-1.43	–	年齢、肥満度指数、喘息／アトピー罹患、農薬使用歴	農薬暴露と呼吸器疾患の関連に関する調査。米国農業健康調査（AHS）コホートによる研究。
EU028	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Hou, L. et al.	米国（アイオワ州及びノースカロライナ州）	横断研究	1993-2006	農薬散布免許取得者	頬細胞DNAの相対テロメア長の減少	唾液サンプルから測定	当該農薬の使用実態	アンケート	1114	–	–	492	–	–	–	唾液採取時の年齢、州、農業従事者／散布事業者の違い、噛みタバコ嗜好、全農薬の散布状況	生涯積算農薬暴露量と頬細胞内のDNAの相対テロメア長の関連を調査。いずれの農薬も相対テロメア長の減少は認められなかった。米国農業健康調査（AHS）コホートによる研究。
EU029	Pesticide use and colorectal cancer risk in the Agricultural Health Study	Lee, W. et al.	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2002	農薬散布免許取得者とその配偶者	大腸がん	各州がん患者登録、死亡記録及び国民死亡指標（National Death Index）とのデータ照合	当該農薬の使用実態	アンケート	56813（他農薬含む）	107	散布経験	–	オッズ比 1.0	0.6-1.7	–	–	農薬暴露と大腸がんの関連に関する調査。当該農薬については対照群との比較データなし。米国農業健康調査（AHS）コホートによる研究。
EU030	Intrauterine Growth Retardation in Iowa Communities with Herbicide-contaminated Drinking Water Supplies	Munger, R. et al.	米国（アイオワ州）	コホート研究	1984-1990	白人新生児	出生時低体重、早産、子宮内発育遅滞	医師による診断	母親の妊娠中の居住地の水道内農薬濃度	州の水道水質調査のデータと母親の居住地データを照合	–	–	–	–	–	–	–	–	新生児の出生時異常と妊娠中の母親の農薬暴露の関連に関する調査。各農薬単体の疫学的データは含まれていない。
EU031	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	Rusiecki, J. et al.	米国（バージニア州及びノースカロライナ州）	コホート研究	1993-2002	農薬散布免許取得者とその配偶者	発がん	医師による診断	当該農薬の使用実態	アンケート	51111	–	–	–	–	–	–	–	メトラクロールのがん誘発性について疫学的に調査。調査対象の6種類のがんについては、いずれも関連が認められなかった。米国農業健康調査（AHS）コホートによる研究。
EU032	Semen Quality in Relation to Biomarkers of Pesticide Exposure	Swan, S. et al.	米国（ミズーリ州及びミネソタ州）	横断研究	1993-1997	配偶者が妊娠中の男性	精子の質	精子提供	血液中の農薬濃度	採血	86（34/52）	–	–	–	オッズ比 MI州 3.0 MI州 3.3 MN州 1.4	MI州 0.7-12.2 MI州 0.8-14.5 MN州 0.3-6.3	–	–	農業地帯と都市部の男性の精子の質の比較及び、農薬濃度との関連を調査。
EU033	Herbicides and nitrates in groundwater of Maryland and childhood cancers: a geographic information systems approach.	Thorpe, N. et al.	米国（メリーランド州）	横断研究	1992-1998	小児がん患者（0－17歳）	発がん	医師の診断	地下水の農薬分布	全米地質調査のデータと照合	1218790（689/1218101）	689	地下水中の農薬の分布状況	–	オッズ比 4種計 1.54 骨がん 2.26 白血病 1.48	4種計 1.14-2.07 骨がん 0.97-5.24 白血病 0.93-2.36	4種計 0.0061 骨がん 0.0995 白血病 0.1256	–	4種類の小児がん患者の発生分布と地下水中の農薬分布との相関から、農薬が小児がんの発症に与える影響を推測。

公表文献に関する報告書

有効成分名：S-メトラクロール

シンジェンタジャパン株式会社 提出

提出日：令和 5 年 9 月 26 日

第 1 回修正日：令和 6 年 1 月 16 日

農薬取締法に基づく農薬有効成分の再評価制度に係る公表文献調査報告書

有効成分名：S-メトラクロール

目次

1. 検索対象有効成分

一般名： メトラクロール、S-メトラクロール、Metolachlor、S-Metolachlor

IUPAC 名：2-chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-methoxy-1-methylethyl)-acetoamide

(1*S*)-2-chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-methoxy-1-methylethyl)-acetoamide

(1*R*)-2-chloro-*N*-(2-ethyl-6-methylphenyl)-*N*-(2-methoxy-1-methylethyl)-acetoamide

CAS 番号： 51218-45-2、87392-12-9、178961-20-1

2. 検索条件

2.1. 文献検索に用いたプラットフォーム/データベース、検索日及び検索期間

文献検索に使用した検索プラットフォームは、英文キーワード検索については Web of Science Core Collection（WOSCC）と J-STAGE、和文キーワード検索については J-STAGE を用いた。

表 2－1－1 文献検索に用いたプラットフォーム/データベース(文献データベース)

分類	データベースの特徴	収載範囲（文献検索時の文献数）	最新更新日 更新頻度	検索日	検索期間
Web of Science Core Collection (WOSCC)	科学技術、社会科学、人文科学における世界最大級の研究情報プラットフォーム。 約 20000 誌の主要な学術雑誌に掲載された約 1.7 億本の論文が 25 の専門分野に分類、収載されている。	1900-現在 （1.7 億件）	2023/2/13 毎日更新	2023/1/27 2023/2/8 2023/2/9 2023/2/13	2014/8/1 - 2023/2/13
J-STAGE	国立研究開発法人科学技術振興機構 (JST) が提供する、日本国内の科学技術情報の電子ジャーナルプラットフォーム。 自然科学、人文・社会科学、学際領域等の分野について、国内 1,500 を超える発行機関が、3,000 誌以上のジャーナルや会議録等の刊行物を公開している。	1999-現在 （550 万件）	2023/2/22 毎日更新	2023/2/22	2014/1/1 - 2023/2/22 （英文） 2008/1/1 - 2023/2/22 （和文）

2.2. 検索に使用した化合物名

表 2－2－1 検索に用いたキーワード (WOSCC)

一般名	Metolachlor、S-Metolachlor
化学名	2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide (1S)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide (1R)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide
CAS 番号	51218-45-2、87392-12-9、178961-20-1

表 2－2－2 検索に用いたキーワード (J-STAGE 英文キーワード検索)

一般名	Metolachlor、S-Metolachlor
化学名	2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide (1S)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide (1R)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide
CAS 番号	51218-45-2、87392-12-9、178961-20-1

表 2－2－3 検索に用いたキーワード (J-STAGE 和文キーワード検索)

一般名	メトラクロール、S-メトラクロール、Metolachlor、S-Metolachlor
化学名	2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide (1S)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide (1R)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)-acetoamide
CAS 番号	51218-45-2、87392-12-9、178961-20-1

なお、以下の理由により、文献検索時の「対象とする農薬」のキーワードに製剤名 "Dual" および ”デュアール” を含めなかった。

① WOSCC において、予備検索として "Metolachlor" を含む文献を検索したところ 1012 件であったのに対し、"Dual" を含む文献は 353,398 件と、膨大な数が該当した。
一方「 "Metolachlor" ＋化学名」では 1012 件（"Metolachlor" のみの場合と同数）であったのに対し、「"Dual"＋化学名」では 3 件（*）のみの該当であった。
これらの状況より、"Dual" で該当したほぼすべての文献は、一般名詞または形容詞の "dual" 、もしくは "individual" や "gradual" 等の単語の一部がヒットしたものと推測される。
*この 3 件の文献は第 1 段階評価に含まれている。

② およそ専門家の文献として、有効成分を明示せずに商品名のみで物質を特定するような例は、除草効果の文献ではあり得ても、毒性、環境関係の研究報告ではきわめて少ないと考えられる。

また、日本の評価結果において、ヒトの健康や環境影響を評価する上で考慮しなければならないとされた化合物、たとえば、有効成分よりも毒性が高いと判断された代謝物、分解物等のその他成分は認められず、検索対象とはしなかった。

2.3. 評価対象となる影響

表２－３－１４分野に関連する文献検索に用いたキーワード(WOSCC)

ヒトに対する毒性	mortality OR skin irritation OR eye irritation OR sensitization OR allergy OR hypersensitivity OR metabolism OR distribution OR absorption OR excretion OR kinetic OR PK OR TK OR cytochrome OR enzyme mutagen OR DNA OR genotoxicity OR carcinogen OR cancer OR tumor OR oncology OR immune OR neurotoxicity OR endocrine disruption/disruptors OR hormone OR development OR developmental toxicity OR reproduction OR malformation OR maternal toxicity OR pregnancy OR embryo OR fetus OR offspring OR dermal OR epidermal OR exposure OR operator OR worker OR occupant OR biomonitoring OR medical OR poison OR apoptosis OR necrosis OR cytotoxic OR cohort OR epidemiology OR adverse effect OR case control
農作物及び畜産物への残留	Uptake OR metabolism OR metabolic OR breakdown OR translocation OR degradation storage OR stability OR residue OR process OR preharvest OR postharvest OR preplant OR pre-emergence OR post-emergence OR processing factor OR conversion factor OR hydroxylation OR photolysis OR rotation OR succeed OR supervised trial OR field trial OR dietary exposure OR MRL OR maximum residue level OR maximum residue limit
生活環境動植物及び家畜に対する毒性	bioaccumulation OR bioconcentration OR biomagnification OR effect OR biodiversity OR protection goals OR eco OR impact OR population OR pest OR endocrine disrupt OR acute OR chronic OR long-term OR ecotoxicology OR colony OR hive OR aquatic OR freshwater OR macro-organism OR micro-organism OR microbial OR biodegradation
環境動態	degradation OR photo OR hydrolysis OR accumulate OR dissipation OR vapor pressure OR mobility OR adsorption OR desorption OR persistent OR pollution OR contamination OR aged residue OR column leaching OR leach OR lysimeter OR drift OR run-off OR atmosphere OR transport OR long-range transport OR short-range transport OR monitoring OR surveillance OR environmental OR exposure OR fate OR residue

表 2－3－2 4 分野に関連する文献検索に用いたキーワード(J-STAGE 英文キーワード検索)

ヒトに対する毒性	mortality OR skin irritation OR eye irritation OR sensitization OR allergy OR hypersensitivity OR metabolism OR distribution OR absorption OR excretion OR kinetic OR PK OR TK OR cytochrome OR enzyme mutagen OR DNA OR genotoxicity OR carcinogen OR cancer OR tumor OR oncology OR immune OR neurotoxicity OR endocrine disruption/disruptors OR hormone OR development OR developmental toxicity OR reproduction OR malformation OR maternal toxicity OR pregnancy OR embryo OR fetus OR offspring OR dermal OR epidermal OR exposure OR operator OR worker OR occupant OR biomonitoring OR medical OR poison OR apoptosis OR necrosis OR cytotoxic OR cohort OR epidemiology OR adverse effect OR case control
農作物及び畜産物への残留	uptake OR metabolism OR metabolic OR breakdown OR translocation OR degradation storage OR stability OR residue OR process OR preharvest OR postharvest OR preplant OR emergence OR processing factor OR conversion factor OR hydroxylation OR photolysis OR rotation OR succeed OR supervised trial OR field trial OR dietary exposure OR MRL OR maximum residue level OR maximum residue limit
生活環境動植物及び家畜に対する毒性	bioaccumulation OR bioconcentration OR biomagnification OR effect OR biodiversity OR protection goals OR eco OR impact OR population OR pest OR endocrine disrupt OR acute OR chronic OR long-term OR ecotoxicology OR colony OR hive OR aquatic OR freshwater OR macro-organism OR micro-organism OR microbial OR biodegradation
環境動態	degradation OR photo OR hydrolysis OR accumulate OR dissipation OR vapor pressure OR mobility OR adsorption OR desorption OR persistent OR pollution OR contamination OR aged residue OR column leaching OR leach OR lysimeter OR drift OR run-off OR atmosphere OR transport OR long-range transport OR short-range transport OR monitoring OR surveillance OR environmental OR exposure OR fate OR residue

表 2－3－3 4 分野に関連する文献検索に用いたキーワード(J-STAGE 和文キーワード検索)

ヒトに対する毒性	死亡率 OR 刺激性 OR 感作性 OR アレルギー OR 過敏症 OR 代謝 OR 分布 OR 吸収 OR 排泄 OR キネティクス OR PK OR TK OR チトクローム OR 酵素 OR 変異原 OR DNA OR 遺伝毒性 OR 発がん性物質 OR 発がん OR 腫瘍 OR 免疫 OR 神経毒性 OR エンドクリン OR 内分泌かく乱化学物質 OR ホルモン OR 発達 OR 毒性 OR 生殖 OR 奇形 OR 母性 OR 妊娠 OR 胚 OR 胎児 OR 子孫 OR 経皮 OR ばく露 OR 作業者 OR 使用者 OR 居住 OR バイオモニタリング OR 毒 OR アポトーシス OR 壊死 OR 細胞毒性 OR コホート OR 疫学 OR 悪影響 OR 事例研究
農作物及び畜産物への残留	取込 OR 代謝 OR 分解 OR 移行 OR 保存 OR 安定性 OR 残留 OR 過程 OR プロセス OR 収穫前 OR 収穫後 OR 移植 OR 播種 OR 加工係数 OR 処理能力 OR 換算係数 OR 加水分解 OR 光分解 OR 輪作 OR 後作 OR 管理試験 OR 圃場試験 OR 食品経由での暴露 OR MRL OR 最大残留
生活環境動植物及び家畜に対する毒性	生物濃縮 OR 蓄積 OR 影響 OR 生物多様性 OR 環境保護目標 OR 生態 OR 集団 OR 病害 OR エンドクリン OR 内分泌かく乱物質 OR 急性 OR 慢性 OR 長期 OR 生態毒性 OR コロニー OR 巣 OR 水生 OR 淡水 OR 微生物 OR 生分解
環境動態	分解 OR 光 OR 加水分解 OR 濃縮 OR 消失 OR 蒸気圧 OR 移行性 OR 吸着 OR 脱着 OR 残留性 OR 汚染 OR 混入 OR カラムリーチング OR ライシメーター OR ドリフト OR 飛散 OR 流亡 OR 大気 OR 移動 OR モニタリング OR サーベイ調査 OR 環境 OR 動態 OR 残留 OR 運命 OR 暴露

2.4. 評価対象の生物種等

表 2－4－1 評価対象となる生物種等に関するキーワード(WOSCC)

ヒトに対する毒性	rat OR mouse OR mice OR dog OR rabbit OR monkey OR pig OR human OR hen OR S. typhimurium OR E. coli
農作物及び畜産物への残留	crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry
生活環境動植物及び家畜に対する毒性	avian OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR fish OR crustacean OR aquatic OR chironomus OR bee OR pollinator OR apis
環境動態	soil OR water OR sediment

表 2－4－2 評価対象となる生物種等に関するキーワード(J-STAGE 英文キーワード検索)

ヒトに対する毒性	rat OR mouse OR mice OR dog OR rabbit OR monkey OR pig OR human OR hen OR S. typhimurium OR E. coli
農作物及び畜産物への残留	crop OR commodity OR feed OR livestock OR hen OR cattle OR goat OR pig OR ruminant OR cow OR poultry
生活環境動植物及び家畜に対する毒性	avian OR bird OR mallard duck OR quail OR bobwhite OR lemna OR algae OR fish OR crustacean OR aquatic OR chironomus OR bee OR pollinator OR apis
環境動態	soil OR water OR sediment

表 2－4－3 評価対象となる生物種等に関するキーワード(J-STAGE 和文キーワード検索)

ヒトに対する毒性	ラット OR マウス OR イヌ OR ウサギ OR サル OR ブタ OR 人間 OR ヒト OR ニワトリ OR チフス菌 OR 大腸菌
農作物及び畜産物への残留	作物 OR 植物 OR 食料 OR 飼料 OR 家畜 OR ニワトリ OR 乳牛 OR ヤギ OR ブタ OR 反すう動物 OR ウシ OR 家きん
生活環境動植物及び家畜に対する毒性	植物 OR 鳥類 OR マガモ OR アヒル OR ウズラ OR ウキクサ OR 藻類 OR 魚 OR 甲殻類 OR ミジンコ OR 水生 OR ユスリカ OR ハチ OR ミツバチ OR 花粉媒介者
環境動態	土壌 OR 水 OR 底質

3. 評価目的との適合性評価及び信頼性評価で設定した判断基準

3.1. 評価目的との適合性（第 1 段階）で設定した判断基準

適合性評価の第 1 段階として、文献の表題及び概要に基づき、下記の①から⑮に該当するものは明らかに評価の目的と適合しない文献と見なして、以降の検討から除いた。

① 当該農薬と関係しない論文（当該農薬の代替剤等）
② 政策、社会、経済分析に関する論文
③ 農産物等の生産、流通に関する論文
④ 薬効、薬害、物理的化学的性状に関する論文
⑤ 分析法やその開発に関する論文
⑥ 新規合成法や基礎化学の観点で記載された論文
⑦ 特許関連文献
⑧ リスク評価をする上で十分なデータや情報を含まない学会発表等の概要や総説、成書
⑨ リスク評価に使用できる新規のデータが提示されていない意見書
⑩ 科学論文や規制についての総説を含む二次情報において、当該文献が参照する一次資料（原著）の確認ができないもの
⑪ 一般的な農薬の暴露に関する論文（当該農薬に限定せず、広範囲の農薬について記載されたもの）
⑫ 異なる有効成分に由来する混合製剤の毒性に関する論文

⑬ 表 2－3－1 に掲げる 4 分野に関係しない論文
⑭ 日本で登録されている処方以外の製剤に関する論文
⑮ コンピュータシミュレーション等を用いたドライラボのみの論文

3.2. 文献の全文に基づく適合性評価（第 2 段階）で設定した判断基準

第 1 段階で除外した以外の公表文献について、文献全文の内容に基づいて、以下の手順に従って評価目的との適合性を検証し、その結果により分類した。

（ア）評価の目的と適合しない文献の除外

① 当該農薬と関係しない論文（当該農薬の代替剤等）
② 政策、社会、経済分析に関する論文
③ 農産物等の生産、流通に関する論文
④ 薬効、薬害、物理的化学的性状に関する論文
⑤ 分析法やその開発に関する論文
⑥ 新規合成法や基礎化学の観点で記載された論文
⑦ 特許関連文献
⑧ リスク評価をする上で十分なデータや情報を含まない学会発表等の概要や総説、成書
⑨ リスク評価に使用できる新規のデータが提示されていない意見書
⑩ 科学論文や規制についての総説を含む二次情報において、当該文献が参照する一次資料（原著）の確認ができないもの
⑪ 一般的な農薬の暴露に関する論文（当該農薬に限定せず、広範囲の農薬について記載されたもの）
⑫ 異なる有効成分に由来する混合製剤の毒性に関する論文
⑬ 表 2－3－1 に掲げる 4 分野に関係しない論文
⑭ 日本で登録されている処方以外の製剤に関する論文
⑮ コンピュータシミュレーション等を用いたドライラボのみの論文
⑯ 試験設計、試験系、試験種、被験物質、暴露経路等が評価に活用する観点で妥当でないもの
　a) 試験方法が記載されていないもの
　b) 適切に評価できる試験種で実施されていないもの
　c) 適切な経路で投与／処理されていないもの
　d) 投与又は処理した被験物質量が明記されていないもの
　e) 被験物質の添加に用いた媒体が確認できないもの
　f) 分析法が記載されていないもの
⑰ 日本の代表的な使用方法／使用条件における評価に活用できない文献（ほ場条件、土性等）

（イ）評価の目的と適合した文献の分類

（ア）で除外した以外の文献については適合性があると判断し、下記の分類基準に従っ

て、全文をレビューし３つの区分に分類した。

＜分類基準＞

- 実施している試験環境がテストガイドライン（TG）で定める条件と合っていること
- 投与又は処理した被験物質の純度が明記されていること
- 統計解析が可能な動物数／例数が確保されていること
- 複数の用量で実施されていること（最低 3 用量で実施）
- 無処理区（コントロール区）が設定されており、TG に照らしその結果が適正であること
- 解析方法及び結果が報告されていること

ヒトに対する毒性に関して、区分 a に該当するかどうかについては、食品安全委員会で示された「定量的データ」として分類される下記基準を参考とした。

- 公表文献で用いられた用量が、研究内容と同等である安全性試験で用いられた最低用量よりも低いこと
- 公表文献の研究結果が、他の試験結果と比較できる単位を用いて報告されていること
- 研究の結論、エンドポイント及び用量が正確で、信頼でき、妥当であることを実証するための十分な情報が公表文献中に提供されており、研究結果が再現される可能性があると判断できること

表 3－2－1 評価目的への適合性がある文献の分類

区分	該当する文献
a	リスク評価パラメーター(ADI、ARfD、AOEL、残留基準、生活環境動植物の登録基準、水産 PEC 等)を設定又は見直すために利用可能と判断される文献
b	リスク評価パラメーターを設定する際の補足データとして利用が可能と想定される文献
c	a 又は b に分類されない文献

3.3. 論文の信頼性の評価基準

評価目的への適合性評価において「区分 a 」に分類した文献については、論文の信頼性を評価する方法として国際的に広く用いられている Klimisch 基準（表 3－3－1）における分類を参考として、適切な分類基準を設定し、信頼性を評価した。

表 3－3－1 Klimisch 基準の概要

分類	信頼性	判断基準
1	信頼性あり（制限なし）	以下のいずれかの試験/データに該当する場合。 ・有効性が確認された方法又は国際的に認められたテストガイドラインに基づいて実施されている(GLP 適合が望ましい)。 ・試験項目(評価パラメーター)が特定(国レベル)のテストガイドラインに基づいている。 ・全ての試験項目がテストガイドラインに示された方法と関連性が強い/同等により報告されている。
2	信頼性あり（制限あり）	以下のいずれかの試験/データに該当する場合(非 GLP 試験のことが多い）。 ・試験項目は特定のテストガイドラインに完全には準拠していないが、内容が受け入れ可能である。 ・試験方法がテストガイドラインから逸脱しているものの、詳細な報告に基づき科学的に受け入れ可能な結果が示されている。
3	信頼性なし	試験系、被験物質又はばく露経路の妥当性、記載情報の不十分さ等の観点から、エキスパートジャッジのためには許容できないと考えられる試験/データ。
4	評価不能	試験の詳細が不明であり、要約のみの記載又は二次情報(書籍、総論等)として記載された試験/データ。

1. ヒトに対する毒性については、ToxRtool (Toxicological data Reliability assessment Tool)を分類基準として活用した。
（https://joint-research-centre.ec.europa.eu/scientific-tools-and-databases/toxrtool-toxicological-data-reliability-assessment-tool_en）
2. それ以外の 3 分野については、6278 号局長通知で定めるテストガイドラインへの適用状況を中心に以下のような分類基準を設定し、Klimisch 基準のどの分類に該当するかを判断した。

(ア) 農作物及び畜産物への残留

① 試験した作物が TG で定める代表的な作物か

② 試験系の条件が明記されているか（たとえば、作物の生育ステージ、ほ場の状況、処理量、処理方法、処理時期、PHI、サンプリング方法）

③ サンプリング後の試料保管中の被験物質の安定性が検証されているか

④ サンプリング後の試料の保管条件が明記されているか

⑤ 栽培条件（密度や仕立て）が適切であるか

⑥ 処理量が登録で定める GAP の範囲内であるか

(イ) 生活環境動植物及び家畜に対する毒性

① 水生生物試験では、被験物質が水に溶解していること

② 供試した生物種の由来、飼育条件、系統、週齢、体重あるいは体長、等が明らかであること

③ 試験期間の環境（温度等）が TG に照らし適切であること

④ 試験期間を通じて計画した濃度で被験物質に暴露していること

⑤ 経時的な観察記録や結果の確認がなされていること

(ウ) 環境動態

① 試験系の条件が明記されていること（たとえば、土壌の試験であれば、土質、pH、有機炭素含量、密度、水分含量、微生物活性等）

② 試験に使用した土壌等が TG で定める条件を満たしていること

③ サンプリング方法が TG で定めた条件をみたしていること

④ サンプリング後の試料の保管中の被験物質の安定性が検証されていること

⑤ サンプリング後の試料の保管条件が明記されていること

4. 評価目的との適合性評価及び信頼性評価の結果

4.1. 各データベースを検索した結果のまとめ

表 4－1－1 Web of Science Core Collection における論文検索結果

データベース名	Web of Science Core Collection (WOSCC)		
検索日	2023 年 1 月 27 日-2023 年 2 月 13 日		
検索対象期間	2014 年 8 月 1 日-2023 年 2 月 13 日		
最終の更新日	2023 年 2 月 13 日		
検索に用いたキーワード	①：表 2－2－1		
	②：表 2－3－1		
	③：表 2－4－1		
検索結果 検索条件(キーワード)	①	① AND ②	(① AND ②) AND ③
対象とする農薬名で検索抽出した総論文数	1012	N/A	N/A
ヒトに対する毒性	N/A	*452	*62
農作物及び畜産物への残留	N/A	*479	*260
生活環境動植物及び家畜に対する毒性	N/A	*574	*156
環境動態	N/A	*646	*566

*4 分野間での重複あり
N/A：該当するデータなし

表 4－1－2 J-STAGE における論文検索結果

データベース名	J-STAGE				
検索日	2023 年 2 月 22 日				
検索対象期間	英文キーワード検索：2014 年 1 月 1 日-2023 年 2 月 22 日 和文キーワード検索：2008 年 1 月 1 日-2023 年 2 月 22 日				
最終の更新日	2023 年 2 月 22 日				
検索に用いたキーワード	①：表 2－2－2（英文キーワード検索）または表 2－2－3（和文キーワード検索）				
	②：表 2－3－2（英文キーワード検索）または表 2－3－3（和文キーワード検索）				
	③：表 2－4－2（英文キーワード検索）または表 2－4－3（和文キーワード検索）				
検索結果 検索条件(キーワード)	①	① AND ②		(① AND ②) AND ③	
		英文 キーワード 検索	和文 キーワード 検索	英文 キーワード 検索	和文 キーワード 検索
対象とする農薬名で検索抽出した総論文数	114	N/A	N/A	N/A	N/A
ヒトに対する毒性	N/A	*38	*52	*21	*26
農作物及び畜産物への残留	N/A	*34	*66	*19	*63
生活環境動植物及び家畜に対する毒性	N/A	*43	*63	*15	*43
環境動態	N/A	*39	*61	*37	*40

*4 分野間及び英・和文間での重複あり
N/A：該当するデータなし

表 4－1－3 すべてのデータベースの検索結果を統合したまとめ（データベース間の重複なし）

分野	論文数			
	WOSCC(†)	J-STAGE		計
		英文 キーワード 検索	和文 キーワード 検索	
対象とする農薬名で検索抽出した総論文数 (全データベースの合計)	1012	46	68	1126
ヒトに対する毒性に関する論文数	*62	*21	*26	*109
農作物及び畜産物への残留に関する論文数	*260	*19	*63	*342
生活環境動植物及び家畜に対する毒性に関する論文数	*156	*15	*43	*214
環境動態に関する論文数	*566	*37	*40	*643

*4 分野間での重複あり
†4 分野に該当しないことが明白な文献等は第 1 段階の評価以前に「上記以外」に分類したため、表 4－2－1 の「該当する論文数」の数値には合致しない。

4.2. 評価目的との適合性評価（第 1 段階、第 2 段階）の結果のまとめ

表 4－2－1 評価目的との適合性評価(第 1 段階、第 2 段階)の結果のまとめ（WOSCC）

分野	該当する論文数(†)	第 1 段階		第 2 段階	
		適合性なし	それ以外(第 2 段階へ)	適合性なし	適合性あり
ヒトに対する毒性	*45	*37	8	1	7
農作物及び畜産物への残留	*226	*213	13	10	3
生活環境動植物及び家畜に対する毒性	*133	*90	44	12	32
環境動態	*534	*397	136	23	113
上記以外	*267	*267	0	0	0
合計	1012	811	201	46	155

*4 分野間での重複あり
†4 分野に該当しないことが明白な文献等は第 1 段階の評価以前に「上記以外」に分類したため、表 4－1－3 の「論文数 WOSCC」の数値には合致しない。

表 4－2－2 評価目的との適合性評価(第 1 段階、第 2 段階)の結果のまとめ
（J-STAGE、英文キーワード検索）

分野	該当する論文数	第 1 段階		第 2 段階	
		適合性なし	それ以外(第 2 段階へ)	適合性なし	適合性あり
ヒトに対する毒性	*21	*21	0	0	0
農作物及び畜産物への残留	*19	*19	0	0	0
生活環境動植物及び家畜に対する毒性	*15	*15	0	0	0
環境動態	*37	*37	0	0	0
上記以外	0	0	0	0	0
合計	46	46	0	0	0

*4 分野間での重複あり

表 4－2－3 評価目的との適合性評価(第 1 段階、第 2 段階)の結果のまとめ
（J-STAGE、和文キーワード検索）

分野	該当する論文数	第 1 段階		第 2 段階	
		適合性なし	それ以外(第 2 段階へ)	適合性なし	適合性あり
ヒトに対する毒性	*26	*26	0	0	0
農作物及び畜産物への残留	*63	*63	0	0	0
生活環境動植物及び家畜に対する毒性	*43	*41	2	2	0
環境動態	*40	*38	2	1	1
上記以外	0	0	0	0	0
合計	68	64	4	3	1

*4 分野間での重複あり

4.3. 適合性評価第 2 段階で適合性ありとされた文献と分類結果

表 4－3－1 適合性評価第 2 段階で適合性ありとされた文献と分類結果（WOSCC）

分野	該当する論文数		
	区分 a	区分 b	区分 c
ヒトに対する毒性	0	2	5
農作物及び畜産物への残留	0	2	1
生活環境動植物及び家畜に対する毒性	2	4	26
環境動態	1	16	96
合計	3	24	128

表 4－3－2 適合性評価第 2 段階で適合性ありとされた文献と分類結果（J-STAGE）

分野	該当する論文数		
	区分 a	区分 b	区分 c
ヒトに対する毒性	0	0	0
農作物及び畜産物への残留	0	0	0
生活環境動植物及び家畜に対する毒性	0	0	0
環境動態	0	0	1
合計	0	0	1

4.4. 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由

表 4－4－1 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(ヒトに対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
179	IIA 5.5.2	Cowie, DE	2019	(S-)Metolachlor - human relevance framework assessment of liver tumour induction in female rats	TOXICOLOGY LETTERS, 314, pp193-193	⑧試験データを含まない短報であり評価不能。

＊：○囲み数字は、3.2 に記載した判断理由の項目番号を示す。

表 4－4－2 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(農作物及び畜産物への残留、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
246	-	Shah, SH	2016	ALLELOPATHIC SORGHUM WATER EXTRACT HELPS TO IMPROVE YIELD OF SUNFLOWER (HELIANTHUS ANNUUS L.)	PAKISTAN JOURNAL OF BOTANY, 48(3), pp1197-1202	①⑬ソルガム水抽出物のアレロパシー作用についての文献。
281	-	Figueroa, R	2016	Effects of Preemergence Herbicides on Bell Pepper, Crop Injury, and Weed Management in Irrigated Chilean Fields	WEED TECHNOLOGY, 30(2), pp587-594 http://dx.doi.org/10.1614/WT-D-15-00124.1	④薬効に関する研究。
288	-	Achdari, G	2022	Bean (Phaseolus vulgaris L.) response and weed control efficacy of pre-plant-incorporated of pendimethalin	PHYTOPARASITICA, 50(3), pp579-587 http://dx.doi.org/10.1007/s12600-021-00974-0	④薬効に関する研究

表 4−4−2 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(農作物及び畜産物への残留、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
293	-	Boyd, NS	2020	Preemergence Herbicides for Purple Nut sedge (Cyperus rotundus L.) Control in Strawberry (Fragaria xananessa Duchesne)	PROCEEDINGS OF THE FLORIDA STATE HORTICULTURAL SOCIETY, 129, pp165-166	④薬効に関する研究
330	-	Soltani, N	2020	Multiple-resistant waterhemp control in herbicide-resistant 3 (HT3) soybean	CANADIAN JOURNAL OF PLANT SCIENCE, 100(6), pp692-696 http://dx.doi.org/10.1139/cjps-2019-0251	④薬効に関する研究
333	-	de Carvalho, DR	2022	Weed control in melon with preemergence herbicides	PESQUISA AGROPECUARIA BRASILEIRA, 57 http://dx.doi.org/10.1590/S1678-3921.pab2022.v57.02334	④薬効に関する研究
344	-	Godwin, J	2018	Selectivity of Very-Long-Chain Fatty Acid-Inhibiting Herbicides in Rice as Influenced by Application Timing and Soil Texture	CROP FORAGE & TURFGRASS MANAGEMENT, 4(1) http://dx.doi.org/10.2134/cftm2018.03.0016	④薬害に関する研究
400	-	Flessner, ML	2020	Evaluating herbicide tolerance of industrial hemp (Cannabis sativa L.)	CROP SCIENCE, 60(1), pp419-427 http://dx.doi.org/10.1002/csc2.20055	④薬効及び薬害に関する研究

表 4−4−2 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(農作物及び畜産物への残留、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
470	-	Richburg, JT	2020	Tolerance of corn to PRE- and POST-applied photosystem II-inhibiting herbicides	WEED TECHNOLOGY, 34 (2), pp277-283 http://dx.doi.org/10.1017/wet.2019.119	④薬効及び薬害に関する研究
539	-	Mobli, A	2020	Effects of sorghum residue in presence of pre-emergence herbicides on emergence and biomass of Echinochloa colona and Chloris virgata	PLOS ONE, 15(3) http://dx.doi.org/10.1371/journal.pone.0229817	④薬効に関する研究

＊：〇囲み数字は、3.2 に記載した判断理由の項目番号を示す。

表 4−4−3 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
22	-	Mermana, J	2017	Photocatalysis of S-metolachlor in aqueous suspension of magnetic cerium-doped mTiO(2) core-shell under simulated solar light	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 24(4), pp4077-4092 http://dx.doi.org/10.1007/s11356-016-8151-6	⑬酸化チタンを用いた農薬除去法の開発
49	IIA 8.4	Liu, HJ	2017	Enantioselective oxidative stress and oxidative damage caused by Rac- and S-metolachlor to *Scenedesmus obliquus*	CHEMOSPHERE, 173(0), pp22-30 http://dx.doi.org/10.1016/j.chemosphere.2017.01.028	⑯b 適切に評価できる試験種ではないイカダモ（*Scenedesmus obliquus*）に対するメトラクロール異性体間の影響比較

表 4－4－3 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
322	-	Liu, C	2019	From rice straw to magnetically recoverable nitrogen doped biochar: Efficient activation of peroxymonosulfate for the degradation of metolachlor	APPLIED CATALYSIS B-ENVIRONMENTAL, 254, pp312-320 http://dx.doi.org/10.1016/j.apcatb.2019.05.014	⑬水系からの農薬除去法開発に関する研究
332	-	Liu, L	2021	Strong adsorption of metolachlor by biochar prepared from walnut shells in water	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 28(35), pp48379-48391 http://dx.doi.org/10.1007/s11356-021-14117-9	⑬バイオチャーによるメトラクロールの除去法開発に関する研究
363	IIA 8.1	Agostinetto, D	2020	Selectivity of pre-emergent herbicides in bird's-foot trefoil crops	REVISTA BRASILEIRA DE CIENCIAS AGRARIAS-AGRARIA, 15(3) http://dx.doi.org/10.5039/agraria.v15i3a8383	④薬効薬害に関する研究。
411	IIA 6.6.3 IIA 7	Wallace, JM	2017	Tolerance of Interseeded Annual Ryegrass and Red Clover Cover Crops to Residual Herbicides in Mid-Atlantic Corn Cropping Systems	WEED TECHNOLOGY, 31(5), pp641-650 http://dx.doi.org/10.1017/wet.2017.48	④薬効薬害に関する研究。
532	IIA 8.2	Liu, SH	2021	Developmental toxicity and transcriptome analysis of zebrafish (Danio rerio) embryos following exposure to chiral herbicide safener benoxacor	SCIENCE OF THE TOTAL ENVIRONMENT, 761 http://dx.doi.org/10.1016/j.scitotenv.2020.143273	①メトラクロールのセーフナーのゼブラフィッシュ毒性

表 4－4－3 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
555	IIA 7.8 IIA 8.6	Zheng, YC	2022	Stereoselective degradation pathway of amide chiral herbicides and its impacts on plant and bacterial communities in integrated vertical flow constructed wetlands	BIORESOURCE TECHNOLOGY, 351 http://dx.doi.org/10.1016/j.biortech.2022.126997	⑪⑬統合垂直流湿地（IVCW）を用いた広範囲の農薬の除去法開発研究。
556	-	Wagner, T	2022	The statistical power to detect regional temporal trends in riverine contaminants in the Chesapeake Bay Watershed, USA	SCIENCE OF THE TOTAL ENVIRONMENT, 812 http://dx.doi.org/10.1016/j.scitotenv.2021.152435	⑪⑬海域における農薬分布の解析法の開発
557	-	Gil, FN	2018	Comparative analysis of transcriptomic responses to sub-lethal levels of six environmentally relevant pesticides in Saccharomyces cerevisiae	ECOTOXICOLOGY, 27(7), pp871-889 http://dx.doi.org/10.1007/s10646-018-1929-1	⑪⑬農薬が酵母の転写プロファイルに及ぼす影響
677	IIA 8.3	Barbieri, MV	2019	Analysis of 52 pesticides in fresh fish muscle by QuEChERS extraction followed by LC-MS/MS determination	SCIENCE OF THE TOTAL ENVIRONMENT, 653, pp958-967 http://dx.doi.org/10.1016/j.scitotenv.2018.10.289	⑪⑬QUEChERS 法を用いた淡水魚体内の農薬の一斉分析法開発
833	IIA 8.2	Main, AR	2020	Beyond neonicotinoids - Wild pollinators are exposed to a range of pesticides while foraging in agroecosystems	SCIENCE OF THE TOTAL ENVIRONMENT, 742 http://dx.doi.org/10.1016/j.scitotenv.2020.140436	⑪野生ミツバチ体内の農薬残留調査。一般的な農薬の暴露に関する論文。

＊：○囲み数字は、3.2 に記載した判断理由の項目番号を示す。

表 4−4−4 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
36	IIA 7	Vieira, BC	2022	Spray drift potential of dicamba plus S-metolachlor formulations	PEST MANAGEMENT SCIENCE ,78(4), pp1538-1546 http://dx.doi.org/10.1002/ps.6772	④混合製剤の薬効研究（新規散布法の開発）。
39	IIA 7.4	Pena, D	2019	Effects of olive mill wastes with different degrees of maturity on behaviour of S-metolachlor in three soils	GEODERMA, 348, pp86-96 http://dx.doi.org/10.1016/j.geoderma.2019.04.022	⑬オリーブの加工廃棄物を用いる S-メトラクロール除去法の開発に関する研究。
63	-	Chuah, TS	2021	COMBINATION RATIO AFFECTS SYNERGISTIC ACTIVITY OF OIL PALM FROND RESIDUE AND S-METOLACHLOR ON GOOSEGRASS (ELEUSINE INDICA)	PAKISTAN JOURNAL OF BOTANY, 53(4), pp1473-1478 http://dx.doi.org/10.30848/PJB2021-4(37)	④薬効に関する研究
144	-	Gluhar, S	2019	Dissipation of mecoprop-P, isoproturon, bentazon and S-metolachlor in heavy metal contaminated acidic and calcareous soil before and after EDTA-based remediation	CHEMOSPHERE, 237 http://dx.doi.org/10.1016/j.chemosphere.2019.124513	⑬汚染土壌の EDTA 処理による除去技術に関する研究
186	IIA 7.1	Li, XJ	2020	The metolachlor degradation kinetics and bacterial community evolution in the soil bioelectrochemical remediation	CHEMOSPHERE, 248 http://dx.doi.org/10.1016/j.chemosphere.2020.125915	⑬生物電気化学的修復システムによる農薬除去法の開発に関する研究。

表 4−4−4 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
238	-	Liu, C	2019	Sulfate radical induced catalytic degradation of metolachlor: Efficiency and mechanism	CHEMICAL ENGINEERING JOURNAL, 368, pp606-617 http://dx.doi.org/10.1016/j.cej.2019.03.001	⑬水系からのメトラクロール除去法の開発
312	IIA 7.4	Liu, L	2022	Metolachlor adsorption using walnut shell biochar modified by soil minerals	ENVIRONMENTAL POLLUTION, 308 http://dx.doi.org/10.1016/j.envpol.2022.119610	⑬クルミの殻のバイオ炭を用いた農薬除去法の開発に関する研究。
315	IIA 7.7	Nykiel-Szymanska, J	2020	Biotransformation and detoxification of chloroacetanilide herbicides by Trichoderma spp. with plant growth-promoting activities	PESTICIDE BIOCHEMISTRY AND PHYSIOLOGY, 163, pp216-226 http://dx.doi.org/10.1016/j.pestbp.2019.11.018	⑬真菌 Trichoderma による農薬分解法の開発に関する研究。
340	-	Wettstein, FE	2016	Leaching of the Neonicotinoids Thiamethoxam and Imidacloprid from Sugar Beet Seed Dressings to Subsurface Tile Drains	JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY, 64(33), pp6407-6415 http://dx.doi.org/10.1021/acs.jafc.6b02619	①メトラクロールを対象としていない研究
388	-	Wei, L	2020	The ratio of H/C is a useful parameter to predict adsorption of the herbicide metolachlor to biochars	ENVIRONMENTAL RESEARCH, 184 http://dx.doi.org/10.1016/j.envres.2020.109324	⑬バイオチャーを用いたメトラクロール除去法開発に関する研究

表 4−4−4 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
408	-	Guan, SH	2018	Determination of Atrazine, Simazine, Alachlor, and Metolachlor in Surface Water Using Dispersive Pipette Extraction and Gas Chromatography-Mass Spectrometry	ANALYTICAL LETTERS, 51 (4), pp613-625 http://dx.doi.org/10.1080/00032719.2017.1341904	⑬水系における農薬分布の測定法に関する研究
461	IIA 7.4	Su, L	2019	Safener benoxacor induces herbicide metolachlor photolysis on simulated soil surface	ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, 257	⑧学会報告の要旨
467	IIA 7.8	Anderson, JC	2021	Prioritization of Pesticides for Assessment of Risk to Aquatic Ecosystems in Canada and Identification of Knowledge Gaps	REVIEWS OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY, 259, pp171-231 https://doi.org/10.1007/398_2021_81	⑧新たな情報や試験データを含まない総説
518	-	Stowik-Borowiec, M	2015	Gas chromatographic determination of pesticide residues in white mustard	FOOD CHEMISTRY, 173, pp997-1005 http://dx.doi.org/10.1016/j.foodchem.2014.06.125	⑪⑬作物中の残留農薬の分析法開発
534	-	Mendes, KF	2020	Role of raw feedstock and biochar amendments on sorption-desorption and leaching potential of three H-3- and C-14-labelled pesticides in soils	JOURNAL OF RADIOANALYTICAL AND NUCLEAR CHEMISTRY, 324(3), pp1373-1386 http://dx.doi.org/10.1007/s10967-020-07128-2	⑬土壌中からのメトラクロール除去法の開発

表 4−4−4 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
537	-	Jennings, AA	2017	Worldwide Regulatory Guidance Values Applied to Direct Contact Surface Soil Pesticide Contamination: Part II-Noncarcinogenic Pesticides	AIR SOIL AND WATER RESEARCH, 10, pp1-14 http://dx.doi.org/10.1177/1178622117711931	②法規制に関する総説
552	-	Owens, PN	2021	The bioremediation of metolachlor in soil using Rhodospirillum rubrum after wastewater treatment. (Retraction of Vol 19, Pg 3534, 2019)	JOURNAL OF SOILS AND SEDIMENTS, 21(1), pp663-663 https://doi.org/10.1007/s11368-019-02279-6	⑬土壌中のメトラクロールの生分解による除去方法の開発
624	IIA 7.8	Piffady, J	2021	ARPEGES: A Bayesian Belief Network to Assess the Risk of Pesticide Contamination for the River Network of France	INTEGRATED ENVIRONMENTAL ASSESSMENT AND MANAGEMENT, 17(1), pp188-201 http://dx.doi.org/10.1002/ieam.4343	⑪⑬水域における農薬動態に関する、ベイジアンネットワークを用いた新しい解析手法の開発研究。
676	-	Li, HH	2018	Analytical Confirmation of Various Herbicides in Drinking Water Resources in Sugarcane Production Regions of Guangxi, China	BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY, 100(6), pp815-820 http://dx.doi.org/10.1007/s00128-018-2324-6	⑪上水道中の農薬分布調査

表 4－4－4 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由*
724	IIA 7.8	Antic, N	2015	Pesticide Residues in the Danube River Basin in Serbia - a Survey during 2009-2011	CLEAN-SOIL AIR WATER, 43(2), pp197-204 http://dx.doi.org/10.1002/clen.201200360	⑪セルビアの河川における 38 種類の農薬の分布に関する調査。
862	IIA 7.6	Sarti, O	2021	Integrated assessment of groundwater quality beneath the rural area of R'mel, Northwest of Morocco	GROUNDWATER FOR SUSTAINABLE DEVELOPMENT, 14 http://dx.doi.org/10.1016/j.gsd.2021.100620	⑪海外農業地帯における地下水中の化学物質分布調査。
877	-	Fernandez-Pascual, E	2020	Hydrological tracers for assessing transport and dissipation processes of pesticides in a model constructed wetland system	HYDROLOGY AND EARTH SYSTEM SCIENCES, 24(1), pp41-60 http://dx.doi.org/10.5194/hess-24-41-2020	①他剤に関する土壌中の分布の分析法開発
890	IIA 7.8	Palma, P	2018	Ecological and ecotoxicological responses in the assessment of the ecological status of freshwater systems: A case-study of the temporary stream Brejo of Cagarrao (South of Portugal)	SCIENCE OF THE TOTAL ENVIRONMENT, 634, pp394-406 http://dx.doi.org/10.1016/j.scitotenv.2018.03.281	⑪25 種類の農薬に関する環境モニタリング研究

＊：○囲み数字は、3.2 に記載した判断理由の項目番号を示す。

表 4−4−5 適合性評価の第 2 段階で「適合しない」と判断した論文とその理由(J-STAGE)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
J08	-	原田 孝則	2010	Invited Lectures: Session 3 Environmental Science	Journal of Pesticide Science 2010 年 35 巻 2 号 189-190 https://doi.org/10.1584/jpestics.35.189	⑧学会発表の要旨
J66	-		2010	第 1 回日中韓農薬科学ワークショップ全プログラム	Journal of Pesticide Science 2010 年 35 巻 2 号 200-205 https://doi.org/10.1584/jpestics.35.200	⑧学会ワークショップ記録誌の目次ページ
J84	-	栗山 光博, 片山 新太, 田村 廣人, 井藤 和人, 上原 正浩, 渡邊 裕純	2011	第 12 回 IUPAC 農業化学国際会議	Journal of Pesticide Science 2011 年 36 巻 1 号 172-187 https://doi.org/10.1584/jpestics.W10-66	⑧学会発表の要旨

＊：〇囲み数字は、3.2 に記載した判断理由の項目番号を示す。

4.5. 適合性評価の第2段階で「区分b」と判断した論文とその理由

表 4－5－1 適合性評価の第2段階で「区分b」と判断した論文とその理由(ヒトに対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
744	IIA 5.4.2	Moshou, H	2020	Assessment of genetic effects and pesticide exposure of farmers in NW Greece	ENVIRONMENTAL RESEARCH, 186 http://dx.doi.org/10.1016/j.envres.2020.109558	複数の農薬の使用歴がある農業従事者の血液サンプルを用いた遺伝毒性/細胞毒性研究。 農薬暴露と細胞内の小核の量との相関が示されているが、S-メトラクロール単体の毒性に関するデータを含まない。
804	IIA 5.6	Houtman, CJ	2021	Characterisation of (anti-)progestogenic and (anti-)androgenic activities in surface and wastewater using high resolution effectdirected analysis	ENVIRONMENT INTERNATIONAL, 153 http://dx.doi.org/10.1016/j.envint.2021.106536	水道施設取水域の表層水及び下水処理場の流入水と流出水が黄体ホルモン及び卵胞ホルモンに与える影響に関する研究。 これらのホルモンへのメトロラクロール単体の影響が示されているが、農薬の評価に活用可能なエンドポイントの記載はない。

表 4－5－2 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(農作物及び畜産物への残留、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
387	IIA 6.3	Suk, J	2021	Dynamics of herbicides degradation in carrot (Daucus carota L.) roots and leaves	PLANT SOIL AND ENVIRONMENT, 67(6), pp353-359 http://dx.doi.org/10.17221/46/2021-PSE	ニンジンを用いた複数農薬の残留分析試験。 日本の残留農薬基準値を大きく下回っているが、補足データとして利用が可能と判断した。
488	IIA 6.3	Suk, J	2018	Dynamics of herbicide degradation in cauliflower	PLANT SOIL AND ENVIRONMENT, 64(11), pp551-556 http://dx.doi.org/10.17221/312/2018-PSE	カリフラワーを用いた複数農薬の残留分析試験。 すべての検体で S-メトラクロールは検出されなかったが、補足データとして利用が可能と判断した。

表 4－5－3 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
41	IIA 8.4	Maronic, DS	2018	S-metolachlor promotes oxidative stress in greenmicroalga Parachlorella kessleri - A potential environmental and health risk for higher organisms	SCIENCE OF THE TOTAL ENVIRONMENT, 637, pp41-49 http://dx.doi.org/10.1016/j.scitotenv.2018.04.433	クロレラ（適切に評価できる試験種ではない）に対する毒性研究。 EC_{50} 値の 1/10～1/20 程度の低濃度の S-メトラクロールが被験生物の各種活性に与える影響が示されているが、農薬の評価に直接活用可能なエンドポイントは得られていない。 補足データとして利用が可能と判断した。

表 4－5－3 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
42	IIA 8.2	Quintaneiro, C	2017	Endocrine and physiological effects of linuron and S-metolachlor in zebrafish developing embryos	SCIENCE OF THE TOTAL ENVIRONMENT, 586, pp390-400 http://dx.doi.org/10.1016/j.scitotenv.2016.11.153 《海外評価書引用：USEPA Comment submitted by Olga Naidenko, Vice President, Science Investigations, Environmental Working Group (EWG), p3, EPA-HQ-OPP-2014-0772-0033》	ゼブラフィッシュの胚に対する発生毒性研究。 主として毒性の作用機構に関する定性的研究だが、成魚に対する既知の LC_{50} 値よりも低い LC_{50} 値が示されており、補足データとして利用が可能と判断した。
198	IIA 8.4	Machado, MD	2020	Reproductive cycle progression arrest and modification of cell morphology (shape and biovolume) in the alga Pseudokirchneriella subcapitata exposed to metolachlor	AQUATIC TOXICOLOGY, 222 http://dx.doi.org/10.1016/j.aquatox.2020.105449	ムレミカヅキモに対する S-メトラクロールの作用機序に関する研究。 代謝活性、クロロフィル含有量、光合成活性等への影響が示されている。 農薬の評価に直接活用可能なエンドポイントは示されていないが、補足データとして利用が可能と判断した。

表 4－5－3 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
268	IIA 8.4	Machado, MD	2021	Exposure of the alga Pseudokirchneriella subcapitata to environmentally relevant concentrations of the herbicide metolachlor: Impact on the redox homeostasis	ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY, 207 http://dx.doi.org/10.1016/j.ecoenv.2020.111264	ムレミカヅキモの酸化還元ホメオスタシスに対するメトラクロールの影響を調査。 既知の NOEC や EC 値を元に被験物質の濃度を設定しており、新たなエンドポイントは得られていないが、補足データとして利用が可能と判断した。

表 4－5－4 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
66	IIA 7.4	Sidoli, P	2020	Reactivity of vadose-zone solids to S-metolachlor and its two main metabolites: case of a glaciofluvial aquifer	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 27(18), pp22865-22877 http://dx.doi.org/10.1007/s11356-020-08579-6	S-メトラクロール及び 2 種類の代謝物の土壌中における吸着動態を調査。 日本における評価に直接活用できる試験条件ではないが、吸着係数の記載があり、補足データとして利用が可能と判断した。
68	IIA 7.3.2	Schuhmann, A	2019	Degradation and leaching of bentazone, terbuthylazine and S-metolachlor and some of their metabolites: A long-term lysimeter experiment	PLANT SOIL AND ENVIRONMENT, 65(5), pp273-281 http://dx.doi.org/10.17221/803/2018-PSE	ライシメーターを用いた S-メトラクロール及びその代謝物の 3 年間の残存モニタリング調査。 日本における評価に直接活用できる試験条件ではないが、補足データとして利用が可能と判断した。

表 4−5−4 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
78	IIA 7.3.2	Canero, AI	2015	Different Effects of a By-product From Olive Oil Extraction on S-Metolachlor and Bentazone Soil Fate	CLEAN-SOIL AIR WATER, 43(6), pp948-957 http://dx.doi.org/10.1002/clen.201400233	有機廃棄物を添加した土壌における S-メトラクロールの動態に関する文献。日本における評価に直接活用できる試験条件ではないが、土壌吸着係数、滲出率、半減期等が算出されており、補足データとして利用が可能と判断した。
128	IIA 7.3.2	Wu, XM	2015	Degradation of Metolachlor in Tobacco Field Soil	SOIL & SEDIMENT CONTAMINATION, 24(4), pp398-410 http://dx.doi.org/10.1080/15320383.2015.968765	中国のたばこ圃場における S-メトラクロールの土壌動態調査。日本における評価に直接活用できる試験条件ではないが、分解速度定数、半減期等が算出されており、補足データとして利用が可能と判断した。
170	IIA 7.3.2	Jaikaew, P	2015	Potential impacts of seasonal variation on atrazine and metolachlor persistence in andisol soil	ENVIRONMENTAL MONITORING AND ASSESSMENT, 187(12) http://dx.doi.org/10.1007/s10661-015-4986-4 《海外評価書引用：EFSA（2018）Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	日本の圃場におけるメトラクロールの土壌中動態モニタリング研究。夏期と冬期で半減期が大きく異なることが示されており、補足データとして利用が可能と判断した。

表 4－5－4 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
484	IIA 7.4.6	Lammoglia, SK	2018	Modelling pesticides leaching in cropping systems: Effect of uncertainties in climate, agricultural practices, soil and pesticide properties	ENVIRONMENTAL MODELLING & SOFTWARE, 109, pp342-352 http://dx.doi.org/10.1016/j.envsoft.2018.08.007	海外のトウモロコシ圃場における S-メトラクロールの土壌中動態モニタリング研究。日本における評価に直接活用できる試験条件ではないが、土壌吸着係数、半減期等が算出されており、補足データとして利用が可能と判断した。
498	IIA 7.1	Elsayed, OF	2015	Degradation of chloroacetanilide herbicides and bacterial community composition in lab-scale wetlands	SCIENCE OF THE TOTAL ENVIRONMENT, 520, pp222-231 http://dx.doi.org/10.1016/j.scitotenv.2015.03.061	垂直アップフローカラムを用いた土壌中動態研究。日本における評価に直接活用できる試験条件ではないが、メトラクロール異性体間の生分解活性の差異が示されており、補足データとして利用が可能と判断した。
691	IIA 7.1.2	Liu, JW	2022	Anaerobic biodegradation and detoxification of chloroacetamide herbicides by a novel Proteiniclasticum sediminis BAD-10(T)	ENVIRONMENTAL RESEARCH, 209 http://dx.doi.org/10.1016/j.envres.2022.112859	嫌気性細菌による 6 種類の農薬の生分解動態研究。アセトクロールを主たる試験対象とした研究でありメトラクロールに関する記述は少ないが、嫌気条件下での各農薬の吸着係数が示されており、補足データとして利用が可能と判断した。

表 4－5－4 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
761	IIA 7.3.2	Kosubova, P	2020	Spatial and temporal distribution of the currently-used and recently-banned pesticides in arable soils of the Czech Republic	CHEMOSPHERE, 254 http://dx.doi.org/10.1016/j.chemosphere.2020.126902	海外における土壌中の農薬分布モニタリング調査。 広範囲の農薬を対象とした研究だが、S-メトラクロールを含む使用停止後の農薬についても調べられており、補足データとして利用が可能と判断した。
809	IIA 7.6	Mottes, C	2017	Relationships between past and present pesticide applications and pollution at a watershed outlet: The case of a horticultural catchment in Martinique, French West Indies	CHEMOSPHERE, 184, pp762-773 http://dx.doi.org/10.1016/j.chemosphere.2017.06.061	熱帯農業地帯の表層水中の農薬分布モニタリング調査。 広範囲の農薬を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、メトラクロールの吸着係数や半減期等が記載されており、補足データとして利用が可能と判断した。
838	IIA 7.6	Loken, LC	2023	Prioritizing Pesticides of Potential Concern and Identifying Potential Mixture Effects in Great Lakes Tributaries Using Passive Samplers	ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY, 42(2), pp340-366 http://dx.doi.org/10.1002/etc.5491	海外の農業地帯における農薬及びその代謝物の分布調査。 広範囲の化学物質を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、毒性データベースとの照合により環境への影響度を数値化しており、補足データとして利用が可能と判断した。

表 4－5－4 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
843	IIA 7.6	Picard, JC	2021	Longitudinal and vertical variations of waterborne emerging contaminants in the St. Lawrence Estuary and Gulf during winter conditions	SCIENCE OF THE TOTAL ENVIRONMENT, 777 http://dx.doi.org/10.1016/j.scitotenv.2021.146073	海外の河口域における化学物質分布モニタリング調査。 広範囲の化学物質を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、汽水域/海域における S-メトラクロールとその代謝物の垂直分布が示されており、補足データとして利用が可能と判断した。
845	IIA 7.8	Toth, G	2022	Spatiotemporal analysis of multi-pesticide residues in the largest Central European shallow lake, Lake Balaton, and its sub-catchment area	ENVIRONMENTAL SCIENCES EUROPE, 34(1) http://dx.doi.org/10.1186/s12302-022-00630-2	海外の浅水湖における農薬及びその代謝物の分布調査。 広範囲の農薬を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、メトラクロールのリスク比が示されており、補足データとして利用が可能と判断した。

表 4－5－4 適合性評価の第 2 段階で「区分 b」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
846	IIA 7.6	Sanford, M	2020	High-Frequency Sampling of Small Streams in the Agroecosystems of Southwestern Ontario, Canada, to Characterize Pesticide Exposure and Associated Risk to Aquatic Life	ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY, 39(12), pp2570-2587 http://dx.doi.org/10.1002/etc.4884	海外の農業地帯の水域における農薬の分布調査。広範囲の農薬を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、メトラクロールのハザード比が示されており、補足データとして利用が可能と判断した。
850	IIA 7.10	Zaller, JG	2022	Pesticides in ambient air, influenced by surrounding land use and weather, pose a potential threat to biodiversity and humans	SCIENCE OF THE TOTAL ENVIRONMENT, 838 http://dx.doi.org/10.1016/j.scitotenv.2022.156012	オーストリアにおける大気中の農薬分布調査。広範囲の化学物質を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、揮発性のあるメトラクロールの大気中濃度データが示されており、補足データとして利用が可能と判断した。
857	IIA 7.6	Baldwin, AK	2016	Organic contaminants in Great Lakes tributaries: Prevalence and potential aquatic toxicity	SCIENCE OF THE TOTAL ENVIRONMENT, 554, pp42-52 http://dx.doi.org/10.1016/j.scitotenv.2016.02.137	海外の広範な地域における表層水中の農薬分布モニタリング調査。広範囲の化学物質を対象とした研究であり、また日本における評価に直接活用できる試験条件ではないが、農薬分布の季節的変動に加え、農業地域と都市部の比較が行われており、補足データとして利用が可能と判断した。

4.6. 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由

表 4−6−1 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(ヒトに対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
185	IIA 5.5	Silver, SR	2015	Cancer incidence and metolachlor use in the Agricultural Health Study: An update	INTERNATIONAL JOURNAL OF CANCER, 137(11), pp2630-2643 http://dx.doi.org/10.1002/ijc.29621 《海外評価書引用：EFSA（2018）Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》 《海外評価書引用：USEPA（2019）Metolachlor and S-Metolachlor: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment p6 EPA-HQ-OPP-2014-0772-0032》	米国の農業従事者に対する肝がんとメトラクロールの関連性に関する疫学調査。 統計的に有意な結果が得られておらず、農薬評価に活用できるデータを含まない。

表 4－6－1 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(ヒトに対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
454	IIA 5.6	Rappazzo, KM	2019	Maternal residential exposure to specific agricultural pesticide active ingredients and birth defects in a 2003-2005 North Carolina birth cohort	BIRTH DEFECTS RESEARCH, 111(6), pp312-323 http://dx.doi.org/10.1002/bdr2.1448	7 種類の農薬と 10 種類の先天性異常との関連性に関する疫学調査。 暴露の定義（妊娠期間中の居住地から 500m 以内での農薬散布の平均的回数）が厳密性に乏しく、またオッズ比の具体的な数値が示されていない。
716	IIA 5	Shrestha, S	2019	Pesticide use and incident hyperthyroidism in farmers in the Agricultural Health Study	OCCUPATIONAL AND ENVIRONMENTAL MEDICINE, 76(5), pp332-335 http://dx.doi.org/10.1136/oemed-2018-105518 《海外評価書引用：USEPA（2019）Metolachlor and S-Metolachlor: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment p54 EPA-HQ-OPP-2014-0772-0032》	米国の農業従事者に対する甲状腺機能亢進症と農薬の関連性に関する疫学調査。 「メトラクロール等の農薬の使用が甲状腺機能亢進症の発症リスクを低減させる」との結果が示されており、考察内で著者自身が調査結果の信頼性への疑義を述べている。 "Nevertheless, several limitations necessitate careful interpretation of the findings.”

表 4－6－1 適合性評価の第２段階で「区分 c」と判断した論文とその理由(ヒトに対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
811	IIA 5.5	Lebov, JF	2016	Pesticide use and risk of end-stage renal disease among licensed pesticide applicators in the Agricultural Health Study	OCCUPATIONAL AND ENVIRONMENTAL MEDICINE, 73(1), pp3-12 http://dx.doi.org/10.1136/oemed-2014-102615 《海外評価書引用：EFSA（2018）Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》 《海外評価書引用：USEPA（2019）Metolachlor and S-Metolachlor: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment p39 EPA-HQ-OPP-2014-0772-0032》	海外の特定の地域における、39 種類の農薬と腎不全の関連に関する疫学調査。 日本における評価に直接活用できる試験条件ではない。
892	IIA 5.5	Schwingl, PJ	2021	A tiered approach to prioritizing registered pesticides for potential cancer hazard evaluations: implications for decision making	ENVIRONMENTAL HEALTH, 20(1) http://dx.doi.org/10.1186/s12940-021-00696-0	広範囲の農薬の発がん性への関与に関する文献研究。 新たな試験データを含まない。

表 4−6−2 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(農作物及び畜産物への残留、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
672	IIA 6.3 IIA 7.3.2	Cui, Y	2022	Organochlorine pesticides and other pesticides in peanut oil: Residue level, source, household processing factor and risk assessment	JOURNAL OF HAZARDOUS MATERIALS, 429 http://dx.doi.org/10.1016/j.jhazmat.2022.128272	落花生及び土壌中の農薬残留濃度に関するフィールド調査。 農薬散布量や頻度に関する具体的なデータが示されていない。

表 4−6−3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
53	IIA 8.2	Liu, SH	2022	Combined effects of S-metolachlor and benoxacor on embryo development in zebrafish (Danio rerio)	ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY, 238 http://dx.doi.org/10.1016/j.ecoenv.2022.113565	S-メトラクロールのセーフナーであるベノキサコールの、魚の胚発達毒性研究。 S-メトラクロール単体に関する研究ではない。
76	IIA 8.2	Quintaneiro, C	2018	Effects of the herbicides linuron and S-metolachlor on Perez's frog embryos	CHEMOSPHERE, 194, pp595-601 http://dx.doi.org/10.1016/j.chemosphere.2017.11.171	カエルに対する発生毒性研究。 EC_{50}、LC_{50}、NOEC、LOEC が示されているが、適切に評価できる試験種ではない。
80	IIA 8.2	Stara, A	2019	Effects of S-metolachlor and its degradation product metolachlor OA on marbled crayfish (Procambarus virginalis)	CHEMOSPHERE, 224, pp616-625 http://dx.doi.org/10.1016/j.chemosphere.2019.02.187	ザリガニに対する S-メトラクロール及びその代謝物の影響に関する研究。 鰓及び肝膵等への影響が報告されているが、適切に評価できる試験種ではない。

表 4−6−3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
90	IIA 8.2	Yang, LH	2021	The agrochemical S-metolachlor disrupts molecularediators and morphology of the swim bladder: Implications for locomotor activity in zebrafish (Danio rerio)	ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY, 208 http://dx.doi.org/10.1016/j.ecoenv.2020.111641	S-メトラクロールがゼブラフィッシュ胚の浮袋形成に与える影響に関する文献。 EC_{50} や NOAEC 等の主要エンドポイントが示されておらず、農薬評価に直接活用できない。
200	IIA 7.8 IIA 8.2	Mettler, CA	2021	Effects of the Herbicide Metolachlor and Fish Presence on Pond Mesocosm Communities	AMERICAN MIDLAND NATURALIST, 186(2), pp199-214 http://dx.doi.org/10.1674/0003-0031-186.2.199	メトラクロールが池の生態に与える影響を調査。 主に両生類や腹足類の個体数の増減や行動変化をエンドポイントとして採用しており、農薬評価に直接活用できない。
210	IIA 8.2	Gamain, P	2017	Do Temporal and Spatial Parameters or Lifestyle of the Pacific Oyster Crasssostrea gigas Affect Pollutant Bioaccumulation, Offspring Development, and Tolerance to Pollutants?	FRONTIERS IN MARINE SCIENCE, 4 http://dx.doi.org/10.3389/fmars.2017.00058	フランスにおける牡蠣に対する環境毒性研究。 日本における評価に直接活用できる試験種/条件ではない。
232	IIA 7.1	Imfeld, G	2018	Toward Integrative Bacterial Monitoring of Metolachlor Toxicity in Groundwater	FRONTIERS IN MICROBIOLOGY, 9 http://dx.doi.org/10.3389/fmicb.2018.02053	フランス南西部の帯水層のバクテリアに対するメトラクロールの影響調査。 日本における評価に直接活用できる試験種/環境ではない。

表 4−6−3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
362	IIA 8.2	Coquille, N	2018	The influence of natural dissolved organic matter on herbicide toxicity to marine microalgae is species-dependent	AQUATIC TOXICOLOGY, 198, pp103-117 http://dx.doi.org/10.1016/j.aquatox.2018.02.019	海洋性微細藻類に対する毒性研究。日本における評価に直接活用できる試験種/環境ではない。
397	IIA 8.2	Korkaric, M	2015	Multiple stressor effects in Chlamydomonas reinhardtii - Toward understanding mechanisms of interaction between effects of ultraviolet radiation and chemical pollutants	AQUATIC TOXICOLOGY, 162, pp18-28 http://dx.doi.org/10.1016/j.aquatox.2015.03.001	紫外線が緑藻(クラミドモナス）に対する農薬の毒性に与える影響について調査。日本における評価に直接活用できる試験種/環境ではない。
407	IIA 8.3 IIA 8.4	Sanford, M	2021	Pulsed exposure of the macrophyte Lemna minor to herbicides and the mayfly Neocloeon triangulifer to diamide insecticides	CHEMOSPHERE, 273 http://dx.doi.org/10.1016/j.chemosphere.2020.128582	コウキクサに対する環境毒性調査。実際の農地での農薬適用状況に近い条件で各種パラメーターを得ているが、特殊な暴露条件（24/48 時間の暴露を 5 日の間隔を空けて 2 回実施）での調査であり、評価に直接活用できない。
446	IIA 8	Schmidt-Jeffris, RA	2019	Non-target effects of herbicides on Tetranychus urticae and its predator, Phytoseiulus persimilis: implications for biological control	PEST MANAGEMENT SCIENCE, 75(12), pp3226-3234 http://dx.doi.org/10.1002/ps.5443	2 種のダニに対する環境毒性研究。日本における評価に直接活用できる試験種/環境ではない。

表 4−6−3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
479	IIA 8.10	Han, LX	2022	Indigenous functional microbial communities for the preferential degradation of chloroacetamide herbicide S-enantiomers in soil	JOURNAL OF HAZARDOUS MATERIALS, 423 http://dx.doi.org/10.1016/j.jhazmat.2021.127135	農薬の鏡像異性体間の生分解活性の比較と、生分解に関与する主たる細菌の特定、及び関与遺伝子の同定が行われている。 農薬評価に直接活用できる定量的データを含まない。
515	IIA 8	Olaya-Arenas, P	2020	Larval pesticide exposure impacts monarch butterfly performance	SCIENTIFIC REPORTS, 10 (1) http://dx.doi.org/10.1038/s41598-020-71211-7	蝶類に対する環境毒性研究。 日本における評価に直接活用できる試験種/環境ではない。
522	IIA 7.6 IIA 8.2	Roulova, N	2022	Removal of Chloroacetanilide Herbicides from Water Using Heterogeneous Photocatalysis with TiO2/UV-A	CATALYSTS, 12(6) http://dx.doi.org/10.3390/catal12060597	酸化チタンと紫外線を用いた農薬除去法の開発、及び分解物の藻類に対する毒性研究。 農薬評価に直接活用できるデータを含まない。
544	IIA 8.2	Gandar, A	2016	Multistress effects on goldfish (Carassius auratus) behavior and metabolism	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 23(4), pp3184-3194 http://dx.doi.org/10.1007/s11356-015-5147-6	混合製剤の魚に対する毒性の研究。 S-メトラクロールの評価に直接活用できるデータを含まない。

表 4－6－3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
551	IIA 8.2	Elias, D	2017	Effects of Individual and Combined Pesticide Commercial Formulations Exposure to Egestion and Movement of Common Freshwater Snails, Physa acuta and Helisoma anceps	AMERICAN MIDLAND NATURALIST, 178(1), pp97-111 http://dx.doi.org/10.1674/0003-0031-178.1.97	腹足類に対する毒性研究。 日本における評価に直接活用できる試験種/環境ではない。
554	IIA 8.2	Alacantara, F	2019	Variable Background Flow on Aquatic Toxicant Exposure Alters Foraging Patterns on Crayfish	BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY, 103(5), pp663-669 http://dx.doi.org/10.1007/s00128-019-02707-w	ザリガニの摂餌行動に及ぼす影響に関する研究。 日本における評価に直接活用できる試験種/環境ではない。
562	IIA 8.2	Jacquin, L	2019	High temperature aggravates the effects of pesticides in goldfish	ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY, 172, pp255-264 http://dx.doi.org/10.1016/j.ecoenv.2019.01.085	金魚に対する複数農薬の混合製剤の毒性研究。 S-メトラクロールの評価に直接活用できるデータを含まない。
583	IIA 8.2	Gandar, A	2017	Adaptive response under multiple stress exposure in fish: From the molecular to individual level	CHEMOSPHERE, 188, pp60-72 http://dx.doi.org/10.1016/j.chemosphere.2017.08.089	環境ストレスと農薬混合物との組み合わせが魚に及ぼす影響を調査。 S-メトラクロール単体の毒性データを含まない。

表 4－6－3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
595	IIA 8.2	Finizio, A	2022	Use of large datasets of measured environmental concentrations for the ecological risk assessment of chemical mixtures in Italian streams: A case study	SCIENCE OF THE TOTAL ENVIRONMENT, 806 http://dx.doi.org/10.1016/j.scitotenv.2021.150614	水系中の様々な物質総体の毒性に関する研究。 S-メトラクロール単体の毒性に関する知見を含まない。
607	IIA 8.2	Fekete-Kertesz, I	2015	Assessing Toxicity of Organic Aquatic Micropollutants Based on the Total Chlorophyll Content of Lemna minor as a Sensitive Endpoint	PERIODICA POLYTECHNICA-CHEMICAL ENGINEERING, 59(4), pp262-271 http://dx.doi.org/10.3311/PPch.8077	コウキクサに対する多数（11 種類）の化学物質の毒性研究。 LOEC が求められているが（5μg/L）、用量設定幅が 10 倍のオーダーであり、農薬の評価に活用できる精度ではない。
610	IIA 5.5	Santana, LMBM	2020	Simultaneous determination of multi-class pesticide metabolites in fish (Siluriformes: Ariidae): protocol developed for human dietary risk in Ceara coast, Brazil	ACCREDITATION AND QUALITY ASSURANCE, 25(3), pp185-199 http://dx.doi.org/10.1007/s00769-020-01431-x	ブラジルにおける食用ナマズ体内の農薬及びその代謝物の残存に関する調査。 日本における評価に直接活用できる試験種/環境ではない。
748	IIA 8.2	Glinski, DA	2018	Effect of hydration status on pesticide uptake in anurans following exposure to contaminated soils	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 25(16), pp16192-16201 http://dx.doi.org/10.1007/s11356-018-1830-8	米国産のカエルの脱水状態が、農薬の経皮摂取に与える影響を調査。 日本における評価に直接活用できる試験種/環境ではない。

表 4−6−3 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(生活環境動植物及び家畜に対する毒性、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
787	IIA 8.2	Ali, JM	2017	Compensatory response of fathead minnow larvae following a pulsed in-situ exposure to a seasonal agricultural runoff event	SCIENCE OF THE TOTAL ENVIRONMENT, 603, pp817-826 http://dx.doi.org/10.1016/j.scitotenv.2017.03.093	混合農薬のハヤ類（Fathead Minnow）仔魚への影響。日本における評価に直接活用できる試験種ではなく、また S-メトラクロール単体のデータを含まない。
790	IIA 8.2	Finlayson, KA	2019	Primary green turtle (Chelonia mydas) skin fibroblasts as an in vitro model for assessing genotoxicity and oxidative stress	AQUATIC TOXICOLOGY, 207, pp13-18 http://dx.doi.org/10.1016/j.aquatox.2018.11.022	ウミガメに対する 16 種類の化学物資の遺伝毒性について、皮膚線維芽細胞を用いて調査。日本における評価に直接活用できる試験種ではない。
907	IIA 8.2	Lencioni, V	2018	Response of Diamesa spp. (Diptera: Chironomidae) from Alpine streams to newly emergent contaminants and pesticides	JOURNAL OF LIMNOLOGY, 77, pp131-140 http://dx.doi.org/10.4081/jlimnol.2018.1802	海外の高山性のユスリカ類 2 種に対する農薬の急性毒性調査。メトラクロールの LC_{50} が示されているが、供試個体数等、基本的な試験条件の多くが記載されていない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
21	IIA 7.4	Filimon, MN	2021	Assessment of the Effect of Application of the Herbicide S-Metolachlor on the Activity of Some Enzymes Found in Soil	AGRICULTURE-BASEL, 11 (6) http://dx.doi.org/10.3390/agriculture11060469	S-メトラクロールが土壌中の酵素活性に与える影響に関する研究。農薬の評価に直接利用可能なデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
23	IIA 7.2	Wolejko, E	2017	Dissipation of S-metolachlor in plant and soil and effect on enzymatic activities	ENVIRONMENTAL MONITORING AND ASSESSMENT, 189(7) http://dx.doi.org/10.1007/s10661-017-6071-7	ポーランドのトウモロコシ圃場における土壌中動態研究。土壌中の半減期等のパラメーターが示されているが、日本における評価に直接活用できる環境条件ではない。
47	IIA 7.4	Fernandez, JV	2020	Field dissipation of S-metolachlor in organic and mineral soils used for sugarcane production in Florida	WEED TECHNOLOGY, 34 (3), pp362-370 http://dx.doi.org/10.1017/wet.2019.121	米国フロリダ州の土壌を用いた S-メトラクロールの動態研究。土壌中の有機物量及び水分量と農薬半減期との間の関連性を示しているが、日本における評価に直接活用できる環境条件ではない。
58	IIA 7	Dollinger, J	2022	Leaching and degradation of S-Metolachlor in undisturbed soil cores amended with organic wastes	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 29(14), pp20098-20111 http://dx.doi.org/10.1007/s11356-021-17204-z	下水処理場の汚泥等の有機廃棄物が S-メトラクロールの土壌中動態に与える影響に関するカラムリーチング研究。日本における評価に直接活用できる試験条件ではない。
64	IIA 7	Marin-Benito, JM	2021	The role of two organic amendments to modify the environmental fate of S-metolachlor in agricultural soils	ENVIRONMENTAL RESEARCH, 195 http://dx.doi.org/10.1016/j.envres.2021.110871	有機廃棄物が S-メトラクロールの土壌中動態に与える影響を調査。農薬の評価に直接利用可能なデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
67	IIA 7.1	da Silva, AP	2022	Leaching potential of S-metolachlor in a medium-textured Oxisol soil with bioindicator plants	REVISTA BRASILEIRA DE ENGENHARIA AGRICOLA E AMBIENTAL, 26(3), pp159-165 http://dx.doi.org/10.1590/1807-1929/agriambi.v26n3p159-165	熱帯オキシソル土壌を用いた S-メトラクロールの滲出動態に関する研究。リスク評価に関連するデータを含まず、また日本における評価に直接活用できる試験条件ではない。
74	IIA 7.4	Farlin, J	2018	Breakthrough dynamics of s-metolachlor metabolites in drinking water wells: Transport pathways and time to trend reversal	JOURNAL OF CONTAMINANT HYDROLOGY, 213, pp62-72 http://dx.doi.org/10.1016/j.jconhyd.2018.05.002	海外の特定の地域における地下水中の S-メトラクロール代謝物の環境動態研究。日本における評価に直接活用できる環境条件ではない。
77	IIA 7	Bedos, C	2017	Observed volatilization fluxes of S-metolachlor and benoxacor applied on soil with and without crop residues	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 24(4), pp3985-3996 http://dx.doi.org/10.1007/s11356-016-8124-9	S-メトラクロールの室内及び圃場における揮発による散逸動態の研究。全試験でセーフナー（ベノキサコール）との混合剤が用いられており、S-メトラクロール単体のデータを含まない。
81	IIA 7.4	Cassigneul, A	2018	Behaviour of S-metolachlor and its oxanilic and ethanesulfonic acids metabolites under fresh vs. partially decomposed cover crop mulches: A laboratory study	SCIENCE OF THE TOTAL ENVIRONMENT, 631-632, pp1515-1524 http://dx.doi.org/10.1016/j.scitotenv.2018.03.143	カバー作物の適用が土壌中の S-メトラクロールの動態に与える影響に関する研究。カバー作物の分解の度合いと S-メトラクロールの分解速度の間の相関が示されているが、農薬の評価に直接利用可能なデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
91	IIA 7.4	Maillard, E	2016	Dissipation of hydrological tracers and the herbicide S-metolachlor in batch and continuous-flow wetlands	CHEMOSPHERE, 144, pp2489-2496 http://dx.doi.org/10.1016/j.chemosphere.2015.11.027	砂質の湛水圃場を用いた S-メトラクロールの散逸動態研究。 散逸率は提示されているが、半減期等の主要な指標を含まず、また日本における評価に直接活用できる環境条件ではない。
93	IIA 7.3.2 IIA 7.4.1 IIA 7.4.2	Mendes, KF	2016	Sorption and desorption of mesotrione alone and mixed with S-metolachlor plus terbuthylazine in Brazilian soils	GEODERMA, 280, pp22-28 http://dx.doi.org/10.1016/j.geoderma.2016.06.014	海外の特定の環境における他剤（メソトリオン）とその混合剤の土壌中動態に関する研究。 S-メトラクロール単体のデータを含まない。
96	IIA 7.6	Drouin, G	2021	Direct and indirect photodegradation of atrazine and S-metolachlor in agriculturally impacted surface water and associated C and N isotope fractionation	ENVIRONMENTAL SCIENCE-PROCESSES & IMPACTS, 23(11), pp1791-1802 http://dx.doi.org/10.1039/d1em00246e	水域における S-メトラクロールの光分解に硝酸塩と溶存有機物が与える影響に関する室内試験研究。 農薬の評価に直接利用可能なデータを含まない。
99	IIA 7.1	Bedmar, F	2017	Persistence of acetochlor, atrazine, and S-metolachlor in surface and subsurface horizons of 2 typic argiudolls under no-tillage	ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY, 36(11), pp3065-3073 http://dx.doi.org/10.1002/etc.3874	海外の不耕起栽培における農薬動態に関する研究。 日本における評価に直接活用できる試験条件ではない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
121	IIA 7.1	Marie, L	2017	Degradation and Transport of the Chiral Herbicide S-Metolachlor at the Catchment Scale: Combining Observation Scales and Analytical Approaches	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 51(22), pp13231-13240 http://dx.doi.org/10.1021/acs.est.7b02297	海外の特定の農業地域における S-メトラクロールの環境動態に関するフィールド研究。 日本における評価に直接活用できる試験条件ではない。
125	IIA 7.3	Rose, CE	2018	Holistic assessment of occurrence and fate of metolachlor within environmental compartments of agricultural watersheds	SCIENCE OF THE TOTAL ENVIRONMENT, 612, pp708-719 http://dx.doi.org/10.1016/j.scitotenv.2017.08.154	農業用水系におけるメトラクロールの環境動態に関する総説。 新たな試験データを含まない。
137	IIA 7.1	Mendes, KF	2018	Glucose mineralization in soils of contrasting textures under application of S-metolachlor, terbuthylazine, and mesotrione, alone and in a mixture	BRAGANTIA, 77(1), pp152-159 http://dx.doi.org/10.1590/1678-4499.2016420	農薬が熱帯土壌のグルコース分解活性に与える影響に関する研究。 日本における評価に直接活用できる試験条件ではない。
187	IIA 7.4	Carretta, L	2018	Dissipation of terbuthylazine, metolachlor, and mesotrione in soils with contrasting texture	JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B-PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES, 53(10), pp661-668 http://dx.doi.org/10.1080/03601234.2018.1474556	海外の特定の地域の土壌における農薬散逸動態に関する研究。 日本における評価に直接活用できる試験条件ではない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
192	IIA 7.3	Cwielag-Piasecka, I	2021	Effectiveness of Carbaryl, Carbofuran and Metolachlor Retention in Soils under the Influence of Different Colloid	MINERALS, 11(9) http://dx.doi.org/10.3390/min11090924	ポーランドの特定の土壌に様々な鉱物を添加して、農薬の吸着/離脱に与える影響を調査している。 具体的な吸着係数／吸着定数等の記載はなく、農薬の評価に直接利用可能なデータを含まない。
196	IIA 7.1	Ghosh, RK	2016	Effect of fly ash amendment on metolachlor and atrazine degradation and microbial activity in two soils	ENVIRONMENTAL MONITORING AND ASSESSMENT, 188(8) http://dx.doi.org/10.1007/s10661-016-5486-x	海外の特定の土壌にフライアッシュを添加して、農薬の分解に与える影響を調査。 メトラクロールの半減期が示されているが、日本における評価に直接活用できる試験条件ではない。
212	IIA 7	Cox, L	2014	Olive oil mill waste as soil amendment: Impact on bentazone and S-metolachlor fate in soils	ABSTRACTS OF PAPERS OF THE AMERICAN CHEMICAL SOCIETY, 248	オリーブの加工廃棄物が S-メトラクロールの土壌吸着に与える影響を調査。 日本における評価に直接活用できる試験条件ではない。
235	IIA 7.1	Kanissery, R	2021	Impact of Soil Aeration on the Environmental Fate of Pre-Emergent Herbicide Metolachlor	APPLIED SCIENCES-BASEL, 11(18) http://dx.doi.org/10.3390/app11188567	好気的/嫌気的条件下における、メトラクロールの吸着動態の研究。 両条件下での吸着係数、半減期等が示されているが、海外の特定の土壌を用いた試験であり、日本における評価に直接活用できない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
245	IIA 7	Lizotte, R	2017	Effectiveness of Integrated Best Management Practices on Mitigation of Atrazine and Metolachlor in an Agricultural Lake Watershed	BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY, 98(4), pp 447-453 http://dx.doi.org/10.1007/s00128-016-2020-3	作付パターンの変更や農業最適管理法導入が、周辺水系への農薬流出に与える影響に関するフィールド調査。 日本における評価に直接活用できる試験条件ではない。
297	IIA 7.3	Sun, ZZ	2022	Enantioselectivity and mechanisms of chiral herbicide biodegradation in hydroponic systems	CHEMOSPHERE, 307 http://dx.doi.org/10.1016/j.chemosphere.2022.135701	ヨシの水耕系におけるメトラクロールのエナンチオ選択的分解に関する研究。 各異性体の半減期が示されているが、日本における評価に直接活用できる試験条件ではない。
310	IIA 7.1	Meite, F	2018	Impact of rainfall patterns and frequency on the export of pesticides and heavy-metals from agricultural soils	SCIENCE OF THE TOTAL ENVIRONMENT, 616, pp500-509 http://dx.doi.org/10.1016/j.scitotenv.2017.10.297	海外の特定の土壌を用いて、降雨パターンが農薬の流出に与える影響を調査した室内試験研究。 日本における評価に直接活用できる試験条件ではない。
331	IIA 7.1	Droz, B	2021	Phase Transfer and Biodegradation of Pesticides in Water-Sediment Systems Explored by Compound-Specific Isotope Analysis and Conceptual Modeling	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 55(8), pp4720-4728 http://dx.doi.org/10.1021/acs.est.0c06283	農薬の土壌への吸脱着動態に関する研究。 室内条件下での有酸素/無酸素下での農薬の半減期が示されているが、農薬の評価に直接利用可能なデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
349	IIA 7.1	Jursik, M	2020	Effect of different soil and weather conditions on efficacy, selectivity and dissipation of herbicides in sunflower	PLANT SOIL AND ENVIRONMENT, 66(9), pp468-476 http://dx.doi.org/10.17221/223/2020-PSE	薬効/薬害研究を主とした文献。S-メトラクロールの滲出について調査が行われているが具体的な数値が示されておらず、農薬の評価に利用可能なデータを含まない。
351	IIA 7.8	Charalampous, AC	2015	The spatial and temporal distribution/variation of pesticide residues in Viotikos Kifissos basin before and after the application of a low input crop management system. A three-year study	INTERNATIONAL JOURNAL OF ENVIRONMENTAL ANALYTICAL CHEMISTRY, 95(13), pp1263-1282 http://dx.doi.org/10.1080/03067319.2015.1090564	海外の特定の地域における残留農薬のモニタリング調査。日本における農薬評価に活用できるデータを含まない。
365	IIA 7.8	Sarrazin, B	2022	Pesticide contamination of fish ponds in relation to crop area in a mixed farmland-pond landscape (Dombes area, France)	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 29(44), pp66858-66873 http://dx.doi.org/10.1007/s11356-022-20492-8	海外の特定の地域の養魚池における、広範囲の農薬に関する分布モニタリング調査。日本における農薬評価に活用できるデータを含まない。
402	IIA 7.4	Santos, EA	2015	HERBICIDE DETECTION IN GROUNDWATER IN CORREGO RICO-SP WATERSHED	PLANTA DANINHA, 33(1), pp147-155 http://dx.doi.org/10.1590/S0100-83582015000100017	海外の特定の地域の地下水における広範囲の農薬の分布モニタリング調査。S-メトラクロールは調査対象のすべての調査地点で検出されておらず、S-メトラクロールの評価に利用可能なデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
406	IIA 7.1	Mendes, KF	2018	Assessment of Mesotrione Leaching Applied Alone and Mixed in Seven Tropical Soils Columns under Laboratory Conditions	AGRICULTURE-BASEL, 8(1) http://dx.doi.org/10.3390/agriculture8010001	他剤（メソトリオン）の浸出動態に関する研究。 S-メトラクロールはメソトリオンとの混合対象としてのみ用いられており、S-メトラクロール単体に関する知見を含まない。
426	IIA 7.4	Pinna, MV	2014	Soil sorption and leaching of active ingredients of Lumax (R) under mineral or organic fertilization	CHEMOSPHERE, 111, pp372-378 http://dx.doi.org/10.1016/j.chemosphere.2014.03.124	海外の特定の土壌における、有機物が混合農薬製剤の滲出動態に与える影響を調査。 農薬の評価に直接利用可能な試験条件ではない。
432	IIA 7.4	Sharipov, U	2021	Adsorption and degradation behavior of six herbicides in different agricultural soils	ENVIRONMENTAL EARTH SCIENCES, 80(20) http://dx.doi.org/10.1007/s12665-021-10036-7	海外の特定の土壌における、農薬の動態研究。 吸着係数、半減期のパラメーターや、有機物や CEC 等との相関性が示されているが、日本における評価に直接活用できる試験条件ではない。
435	IIA 7.1	Dusek, J	2015	Transport of bromide and pesticides through an undisturbed soil column: A modeling study with global optimization analysis	JOURNAL OF CONTAMINANT HYDROLOGY, 175, pp1-16 http://dx.doi.org/10.1016/j.jconhyd.2015.02.002	カラム滲出実験のデータを用いて、熱帯土壌中の農薬動態モデルの実証試験を実施。 S-メトラクロールの半減期及び吸着分配係数が示されているが、日本における評価に直接活用できる試験条件ではない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
440	IIA 7.4	Mendes, KF	2017	Quantification of the fate of mesotrione applied alone or in a herbicide mixture in two Brazilian arable soils	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 24(9), pp8425-8435 http://dx.doi.org/10.1007/s11356-017-8535-2	他剤（メソトリオン）の浸出動態に関する研究。S-メトラクロールはメソトリオンとの混合対象としてのみ用いられており、S-メトラクロール単体に関する知見を含まない。
447	IIA 7.4	Perez-Rodriguez, P	2021	Plants affect the dissipation and leaching of anilide pesticides in soil mesocosms: Insights from compound-specific isotope analysis (CSIA)	AGRICULTURE ECOSYSTEMS & ENVIRONMENT, 308 http://dx.doi.org/10.1016/j.agee.2020.107257	海外の特定の土壌における農薬の動態に関する研究。日本における評価に直接活用できる試験条件ではない。
458	IIA 7.4	Elias, D	2017	Pesticide and nitrate transport in an agriculturally influenced stream in Indiana	ENVIRONMENTAL MONITORING AND ASSESSMENT, 189(4) http://dx.doi.org/10.1007/s10661-017-5870-1	海外の特定の地域の河川における農薬の分布調査。日本における評価に直接活用できる試験条件ではない。
485	IIA 7.8	Alvarez-Zaldivar, P	2018	Pesticide degradation and export losses at the catchment scale: Insights from compound-specific isotope analysis (CSIA)	WATER RESEARCH, 139, pp198-207 http://dx.doi.org/10.1016/j.watres.2018.03.061	化合物特異的同位体分析法を用いた、水圏中の S-メトラクロールの動態研究。日本における評価に直接活用できる試験条件ではない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
492	IIA 7.1	Potter, TL	2017	Assessing pesticide wet deposition risk within a small agricultural watershed in the Southeastern Coastal Plain (USA)	SCIENCE OF THE TOTAL ENVIRONMENT, 580, pp158-167 http://dx.doi.org/10.1016/j.scitotenv.2016.11.020	海外の特定の小湖沼における広範囲の農薬の分布モニタリング調査。 日本における評価に活用できるデータを含まない。
563	IIA 7.1	Jaikaew, P	2017	INVESTIGATION OF LEACHING PROCESSES OF HERBICIDES IN SOIL COLUMN SIMULATING BY HYDRUS-1D MODEL	SURANAREE JOURNAL OF SCIENCE AND TECHNOLOGY, 24(4), pp423-432	メトラクロールのカラム滲出試験を用いた、HYDRUS モデルの実証研究。 カラム滲出試験から得られた半減期や分解速度定数が示されていが、HYDRUS モデルの数値との比較が主要な論点であり、また土壌試料の詳細な性質の記述がなく、農薬の評価に活用できない。
621	IIA 7.4	Otto, S	2016	Vegetated Ditches for the Mitigation of Pesticides Runoff in the Po Valley	PLOS ONE, 11(4) http://dx.doi.org/10.1371/journal.pone.0153287	海外の特定の地域における、植生を伴う溝を用いて農薬流出を低減する管理法に関する研究。 日本における評価に活用できるデータを含まない。
634	IIA 7.8	Rossi, F	2018	Interactive Effects of Pesticides and Nutrients on Microbial Communities Responsible of Litter Decomposition in Streams	FRONTIERS IN MICROBIOLOGY, 9 http://dx.doi.org/10.3389/fmicb.2018.02437	河川の落葉分解に関与する微生物群集に対する、農薬と栄養素の影響に関する調査。 農薬の評価に利用可能なデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
635	IIA 7.1	Meite, F	2022	Ageing of copper, zinc and synthetic pesticides in particle-size and chemical fractions of agricultural soils	SCIENCE OF THE TOTAL ENVIRONMENT, 824 http://dx.doi.org/10.1016/j.scitotenv.2022.153860	土壌中の重金属が農薬の動態に与える影響に関する研究。 農薬の評価に利用可能なデータを含まない。
640	IIA 7.1	Baran, N	2021	Pesticides in groundwater at a national scale (France): Impact of regulations, molecular properties, uses, hydrogeology and climatic conditions	SCIENCE OF THE TOTAL ENVIRONMENT, 791 http://dx.doi.org/10.1016/j.scitotenv.2021.148137	地下水中の農薬分布について、フランス全土のモニタリング調査を渉猟した文献研究。 農薬の評価に利用可能なデータを含まない。
641	IIA 7.8 IIA 8.2	Santarossa, MAD	2020	Contamination of fee-fishing ponds with agrochemicals used in sugarcane crops	SN APPLIED SCIENCES, 2 (9) http://dx.doi.org/10.1007/s42452-020-03274-0	海外の特定の地域の釣り堀における農薬分布調査。 日本における評価に直接活用できるデータを含まない。
642	IIA 7.8	Hong, W	2017	Research about impacts of specific pollutants like herbicides upon microbial activity of activated sludge systems in wastewater treatment plants	3RD INTERNATIONAL CONFERENCE ON ENERGY MATERIALS AND ENVIRONMENT ENGINEERING, 61 http://dx.doi.org/10.1088/1755-1315/61/1/012001	下水処理施設の活性汚泥システムの微生物活性に対する除草剤の影響に関する調査。 日本における評価に直接活用できるデータを含まず、また検体採取方法等の具体的な記述がない。
643	IIA 7.8	Glinski, DA	2018	Analysis of pesticides in surface water, stemflow, and throughfall in an agricultural area in South Georgia, USA	CHEMOSPHERE, 209, pp496-507 http://dx.doi.org/10.1016/j.chemosphere.2018.06.116	海外の特定の地域における環境中の農薬分布調査。 日本における評価に直接活用できるデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
645	IIA 7.4	Carretta, L	2017	Effect of Vegetative Buffer Strips on Herbicide Runoff From a Nontilled Soil	SOIL SCIENCE, 182(8), pp285-291 http://dx.doi.org/10.1097/SS.0000000000000221	イタリアでの不耕起農法における、周縁緩衝帯が農薬の流出に与える効果に関する研究。 日本における評価に直接活用できるデータを含まない。
648	IIA 7.1	Thompson, TJ	2021	Groundwater discharges as a source of phytoestrogens and other agriculturally derived contaminants to streams	SCIENCE OF THE TOTAL ENVIRONMENT, 755 http://dx.doi.org/10.1016/j.scitotenv.2020.142873	海外の農業地帯における地下水中の農薬分布に関する調査。 日本における評価に直接活用できるデータを含まない。
651	IIA 7.1	Parlakidis, P	2022	Occurrence of Banned and Currently Used Herbicides, in Groundwater of Northern Greece: A Human Health Risk Assessment Approach	INTERNATIONAL JOURNAL OF ENVIRONMENTAL RESEARCH AND PUBLIC HEALTH, 19(14) http://dx.doi.org/10.3390/ijerph19148877	特定の地域における地下水中の農薬分布に関する調査。 日本における評価に直接活用できるデータを含まない。
652	IIA 7.8	Powell, KW	2017	A Retrospective Analysis of Agricultural Herbicides in Surface Water Reveals Risk Plausibility for Declines in Submerged Aquatic Vegetation	TOXICS, 5(3) http://dx.doi.org/10.3390/toxics5030021	特定の地域における表層水中の農薬分布調査。 日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
653	IIA 7.1	Domergue, L	2022	Adsorption onto granular activated carbons of a mixture of pesticides and their metabolites at trace concentrations in groundwater	JOURNAL OF ENVIRONMENTAL CHEMICAL ENGINEERING, 10(5) http://dx.doi.org/10.1016/j.jece.2022.108218	活性炭による農薬及びその代謝物の吸着機序に関する研究。 農薬の評価に利用可能なデータを含まない。
654	IIA 7.1	Boulange, J	2016	Development and validation of the SPEC model for simulating the fate and transport of pesticide applied to Japanese upland agricultural soil	JOURNAL OF PESTICIDE SCIENCE, 41(44989), pp152-162 http://dx.doi.org/10.1584/jpestics.D16-027	残存農薬に関する新しい動態予測モデルの開発に関する文献。 モデルの検証のためのフィールド試験の結果は当文献に含まれておらず、農薬の評価に利用可能なデータを含まない。
657	IIA 7.8	Fingler, S	2017	Herbicide micropollutants in surface, ground and drinking waters within and near the area of Zagreb, Croatia	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 24(12), pp11017-11030 http://dx.doi.org/10.1007/s11356-016-7074-6	海外の特定の地域における飲料水中の農薬分布調査。 日本における評価に直接活用できるデータを含まない。
658	IIA 7.1	Chaumet, B	2022	Pond mitigation in dissolved and particulate pesticide transfers: Influence of storm events and seasonality (Aurade agricultural catchment, SW-France)	JOURNAL OF ENVIRONMENTAL MANAGEMENT, 320 http://dx.doi.org/10.1016/j.jenvman.2022.115911	海外の特定の地域における小湖沼中の農薬動態に関する研究。 日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
661	IIA 7.8	Terzopoulou, E	2016	Active and passive sampling for the assessment of hydrophilic organic contaminants in a river basin-ecotoxicological risk assessment	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 23(6), pp5577-5591 http://dx.doi.org/10.1007/s11356-015-5760-4	海外の特定の地域における、広範囲の化学物質の分布調査。 日本における評価に直接活用できるデータを含まない。
663	IIA 7.1	Grantz, EM	2020	Residual herbicide concentrations in on-farm water storage-tailwater recovery systems: Preliminary assessment	AGRICULTURAL & ENVIRONMENTAL LETTERS, 5(1) http://dx.doi.org/10.1002/ael2.20009	海外の特定地域の循環灌漑システムにおける農薬動態研究。 日本における評価に直接活用できるデータを含まない。
665	IIA 7.8	Vera-Candioti, J	2021	Pesticides detected in surface and groundwater from agroecosystems in the Pampas region of Argentina: occurrence and ecological risk assessment	ENVIRONMENTAL MONITORING AND ASSESSMENT, 193(10) http://dx.doi.org/10.1007/s10661-021-09462-8	海外の特定の地域における広範囲の農薬の分布調査。 日本における評価に直接活用できるデータを含まない。
670	IIA 7.8	Van Opstal, NV	2022	Quality of the surface water of a basin affected by the expansion of the agricultural frontier over the native forest in the Argentine Espinal region	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 29(38), pp57395-57411 https://doi.org/10.1007/s11356-022-19760-4	海外の特定の地域における、広範囲の農薬の分布調査。 日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第2段階で「区分c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
674	IIA 7.4	Cheng, Z	2022	Effects of the presence of triclocarban on the degradation and migration of co-occurring pesticides in soil	ENVIRONMENTAL POLLUTION, 310 http://dx.doi.org/10.1016/j.envpol.2022.119840	殺菌剤トリクロカルバンが土壌中の他の農薬の動態に与える影響に関する研究。S-メトラクロールの評価に利用可能なデータを含まない。
678	IIA 7.3.2	Parajulee, A	2018	Comparing winter-time herbicide behavior and exports in urban, rural, and mixed-use watersheds	ENVIRONMENTAL SCIENCE-PROCESSES & IMPACTS, 20(5), pp767-779 http://dx.doi.org/10.1039/c7em00596b	海外の特定地域における水圏中の農薬モニタリング調査。日本における評価に直接活用できるデータを含まない。
680	IIA 7.8	Wang, SR	2021	Occurrence, Spatial, and Seasonal Variations, and Gas-Particle Partitioning of Atmospheric Current-Use Pesticides (CUPs) in the Great Lakes Basin	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 55(6), pp3539-3548 http://dx.doi.org/10.1021/acs.est.0c06470	海外の特定地域における大気中の農薬分布調査。日本における評価に直接活用できるデータを含まない。
701	IIA 7.8	Fairbairn, DJ	2016	Sources and transport of contaminants of emerging concern: A two-year study of occurrence and spatiotemporal variation in a mixed land use watershed	SCIENCE OF THE TOTAL ENVIRONMENT, 551, pp605-613 http://dx.doi.org/10.1016/j.scitotenv.2016.02.056	海外特定地域の水域における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
702	IIA 7.8	Wang, TL	2021	Occurrence, spatiotemporal distribution, and risk assessment of current-use pesti cides in surface water: A case study ne ar Taihu Lake, China	SCIENCE OF THE TOTAL ENVIRONMENT, 782 http://dx.doi.org/10.1016/j.scitotenv.2021.146826	海外特定地域の表層水における広範囲の農薬の分布調査。日本における評価に直接活用できるデータを含まない。
711	IIA 7.4 IIA 7.8	Rocha, AA	2015	Monitoring of Pesticide Residues in Sur face and Subsurface Waters, Sediments, and Fish in Center-Pivot Irrigation Area s	JOURNAL OF THE BRAZIL IAN CHEMICAL SOCIETY, 26(11), pp2269-2278 http://dx.doi.org/10.5935/0103-5053.20150215	海外特定地域の水圏における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。
713	IIA 7.8	O'Brien, D	2016	Spatial and Temporal Variability in Pest icide Exposure Downstream of a Heavil y Irrigated Cropping Area: Application of Different Monitoring Techniques	JOURNAL OF AGRICULTU RAL AND FOOD CHEMIST RY, 64(20), pp3975-3989 http://dx.doi.org/10.1021/acs.jafc.5b04710	海外特定地域の表層水における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。
728	IIA 7.8	Kacikoc, M	2022	Environmental monitoring of pesticide r esidues in surface waters of Buyuk Me nderes RiverMeltem	SIGMA JOURNAL OF ENGI NEERING AND NATURAL SCIENCES-SIGMA MUHEND ISLIK VE FEN BILIMLERI DERGISI, 40(4), pp762-771 http://dx.doi.org/10.14744/sigma.2022.00092	海外特定地域の表層水における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
730	IIA 7.8	Fingler, S	2021	Seasonal distribution of multiclass pesticide residues in the surface waters of northwest Croatia	ARHIV ZA HIGIJENU RADA I TOKSIKOLOGIJU-ARCHIVES OF INDUSTRIAL HYGIENE AND TOXICOLOGY, 72(4), pp280-288 http://dx.doi.org/10.2478/aiht-2021-72-3598	海外特定地域の表層水における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。
732	IIA 7.8	Berton, A	2018	Grab and passive sampling applied to pesticide analysis in the Sao Lourenco river headwater in Campo Verde - MT, Brazil	JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B-PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES, 53(4) pp237-245 http://dx.doi.org/10.1080/03601234.2017.1410412	海外特定地域の表層水における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。
733	IIA 8.2	Ojemaye, CY	2020	Herbicides in the tissues and organs of different fish species (Kalk Bay harbour, South Africa): occurrence, levels and risk assessment	INTERNATIONAL JOURNAL OF ENVIRONMENTAL SCIENCE AND TECHNOLOGY, 17(3), pp1637-1648 http://dx.doi.org/10.1007/s13762-019-02621-y	海外の特定地域における淡水魚体内の農薬残留に関する研究。日本における評価に直接活用できるデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
737	IIA 7.8	Machete, M	2019	Detection of selected agricultural pesticides in river and tap water in Letsitele, Lomati and Vals-Renoster catchments, South Africa	WATER SA, 45(4), pp716-720 http://dx.doi.org/10.17159/wsa/2019.v45.i4.7554	海外特定地域の水圏における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。
749	IIA 8.2	Lerebours, A	2021	Pesticides, nonylphenols and polybrominated diphenyl ethers in marine bivalves from France: A pilot study	MARINE POLLUTION BULLETIN, 172 http://dx.doi.org/10.1016/j.marpolbul.2021.112956	海外の特定地域における海産二枚貝類体内の化学物質分布に関する研究。日本における評価に直接活用できるデータを含まない。
754	IIA 7.8	Spirhanzlova, P	2019	Composition and endocrine effects of water collected in the Kibale national park in Uganda	ENVIRONMENTAL POLLUTION, 251 pp460-468 http://dx.doi.org/10.1016/j.envpol.2019.05.006	海外特定地域の河川における広範囲の農薬の分布調査および環境影響調査。日本における評価に直接活用できるデータを含まない。
758	IIA 7.8	Barizon, RRM	2020	Pesticides in the surface waters of the Camanducaia River watershed, Brazil	JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B-PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES, 55(3), pp283-292 http://dx.doi.org/10.1080/03601234.2019.1693835	海外特定地域の河川における広範囲の農薬の分布調査および環境影響調査。日本における評価に直接活用できるデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
760	IIA 7.8	Piel, S	2021	Understanding the origins of herbicides metabolites in an agricultural watershed through their spatial and seasonal variations	JOURNAL OF ENVIRONMENTAL SCIENCE AND HEALTH PART B-PESTICIDES FOOD CONTAMINANTS AND AGRICULTURAL WASTES, 56(4), pp313-332 http://dx.doi.org/10.1080/03601234.2021.1883390	海外特定地域の水域における広範囲の農薬の分布調査および環境影響調査。日本における評価に直接活用できるデータを含まない。
762	IIA 5.8 IIA 7	Bexfield, LM	2021	Pesticides and Pesticide Degradates in Groundwater Used for Public Supply across the United States: Occurrence and Human-Health Context	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 55(1), pp362-372 http://dx.doi.org/10.1021/acs.est.0c05793	海外の特定の地域における水道用水中の農薬分布調査。日本における評価に直接活用できるデータを含まない。
764	IIA 7.8	Carpenter, CMG	2018	Widespread Micropollutant Monitoring in the Hudson River Estuary Reveals Spatiotemporal Micropollutant Clusters and Their Sources	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 52(11), pp6187-6196 http://dx.doi.org/10.1021/acs.est.8b00945	海外特定地域の水域における広範囲の化学物質の分布調査。日本における評価に直接活用できるデータを含まない。
772	IIA 5.8 IIA 7	Mas, LI	2020	Pesticides in water sources used for human consumption in the semiarid region of Argentina	SN APPLIED SCIENCES, 2(4) http://dx.doi.org/10.1007/s42452-020-2513-x	海外特定地域の水域における広範囲の化学物質の分布調査。日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
776	IIA 7.8	Bradley, PM	2017	Expanded Target-Chemical Analysis Reveals Extensive Mixed Organic-Contaminant Exposure in US Streams	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 51(9), pp4792-4802 http://dx.doi.org/10.1021/acs.est.7b00012	海外特定地域の水域における広範囲の化学物質の分布調査。日本における評価に直接活用できるデータを含まない。
778	IIA 7.8	Liu, W	2020	Suspect screening and risk assessment of pollutants in the wastewater from a chemical industry park in China	ENVIRONMENTAL POLLUTION, 263 http://dx.doi.org/10.1016/j.envpol.2020.114493	海外特定地域の下水道系における広範囲の化学物質の分布調査。日本における評価に直接活用できるデータを含まない。
779	IIA 7.8	Korosa, A	2015	Pharmaceuticals and pesticides in urban groundwater: a case study - Maribor, Slovenia	WATER RESOURCES MANAGEMENT VIII, 196, pp413-422 http://dx.doi.org/10.2495/WRM150351	海外特定地域の水域における広範囲の化学物質の分布調査。日本における評価に直接活用できるデータを含まない。
785	IIA 7.8	Karpuzcu, ME	2014	Identifying sources of emerging organic contaminants in a mixed use watershed using principal components analysis	ENVIRONMENTAL SCIENCE-PROCESSES & IMPACTS, 16(10), pp2390-2399 http://dx.doi.org/10.1039/c4em00324a	海外特定地域の水域における広範囲の農薬の分布調査。日本における評価に直接活用できるデータを含まない。
788	IIA 7	Santolaria, Z	2015	Evaluation of Airborne Organic Pollutants in a Pyrenean Glacial Lake (The Sabocos Tarn)	WATER AIR AND SOIL POLLUTION, 226(11) http://dx.doi.org/10.1007/s11270-015-2648-3	海外特定地域の水域における広範囲の化学物質の分布調査。日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求(項目番号)	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
789	IIA 7.8	Zhang, YP	2021	Suspect and target screening of emerging pesticides and their transformation products in an urban river using LC-QTOF-MS	SCIENCE OF THE TOTAL ENVIRONMENT, 790 http://dx.doi.org/10.1016/j.scitotenv.2021.147978	海外特定地域の水域における広範囲の農薬の分布調査。日本における評価に直接活用できるデータを含まない。
798	IIA 8.2	Ernst, F	2018	Occurrence of pesticide residues in fish from south American rainfed agroecosystems	SCIENCE OF THE TOTAL ENVIRONMENT, 631-632, pp169-179 http://dx.doi.org/10.1016/j.scitotenv.2018.02.320	海外特定地域の魚類における広範囲の農薬の残留調査。日本における評価に直接活用できるデータを含まない。
799	IIA 7.8	Raby, M	2022	Characterizing the exposure of streams in southern Ontario to agricultural pesticides	CHEMOSPHERE, 294 http://dx.doi.org/10.1016/j.chemosphere.2022.133769	海外の特定地域における広範囲の農薬の土壌中分布調査。日本における評価に直接活用できるデータを含まない。
801	IIA 7.8	Spilsbury, FD	2020	Risk Assessment of Pesticide Mixtures in Australian Rivers Discharging to the Great Barrier Reef	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 54(22), pp14361-14371 http://dx.doi.org/10.1021/acs.est.0c04066	海外の特定地域における広範囲の農薬のリスクアセスメント調査。日本における評価に直接活用できるデータを含まない。
807	IIA 7.8	Moeder, M	2017	Potential of vegetated ditches to manage organic pollutants derived from agricultural runoff and domestic sewage: A case study in Sinaloa (Mexico)	SCIENCE OF THE TOTAL ENVIRONMENT, 598, pp1106-1115 http://dx.doi.org/10.1016/j.scitotenv.2017.04.149	海外の特定の地域における植生を伴う溝を用いて農薬流出を低減する管理法に関する研究。日本における評価に活用できるデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
814	IIA 7.8	Diarnanti, KS	2020	Assessment of the chemical pollution status of the Dniester River Basin by wide-scope target and suspect screening using mass spectrometric techniques	ANALYTICAL AND BIOANALYTICAL CHEMISTRY, 412(20), pp4893-4907 http://dx.doi.org/10.1007/s00216-020-02648-y	海外特定地域の水域における広範囲の農薬の分布調査。日本における評価に直接活用できるデータを含まない。
848	IIA 7.8	Herrero-Hernandez, E	2017	Seasonal distribution of herbicide and insecticide residues in the water resources of the vineyard region of La Rioja (Spain)	SCIENCE OF THE TOTAL ENVIRONMENT, 609, pp161-171 http://dx.doi.org/10.1016/j.scitotenv.2017.07.113	海外特定地域の水域における広範囲の農薬の分布モニタリング調査。日本における評価に直接活用できるデータを含まない。
853	IIA 7.4	Korosa, A	2016	Determination of micro-organic contaminants in groundwater (Maribor, Slovenia)	SCIENCE OF THE TOTAL ENVIRONMENT, 571, pp1419-1431 http://dx.doi.org/10.1016/j.scitotenv.2016.06.103	海外特定地域の水域における広範囲の農薬の分布調査。日本における評価に直接活用できるデータを含まない。
856	IIA 7.8	Tyohemba, RL	2020	Herbicide residues in sediments from Lake St Lucia (iSimangaliso World Heritage Site, South Africa) and its catchment areas: Occurrence and ecological risk assessment	ENVIRONMENTAL POLLUTION, 267 http://dx.doi.org/10.1016/j.envpol.2020.115566	海外特定地域の水域における広範囲の農薬の分布調査及びリスクアセスメント研究。日本における評価に直接活用できるデータを含まない。

表 4－6－4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
867	IIA 7.8	Mutzner, L	2020	Spatial Differences among Micropollutants in Sewer Overflows: A Multisite Analysis Using Passive Samplers	ENVIRONMENTAL SCIENCE & TECHNOLOGY, 54(11), pp6584-6593 http://dx.doi.org/10.1021/acs.est.9b05148	海外特定地域の下水処理排水における農薬の分布調査。 日本における評価に直接活用できるデータを含まない。
879	IIA 7.8	Nowell, LH	2018	Complex mixtures of dissolved pesticides show potential aquatic toxicity in a synoptic study of Midwestern US streams	SCIENCE OF THE TOTAL ENVIRONMENT, 613, pp1469-1488 http://dx.doi.org/10.1016/j.scitotenv.2017.06.156	海外特定地域の水域における広範囲の農薬の分布調査及びリスクアセスメント研究。 日本における評価に直接活用できるデータを含まない。
881	IIA 5.5 IIA 7	Busetti, F	2015	Target screening of chemicals of concern in recycled water	ENVIRONMENTAL SCIENCE-WATER RESEARCH & TECHNOLOGY, 1(5), pp659-667 http://dx.doi.org/10.1039/c4ew00104d	海外特定地域の汚水リサイクル水における広範囲の化学物質の分布調査。 日本における評価に直接活用できるデータを含まない。

表 4−6−4 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(環境動態、WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
884	IIA 7.8	Papadakis, EN	2015	A pesticide monitoring survey in rivers and lakes of northern Greece and its human and ecotoxicological risk assessment	ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY, 116, pp1-9 http://dx.doi.org/10.1016/j.ecoenv.2015.02.033 《海外評価書引用：EFSA（2018）Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted》	海外特定地域の水域における広範囲の農薬の分布調査及びリスクアセスメント研究。 日本における評価に直接活用できるデータを含まない。
887	IIA 7.1	Kiefer, K	2021	Identification of LC-HRMS nontarget signals in groundwater after source related prioritization	WATER RESEARCH, 196 http://dx.doi.org/10.1016/j.watres.2021.116994	海外特定地域の地下水における広範囲の農薬の分布調査。 日本における評価に直接活用できるデータを含まない。

表 4−6−5 適合性評価の第 2 段階で「区分 c」と判断した論文とその理由(J-STAGE)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	判断理由
J17	IIA 7	Julien Boulange, Dang Quoc Thuyet, Piyanuch Jaikaew, 石原 悟, 渡邊 裕純	2016	日本の畑土壌に処理された農薬の動態予測のための SPEC モデルの開発と検証	Journal of Pesticide Science 2016 年 41 巻 4 号 152-162 https://www.jstage.jst.go.jp/article/jpestics/41/4/41_D16-027/_pdf/-char/ja	土壌中の農薬の動態に関するドライラボ研究。

4.7. 適合性評価の第 2 段階で「区分 a」と判断した論文とその理由

表 4−7−1 適合性評価の第 2 段階で「区分 a」と判断した論文とその理由(WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	Klimisch 分類
155	IIA 7.6	Gutowski, L	2015	A comparative assessment of the transformation products of S-metolachlor and its commercial product Mercantor Gold (R) and their fate in the aquatic environment by employing a combination of experimental and in silico methods	SCIENCE OF THE TOTAL ENVIRONMENT, 506, pp369-379 https://dx.doi.org/10.1016/j.scitotenv.2014.11.025	1
	判断理由					
	S-メトラクロール原体と製剤（商品名「メルカンタールゴールド」）の、水中での光分解性及び生分解性に関する調査。原体、製剤とも生分解は生じなかったが、光分解では製剤と原体の分解速度に違いが見られ、光分解に対する製剤中の補助剤の影響が示唆された。 また光分解生成物はさらに生分解により新たな生成物となるが、この新たな生成物は元の S-メトラクロールよりも強い毒性を持つ可能性があり、市販製剤によるより現実的な環境下での動態調査の重要性が指摘されている。 OECD ガイドライン準拠（301D 好気性生分解試験及び 301F 好気性生分解試験）。					

表 4－7－1 適合性評価の第 2 段階で「区分 a」と判断した論文とその理由(WOSCC)

文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	Klimisch 分類
316	IIA 8.7	Helmer, SH	2015	Effects of realistic doses of atrazine, metolachlor, and glyphosate on lipid peroxidation and diet-derived antioxidants in caged honey bees (Apis mellifera)	ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH, 22(11), pp8010-8021 http://dx.doi.org/10.1007/s11356-014-2879-7	2
	判断理由					
	トウモロコシ圃場周辺の植物体内と同程度の濃度の農薬をミツバチに投与し、ミツバチのカロテノイド-レチノイド代謝系への影響を調査。 メトラクロールを投与された個体では、食餌摂取量の顕著な増加及びオールトランス-レチノール（AT-ROH）の増加が見られ、野外の植物に実際に生じうる濃度のメトラクロールがミツバチの代謝に影響を与える可能性が示唆された。 試験は LD_{50} 値の算出を目的としておらず、OECD ガイドライン（213 成虫単回経口毒性／245 成虫単回経口毒性）に準拠していないが、詳細な報告に基づき科学的に受け入れ可能な結果が示されている。					
文献番号	データ要求（項目番号）	著者	出版年	論文表題	掲載誌名、号、ページ等	Klimisch 分類
382	IIA 8.4	Machado, MD	2019	Sensitivity of freshwater and marine green algae to three compounds of emerging concern	JOURNAL OF APPLIED PHYCOLOGY, 31(1), pp399-408 http://dx.doi.org/10.1007/s10811-018-1511-5	2
	判断理由					
	ムレミカヅキモを含む 3 種の緑藻に対する毒性調査。 メトラクロールのムレミカヅキモに対する EC_{10} 値として 45μg/L、EC_{50} 値として 118μg/L が示されており、この値は、過去の報告で土壌中及び表層水中に存在するメトラクロールの濃度範囲に含まれている。 試験は OECD ガイドライン（201 藻類成長阻害）に準拠していないが、詳細な報告に基づき科学的に受け入れ可能な結果が示されている。					

5.　食品安全委員会における検討対象となるヒトに対する毒性に関する論文の一覧

「残留農薬の食品健康影響評価における公表文献の取扱いについて　（令和 3 年 3 月 18 日農薬第一専門調査会決定)」に基づき、食品安全委員会における検討対象となるヒトに対する毒性に関する論文の一覧を下記の通り別途添付する。

- 別添１　S-メトラクロール　食品安全委員会フォーマット表

6.　海外評価機関等の評価書に引用のある文献

「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 日農薬資材審議会農薬分科会決定、令和 5 年 7 月 27 日一部改正)」に基づき該当する評価書を調査したところ、EFSA で 3 件、USEPA で 18 件の評価書が認められ、258 件（延べ 293 件）の文献が引用されていた。なおメトラクロールおよび S-メトラクロールは JMPR においては評価されていない。

① EFSA, USEPA の評価書の検索を実施したサイト
　EFSA ：EFSA journal https://efsa.onlinelibrary.wiley.com/journal/18314732
　EPA ：Regulation.gov https://www.regulations.gov/search?filter＝metolachlor
② 検索日：2023 年 6 月 13 日
③ 検索ワード：metolachlor

EU、USEPA の関連する評価書の一覧と、それらの評価書に結果が引用されている文献の一覧、及び検討対象となる公表文献（ヒトに対する毒性における検討対象）の一覧は、下記の通り別途添付する。

- 別添２　S-メトラクロール　海外評価書リスト
- 別添３　S-メトラクロール　海外評価書引用文献リスト
- 別添４　S-メトラクロール　海外評価書引用文献食品安全委員会フォーマット表

7.　結果および結論

S-メトラクロールについて、系統的な文献調査を実施した。文献検索は、Web of Science Core Collection（WOSCC）及び J-STAGE で実施した。WOSCC の検索期間は 2014 年 8 月 1 日-2023 年 2 月 13 日、J-STAGE の検索期間は 2014 年 1 月 1 日-2023 年 2 月 22 日（英文キーワード検索)、2008 年 1 月 1 日-2023 年 2 月 22 日（和文キーワード検索）で実施した。

WOSCC 検索においては、化合物名等で 1012 件のヒットとなった。1012 の文献を文献タイトル及び要旨を基に第 1 段階の適合性評価を行い、201 の文献を選抜し、この 201 件の文献について文献全文を用いた第 2 段階評価を実施し、155 件を適合性ありと判断した。

これら 155 件につき、評価目的への適合性分類（表 3－2－1）に基づき「区分 a」: 生活環境動植物及び家畜に対する毒性 2 件、環境動態 1 件、「区分 b」: ヒトに対する毒性 2 件、農作物及び畜産物への残留 2 件、生活環境動植物及び家畜に対する毒性 4 件、環境動態 16 件、「区分 c」: ヒトに対する毒性 5 件、農作物及び畜産物への残留 1 件、生活環境動植物及び家畜に対する毒性 26 件、環境動態 96 件に分類した。

J-STAGE 検索においては、114 件の文献がヒットし、この 114 件を第 1 段階評価して 4 件を選抜し、この 4 件の文献について文献全文を用いた第 2 段階評価を実施し、1 件を適合性ありと判断した。

この 1 件につき、評価目的への適合性分類（表 3－2－1）に基づき「区分 c」: 環境動態 1 件に分類した。

海外の代表的な 3 評価機関（EFSA、USEPA、JMPR）による評価書を調査したところ、EFSA で 3 件、USEPA で 19 件の評価書が認められ、両機関合わせて 258 件（延べ 293 件）の文献が引用されていた。なおメトラクロールおよび S-メトラクロールは JMPR においては評価されていない。

食品安全委員会の「残留農薬の食品健康影響評価における公表文献の取扱いについて」に基づき、ヒトに対する毒性に関する文献につき、疫学研究に関する文献 4 件と疫学以外に関する文献 3 件を検討対象として選抜し、「食品安全委員会フォーマット表」として別添した。

別添１

No.	文献名	ジャーナル名等	公表年	著者	著者の所属機関	書誌情報	研究分野	原著/総説	海外評価書での引用の有無	ドシエでの引用の有無	*in vivo* (動物種) / *in vitro*	用量 (mg/kg体重又はg/kg体重/日)	NOAEL /NOEL	LOEAL /LOEL	Klimisch コード	評価の目的との適合性に関する情報	備考
744	Assessment of genetic effects and pesticide exposure of farmers in NW Greece	ENVIRONMENTAL RESEARCH 186	2020	Moshou, H, et al.	University of Patras, Greece	http://dx.doi.org/10.1016/j.envres.2020.109558	遺伝	原著	無	無	*in vitro*	–	–	–	–	複数農薬へのばく露に関する研究であり、メトラクロール単体の毒性データを含まない。	農薬混合物への職業的暴露の遺伝毒性学的影響
804	Characterisation of (anti-)progestogenic and (anti-)androgenic activities in surface and wastewater using high resolution effectdirected analysis	ENVIRONMENT INTERNATIONAL 153	2021	Houtman, CJ, et al.	The Water Laboratory, the Netherlands	http://dx.doi.org/10.1016/j.envint.2021.106536	生殖発生	原著	無	無	*in vitro*	–	–	–	–	食品健康影響評価に利用可能なデータを含まない。	環境水中の農薬等の物質がホルモン活性に与える影響と環境モニタリング調査。 抗エストロゲン、アンドロゲン活性に寄与すると同定。
892	A tiered approach to prioritizing registered pesticides for potential cancer hazard evaluations: implications for decision making	ENVIRONMENTAL HEALTH 20 1	2021	Schwingl, PJ, et al.	National Institute of Environmental Health Sciences, USA	http://dx.doi.org/10.1186/s12940-021-00696-0	発がん性	総説	無	無	–	–	–	–	–	新たな実験データを含まない総説。	代表的な農薬20種類の発がん性への関与に関する総説。

No.	文献名	ジャーナル名等	公表年	著者名	著者の所属機関	書誌情報	原著/総説	海外評価書での引用の有無	ドシエでの引用の有無	備考
185	Cancer incidence and metolachlor use in the Agricultural Health Study: An update	INTERNATIONAL JOURNAL OF CANCER 137 11 pp2630-2643	2015	Silver, SR, et al.	National Institute for Occupational Safety and Health, USA	https://doi.org/10.1002/ijc.29621	原著	EFSA Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted Rev. 0 - 06 September 2018	無	
454	Maternal residential exposure to specific agricultural pesticide active ingredients and birth defects in a 2003-2005 North Carolina birth cohort	BIRTH DEFECTS RESEARCH 111 6 pp312-323	2019	Rappazzo, KM, et al.	US Environmental Protection Agency	https://doi.org/10.1002/bdr2.1448	原著	無	無	
716	Pesticide use and incident hyperthyroidism in farmers in the Agricultural Health Study	OCCUPATIONAL AND ENVIRONMENTAL MEDICINE 76 5 pp332-335	2019	Shrestha, S, et al.	National Institute of Environmental Health Sciences	https://doi.org/10.1136/oemed-2018-105518	原著	EPA2019 Metolachlor and S-Metolachlor: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment	無	
811	Pesticide use and risk of end-stage renal disease among licensed pesticide applicators in the Agricultural Health Study	OCCUPATIONAL AND ENVIRONMENTAL MEDICINE 73 1 pp3-12	2016	Lebov, JF, et al.	Univ. of North Carolina at Chapel Hill	https://doi.org/10.1136/oemed-2014-102615	原著	EFSA Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted Rev. 0 - 06 September 2018	無	

			研究デザイン								健康関連の事象の情報								
No.	文献名	著者名	国名（地域名、研究名）	試験設計	調査時期	対象者、年齢	アウトカムの定義	アウトカムの確認方法	ばく露指標の定義	ばく露の確認方法	試験全体のN数（症例/対照）	アウトカムのN数（症例）	分析カテゴリー	ばく露に係るN数（症例/対照）	相対リスク/オッズ比等	95%信頼区間	p値	交絡因子の考慮	備考
185	Cancer incidence and metolachlor use in the Agricultural Health Study: An update	Silver, SR	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2011	農薬散布免許取得者	がん発症	各州がん登録/死亡記録及び国民死亡指標（National Death Index）とのデータ照合	当該農薬の使用実態	アンケート	49,580	–	散布経験	–	–	–	–	年齢、喫煙状況、飲酒状況、家族の発がん履歴、散布業者/個人散布の別、州	農薬暴露と各種がんの関連に関する調査。
454	Maternal residential exposure to specific agricultural pesticide active ingredients and birth defects in a 2003-2005 North Carolina birth cohort	Rappazzo, KM	米国ノースカロライナ州	コホート研究	2003-2005	単生児	出生時異常	州の出生時異常モニタリングプログラムとのデータ照合	妊娠初期の居住地での農薬散布記録	州の農薬散布記録と妊娠初期の母親の住所を照合	302,460	1,286	居住地の散布履歴	89,786	–	–	–	母親の 人種、学歴、婚姻状況、喫煙状況	農薬暴露と出生時異常の関連に関する調査。
716	Pesticide use and incident hyperthyroidism in farmers in the Agricultural Health Study	Shrestha, S	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2016	農薬散布免許取得者	甲状腺機能亢進症発症	インタビュー（医師による診断歴を自己申告）	当該農薬の使用実態	アンケート	35,150	1,100	散布経験	–	–	–	–	性別、学歴、飲酒状況	農薬暴露と甲状腺機能異常の関連に関する調査。
811	Pesticide use and risk of end-stage renal disease among licensed pesticide applicators in the Agricultural Health Study	Lebov, JF	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2011	男性農薬散布免許取得者	重症の腎臓病	アンケートによる自己申告（医師の診断）	当該農薬の使用実態	アンケート	22,922	38 38 40	散布経験	9,244 7,195 6,483	ハザード比 1.02 1.39 1.53	0.71-1.47 0.96-1.49 1.08-1.49	–	年齢、州	農薬暴露と重症腎臓病の関連に関する調査。

	評価書名	書誌情報、発行部署名、発行日等の評価書に付随する情報	入手先	備考
EFSA01	Review of the existing maximum residue levels (MRLs) for S-metolachlor according to Article 12 of Regulation (EC) No 396/20051	EFSA Journal 2012;10(2):2586	https://www.efsa.europa.eu/en/efsajournal/pub/2586	S-メトラクロールの残留に関する評価
EFSA02	Renewal Assessment Report S-Metolachlor Volume 2 List of the tests, studies and information submitted	EFSA Journal APPROVED: 27 January 2023 doi: 10.2903/j.efsa.2023.7852中の再評価で利用された引用文献すべてを収集	https://www.efsa.europa.eu/en/consultations/call/181129-1	EU-再評価幹事国評価書
EFSA03	Peer review of the pesticide risk assessment of the active substance S-metolachlor excluding the assessment of the endocrine disrupting properties	EFSA JournalVolume 21, Issue 2 e07852	Peer review of the pesticide risk assessment of the active substance S - metolachlor excluding the assessment of the endocrine disrupting properties (wiley.com)	内分泌かく乱特性の評価を除く、有効成分 S-メトラクロールの農薬リスク評価のピアレビュー
USEPA01	Metolachlor	Health Advisdry Office of Drinking Water U.S. Environmental Protection Agency August 1987	https://nepis.epa.gov/Exe/ZyPDF.cgi/2000SP8V.PDF?Dockey=2000SP8V.PDF	EPA飲料水中のメトラクロールの健康評価
USEPA02	GUIDANCE FOR THE REREGISTRATION OF PESTICIDE PRODUCTS CONTAINING AS THE ACTIVE INGREDIENT METOLACHLOR	U.S. ENVIRONMENTAL PROTECTION AGENCY OFFICE OF PESTICIDE PROGRAMS WASHINGTON, D.C. 20460 JANUARY 1987	https://nepis.epa.gov/Exe/ZyPDF.cgi/91012W2Z.PDF?Dockey=91012W2Z.PDF	EPAメトラクロール登録のガイダンス 1987年Review
USEPA03	Reregistration Eligibility Decision (RED) Metolachlor	EPA 738-R-95-006 April 1995	https://archive.epa.gov/pesticides/reregistration/web/pdf/0001.pdf	EPAのメトラクロール再登録の適格性決定書　人体、環境に対するリスク評価を含む
USEPA04	R.E.D. FACTS Metolachlor	EPA-738-F-95-007 April 1995	https://www3.epa.gov/pesticides/chem_search/reg_actions/reregistration/fs_PC-108801_1-Apr-95.pdf	EPAのメトラクロール　FactSheet
USEPA05	Toxicology Chapter for Metolachlor/S-Metolachlor	UNITED STATES ENVIRONMENTAL PROTECTION AGENCY WASHINGTON, D.C. 20460 Office of Prevention, Pesticides and Toxic Substances Jan 2002	https://www3.epa.gov/pesticides/endanger/litstatus/effects/redleg-frog/2010/metolachlor-s/appendix-j1.pdf	EPAのメトラクロールおよびS-メトラクロールの毒性評価
USEPA06	SECONDARY VALUES FOR METOLACHLOR (CAS No. 51218-45-2)	Date: May 1, 2003 Calculator: Elisabeth Harrahy, Ph.D.	https://www.epa.gov/sites/default/files/2015-06/documents/wi_282_05012003.pdf	メトラクロールの毒性、環境毒性に関するデータの集積
USEPA07	Regulatory Determinations Support Document for Selected Contaminants from the Second Drinking Water Contaminant Candidate List (CCL 2) Part III: What About the Remaining CCL 2 Contaminants?	EPA – OGWDW Regulatory Determinations Support Document for CCL 2 June 2008	https://www.epa.gov/sites/default/files/2014-09/documents/report_ccl2-reg2_supportdocument_full.pdf	メトラクロールの環境動態と健康影響に関する文書を含む文書
USEPA08	Registration Review Problem Formulation for Metolachlor and S-Metolachlor	Date: December 3, 2014 DP Barcode: 420467	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0002	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA09	Metolachlor: Tier 1 Review of Human Incidents	Date: September 16, 2014 DP Barcode: D420801	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0004	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA10	EDSP Weight of Evidence Conclusions on the Tier 1 Screening Assays for the List 1 Chemicals	Date: June 29, 2015 DP Barcode: NA	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0022	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA11	Response to Public Comments on the EFED Registration Review Problem Formulation for Metolachlor and S-Metolachlor	Date: May 8, 2015 DP Barcode: D426907	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0020	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA12	BEAD Response to Public Comments in Support of Registration Review (EPA Docket ID No.: EPA-HQ-OPP-2014-0772)-Metolachlor Case [S-metolachlor (108800) and Metolachlor (108801)]	Date: MAY 21 2015	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0018	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA13	Metolachlor/S-metolachlor: Report of the Cancer Assessment Review Committee (5th Evaluation)	DATE: 11/6/2017 Decision No.: 518226	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0026	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA14	Region 4 Ecological Risk Assessment Supplemental Guidance	Supplemental Guidance to ERAGS: Region 4, Ecological Risk Assessment. Originally published November 1995 and updated March 2018 Region 4 Risk Assessment Resources	https://www.epa.gov/risk/regional-ecological-risk-assessment-era-supplemental-guidance	環境リスクアセスメントについての補足的ガイダンス
USEPA15	Metolachlor & S-metolachlor: Drinking Water Exposure Assessment for Registration Review	Date: October 31, 2018 DP Barcode: 448964	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0029	Metolachlor and S-Metolachlor Registration Review ドケット内文書

USEPA16	Metolachlor and S-Metolachlor: Tier I Update Review of Human Incidents and Epidemiology for Draft Risk Assessment	Date: September 12, 2019 DP Barcode: D452762	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0032	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA17	Metolachlor/S-Metolachlor: Draft Ecological Risk Assessment for Registration Review	Date: September 19, 2019 DP Barcodes: 448940	https://www.regulations.gov/document/EPA-HQ-OPP-2014-0772-0028	Metolachlor and S-Metolachlor Registration Review ドケット内文書
USEPA18	MetolachlorS-Metolachlor Draft Human Health Risk Assessment for Registration Review	Date: January 10, 2020	https://www.regulations.gov/comment/EPA-HQ-OPP-2014-0772-0033	Metolachlor and S-Metolachlor Registration Review ドケット内文書

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282	Curwin, B. D., Hein, M. J., Sanderson, W. T., Nishioka, M.G., Reynolds, S. J., Ward, E. M., & Alavanja, M. C.	2005	Pesticide contamination inside farm and nonfarm homes.	J Occup Environ Hyg, 2(7), 357-367. doi: 10.1080/15459620591001606	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	123と重複
283	Dennis, L. K., Lynch, C. F., Sandler, D. P., & Alavanja, M. C.	2010	Pesticide use and cutaneous melanoma in pesticide applicators in the agricultural heath study.	Environ Health Perspect, 118(6), 812-817. doi: 10.1289/ehp.0901518	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	
284	Engel, L. S., Hill, D. A., Hoppin, J. A., Lubin, J. H., Lynch, C. F., Pierce, J., ... Alavanja, M. C.	2005	Pesticide use and breast cancer risk among farmers' wives in the agricultural health study.	Am J Epidemiol, 161(2), 121-135. doi: 161/2/121 [pii] 10.1093/aje/kwi022	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	
285	Hou, L., Andreotti, G., Baccarelli, A. A., Savage, S., Hoppin, J. A., Sandler, D.P., ... Alavanja, M. C.	2013	Lifetime Pesticide Use and Telomere Shortening among Male Pesticide Applicators in the Agricultural Health Study.	Environ Health Perspect. doi: 10.1289/ehp.1206432	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	136と重複
286	Koutros, S., Beane Freeman, L. E., Lubin, J. H., Heltshe, S. L., Andreotti, G., Barry, K. H., ... Alavanja, M. C.	2013	Risk of total and aggressive prostate cancer and pesticide use in the Agricultural Health Study.	Am J Epidemiol, 177(1), 59-74. doi: 10.1093/aje/kws225	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	

287	Lee, W. J., Sandler, D. P., Blair, A., Samanic, C., Cross, A. J., & Alavanja, M. C. R.	2007	Pesticide use and colorectal cancer risk in the Agricultural Health Study.	International Journal of Cancer, 121(2), 339-346. doi: 10.1002/ijc.22635	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	143と重複
288	Rusiecki, J. A., Hou, L., Lee, W. J., Blair, A., Dosemeci, M., Lubin, J. H., … Alavanja, M. C.	2006	Cancer incidence among pesticide applicators exposed to metolachlor in the Agricultural Health Study.	Int J Cancer, 118(12), 3118-3123. doi: 10.1002/ijc.21758	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	150と重複
289	Slager, R. E., Poole, J. A., LeVan, T. D., Sandler, D.P., Alavanja, M. C. R., & Hoppin, J. A.	2009	Rhinitis associated with pesticide exposure among commercial pesticide applicators in the Agricultural Health Study.	Occupational and Environmental Medicine, 66(11), 718-724. doi:10.1136/oem.2008.041798	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	154と重複
290	Slager, R. E., Simpson, S. L., Levan, T. D., Poole, J. A., Sandier, D.P., & Hoppin, J. A.	2010	Rhinitis associated with pesticide use among private pesticide applicators in the agricultural health study.	J Toxicol Environ Health A, 73(20), 1382-1393. doi: 10.1080/15287394.2010.497443	EPA	EPA-HQ-OPP-2014-0772-0004 (2014) Metolachlor: Tier I Review of Human Incidents.	155と重複
291	Mathias FT, Romano RM, Sleiman HK, de Oliveira CA, Romano MA.	2012	Herbicide metolachlor causes changes in reproductive endocrinology of male Wistar rats.	Toxicol. 2012:130846. doi: 10.5402/2012/130846	EPA	EPA-HQ-OPP-2014-0772-0033 (2014) Comment submitted by Olga Naidenko, Vice President, Science Investigations, Environmental Working Group (EWG)	87と重複
292	Quintaneiro C, Patrício D, Novais SC, Soares AMVM, Monteiro MS.	2017	Endocrine and physiological effects of linuron and S-metolachlor in zebrafish developing embryos.	Sci Total Environ. 586:390-400. doi: 10.1016/j.scitotenv.2016.11.153	EPA	EPA-HQ-OPP-2014-0772-0033 (2014) Comment submitted by Olga Naidenko, Vice President, Science Investigations, Environmental Working Group (EWG)	
293	Shaner DL, Brunk G, Belles D, Westra P, and Nissen P. 2006.	2006	Soil Dissipation and Biological Activity of Metolachlor and S-metolachlor in Five Soils.	Pesticide Management Science 62: 617-623.	EPA	EPA-HQ-OPP-2014-0772-0018 (2015) BEAD Response to Public Comments in Support of Registration Review-Metolachlor Case and Metolachlor	

No.	文献名	ジャーナル名等	公表年	著者名	著者の所属機関	書誌情報	研究分野	原著/総説	海外評価書での引用の有無	ドシエでの引用の有無	*in vivo*（動物種）/ *in vitro*	用量（mg/kg体重又はg/kg体重/日）	NOAEL/NOEL	LOEAL/LOEL	Klimischコード	評価の目的との適合性に関する情報	備考
61	An evaluation of the genotoxic properties of herbicides following plant and animal activation.	Mutation Research/Genetic Toxicology 136 (3) 233-245 1984 Published: Y TOX9652116, BVL 2851224	1984	Plewa, M. J., et al.	Univ. of Illinois at Urbana, etc.	https://doi.org/10.1016/0165-1218(84)90057-0	遺伝	原著	○ EFSA 2018年	無	in vitro （ラット肝細胞）	-	-	-	-	-	b 植物酵素及び動物酵素での活性化した後の農薬代謝物に関する遺伝毒性の調査。 メトラクロール単独、及び他の農薬との混合物で毒性が確認された。
62	Cytogenetic effects of cyanazine and metolachlor on human lymphocytes exposed in vitro	Mutation Research Letters 281 (4) 295-298 1992 Published: Y ASB2015-10979, BVL 2851227	1992	Roloff, B., et al.	Univ. of Wisconsin, etc.	https://doi.org/10.1016/0165-7992(92)90024-C	遺伝	原著	○ EFSA 2018年	無	in vitro （ヒト リンパ球）	0.01,0.1,1μg/ml	-	-	-	-	b 農薬によるヒトリンパ球クロモソーム損傷に関する調査。
63	Dialkylquinoneimine metabolites of chloroacetanilide herbicides induce sister chromatid exchanges in cultured human lymphocytes	Mutation Research - Genetic Toxicology and Environmental Mutagenesis 395 (2-3) 159-171 1997 Published: Y TOX2002-925, BVL 2851202	1997	Hill, A. B., et al.	Univ. of California, etc.	https://doi.org/10.1016/S1383-5718(97)00163-0	生殖発生	原著	○ EFSA 2018年	無	in vitro （ヒト リンパ球）	10μM	-	-	-	-	b 農薬代謝物がヒトリンパ球の姉妹染色分体交換に与える影響を調査。 クロロアセトアニリド系農薬の代謝物の遺伝毒性が示唆された。
64	In vitro transformation of chloroacetanilide herbicides by rat liver enzymes: A comparative study of Metolachlor and Alachlor	J. Agric. Food Chem. 37 (4) 1088-1093 1989 Published: Y Z72454, BVL 2851194	1989	Feng, P. C. C., et al.	Monsant Agricultural Company, etc.	https://pubs.acs.org/doi/pdf/10.1021/jf00088a060	代謝	原著	○ EFSA 2018年	無	in vitro （ラット肝細胞）	0.05μmol/ml	-	-	-	-	b アラクロールとメトラクロールについて、ラット肝臓酵素の活性を比較調査。
65	Comparative metabolism and elimination of acetanilide compounds by rat	Xenobiotica 24 (10) 1003-1012 1994 Published: Y ASB2015-10972, BVL 2851177	1994	Davison, K. L., et al.	US Dept. of Agriculture, etc.	https://doi.org/10.3109/00498259409043297	代謝	原著	○ EFSA 2018年	無	in vivo ラット	2μmol/個体（271g-440g）	-	-	-	-	b 農薬代謝物の動物体内からの排出に関する研究。 主にメルプツール結合体として胆汁及び尿中に排出されることが示された。
66	Formamidine insecticides and chloroacetanilide herbicides: Disubstituted anilines and nitrosobenzenes as mammalian metabolites and bacterial mutagens	Journal of Agricultural and Food Chemis- try 34 (2) 157-161 1986 Published: Y ASB2015-10974, BVL 2851195	1994	Kimmel, E. C., et al.	Univ. of California, etc.	https://pubs.acs.org/doi/pdf/10.1021/jf00068a002	代謝	原著	○ EFSA 2018年	無	in vivo ラット	250mg/kg体重	-	-	-	-	b ラットの肝抽出物による農薬代謝物の同定と、その遺伝毒性を調査。 水酸基／ニトロソ基代謝物がメトラクロールの毒性に関与していると示唆された。
68	Dialkylquinonimines validated as in vivo metabolites of alachlor, acetochlor and metolachlor herbicides in rats	Chemical Research in Toxicology 11 (4) 353-359 1998 Published: Y ASB2015-10971, BVL 2851201	1998	Jeffries, P. R., et al.	Univ. of California, etc.	https://doi.org/10.1021/tx970209z	代謝	原著	○ EFSA 2018年	無	in vivo ラット	0.74mmol/kg	-	-	-	-	b 6種類の農薬のin vivoでの代謝物質の特定。 メトラクロールの代謝物はキノンイミンであることが示された。
71	Preliminary analysis of an aquatic toxicitydataset and assessment of QSAR modelsfor narcosis EUR 21749 EN EC, 2005 Published: Y ASB2016-838, BVL 3288494	Joint Research Centre's Publications	2005	Pavan, M., et al.	EC Institute for Health and Consumer Protection, etc.	https://publications.jrc.ec.europa.eu/repository/handle/JRC31399	一般毒性	原著	○ EFSA 2018年	無	-	-	-	-	-	-	メトラクロールと関係しない。
72	A QSAR, pharmacokinetic and toxicologi-cal study of new artemisinin compoundswith anticancer activity	Molecules 2014, 19, 10670-10697; doi:10.3390/molecules190810670 2014 Published: Y ASB2016-839, BVL 3288513	2014	Vieira, J. B., et al.	Federal Univ. of Amapa, Brazil, etc.	https://doi.org/10.3390/molecules190810670	発がん性	原著	○ EFSA 2018年	無	-	-	-	-	-	-	C QSAR手法による毒性予測法の開発。
73	Study on the biochemical characterization of herbicide detoxification enzyme, glutathione S-transferase.	BioFactors 30(4): 281-287. Published. ASB2018-2558	2007	Cho, H. Y., et al.	Chung-Ang Univ. Korea, etc.	https://doi.org/10.1002/biof.5520300410	代謝	原著	○ EFSA 2018年	無	in vitro（ヒト及びイネ）	-	-	-	-	-	c イネ及びヒトのGST酵素の、７種類の農薬に対する解毒活性に関する研究。 GST酵素がこれの農薬への特異性を持つこと、植物体内での無毒化に大きな役割を果たしていることが示された。
74	Comparative metabolism of chloroacetamide herbicides and selected metabolites in human and rat liver microsomes.	Environmental Health Perspectives 108(12): 1151-1157. Published. ASB2018-2559	2000	Coleman, S., et al.	North Carolina State Univ., etc.	https://doi.org/10.1289/ehp.001081151	代謝	原著	○ EFSA 2018年	無	in vitro（ヒト及びラット）	50μM	-	-	-	-	c ヒト及びラットのミクロソームによる農薬の代謝に関する研究。 メトラクロールのヒト体内での代謝にはCYP3A4とCYP2B6の2つのP450シトクロームが関わっていることが見いだされた。
75	Metabolism of herbicides and other chemicals in human cytochrome P450 species and in transgenic potato plants Coexpressing human CYP1A1, CYP2B6 and CYP2C19.	Journal of Pesticide Sciences 26(1): 28-40. Published. ASB2018-2560	2001	Inui, H., et al.	神戸大学	https://doi.org/10.1584/jpestics.26.28	代謝	原著	○ EFSA 2018年	無	in vitro（ヒト）	100μM	-	-	-	-	c 11種類のヒトシトクロームP450による27種類の農薬の代謝の比較研究。 ヒトのシトクロームP450を発現させた遺伝子組み換え植物により、農薬残留を低減させられる可能性を示し
77	Comparative cytotoxicity of alachlor, acetochlor, and metolachlor herbicides in isolated rat and cryopreserved human hepatocytes.	Journal of Biochemical and Molecular Toxicology 22(1): 41-50. Published. ASB2018-2562	2008	Kale, V. M., et al.	Univ. Luisiana at Monroe, etc.	https://doi.org/10.1002/jbt.20213	遺伝	原著	○ EFSA 2018年	無	in vitro（ヒト及びラット）	100,200,400,800,1600μM	-	-	-	-	b ヒト及びラットの肝細胞に対する3種類の農薬の影響比較。 ラットの肝細胞ではメトラクロールの活性はアセトクロール及びアラクロールと異なるが、ヒト肝細胞の場合は3者の活性が同様であることが示された。
78	Structural elucidation of metolachlor photoproducts by liquid chromatography/high-resolution tandem mass spectrometry.	Rapid Commun Mass Spectrom 29(23): 2279-2286. Published. ASB2018-2825	2015	Nicol, E., et al.	Ecole Polytechnique, France	https://doi.org/10.1002/rcm.7382	一般毒性	原著	○ EFSA 2018年	無	-	-	-	-	-	-	メトラクロール代謝物に関するドライラボ研究
79	In vitro and in vivo studies demonstrate non-mutagenicity of the herbicide metolachlor.	Brazilian Journal of Genetics 20(3): 411- 414. Published. ASB2018-2826	1997	Grisolia, C. K. Ferrari, I.	Univ. de Brazillia, Brazil	https://doi.org/10.1590/S0100-84551997000300009	遺伝	原著	○ EFSA 2018年	無	in vivo（マウス） in vitro（ヒトリンパ球）	10,20,40mg/kg体重（マウス） 0.5,1.0,2.0mg/ml（ヒトリンパ球）	-	-	-	-	b ヒトリンパ球及びマウスに対する変異原性に関する研究。 メトラクロルによる染色体異常誘発性の兆候は見られなかった。
80	Analyses of cytogenetic damage in rodents following exposure to simulated groundwater contaminated with pesticides and a fertilizer.	Mutation Research/Genetic Toxicology 300(2): 125-134. Published. ASB2018- 2827	1993	Kligerman, A. D., et al.	US Environmental Protection Agency	https://doi.org/10.1016/0165-1218(93)90130-6	一般毒性	原著	○ EFSA 2018年	無	in vivo（マウス及びラット）	-	-	-	-	-	複数の農薬／肥料の混合製剤の毒性に関する研究。

81	Comparative study of cytotoxic and genotoxic effects induced by herbicide Smetolachlor and its commercial formulation twin pack gold® in human hepatoma (HepG2)	Food and Chemical Toxicology 62: 777- 781. Published. ASB2018-2828	2013	Nikoloff, N., et al.	Univ. Nacional de La Plata, Argentina	https://doi.org/10.1016/j.fct.2013.10.015	遺伝	原著	○ EFSA 2018年	無	in vitro（ヒト肝がん細胞）	-	-	-	-	-	b メトラクロールの原体と製剤との間の、細胞毒性および遺伝毒性の比較調査。
82	Effects of pesticide mixtures at the acceptable daily intake levels on rat carcinogenesis.	Food and Chemical Toxicology 34(11-12): 1091-1096. Published. ASB2018-	1996	Ito, N., et al.	名古屋市立大学 他	https://doi.org/10.1016/S0278-6915(97)00079-3	発がん性	原著	○ EFSA 2018年	無	in vivo（マウス）	-	-	-	-	-	複数農薬の混合剤の毒性に関する研究。
83	Medium-term bioassays for carcinogenicity of chemical mixtures.	Environ Health Perspect 106(Suppl 6): 1331-1336. Published. ASB2018-2830	1998	Ito, N., et al.	名古屋市立大学	https://doi.org/10.1289/ehp.98106s61331	発がん性	原著	○ EFSA 2018年	無	in vivo（マウス）	-	-	-	-	-	複数農薬の混合剤の毒性に関する研究。
84	Pesticider/Fertilizer Mix III (Iowa)	Environ Health Perspect 105(Suppl 1): 375-376. Published. ASB2018-2831	1997	Jerrold J. Jeindel, et al.	Research Triangle Inst., NC, etc.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1470272/pdf/envhper00326-0368.pdf	一般毒性	原著	○ EFSA 2018年	無	in vivo（マウス）	-	-	-	-	-	複数農薬の混合剤の毒性に関する研究。
85	Low-dose agrochemicals and lawn-care pesticides induce developmental toxicity in murine preimplantation embryos.	Environmental Health Perspectives 112(6): 703-709. Published. ASB2016-9889	2004	Greenlee, A. R., et al.	Marshfield Clinic Research Foundation, Wisconcin, etc.	https://doi.org/10.1289/ehp.6774	生殖発生	原著	○ EFSA 2018年	無	in vitro（マウス着床前胚）	0.1μg/mL	-	-	-	-	b マウス着床前胚に対する24種の農薬/混合剤の毒性の研究。 農薬による損傷は発生の最初期に生じることが示された。
86	Assessment of the reproductive and developmental toxicity of pesticide/fertilizer mixtures based on confirmed pesticide contamination in California and Iowa groundwater.	Fundamental and Applied Toxicology 22(4): 605-621. Published. TOX9552727	1994	Heindel, J. J., et al.	Nat'l Inst. of Environmental Sciences,etc.	https://doi.org/10.1006/faat.1994.1067	生殖発生	原著	○ EFSA 2018年	無	in vivo（マウス）	0.07,0.78,7.6μg/kg体重/日	-	-	-	-	複数農薬の混合剤の毒性に関する研究
87	Herbicide metolachlor causes changes in reproductive endocrinology of male wistar rats. ISRN	Toxicol 2012: 130846. Published. ASB2016-9890	2012	Mathias, F. T., et al.	State Univ. of Centro-Oeste, Brazil, etc.	https://doi.org/10.5402/2012/130846	生殖発生	原著	○ EFSA 2018年	無	in vivo（マウス）	5 mg/kg/日 50 mg/kg/日	-	-	-	-	b 思春期前の雄マウスへの、メトラクロールの影響に関する研究。 メトラクロールにより、テストステロン、エストラディオル及びFSHの増加とDHTの減少が見られた。
88	Maternal and fetal toxicity of Wistar rats exposed to herbicide metolachlor.	Acta Scientiarum - Biological Sciences 38(1): 91-98. Published. ASB2016-9891	2016	Vieira, K. C. M. T., et al.	Univ. do Oeste Paulista, Brazil, etc.	https://doi.org/10.4025/actascibiolsci.v38i1.29079	生殖発生	原著	○ EFSA 2018年	無	in vivo（ラット）	150,300,1000mg/kg体重/日	-	-	-	-	b ラット胚に対するメトラクロールの催奇形性の研究。 メトラクロールへの暴露により、胚の消失や先天異常が生じる可能性が示唆された。
89	The herbicide metolachlor induces liver cytochrome P450s 2B1/2 and 3A1/2, but not thyroxine-uridine dinucleotide phosphate glucuronosyltransferase and associated thyroid gland activity.	International Journal of Toxicology 22(4): 287-295. Published. ASB2018-2832	2003	Dalton, S. R., et al.	North Carolina State Univ., etc.	https://doi.org/10.1080/10915810305121	代謝	原著	○ EFSA 2018年	無	in vivo（ラット）	3000ppm	-	-	-	-	b ラットに対する、メトラクロールと催眠剤フェノバルビタールの影響の比較研究。 メトラクロールはシトクロームCYP2B1を活性化することが示された。
90	Glutathione-dependent cytotoxicity of the chloroacetanilide herbicides alachlor, metolachlor, and propachlor in rat and human hepatoma-derived cultured cells.	Cell Biology and Toxicology 15(5): 325- 332. Published. ASB2018-2833	1999	Dierickx, P. J.	Inst. voor Volksgezondheid, Belgium, etc.	https://doi.org/10.1023/A:1007619919336	代謝	原著	○ EFSA 2018年	無	in vitro （ヒト肝がん細胞及びラット肝がん細胞）	100μmol/L（ヒト） 50μmol/L（ラット）	-	-	-	-	b ヒト及びラットの肝細胞に対する3種類の農薬の影響比較。 ヒト肝細胞とラット肝細胞の間の活性の差異が見られた。
91	Activation of soluble glutathione transferase in rat hepatoma-derived Fa32 cells by several pesticides and oxidants	Chemico-Biological Interactions 133(1-3): 342-344. Published. ASB2018-	2001	Dierickx, P. J.	Wetenschappelijk Inst. voor Volksgezondheid, Belgium, etc.	https://doi.org/10.1016/S0009-2797(00)00216-7	代謝	原著	○ EFSA 2018年	無	in vitro （ラット肝がん細胞）	-	-	-	-	-	c ラット肝細胞に対する3種類の農薬の影響比較。 （要旨のみ）
92	Cellular effects of metolachlor exposure on human liver (HepG2) cells.	Chemosphere 90(3): 1258-1266. Published. ASB2018-2835	2013	Hartnett, S., et al.	Univ. of Northern Iowa, etc.	https://doi.org/10.1016/j.chemosphere.2012.09.077	代謝	原著	○ EFSA 2018年	無	in vitro（ヒト肝細胞）	50,100,300,500ppb/日	-	-	-	-	b ヒト肝細胞に対するメトラクロールの影響調査。 メトラクロールは細胞周期のS期、及びS期からG2期への移行時に影響していると見られる。
93	Screening for estrogen and androgen receptor activities in 200 pesticides by in vitro reporter gene assays using Chinese hamster ovary cells.	Environ Health Perspect 112(5): 524-531. Published. ASB2010-14389	2004	Kojima, H., et al.	北海道立衛生研究所	https://doi.org/10.1289/ehp.6649	代謝	原著	○ EFSA 2018年	無	in vitro（ハムスター卵巣細胞）	<10^{-5}M	-	-	-	-	c 200種類の農薬（異性体や代謝物を含む）に対するハムスター卵巣細胞のエストロゲン及びアンドロゲン活性に関する研究。
94	Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line.	Toxicology 228(1): 98-108. Published. ASB2010-14391	2006	Laville, N., et al.	Institut national de l' environnement industriel et des risques, etc., France, etc.	https://doi.org/10.1016/j.tox.2006.08.021	代謝	原著	○ EFSA 2018年	無	in vitro（ヒト絨毛がん細胞）	10μM	-	-	-	-	b 30種類の農薬がアロマターゼ酵素の活性に与える影響に関する研究。 メトラクロールによる同酵素の活性向上が認められ
95	Identification of new human pregnane X receptor ligands among pesticides using a stable reporter cell system.	Toxicological Sciences 91(2): 501-509. Published. ASB2008-2129	2006	Lemaire, G., et al.	Institut national de l' environnement industriel et des risques, France, etc.	https://doi.org/10.1093/toxsci/kfj173	代謝	原著	○ EFSA 2018年	無	in vitro（ヒト子宮頸がん由来細胞 HeLa Cell）	10μM	-	-	-	-	b 28種類の農薬がヒトのプレグナンX受容体に与える影響を調査。
96	Mechanism of metolachlor action due to alterations in cell cycle progression."	Cell Biology and Toxicology 29(4): 283-291. Published. ASB2018-2836	2013	Lowry, D. M., et al.	Univ. of Northern Iowa, etc.	https://doi.org/10.1007/s10565-013-9256-z	一般毒性	原著	○ EFSA 2018年	無	in vitro（ヒト肝がん由来細胞 HepG2）	100,300,500,1000ppb	-	-	-	-	b メトラクロールがヒト肝がん由来細胞に与える影響を調査。 細胞数の減少は、細胞死の誘発ではなく細胞分裂の抑制により引き起こされていることが示唆された。
97	Specific interactions of chloroacetanilide herbicides with human ABC transporter proteins.	Toxicology 248(1): 45-51. Published. ASB2018-2837	2008	Oosterhuis, B., et al.	SOLVO Biotechnology, Hungary, etc.	https://doi.org/10.1016/j.tox.2008.03.003	一般毒性	原著	○ EFSA 2018年	無	in vitro（ヒト結腸がん由来細胞 Caco-2）	5,10,50,100,500,1000μM	-	-	-	-	b 7種類の農薬がABCトランスポーターに与える影響を研究。 メトラクロールはMDR1の基質として働き、細胞の対毒物感度を高めることが示された。
98	Toxicity assessment of the herbicide metolachlor comparative effects on bacterial and mitochondrial model systems.	Toxicology in Vitro 23(8): 1585-1590. Published. ASB2018-2838	2009	Pereira, S. P., et al.	Coimbra Univ., Portugal, etc.	https://doi.org/10.1016/j.tiv.2009.06.032	一般毒性	原著	○ EFSA 2018年	無	in vitro（ラット肝ミトコンドリア及び細菌 Bacillus stearothermophilus）	100,200,300,400,500,600μM（B. stearothermophilus） 400,600,800,1000nmol/mgタンパク質重（ラット肝ミトコンドリア）	-	-	-	-	b メトラクロールのラット肝ミトコンドリアと耐熱性菌への影響を調査。 他の農薬に比べて安全性が高いことが示唆された。
99	Profiling 976 ToxCast Chemicals across 331 Enzymatic and Receptor Signaling Assays. Chem Res Toxicol 26(6): 878-895. Published. ASB2014-8448	Environ Health Perspect 103(Suppl 7): 113-122. Published. ASB2018-2839	2013	Sipes, N. S., et al.	US Environmental Protection Agency, etc.	https://doi.org/10.1021/tx400021f	一般毒性	原著	○ EFSA 2018年	無	in vitro	10μM／25μM	-	-	-	-	c 976種類の化学物質にそれぞれ331種類の生化学的試験を行い、クラスター分析を実施。
100	The E-SCREEN assay as a tool to identify estrogens: an update on estrogenic environmental pollutants.	Environmental Science and Technology 50(1): 435-443. Published. ASB2018-2840	1995	Soto, A. M., et al.	Tufts Univ., etc.	https://doi.org/10.1289/ehp.95103s7113	一般毒性	原著	○ EFSA 2018年	無	in vitro（ヒト乳がん由来細胞 MCF-7）	10mM	-	-	-	-	b 多数の化学物質に対し、エストロゲン特性の有無をスクリーニング調査。 メトラクロールにはエストロゲン特性はなかった。

101	Endocrine-Disrupting Effects of Pesticides through Interference with Human Glucocorticoid Receptor.	Environ. Sci. Technol. 2016, 50, 1, 435-443	2016	Zhang, J., et al.	浙江大学（中国）他	https://doi.org/10.1021/acs.est.5b03731	代謝	原著	○ EFSA 2018年	無	in vitro（ヒトGRαプラスミド組込マウス）	10^{-5}M	-	-	-	-	b 34種類の農薬に対し、ヒト糖質コルチコイド受容体との作動／拮抗活性を調査。 メトラクロールには作動活性も拮抗活性もなかった。
260	IPCS framework for analyzing the relevance of a cancer mode of action for humans.	Crit. Rev. Toxicol. 36: 781-792.	2006	Boobis, A., R. et al.	Imperial College London, UK, etc.	https://doi.org/10.1080/10408440600977677	発がん性	総説	○ EPA 2019年	無	-	-	-	-	-	-	ヒト発がん性MOAフレームワークの見直しに関するレビュー。 新たな試験データを含まない。
261	Mode of action and human relevance analysis for nuclear receptor-mediated liver toxicity: A case study with phenobarbital as a model constitutive androstane receptor (CAR) activator.	Crit. Rev. Toxicol. 44(1): 64-82.	2014	Clifford R. Elcombe, et al.	Biosciences Ltd, UK, etc.	https://doi.org/10.3109/10408444.2013.835786	代謝	総説	○ EPA 2019年	無	-	-	-	-	-	-	PB 誘発齧歯動物肝腫瘍形成に対する作用機序 (MOA) 開発に関する研究。 新たな試験データを含まない。
262	Mode of action in relevance of rodent liver tumors to human cancer risk.	Toxicol. Sci. 89(1): 51-56.	2006	Holsapple, M. P., et al.	ILSI Health and Environmental Sciences Institute, USA, etc.	https://doi.org/10.1093/toxsci/kfj001	代謝	総説	○ EPA 2019年	無	-	-	-	-	-	-	肝臓がんについて齧歯類動物でおきたP450の様なフェノバルビタールによる影響は人にはありそうもない。 エストロゲンは人に対しエストロゲン誘発性腫瘍を発生させる。ポルフィロ精製化合物による、齧歯類肝腫瘍の誘発は人の癌リスクも増加させる。 新たな試験データを含まない。
263	A Framework for Human Relevance Analysis of Information on Carcinogenic Modes of Action.	Crit. Rev. Toxicol. 33(6): 591-653.	2003	Meek, M., Buche, et al.	Health Canada, ,etc.	https://doi.org/10.1080/713608373	発がん性	総説	○ EPA 2019年	無	-	-	-	-	-	-	試験動物による発がん性試験の結果のヒトへの応用における、作用機序を考慮することの重要性について言及した総説。 新たな試験データを含まない。
264	New developments in the evolution and application of the WHO/IPCS framework on mode of action/species concordance analysis.	J. Appl. Toxicol. 34(1): 1-18.	2014	Meek, M. E., et al.	McLaughlin Centre for Population Health Risk Assessment, etc.	https://doi.org/10.1002/jat.2949	一般毒性	総説	○ EPA 2019年	無	-	-	-	-	-	-	WFO/化学物質の安全性に関する国際プログラム、MOA/ヒトとの関連性フレームワークの更新に関するレビュー。 新たな試験データを含まない。
265	Multispecies analyses of direct activators of the constitutive androstane receptor.	Toxicol. Sci. 123(2): 550-562.	2011	Omiecinski, C. J., et al.	Penn Stare Univesity, etc.	https://doi.org/10.1093/toxsci/kfr191	一般毒性	原著	○ EPA 2019年	無	-	-	-	-	-	-	核内受容体CARによる毒性スクリーニングに関する研究

										研究デザイン								健康関連の事象の情報								
No.	文献名	ジャーナル名等	公表年	著者名	著者の所属機関	書誌情報	原著	海外評価書での引用の有無	ドシエでの引用の有無	国名（地域名、研究名）	試験設計	調査時期	対象者、年齢	アウトカムの定義	アウトカムの確認方法	暴露指標の定義	暴露の確認方法	試験全体のN数（症例/対照）	アウトカムのN数	分析カテゴリー	暴露に係るN数	相対リスク/オッズ比等	95%信頼区間	p値	交絡因子の考慮	備考
102	Pesticides and lung cancer risk in the agricultural health study cohort.	American Journal of Epidemiology 160(9): 876-885. Published. ASB2018-2841	2004	Alavanja, M. C. R., et al.	Nat'l Inst. for Health, etc.	https://doi.org/10.1093/aje/kwh290	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許取得者とその配偶者	肺がん発症	アンケート及びインタビュー	農薬の使用実態	アンケート	他農薬含む 57044	240	ロジスティック回帰	54	散布日数（積算） オッズ比 <38.8 0.6 38.8-116 1.0 116.1-457.0 1.0 >457 4.1	散布日数（積算） 区間 8.8 0.4-1.0 38.8-116 0.6-1.6 116.1-457.0 0.4-1.8 >457 1.6-10.0	-	喫煙経験、年齢、性別、全農薬の散布日数	農薬使用と肺がんの関連性の調査。 米国農業健康調査（AHS)コホートによる研究。
103	Agricultural pesticide use and pancreatic cancer risk in the Agricultural Health Study Cohort.	International Journal of Cancer 124(10): 2495-2500. Published. ASB2012-11544	2009	Andreotti, G., et al.	Nat'l Inst. for Health, etc.	https://doi.org/10.1002/ijc.24185	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1998	農薬散布免許取得者とその配偶者	すい臓がん	アンケート及びインタビュー	農薬の使用実態	アンケート	他農薬含む 75808	84	ロジスティック回帰	23120	オッズ比 1.0	0.6-1.7	-	喫煙経験、年齢、糖尿病の有無、事業散布／個人散布の別	農薬使用と膵がんの関連性の調査。 米国農業健康調査（AHS)コホートによる研究。
104	Body mass index, agricultural pesticide use, and cancer incidence in the Agricultural Health Study cohort.	Cancer Causes & Control 21(11): 1759- 1775. Published. ASB2018-2842	2010	Andreotti, G., et al.	Nat'l Inst. for Health, etc.	https://doi.org/10.1007/s10552-010-9603-9	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2005	農薬散布免許取得者とその配偶者	がん	アンケート及びインタビュー	農薬の使用実態	アンケート	他農薬含む 67947	4432 （調査対象の全農薬に対するN）	-	48730 （調査対象の全農薬に対するN）	-	-	-	人種、喫煙状況、野菜摂取、運動、家族の発がん履歴、高血圧、ビタミン剤摂取、果物摂取、州、糖尿、アルコール摂取、教育、肉摂取、日焼け止め使用の有無、出産歴	農薬使用及び肥満度の発がん性との関連性の調査。 米国農業健康調査（AHS)コホートによる研究。
106	Pesticide urinary metabolite levels of children in Eastern North Carolina farmworkers households.	Environmental Health Perspectives 115(8): 1254-1260. Published. ASB2018-2844	2007	Arcury, T. A., et al.	Wake Forest Univ., etc.	https://doi.org/10.1289/ehp.9975	原著	○ EFSA 2018	無	米国（ノースカロライナ州）	横断研究	2004	ヒスパニック系農業従事者の子供（1－6歳）	-	-	尿内の農薬濃度	採尿及びインタビュー	60	-	-	-	-	-	-	-	ヒスパニック系農業従事者の子供に関して尿内の農薬代謝物含有量を調査し、生活環境等との関連を分析 メトラクロールの代謝物は検出されなかった
107	Seasonal variation in the measurement of urinary pesticide metabolites among Latino farmworkers in eastern North Carolina.	International Journal of Occupational and Environmental Health 15(4): 339-350. Published. ASB2018-2845	2009	Arcury, T. A., et al.	Wake Forest Univ., etc.	https://doi.org/10.1179/oeh.2009.15.4.339	原著	○ EFSA 2018	無	米国（ノースカロライナ州）	横断研究	2007	ヒスパニック系季節農業従事者（18歳以上）	-	-	-	-	250	-	-	-	-	-	-	-	ヒスパニック系季節農業従事者の尿内農薬代謝物含有量の季節変化を調査し、作業内容等との関連を分析。
108	Repeated Pesticide Exposure among North Carolina Migrant and Seasonal Farmworkers.	Am J Ind Med 53(8): 802-813. Published. ASB2018-2846	2010	Arcury, T. A., et al.	Wake Forest Univ., etc.	https://doi.org/10.1002/ajim.20856	原著	○ EFSA 2018	無	米国（ノースカロライナ州）	横断研究	2007	ヒスパニック系季節農業従事者（18歳以上）	-	-	-	-	283	-	-	-	-	-	-	-	ヒスパニック系季節農業従事者の尿内農薬代謝物含有量を調査し、作業内容等との関連を分析。
109	Serum acetylcholinesterase and prognosis of acute organophosphate poisoning.	Journal of Toxicology - Clinical Toxicolo- gy 40(7): 903-910. Published. ASB2018- 2847	2002	Aygun, D., et al.	Ondokuz Mayis Univ., Turkey, etc.	https://doi.org/10.1081/CLT-120016962	原著	○ EFSA 2018	無	トルコ	-	1991-2001	-	-	-	-	-	-	-	-	-	-	-	-	-	急性有機リン酸中毒患者における血清アセチルコリンエステラーゼの予後予測への活用に関する研究。 メトラクロールに関する知見を含まない。
110	Pesticide concentrations in maternal and umbilical cord sera and their relation to birth outcomes in a population of pregnant women and newborns in New Jersey.	Science of the Total Environment 408(4): 790-795. Published. ASB2018-2848	2010	Barr, D. B., et al.	Centers for Disease Control and Prevention, etc.	https://doi.org/10.1016/j.scitotenv.2009.10.007	原著	○ EFSA 2018	無	米国（ニュージャージー州）	コホート研究	2003-2004	妊婦及び新生児	血液内の農薬濃度	妊婦と臍帯からの採血	-	-	150	-	-	-	-	-	-	-	妊婦及び新生児における農薬含有量の調査。
111	Genetic Variation in Base Excision Repair Pathway Genes, Pesticide Exposure, and Prostate Cancer Risk.	Environ Health Perspect 119(12): 1726- 1732. Published. ASB2014-9247	2011	Barry, K. H., et al.	Nat'l Inst. for Health, etc.	https://doi.org/10.1289/ehp.1103454	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート内症例対照研究	1993-2004	白人男性の農薬散布免許取得者	前立腺がん	アンケート及びインタビュー	農薬の使用実態	アンケート	他農薬含む 1992	678	ロジスティック回帰	911	オッズ比 1.21 低暴露 0.77 高暴露	0.97-1.52 低暴露 0.60-0.90 高暴露	0.02	年齢及び州	農薬使用歴のある前立腺がん患者における、塩基除去修復関連遺伝子の多型変異の発生状況を調査。 メトラクロールでは、顕著な傾向が見られなかった。 米国農業健康調査（AHS)コホートによる研究。
112	Pesticide Exposure and Self-Reported Incident Depression among Wives in the Agricultural Health Study.	Environ Res 126: 31-42. Published. ASB2018-2849	2013	Beard, J. D., et al.	Univ. of North Carolina at Chapel Hill, etc.	https://doi.org/10.1016/j.envres.2013.06.001	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2010	農薬散布免許取得者の女性配偶者	うつ病	アンケート（医師による診断歴を自己申告）	配偶者による農薬の使用実態	アンケート	他農薬含む 16893	213	ポアソン回帰	3000	相対リスク 0.68	0.45-1.04	-	年齢、糖尿病歴、学歴、州	女性における農薬暴露歴とうつ病の関連性に関する調査。 米国農業健康調査（AHS)コホートによる研究。
113	Pesticide Exposure and Depression among Male Private Pesticide Applicators in the Agricultural Health Study.	Environ Health Perspect 122(9): 984-991. Published. ASB2018-2850	2014	Beard, J. D., et al.	Univ. of North Carolina, Chapel Hill, etc.	https://doi.org/10.1289/ehp.1307450	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2011	男性農薬散布免許取得者	うつ病	アンケート（医師による診断歴を自己申告）	農薬の使用実態	アンケート	他農薬含む 21208	771	ロジスティック回帰	9892	オッズ比 1.1,0.8,1.0	0.9-1.3-0.7-1.0-0.8-1.1	0.20	年齢、糖尿病歴、学歴、州	男性における農薬暴露歴とうつ病の関連性に関する調査。 米国農業健康調査（AHS)コホートによる研究。
114	Suicide and pesticide use among pesticide applicators and their spouses in the Agricultural Health Study.	Environmental Health Perspectives 119(11): 1610-1615. Published. ASB2018- 2851	2011	Beard, J. D., et al.	Univ. of North Carolina, Chapel Hill, etc.	https://doi.org/10.1289/ehp.1103413	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2009	農薬散布免許取得者とその配偶者、19歳以上（登録時）	自殺	各州死亡記録及び国民死亡指標（National Death Index）とのデータ照合	農薬の使用実態	アンケート	他農薬含む 81988	110	ロジスティック回帰	169	オッズ比 0.54	0.35-0.84	-	年齢及び性別	農薬使用と自殺の関連性の調査。 米国農業健康調査（AHS)コホートによる研究。
115	Depression and pesticide exposures in female spouses of licensed pesticide applicators in the agricultural health study cohort.	J Occup Environ Med 48(10): 1005-1013. Published. ASB2018-2852	2006	Beseler, C., et al.	Colorado State Univ., etc.	https://doi.org/10.1097/01.jom.0000235938.70212.dd	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート内症例対照研究	1993-1997	農薬散布免許取得者の女性配偶者	うつ病	アンケート（医師による診断歴を自己申告）	農薬の使用実態	アンケート	他農薬含む 27023	2051	-	-	-	-	-	-	農薬暴露歴とうつ病の関連性に関する調査。 メトラクロールのデータは示されていない。 米国農業健康調査（AHS)コホートによる研究。
116	Mean serum-level of common organic pollutants is predictive of behavioral severity in children with autism spectrum disorders.	Sci Rep 6. Published. ASB2018-2853	2016	Boggess, A., et al.	Duquesne Univ., etc.	https://doi.org/10.1038/srep26185	原著	○ EFSA 2018	無	米国	症例対照研究	-	自閉症スペクトラム症候群を持つ子供と対照群（2-9歳）	自閉症スペクトラム症候群	医師の診断	-	-	60（30/30）	-	-	-	-	-	-	-	自閉症スペクトラム症候群の子供の血中の農薬濃度の調査。 メトラクロールでは対照群との間に有意な差が見られなかった。
117	Measurement of pesticides and other toxicants in amniotic fluid as a potential biomarker of prenatal exposure: a validation study.	Environ Health Perspect 111(14): 1779- 1782. Published. ASB2018-2854	2003	Bradman, A., et al.	Univ. of California, etc.	https://doi.org/10.1289/ehp.6259	原著	○ EFSA 2018	無	米国（カリフォルニア州中部）	バイオモニタリング調査	-	羊水穿刺検査を行った妊婦（18-43歳）	-	-	-	-	100	-	-	-	-	-	-	-	農業地帯の妊婦の羊水内の農薬含有濃度に関する調査。
118	Effect of organic diet intervention on pesticide exposures in young children living in low-income urban and agricultural communities.	Environmental Health Perspectives 123(10): 1086-1093. Published. ASB2018- 2855	2015	Bradman, A., et al.	Univ. of California, etc.	https://doi.org/10.1289/ehp.1408660	原著	○ EFSA 2018	無	米国（カリフォルニア州）	横断研究	2006	低所得家庭のメキシコ系アメリカ人（3-6歳）	-	-	-	-	40	-	-	-	-	-	-	-	慣行栽培食品の摂取中及び有機食品の摂取中の、尿中農薬濃度の比較。
119	Hypospadias and Residential Proximity to Pesticide Applications.	Pediatrics 132(5): e1216-1226. Published. ASB2014-9307	2013	Carmichael, S. L., et al.	Stanford Univ., etc.	https://doi.org/10.1542/peds.2013-1429	原著	○ EFSA 2018	無	米国（カリフォルニア州）	コホート研究	1991-2004	男の新生児	尿道下裂	医師による診断	妊娠初期の妊婦の居住地の農薬散布履歴	州農薬管理局の農薬散布記録と妊婦の居住地を照合	クロロアセトアニリド系除草剤合計 2195	6	ロジスティック回帰	クロロアセトアニリド系除草剤合計 36	オッズ比 2.76	1.12-6.75	-	-	新生児の尿道下裂と母親の妊娠初期の農薬暴露の関係を調査。
120	Comparison of Current-Use Pesticide and Other Toxicant Urinary Metabolite Levels among Pregnant Women in the CHAMACOS Cohort and NHANES.	Environ Health Perspect 118(6): 856-863. Published. ASB2018-2856	2010	Castorina, R., et al.	Univ. of California, etc.	https://doi.org/10.1289/ehp.0901568	原著	○ EFSA 2018	無	米国（カリフォルニア州）	横断研究	1999-2000	18歳以上で妊娠21週未満の妊婦	-	-	妊娠初期の妊婦の居住地の農薬散布履歴	州農薬管理局の農薬散布記録と妊婦の居住地を照合、及びインタビュー	-	-	-	-	-	-	-	-	農業地帯の妊婦の尿中農薬濃度を全国健康栄養調査（NHNANES)のデータと比較。 CHAMACOSコホートによる研究。
121	Urinary biomarkers of prenatal atrazine exposure and adverse birth outcomes in the PELAGIE birth cohort.	Environmental Health Perspectives 119(7): 1034-1041. Published. ASB2018-2857	2011	Chevrier, C., et al.	INSERM, France, etc.	https://doi.org/10.1289/ehp.1002775	原著	○ EFSA 2018	無	フランス	コホート内症例対照研究	2002-2006	妊娠19週未満の妊婦	異常出生	医師による診断	水道水中のアトラジン含有量（推測値）	全国農業統計のとうもろこし農地の比率から、水道水中のアトラジン含有量を推測	579	-	ロジスティック回帰	-	メトラクロール オッズ比 0.8,1.2,1.0	0.4-1.4-0.8-1.9-0.6-1.7	-	-	フランス農業地帯の妊婦の血中農薬濃度と異常出生の関係を調査。
122	Urinary and hand wipe pesticide levels among farmers and nonfarmers in Iowa.	Journal of Exposure Analysis and Environmental Epidemiology 15(6): 500-508. Published. ASB2018-2858	2005	Curwin, B. D., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1038/sj.jea.7500428	原著	○ EFSA 2018	無	米国（アイオワ州）	横断研究	2001	男性農業従事者	-	-	-	-	80（40/40）	-	-	-	-	-	-	-	農業従事者と非農業従事者との間で、尿中と手のひら上の農薬濃度を比較。
123	Pesticide contamination inside farm and nonfarm homes.	Journal of Occupational and Environmental Hygiene 2(7): 357-367. Published. ASB2012-11595	2005	Curwin, B. D., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1080/15459620591001606	原著	○ EFSA 2018	無	米国（アイオワ州）	横断研究	2001	8歳以下の子供を持つ農業従事者	-	-	-	-	50（25/25）	-	-	-	-	-	-	-	農業従事者と非農業従事者との間で、住宅内の農薬分布を比較。
124	Pesticide dose estimates for children of Iowa farmers and non-farmers.	Environmental Research 105(3): 307-315. Published. ASB2012-11596	2007	Curwin, B. D., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1016/j.envres.2007.06.001	原著	○ EFSA 2018	無	米国（アイオワ州）	横断研究	2001	農業従事者の子供（16歳未満）	-	-	-	-	118（66/52）	-	-	-	-	-	-	-	農業従事者の子供と非農業従事者の子供との間で、尿内の農薬濃度を比較。
125	Urinary pesticide concentrations among children, mothers and fathers living in farm and non-farm households in Iowa.	Annals of Occupational Hygiene 51(1): 53- 65. Published. ASB2012-11597	2007	Curwin, B. D., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1093/annhyg/mel062	原著	○ EFSA 2018	無	米国（アイオワ州）	横断研究	2001	農業従事者のいる家庭の父親、母親と子供	-	-	-	-	父親47（24/23） 母親48（24/24） 子供50（25/25）	-	-	-	-	-	-	-	農業従事者の家庭（父親、母親、子供）と非農業従事者の家庭との間の尿中の農薬濃度を比較。 また尿中濃度と各住宅内の埃に含まれる農薬の濃度の関係も調査しているが、相関が見られなかった。
126	Pesticide use and myocardial infarction incidence among farm women in the agricultural health study.	Journal of Occupational and Environmental Medicine 52(7): 693-697. Published. ASB2012-11604	2010	Dayton, S. B., et al.	Univ. of Nevada, Reno, etc.	https://doi.org/10.1097/JOM.0b013e3181e66d25	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1992-2003	女性農薬散布免許取得者、及び男性農薬散布免許取得者の配偶者	心筋梗塞	アンケート（医師による診断歴を自己申告）	農薬の使用実態	アンケート	他農薬含む 22425	23	ロジスティック回帰	868	オッズ比 0.9	0.4-2.2	-	年齢、肥満度指数、喫煙状況、州	女性における農薬暴露歴と心筋梗塞の関連性に関する調査。 メトラクロールは関連性が認められなかった。 米国農業健康調査（AHS)コホートによる研究。
127	Integrative assessment of multiple pesticides as risk factors for non-Hodgkin's lymphoma among men.	Occup Environ Med 60(9): e11. Published. ASB2012-11606	2003	De Roos, A. J., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1136/oem.60.9.e11	原著	○ EFSA 2018	無	米国（中西部5州）	コホート研究	1983-1986 1980-1983 1979-1981	白人（21歳以上） 白人男性（30歳以上） 白人男性（21歳以上）	非ホジキンリンパ腫	医師による診断	農薬の使用実態	自身（死亡時は近親者）へのインタビュー	他農薬含む 3417	13	ロジスティック回帰	50	オッズ比 0.7	0.3-1.6	-	他農薬の使用、年齢、調査地	農業使用と非ホジキンソンリンパ腫の関連性に関する調査。

128	Cancer risk and parental pesticide application in children of Agricultural Health Study participants.	Environ Health Perspect 112(5): 631-635. Published. ASB2012-11620	2004	Flower, K. B., et al.	Univ. of North Carolina, Chapel Hill, etc.	https://doi.org/10.1289/ehp.6586	原著	○ EFSA 2018	無	米国（アイオワ州）	コホート研究	1993-1997 （登録期間）	子供（0-19歳）	がん	親への聞き取り結果をSEERのデータと照合	農薬の使用実態	アンケート	他農薬含む 17280	5	ロジスティック回帰	3032	オッズ比 0.69	0.26-1.84	-	-	胎児期の父親の農薬使用と発がんの関連性に関する調査。 米国農業健康調査（AHS)コホートによる研究。
129	Pesticide Use and Thyroid Disease Among Women in the Agricultural Health Study	Am J Epidemiol 171(4): 455-464. Published. ASB2012-11830	2010	Goldner, W. S., et al.	Univ. of Nebraska, etc.	https://doi.org/10.1093/aje/kwp404	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1998 （登録期間）	農薬散布免許取得者の女性配偶者	甲状腺異常	インタビュー（医師による診断歴を自己申告）	農薬の使用実態	アンケート	他農薬含む 14486	57	ロジスティック回帰	479	オッズ比 1.2,0.66,1.3	0.68-2.1-0.43-1.0-0.82-2.0	-	学歴、年齢、喫煙状況、肥満度指数、ホルモン療法の履歴	女性における農薬暴露と甲状腺異常との関連性に関する調査。 米国農業健康調査（AHS)コホートによる研究。
130	Distributions and determinants of preemergent herbicide exposures among custom applicators.	Annals of Occupational Hygiene 45(3): 227-239. Published. ASB2018-2859	2001	Hines, C. J., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1093/annhyg/45.3.227	原著	○ EFSA 2018	無	米国（オハイオ州）	横断研究	1996	フルタイムの農薬散布者	-	-	環境中の農薬濃度	手のひら、衣服表面、空中の農薬濃度を測定	他農薬含む 30	-	-	-	-	-	-	-	各農薬の業務内容（散布日／非散布日）と暴露量の関係の調査。 散布日と非散布日の間の暴露量の差は、労働者間の暴露量の差を上回った。
131	Biological monitoring for selected herbicide biomarkers in the urine of exposed custom applicators:	Application of mixed- effect models. Annals of Occupational Hygiene 47(6): 503-517. Published. ASB2018-2860	2001	Hines, C. J., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1093/annhyg/meg067	原著	○ EFSA 2018	無	米国（オハイオ州）	バイオモニタリング調査	1996	男性農薬散布者	-	-	尿中の農薬濃度	採尿及びインタビュー	15	-	-	-	-	-	-	-	農薬散布者の尿中の、農薬4種類の濃度測定。 検体採取前日の散布状況が結果に影響する可能性を指摘している。
132	Pesticides and Atopic and Nonatopic Asthma among Farm Women in the Agricultural Health Study.	Am J Respir Crit Care Med 177(1): 11-18. Published. ASB2012-11850	2008	Hoppin, J. A., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1164/rccm.200706-821OC	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許取得者及びその配偶者（20歳以上の女性）	アトピー性喘息及び非アトピー性喘息	アンケートによる自己申告	農薬の使用実態	アンケート	他農薬含む 25814	8 9	ロジスティック回帰	847	オッズ比 0.98 0.64	0.48-2.00 0.33-1.25	-	年齢、州、喫煙状況、肥満度指数、農場での成長	女性における農薬暴露と喘息罹患の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
133	Pesticide use and adult-onset asthma among male farmers in the Agricultural Health Study.	Eur Respir J 34(6): 1296-1303. Published. ASB2012-11851	2009	Hoppin, J. A., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1183/09031936.00005509	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許取得者（20歳以上の男性）	成人喘息	アンケートによる自己申告	農薬の使用実態	アンケート	他農薬含む 19704	58 148	ロジスティック回帰	8830	オッズ比 0.99 1.12	0.69-1.44 0.88-1.43	-	年齢、州、喫煙状況、高濃度農薬への暴露歴、肥満度指数	男性における農薬暴露と喘息罹患の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
134	Pesticides and adult respiratory outcomes in the agricultural health study.	Annals of the New York Academy of Sciences. 1076: 343-354. Published. ASB2018-2861	2006	Hoppin, J. A., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1196/annals.1371.044	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	横断研究	1993-1997	農薬散布免許取得者	成人呼吸器疾患	アンケートによる自己申告（呼吸音の異常）	農薬の使用実態	アンケート	他農薬含む 20175	-	ロジスティック回帰	-	オッズ比 農業従事者1.09 散布業者1.01	0.97-1.21 0.71-1.43	-	年齢、肥満度指数、喘息／アトピー罹患、農薬使用歴	農薬暴露と呼吸器疾患の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
135	Pesticide Use And Chronic Bronchitis Among Farmers in The Agricultural Health Study.	Am J Ind Med 50(12): 969-979. Published. ASB2012-11853	2007	Hoppin, J. A., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1002/ajim.20523	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	横断研究	1993-1997	農薬散布免許取得者	慢性気管支炎	アンケートによる自己申告（医師の診断）	農薬の使用実態	アンケート	他農薬含む 20908	43	ロジスティック回帰	90	オッズ比 0.99	0.84-1.18	-	年齢、州、性別	農薬暴露と気管支炎の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
136	Lifetime pesticide use and telomere shortening among male pesticide applicators in the Agricultural Health Study.	Environmental Health Perspectives 121(8): 919-924. Published. ASB2018-2862	2013	Hou, L., et al.	Northwestern Univ., etc.	https://doi.org/10.1289/ehp.1206432	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	横断研究	1993-2006	農薬散布免許取得者	頬細胞DNAの相対テロメア長の減少	唾液サンプルから測定	農薬の使用実態	アンケート	1114	-	-	492	-	-	-	唾液採取時の年齢、州、農業従事者／散布事業者の違い、噛みタバコ嗜好、全農薬の散布状況	生涯積算農薬暴露量と頬細胞内のDNAの相対テロメア長の関連を調査。 いずれの農薬も相対テロメア長の減少は認められなかった。 米国農業健康調査（AHS)コホートによる研究。
138	Pesticide exposure and amyotrophic lateral sclerosis.	Neurotoxicology 33(3): 457-462. Pub- lished. ASB2014-9586	2012	Kamel, F., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1016/j.neuro.2012.04.001	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究及びメタ分析	1993-2010	農薬散布免許取得者及びその配偶者	筋萎縮性側索硬化症（ALS）	各州死亡記録及び国民死亡指標（National Death Index）とのデータ照合	農薬の使用実態	アンケート	他農薬含む 84739	10	ロジスティック回帰	22737	オッズ比 1.0	0.4-2.2	-	-	農薬暴露とALSの関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
139	Pesticide use modifies the association between genetic variants on chromosome 8q24 and prostate cancer.	Cancer Res 70(22): 9224-9233. Published. ASB2018-2863	2010	Koutros, S., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1158/0008-5472.CAN-10-1078	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2003	男性農薬散布免許取得者	前立腺がん	インタビュー（医師による診断歴を自己申告）および唾液サンプルからの染色体検査	農薬の使用実態	アンケート	他農薬含む 49561	369	ロジスティック回帰	低暴露179 高暴露133	オッズ比 1.15 1.47	0.87-1.53 1.08-2.00	0.05	年齢、州	農薬暴露が、前立腺がんに関連する8q24遺伝子座位の変異に与える影響の調査。 米国農業健康調査（AHS)コホートによる研究。
140	Pesticide exposure and risk of monoclonal gammopathy of undetermined significance in the Agricultural Health Study.	Blood 113(25): 6386-6391. Published. ASB2012-11875	2009	Landgren, O., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1182/blood-2009-02-203471	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	男性農薬散布免許取得者（30-94歳）	モノクローナル免疫グロブリン血症	血液検査	農薬の使用実態	アンケート	他農薬含む 10147	17	ロジスティック回帰	356	オッズ比 0.8	0.4-1.5	-	年齢、学歴	農薬暴露とモノクローナル免疫グロブリン血症の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
141	Pesticide use and risk of end-stage renal disease among licensed pesticide applicators in the Agricultural Health Study.	Occupational and Environmental Medicine 73(1): 3-12. Published. ASB2018-2864	2016	Lebov, J. F., et al	Univ. of North Carolina at Chapel Hill, etc.	https://doi.org/10.1136/oemed-2014-102615	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2011	男性農薬散布免許取得者	重症の腎臓病	アンケートによる自己申告（医師の診断）	農薬の使用実態	アンケート	22922	38 38 40	コックス比例ハザードモデル	9244 7195 6483	ハザード比 1.02 1.39 1.53	0.71-1.47 0.96-1.49 1.08-1.49	-	年齢、州	農薬暴露と重症腎臓病の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
142	Agricultural pesticide use and risk of glioma in Nebraska, United States.	Occupational and Environmental Medicine 62(11): 786-792. Published. ASB2012- 11882	2005	Lee, W. J., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1136/oem.2005.020230	原著	○ EFSA 2018	無	米国（ネブラスカ州）	症例対照研究	1988-1993	21歳以上の男女	グリオーマ	医師の診断	農薬の使用実態	インタビュー	他農薬含む 749（251/498）	6	ロジスティック回帰	20	オッズ比 1.2	0.4-3.6	-	年齢	農薬暴露とグリオーマの関連に関する調査。
143	Pesticide use and colorectal cancer risk in the Agricultural Health Study.	Int J Cancer 121(2): 339-346. Published. ASB2015-8228	2007	Lee, W. J., et al.	Korea Unov., Korea, etc.	https://doi.org/10.1002/ijc.22635	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2002	農薬散布免許取得者とその配偶者	大腸がん	各州がん患者登録、死亡記録及び国民死亡指標（National Death Index）とのデータ照合	農薬の使用実態	アンケート	他農薬含む 56813	107	-	-	-	-	-	-	農薬暴露と大腸がんの関連に関する調査。 メトラクロールについては対照群との比較データなし。 米国農業健康調査（AHS)コホートによる研究。
144	Exposure to herbicides in house dust and risk of childhood acute lymphoblastic leukemia.	Journal of Exposure Science and Environ- mental Epidemiology 23(4): 363-370. Published. ASB2018-2865	2013	Metayer, C., et al.	Univ. of California, etc.	https://doi.org/10.1038/jes.2012.115	原著	○ EFSA 2018	無	米国（カリフォルニア州）	症例対照研究	1995-2008	15歳未満の子供	小児急性リンパ性白血病	医師の診断	住宅内の農薬残存状況	埃の吸引等により測定	2223	997	-	-	-	-	-	-	農薬暴露と小児急性リンパ性白血病の関連に関する調査。 メトラクロールは検出例が少なく、有意なデータが得られていない。
145	Pesticides and Myocardial Infarction Incidence and Mortality Among Male Pesticide Applicators in the Agricultural Health Study.	Am J Epidemiol 170(7): 892-900. Pub- lished. ASB2012-11903	2009	Mills, K. T., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1093/aje/kwp214	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2006	男性農薬散布免許取得者	心筋梗塞（の発症と死亡）	各州がん患者登録、死亡記録及び国民死亡指標（National Death Index）とのデータ照合、及びインタビュー	農薬の使用実態	アンケート	54069 32024	88 92	コックス比例ハザードモデル	41	ハザード比 1.00 1.06	0.82-1.03 0.91-1.25	-	年齢、州、喫煙、肥満度指数	農薬暴露と心筋梗塞の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
146	Incident Diabetes and Pesticide Exposure among Licensed Pesticide Applicators: Agricultural Health Study 1993 – 2003.	Am J Epidemiol 167(10): 1235-1246. Published. ASB2012-11911	2008	Montgomery, M. P., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1093/aje/kwn028	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2003	農薬散布免許取得者	糖尿病発症	アンケート（医師による診断歴を自己申告）	農薬の使用実態	アンケート	他農薬含む 31787	444	ロジスティック回帰	-	オッズ比 1.05	0.92-1.20	-	年齢、州、肥満度指数	農薬暴露と糖尿病の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
147	Intrauterine growth retardation in Iowa communities with herbicide-contaminated drinking water supplies.	Environmental Health Perspectives 105(3): 308-314. Published. ASB2015-10990	1997	Munger, R., et al.	Univ. of Iowa, etc.	https://doi.org/10.1289/ehp.97105308	原著	○ EFSA 2018	無	米国（アイオワ州）	コホート研究	1984-1990	白人新生児	出生時低体重、早産、子宮内発育遅滞	医師による診断	母親の妊娠中の居住地の水道内農薬濃度	州の水道水質調査のデータと母親の居住地データを照合	-	-	-	-	-	-	-	-	新生児の出生時異常と妊娠中の母親の農薬暴露の関連に関する調査。 各農薬単体の疫学的データは含まれていない。
149	Agricultural and residential pesticides in wipe samples from farmworker family residences in North Carolina and Virginia.	Environ Health Perspect 112(3): 382-387. Published. ASB2018-2867	2004	Quandt, S. A., et al.	Wake Forest Univ., etc.	https://doi.org/10.1289/ehp.6554	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	環境モニタリング調査	2001	7歳未満の子供を持つメキシコ系農業従事者の住宅	-	-	住宅内の農薬残存状況	床、おもちゃ、子供の手のひらを拭き取り	41	-	-	-	-	-	-	-	農業従事者の住居内の農薬分の調査。 メトラクロールは調査対象に含まれていない。
150	Cancer incidence among pesticide applicators exposed to Metolachlor in the Agricultural Health Study.	International Journal of Cancer 118(12): 3118-3123. Published. ASB2018-2868	2006	Rusiecki, J. A., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1002/ijc.21758	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2002	農薬散布免許取得者とその配偶者	発がん	医師による診断	農薬の使用実態	アンケート	51111	-	-	-	-	-	-	-	メトラクロールのがん誘発性について疫学的に調査。 調査対象の6種類のがんについては、いずれも関連が認められなかった。 米国農業健康調査（AHS)コホートによる研究。
151	Maternal Pesticide Use and Birth Weight in the Agricultural Health Study.	J Agromedicine 15(2): 127-136. Published. ASB2012-12020	2010	Sathyanarayana, S., et al.	Univ. of Washington, etc.	https://doi.org/10.1080/1059924100 3622699	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許取得者とその配偶者（女性のみ）	出生時低体重	医師による診断	農薬の使用実態	アンケート	2598	-	-	47	相関係数 -8	149-134	-	居住地、肥満度、出産履歴、母親の身長、早産の有無、喫煙	妊娠中の農薬暴露が新生児の身長に与える影響に関する調査。 米国農業健康調査（AHS)コホートによる研究。
153	Cancer incidence and Metolachlor use in the Agricultural Health Study: An update.	International Journal of Cancer 137(11): 2630-2643. Published. ASB2018-2870	2015	Silver, S. R., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1002/ijc.29621	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2011	農薬散布免許取得者とその配偶者	発がん	医師による診断	農薬の使用実態	アンケート	49616	-	-	-	-	-	-	-	メトラクロールのがん誘発性について疫学的に調査(上記94のアップデート)。 肝がんとの関連性が指摘された。 米国農業健康調査（AHS)コホートによる研究。
154	Rhinitis Associated with Pesticide Exposure among Commercial Pesticide Applicators in the Agricultural Health Study.	Occup Environ Med 66(11): 718-724. Published. ASB2012-12030	2009	Slager, R. E., et al.	Wake Forest Univ., etc.	https://doi.org/10.1136/oem.2008.041798	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	フルタイムの農薬散布者	鼻炎	アンケートによる自己申告	農薬の使用実態	アンケート	他農薬含む 2245	434	ロジスティック回帰	579	オッズ比 1.05	0.83-1.32	-	年齢、学歴、過去の居住地での農薬使用	農薬暴露と鼻炎の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
155	Rhinitis associated with pesticide use among private pesticide applicators in the agricultural health study.	Journal of Toxicology and Environmental Health - Part A: Current Issues 73(20): 1382-1393. Published. ASB2012-12031	2010	Slager, R. E., et al.	Wake Forest Univ., etc.	https://doi.org/10.1080/15287394.2010.497443	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許を持つ農業従事者	鼻炎	アンケートによる自己申告	農薬の使用実態	アンケート	他農薬含む 21958	2660	-	3754	-	-	-	-	農薬暴露と鼻炎の関連に関する調査。 メトラクロールの相対リスク／オッズ比等は示されていない。 米国農業健康調査（AHS)コホートによる研究。
156	Semen quality in relation to biomarkers of pesticide exposure.	Environmental Health Perspectives 111(12): 1478-1484. Published. ASB2018- 2871	2003	Swan, S. H., et al.	Univ. of Missouri at Columbia, etc.	https://doi.org/10.1289/ehp.6417	原著	○ EFSA 2018	無	米国（ミズーリ州及びミネソタ州）	横断研究	1993-1997	配偶者が妊娠中の男性	精子の質	精子提供	血液中の農薬濃度	採血	86 （52/34）	-	-	-	-	-	-	-	農業地帯と都市部の男性の精子の質の比較及び、農薬濃度との関連を調査。
157	Herbicides and Nitrates in Groundwater of Maryland and Childhood Cancers: A Geographic Information Systems Approach.	Journal of Environmental Science and Health - Part C Environmental Carcinogenesis and Ecotoxicology Reviews 23(2): 261-278. Published. ASB2018-2872	2005	Thorpe, N.; Shirmohammadi A.	Hagerstown Com. Col. & Univ. of Maryland	https://doi.org/10.1080/1059050050 0235001	原著	○ EFSA 2018	無	米国（メリーランド州）	横断研究	1992-1998	小児がん患者（0－17歳）	発がん	医師の診断	地下水の農薬分布	全米地質調査のデータと照合	1218790 （689/1218101）	689	-	-	オッズ比 1.54	1.14-2.07	0.0061	-	4種類の小児がん患者の発生分布と地下水中の農薬分布との相関から、農薬が小児がんの発症に与える影響を推測。
158	Chronic bronchitis among non-smoking farm women in the agricultural health study.	J Occup Environ Med 49(5): 574-583. Published. ASB2012-12042	2007	Valcin, M., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1097/JOM.0b013e3180577768	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許取得者の非喫煙女性配偶者（20歳以上）	慢性気管支炎	アンケート（医師による診断歴を自己申告）	農薬の使用実態	アンケート	他農薬含む 20541	4	ロジスティック回帰	-	オッズ比 1.07	0.56-2.03	-	年齢、州、農薬のカテゴリー	農薬暴露と女性の慢性気管支炎の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。

159	Pesticide Use and Fatal Injury among Farmers in the Agricultural Health Study.	Int Arch Occup Environ Health 86(2): 177- 187. Published. ASB2018-2873	2013	Waggoner, J. K., et al.	Nat'l Inst. for Occupational Safety and Health, etc.	https://doi.org/10.1007/s00420-012-0752-x	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-2008	農薬散布免許を持つ男性農業従事者	負傷による死亡	各州死亡記録及び国民死亡指標（National Death Index）とのデータ照合	農薬の使用実態	アンケート	他農薬含む 51035	134	コックス比例ハザードモデル	21522	ハザード比 0.98	0.78-1.23	-	年齢、州	農薬暴露と男性の負傷による死亡の関連に関する調査。 米国農業健康調査（AHS)コホートによる研究。
160	Proximity to Crops and Residential Exposure to Agricultural Herbicides in Iowa.	Environ Health Perspect 114(6): 893-897. Published. ASB2018-2874	2006	Ward, M. H., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1289/ehp.8770	原著	○ EFSA 2018	無	米国（アイオワ州）	環境モニタリング調査	1998-2000	非ホジキンリンパ腫患者（20-74歳）の住宅	-	-	住居の周囲750m以内の農地面積	衛星画像データ	111	-	-	-	-	-	-	-	農地から住宅までの距離及び居住地の過去の農地使用歴と、住宅内の農薬濃度の関連を調査。
161	Contemporary-use pesticides in personal air samples during pregnancy and blood samples at delivery among urban minority mothers and newborns.	Environ Health Perspect 111(5): 749-756. Published. ASB2013-3850	2003	Whyatt, R. M., et al	Columbia Univ., etc.	https://doi.org/10.1289/ehp.5768	原著	○ EFSA 2018	無	米国（ニューヨーク市）	バイオモニタリング調査	1998-2001	アフリカ系／ドミニカ系妊婦（18-35歳）と新生児	-	-	住宅内の農薬濃度	埃の吸引等により測定	230	-	-	-	-	-	-	-	住居内の空気中や埃の中の農薬濃度と、妊婦及び新生児（臍帯）の血中の農薬濃度の関連を調査。
162	Reduced birth weight in relation to pesticide mixtures detected in cord blood of full-term infants.	Environment International 47: 80-85. Published. ASB2018-2875	2012	Wickerham, E. L., et al.	Univ. of Mishican, etc.	https://doi.org/10.1016/j.envint.2012.06.007	原著	○ EFSA 2018	無	中国（浙江省）	横断研究	2009	21-39歳の妊婦と新生児	低体重出産	新生児の出生時体重測定	妊婦の血中と新生児の臍帯血中の農薬濃度	採血	112	-	-	-	-	-	-	-	妊婦及び新生児（臍帯）血中農薬濃度と低体重出生との関連の調査。各農薬単体による影響は調べられていない。
163	Community air monitoring for pesticides. Part 3: Using health-based screening levels to evaluate results collected for a year.	Environmental Monitoring and Assessment 186(3): 1355-1370. Published. ASB2018- 2876	2014	Wofford, P., et al.	California Environmental Protecction Agency, etc.	https://doi.org/10.1007/s10661-013-3394-x	原著	○ EFSA 2018	無	米国（カリフォルニア州）	環境モニタリング調査	2006	-	-	-	大気中の農薬濃度	大気中のサンプル採取	3	-	-	-	-	-	-	-	農業地域の大気中の農薬濃度の調査。 メトラクロールは検出されなかった。
209	Sleep apnea and pesticide exposure in a study of US farmers.	Sleep Health: Journal of the National Sleep Foundation, 4(1), 20-26.	2017	Baumert, B. O., et al.	Nat'l Inst. of Health, etc.	https://doi.org/10.1016/j.sleh.2017.08.006	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	2009-2013	農薬散布免許を持つ男性農業従事者	睡眠時無呼吸症候群	アンケートによる自己申告	農薬の使用実態	アンケート	1569	234	ロジスティック回帰	855	オッズ比 0.82	0.86-1.85	-	年齢、州、肥満度、糖尿病、高血圧、喘息、循環器疾患	本論文は米国に農薬散布者における農薬曝露と睡眠時無呼吸症候群との関連性を調査したものである。63 種類の農薬の使用と睡眠時無呼吸症候群 (症例234 件、非症例1,335 件) の関連性を推定している。カルボフランへの曝露が睡眠時無呼吸症候群と正の関連があることを示唆
213	Sex Steroid Hormone Single-Nucleotide Polymorphisms, Pesticide Use, and the Risk of Prostate Cancer: A Nested Case–Control Study within the Agricultural Health Study.	Frontiers in Oncology, 6, 237.	2016	Christensen, C. H., et al.	Center for Tobacco Products, Food and Drug Administration, etc.	https://doi.org/10.3389/fonc.2016.00237	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2004	農薬散布免許を持つ男性農業従事者	前立腺がん	アンケートによる自己申告	農薬の使用実態	アンケート	2220	-	-	-	-	-	-	年齢、州、喫煙歴、肥満度、家族の罹患歴	ホルモン恒常性に関与する一塩基多型（SNP）が前立腺がんリスクに対する農薬曝露の影響を変化させるかどうかを評価。農業健康研究コホートに含まれる776例と1,444例の対照の前立腺がんに関して、39の農薬とSNPの間の農薬-SNP相互作用を評価した。除草剤ジカンバとテストステロン代謝遺伝子 SRD5A1 の rs8192166 の間に有意な相互作用が示唆された
215	Rheumatoid arthritis among women in the Agricultural Health Study: risk associated with farming activities and exposures.	Annals of Epidemiology, 15(10), 762-770.	2005	De Roos, A. J., et al.	University of Washington, etc.	https://doi.org/10.1016/j.annepidem.2005.08.001	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2003	農薬散布免許を持つ女性農業従事者と女性配偶者	関節リュウマチ	アンケートによる自己申告	農薬の使用実態	アンケート	810	135	ロジスティック回帰	505	オッズ比 0.4	0.1-1.7	-	年齢、州	農薬と関節リュウマチ（RA）との関連性研究。57,000人以上の農薬散布者及びその配偶者集団が対象。RA の危険因子は特定されなかった。 。
217	Hypothyroidism and pesticide use among male private pesticide applicators in the agricultural health study.	Journal of Occupational and Environmental Medicine/American College of Occupational and Environmental Medicine, 55(10), 1171.	2013	Goldner, W. S., et al.	University of Nebraska, etc.	https://doi.org/10.1097/JOM.0b013e31829b290b	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-1997	農薬散布免許を持つ男性農業従事者	甲状腺疾患	アンケートによる自己申告	農薬の使用実態	アンケート	22246	919	ロジスティック回帰	-	オッズ比 1.14	0.95-1.38	-	年齢、学歴、肥満度	甲状腺疾患と農薬使用との関連性の評価。22,246人の男性が対象。50種類農薬の使用と甲状腺疾患との関連性を調べた。アラクロール、2,4-D、アルドリン、クロルデン、DDT、リンデン、パラチオン等へのばく露が甲状腺機能低下との関連性を示唆。
218	Cancer Risk and Parental Pesticide Application in Children of Agricultural Health Study Participants	Environmental Health Perspectives • volume 1121 number 51 April 2004	2004	Kori B. Flower,, et al.	University of North Carolina, Chapel Hill, etc.	https://doi.org/10.1289/ehp.6586	原著	○ EFSA 2018	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-1997	農薬散布免許を持つ農業従事者の子供	小児がん	各州がん患者登録との照合	両親の農薬の使用実態	アンケート	17357	50	ロジスティック回帰	3032	オッズ比 0.69	0.26-1.84	-	年齢	小児がんのリスクと親の農薬散布との関連性を調査。農薬散布者の子供 17,357 人が対象。
220	Exacerbation of symptoms in agricultural pesticide applicators with asthma.	International Archives of Occupational and Environmental Health, 87(4), 423-432.	2014	Paul K. Henneberger , et al.	National Institute for Occupational Safety and Health, etc.	https://doi.org/10.1007/s00420-013-0881-x	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許を持つ農業従事者	喘息の悪化	アンケートによる自己申告	農薬の使用実態	アンケート	956	132	ロジスティック回帰	926	オッズ比 1.1	0.7-1.8	-	年齢、州、喫煙歴、アレルギー	喘息症状の悪化が農薬曝露と関連しているかどうかを調査。喘息を有する926人の農薬散布者が対象。36種の農薬。
221	Chemical predictors of wheeze among farmer pesticide applicators in the Agricultural Health Study.	American Journal of Respiratory and Critical Care Medicine, 165(5), 683-689.	2002	Hoppin, J. A., et al.	National institute of Health, etc.	https://doi.org/10.1164/rccm.2106074	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1994-1997	農薬散布免許を持つ農業従事者	喘鳴	アンケートによる自己申告	農薬の使用実態	アンケート	20468	3838	ロジスティック回帰	-	オッズ比 1.07	0.97-1.19	0.26	年齢、州、喫煙歴、喘息、アトピー	農薬と喘鳴との関連性に関するコホート研究。対象は16～88歳までの農薬アプリケーター20,468 人。パラチオンの OR が最も高い (1.5、95% 信頼区間 [CI] 1.0、2.2)、アトラジンとアラクロールは関連性あり。2,4-D は喘鳴と関連
225	Pesticides associated with wheeze among commercial pesticide applicators in the Agricultural Health Study.	American Journal of Epidemiology, 163(12), 1129-1137.	2006	Hoppin, J. A., et al.	National Institutes of Health, etc.	https://doi.org/10.1093/aje/kwj138	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許を持つ農業従事者	喘鳴	アンケートによる自己申告	農薬の使用実態	アンケート	2255	134	ロジスティック回帰	-	オッズ比 1.37	1.05-1.78	-	年齢、喫煙歴、喘息、アトピー	農薬と喘鳴の関連性を調査。AHSにおける農薬散布作業者2,255 人のデータを解析。36農薬、有機リン系殺虫剤と呼吸器疾患の関連性を示唆。
226	Pesticides are Associated with Allergic and Non-Allergic Wheeze among Male Farmers.	Environmental Health Perspectives, 125(4), 535–543.	2017	Hoppin, J. A., et al.	North Carolina State University, etc.	https://doi.org/10.1289/EHP315	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2010	農薬散布免許を持つ農業従事者	喘息	アンケートによる自己申告	農薬の使用実態	アンケート	22139	5249	ロジスティック回帰	-	オッズ比 1.12 1.14	0.91-1.37 1.01-1.28	-	年齢、喫煙歴、喘息、農薬使用歴、トラクター運転歴	農薬とアレルギー性及び非アレルギー性喘息を有する農業従事者との関連性を調査。AHS（2005-2010）における農薬散布作業者 22134人のデータを解析。78農薬。
228	Pesticide exposure and self-reported Parkinson's disease in the agricultural health study.	American Journal of Epidemiology, 165(4), 364-374.	2007	Kamel, F., et al.	National Institute of Environmental Health Sciences, etc.	https://doi.org/10.1093/aje/kwk024	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2003	農薬散布免許を持つ農業従事者	パーキンソン病	アンケートによる自己申告	農薬の使用実態	アンケート	79640	83 78	ロジスティック回帰	-	オッズ比 0.9 1.3	0.5-1.6 0.7-2.3	-	年齢、州、喫煙歴	農薬とパーキンソン病との関連性を調査。AHS(n = 79,557 and follow up調査 n = 55,931。特定の農薬はPDを増加させる可能性を示唆。
230	Retinal degeneration and other eye disorders in wives of farmer pesticide applicators enrolled in the agricultural health study.	American Journal of Epidemiology, 161(11), 1020-1029.	2005	Kirrane, E. F., et al.	National Institutes of Health, etc	https://doi.org/10.1093/aje/kwi140	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	コホート研究	1993-1997	農薬散布免許を持つ農業従事者の女性配偶者	眼疾患/網膜変性症	アンケートによる自己申告	農薬の使用実態	アンケート	31173	281	ロジスティック回帰	-	オッズ比 0.7	0.3-1.5	-	年齢、州	農家の農薬散布者の妻の網膜変成につき1993-1997年にアンケート調査を実施
231	Xenobiotic metabolizing gene variants, pesticide use, and risk of prostate cancer.	Pharmacogenetics and Genomics, 21(10), 615.	2011	Koutros, S., et al.	National Institutes of Health, etc	https://doi.org/10.1097/FPC.0b013e3283493a57	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2003	農薬散布免許を持つ男性農業従事者	前立腺がん	うがい薬リンス液から の頬細胞からのDNA	農薬の使用実態	アンケート	776/1444	776	ロジスティック回帰	-	オッズ比 1.14 0.84	0.91-1.44 0.65-1.07	0.109	年齢、州、家族の既往歴	農業従事者での農薬とSNP(1塩基多型）の相互作用を176例の前立腺がん患者とAHS(農業健康調査）での健常者での1,444例AHS(農業健康調査）を検討した
232	Occupational exposure to pesticides and bladder cancer risk.	International Journal of Epidemiology, 45(3), 792-805.	2016	Koutros, S., et al.	National Institutes of Health, etc	https://doi.org/10.1093/ije/dyv195	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2011	農薬散布免許を持つ農業従事者	膀胱がん	各州死亡記録及び国民死亡指標（National Death Index）とのデータ照合	農薬の使用実態	アンケート	54344	321	ポアソン回帰	-	相対リスク 0.88 0.44 0.63	0.58-1.34 0.49-1.12 0.44-0.99 0.63-1.44	0.73	年齢、人種、州、喫煙歴	農薬を使用する農業従事者の農薬暴露と膀胱がんの関連について、65種類の殺虫剤と321例の膀胱がん患者について調査を実施。
235	Pesticide exposure and end-stage renal disease risk among wives of pesticide applicators in the Agricultural Health Study.	Environmental Research, 143, Part A, 198-210.	2015	Lebov, J., et al.	University of North Carolina, Chapel Hill, etc	https://doi.org/10.1016/j.envres.2015.10.002	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-1997	農薬を使用する農業従事者の女性配偶者	末期腎臓疾患（ESRD）	米国腎臓データシステムとのデータ照合	農薬の使用実態	アンケート	31142	98	コックス比例ハザードモデル	-	ハザード比 1.23	0.71-2.74	-	年齢、喫煙、肥満度、解熱剤服用歴、糖尿病、高血圧	農業従事者の農薬暴露の影響は腎損傷と機能不全を引き起こす事が研究されているが、低レベルの農薬の慢性的暴露による、腎臓への影響について、農薬散布者の妻における末期腎臓疾患（ESRD）と1)個人の農薬使用の関係、2)夫の農薬使用の暴露、3)その他の殺虫剤関連農業と家庭内での活動について調査した。
237	Pesticide use and risk of non-Hodgkin lymphoid malignancies in agricultural cohorts from France, Norway and the USA: a pooled analysis from the AGRICOH consortium.	International Journal of Epidemiology. https://doi.org/10.1093/ije/dyz017	2019	Leon, M., et al.	International Agency for Research on Cancer (IARC), France, etc.	https://doi.org/10.1093/ije/dyz017	原著	○ EPA 2019	無	フランス、ノルウェー、アメリカ	前向きコホート研究	フランス：2005-2009 ノルウェー：1969-2011 USA：1993-2012	AGRICAN、CNAP、AHSに参加の農業従事者	非ホジキンリンパ腫	各国がんデータシステムとの照合	農薬の使用実態	アンケート	316270	2430	コックス比例ハザードモデル	-	ハザード比 0.99 1.02 0.95	0.84-1.17 0.72-1.43 0.64-1.42	0.57 0.45 0.86	性別、年齢、家畜飼育歴、州	3つの大規模な農業従事者コホート：フランス、ノルウェー、USAにおける農業従事者について、14の農薬グループおよび33の農薬有効成分の使用と非ホジキンリンパ性悪性腫瘍の関係を調査
238	Occupational pesticide exposure and subclinical hypothyroidism among male pesticide applicators.	Occupational and Environmental Medicine, 75(2), 79-89.	2018	Lerro, C. C., et al.	National Cancer Institute, etc.	https://doi.org/10.1136/oemed-2017-104431	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2013	農薬散布免許を持つ農業従事者	甲状腺機能低下	血液検査	農薬の使用実態	アンケート	675	127	ロジスティック回帰	-	オッズ比 1.47 1.23 0.65 1.44	0.79-2.71 0.64-2.37 0.30-1.39 0.72-2.88	0.41	年齢、州、肥満度、喫煙歴	動物実験では、殺虫剤の暴露が甲状腺機能が変化する事が示唆されているが、農薬散布者の男性を対象に個々の農薬と甲状腺機能との関係を評価した。
239	Pesticide exposure and risk of rheumatoid arthritis among licensed male pesticide applicators in the Agricultural Health Study.	Environmental Health Perspectives, 125(7).	2017	Meyer, A., et al.	National Instltutes of Health, etc.	https://doi.org/10.1289/EHP1013	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2015	農薬散布免許を持つ男性農業従事者	関節リウマチ（RA）	アンケートによる自己申告	農薬の使用実態	アンケート	28650	220	ロジスティック回帰	-	オッズ比 0.90	0.67-1.20	-	年齢、州、喫煙歴、学歴	農業従事者のうち、男性の農薬散布許可者の農薬曝露と関節リウマチの関係を調査
242	Pesticide Use and Age-Related Macular Degeneration in the Agricultural Health Study.	Environmental Health Perspectives, 125(7).	2017	Montgomery, M. P., et al.	National Instltutes of Health, etc.	https://doi.org/10.1289/EHP793	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2010	50歳以下は除外	AMD疾患	医師による診断	農薬の使用実態	アンケート	39108	161	ロジスティック回帰	-	オッズ比 1.2	0.8-1.8	-	年齢、州、喫煙歴、学歴	医師が確認したAMD患者(Age-Related Macular Degeneration:加齢性黄斑変性症）と農薬使用の関係を調査した。
243	Agricultural exposures and stroke mortality in the Agricultural Health Study.	Journal of Toxicology and Environmental Health, Part A, 76(13), 798-814.	2013	Rinsky, Jessica L., et al.	University of North Carolina, Chapel Hill, etc	https://doi.org/10.1080/15287394.2013.819308	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2008	農薬散布免許を持つ男性農業従事者	脳卒中による死亡	国民死亡指標（National Death Index）とのデータ照合	農薬の使用実態	アンケート	51603	308	-	-	-	-	-	肥満度、糖尿病、手袋使用の有無、年齢、州、人種、学歴	農業従事者の農薬曝露は脳卒中のリスクを高める可能性がある。AHSの農薬使用者の農薬暴露と脳卒中の関連を調査した。
245	High pesticide exposure events and olfactory impairment among US farmers.	Environmental Health Perspectives, 127(01), 017005.	2019	Shrestha, S., et al.	National Instltutes of Health, etc.	https://doi.org/10.1289/EHP3713	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2015	農薬散布免許を持つ農業従事者	嗅覚障害	アンケート調査	農薬の使用実態	アンケート	11232	1186	ロジスティック回帰	-	オッズ比 3.20	1.69-6.06	-	年齢、性別、州、学歴、婚姻歴、喫煙歴、飲酒歴	農薬使用者の嗅覚障害(OI)について、高農薬曝露の影響を調査した。

246	Factors associated with dream enacting behaviors among US farmers.	Parkinsonism & Related Disorders, 57, 9-15.	2018	Shrestha, S., et al.	National Institutes of Health, etc	https://doi.org/10.1016/j.parkreldis.2018.07.003	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2015	農薬散布免許を持つ男性農業従事者	DEB（夢の行動化）	アンケート調査	農薬の使用実態	アンケート	20591	1623	ロジスティック回帰	-	オッズ比 1.0	0.9-1.2	-	年齢、性別、州、学歴、婚姻歴、喫煙歴、飲酒歴、頭痛	20,591人の男性農業従事者を対象にDEB障害者のスクリーニングを行い、約20年前に報告された農薬使用やその他の潜在的な危険因子との関連性を検討 ＊メトラクロールは1対象薬剤、言及なし
247	Pesticide use and incident hypothyroidism in pesticide applicators in the Agricultural Health Study.	Environmental Health Perspectives, 126(9),	2018	Shrestha, S., et al.	National Institutes of Health, etc.	https://doi.org/10.1289/EHP3194	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2016	農薬散布免許を持つ農業従事者	甲状腺疾患	アンケート調査	農薬の使用実態	アンケート	35150	829	コックス比例ハザードモデル	-	ハザード比 0.98	0.85-1.13	0.8	性別、学歴、州、喫煙歴	農業健康調査（AHS）において、特定の農薬の使用と農薬散布者における甲状腺機能低下症の発症との関連性を評価。 ＊メトラクロールは1対象薬剤、言及なし
248	Pesticide use and incident hyperthyroidism in farmers in the Agricultural Health Study.	Occupational and Environmental Medicine, 76(5), 332-335.	2019	Shrestha, S., et al.	National Institutes of Health, etc.	https://doi.org/10.1136/oemed-2018-105518	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2016	農薬散布免許を持つ農業従事者	甲状腺機能亢進	アンケート調査	農薬の使用実態	アンケート	35150	271	コックス比例ハザードモデル	-	ハザード比 0.75 0.68	0.57-0.99 0.39-1.16	-	性別、学歴、州、喫煙歴	AHSにおける特定の農薬と農薬散布者における甲状腺機能亢進症との関連性を評価 ＊メトラクロールは1対象薬剤、甲状腺機能亢進症リスクを軽減
249	Incident thyroid disease in female spouses of private pesticide applicators.	Environment International, 118, 282-292.	2018	Shrestha, S., et al.	National Institutes of Health, etc.	https://doi.org/10.1016/j.envint.2018.05.041	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2016	農薬散布免許を持つ農業従事者の女性配偶者	甲状腺疾患	アンケート調査	農薬の使用実態	アンケート	24092	1627人(甲状腺機能低下症) 531人（甲状腺機能亢進症）	コックス比例ハザードモデル	-	ハザード比 0.70 0.72	0.51-0.96 0.48-1.08	-	学歴、州、喫煙歴、他農薬の使用歴	農業健康調査（AHS）において、農薬と農場曝露における甲状腺機能低下症および甲状腺機能亢進症との関連性を評価　＊メトラクロールは1対象薬剤、甲状腺機能亢進症リスクを軽減
252	Pesticide use and incident diabetes among wives of farmers in the Agricultural Health Study.	Occupational and Environmental Medicine, 71(9), 629-635.	2014	Starling, A. P., et al.	National Institutes of Health, etc.	https://doi.org/10.1136/oemed-2013-101659	原著	○ EPA 2019	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2016	農薬散布免許を持つ農業従事者の女性配偶者	糖尿病	アンケート調査	農薬の使用実態	アンケート	13637	688	コックス比例ハザードモデル	-	ハザード比 0.78	0.54-1.11	-	州、肥満度	農薬の使用と女性における糖尿病発症との関連性を評価 ＊メトラクロールは1対象薬剤、言及なし
277	Use of agricultural pesticides and prostate cancer risk in the Agricultural Health Study cohort.	Am J Epidemiol, 157(9), 800-814.	2003	Alavanja, M. C.R., et al.	National Cancer Institute, etc.	https://doi.org/10.1093/aje/kwk040	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2005	農薬散布免許を持つ男性農業従事者	前立腺がん	アンケート調査	農薬の使用実態	アンケート	54766	566	ロジスティック回帰	-	-	-	-	-	前立腺がんの既往歴のないアイオワ州とノースカロライナ州の男性農業散布者55,332人を対象とした前向きコホート研究（AHS）において、45種類の農薬と前立腺がん発生率との関係を評価 ＊メトラクロールは1対象薬剤、言及なし
280	Pesticide use and practices in an Iowa farm family pesticide exposure study.	J Agric Saf Health, 8(4), 423-433.	2002	Curwin, B., et al.	University of Iowa, etc.	https://doi.org/10.13031/2013.10222	原著	○ EPA 2014	無	米国（アイオワ州）	環境モニタリング調査	2001年	25農家家族と25非農家家族（大人95人、子供118人）	農薬ばく露	アンケート調査	農薬の使用実態	アンケート	213	-	-	-	-	-	-	-	アイオワ州における農薬の使用と農薬暴露に関する研究
283	Pesticide use and cutaneous melanoma in pesticide applicators in the agricultural heath study.	Environ Health Perspect, 118(6), 812-817.	2010	Dennis, L. K., et al.	University of Iowa, etc.	https://doi.org/10.1289/ehp.0901518	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-1997	-	皮膚黒色腫	アンケート調査	農薬の使用実態	アンケート	57310	-	ロジスティック回帰	-	-	-	-	-	農業散布者の農業健康研究コホートにおける50種類の農薬と皮膚黒色腫の発生率の用量反応関係を評価 ＊メトラクロールは対象薬剤として含まれるが言及なし
284	Pesticide use and breast cancer risk among farmers' wives in the agricultural health study.	Am J Epidemiol, 161(2), 121-135.	2005	Engel, L. S., et al.	National Institutes of Health, etc.	https://doi.org/10.1093/aje/kwi022	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-1997	農薬散布免許を持つ農業従事者の女性配偶者	乳がん	アンケート調査	農薬の使用実態	アンケート	30454	309	ポアソン回帰	-	相対リスク 1.3 1.0	0.8-2.4 0.7-1.5	-	年齢、人種、州	農薬使用と乳がんとの関連性の調査。 ＊メトラクロールは対象薬剤として含まれるが言及なし
286	Risk of total and aggressive prostate cancer and pesticide use in the Agricultural Health Study.	Am J Epidemiol, 177(1), 59-74.	2013	Koutros, S., et al.	National Cancer Institute, etc.	https://doi.org/10.1093/aje/kws225	原著	○ EPA 2014	無	米国（アイオワ州及びノースカロライナ州）	前向きコホート研究	1993-2007	農薬散布免許を持つ男性農業従事者	前立腺がん	アンケート調査	農薬の使用実態	アンケート	54412	1962	ポアソン回帰	-	-	-	-	-	AHSにおける特定の農薬と前立腺がんとの関連性を評価 ＊メトラクロールは対象薬剤として含まれるが言及なし