[redacted]

Literature Review Report (LRR)
on metamitron and its metabolite desamino-metamitron

October 2023

Project number ADA23027

Prepared by:

[redacted]

This document has been prepared as part of the required assessment of scientific peer-reviewed open literature for any potential impact on human health and/or the environment associated with exposure to metamitron and its metabolite desamino-metamitron

[redacted]

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OBJECTIVE OF THE REVIEW

This Literature Review Report (LRR) collates information on the active substance metamitron and its metabolite desamino-metamitron that has been published in the scientific peer-reviewed open literature from October 2019-June 2023 (inclusive).

The active substance is identified as:

- Metamitron
  [CAS RN[1] 41394-05-2]

and its metabolite as:

- desamino-Metamitron
  [CAS RN 36993-94-9]

The LRR describes the search and selection process for relevant and reliable information on the toxicity, metabolism, ecotoxicity, environmental fate, environmental behaviour or residues of metamitron and its metabolite desamino-metamitron. Summaries of the pertinent studies relating to ecotoxicity and environmental fate/behaviour are presented in Appendix 3. The client does not require the summary of mammalian toxicology studies in 2023.

The search process and LRR documentation have taken into consideration the European Crop Protection Association (ECPA) "Technical guidance on the application of the EFSA Guidance Document 'Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009'" (ECPA, 2012).

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[1] Chemical Abstracts Service Registry Number is a Registered Trademark of the American Chemical Society.

SEARCH AND SELECTION STRATEGY

In July 2023, a search strategy based on a single concept[2] was performed by [redacted] in the Agricola, Analytical abstracts, BIOSIS Toxicology, CAB Abstracts, Embase, Environment Abstracts, Medline, Toxfile, Toxicology Abstracts, Toxline and PubMed databases[3] and TRACE[4], for information on the active substance (metamitron). This used its specific CAS RN and appropriate synonyms and name fragments. Similar searches were also performed at this time, using the same databases, for its metabolite desamino-metamitron, using its specific CAS RN, synonyms and name fragments.

The search strategy, including database coverage, the specific search terms used and an overview of the results obtained, is described in Appendix 1. The search results themselves are documented and tabulated in Appendix 2.

The selection process resulted in three categories of publication:

- Publications judged by rapid assessment (and from their titles alone) to be of clear irrelevance to the fields outlined above (in the "Objective of the review" section). These references were immediately rejected during the literature search phase and are not documented within the LRR. Examples of publications immediately rejected as irrelevant under rapid assessment included (but were not limited to) those considering "thinning" in the context of efficacy, and benefit studies (unless the title and/or available preview suggested that adverse effects may also have been assessed).

- Publications initially judged to be of potential relevance to the fields listed above (in the "Objective of the review" section) which, upon closer inspection of the abstract, were deemed to be either irrelevant or unreliable. These are documented in Appendix 2, with justifications for (ir)relevance and/or (un)reliability.

- Publications of certain relevance to the fields listed above (in the "Objective of the review" section) which, upon inspection of the full-text document, were deemed to be either reliable or unreliable. Where appropriate, reasons for (un)reliability are documented in Appendix 2.

No assessments conducted by the European Food Safety Authority (EFSA), the Joint FAO/WHO[5] Meeting on Pesticide Residues (JMPR) or the United States Environmental

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[2] A single concept search strategy captures all data in one search, for example by searching using terms for the substance of interest and its synonyms only. This is in contrast to a strategy using separate focused searches for individual or grouped endpoints (such as toxicity or ecotoxicity etc.), for example by combining searches for the substance of interest (and its synonyms) with one or more other concepts relating to each endpoint/group of endpoints of interest.

[3] Searches are considered to be valid and complete as of the date of searching. [redacted] holds no responsibility for the accuracy or completeness of the databases consulted, for the maintenance or sufficiency of any multi-database platform utilised for search purposes, or for results omitted as a direct consequence of failings in such aspects at the time of searching.

[4] Bibra's in-house database and databank https://www.bibra-information.co.uk/scientific-support/trace.

[5] Food and Agriculture Organization/World Health Organization.

Protection Agency (US EPA) were identified in the searches, so could not be consulted for any primary papers published during the designated dates.

CRITERIA FOR RELEVANCE

The following criteria for relevance were used in the selection of mammalian **toxicology** and **metabolism** studies for the LRR:

- Appropriate test substance and physical form (excluding salts), and
- Appropriate test species for mammalian toxicological risk assessment (i.e. mammalian species for all endpoints except genotoxicity and endocrine disruption), and
- Relevant route of administration (i.e. oral, dermal or inhalation for all endpoints except genotoxicity and endocrine disruption), and
- Information relating to human or animal health, toxicology or metabolism

or:

- Epidemiological studies associating health effects with exposure were considered relevant due to their potential implications if assessed as part of a weight-of-evidence evaluation.

The following criteria for relevance were used in the selection of **ecotoxicology** studies for the LRR:

Experimental studies

- Appropriate test substance (excluding salts or individual enantiomers), and
- Appropriate test species (i.e. a species able to inform with respect to ecotoxicology endpoints, including non-standard species if these can be used to provide supplementary information, and non-target plants[6]), and
- Appropriate number of individuals tested, and
- Test conditions representative of European geoclimatic conditions, and
- The test substance is applied alone or as part of a solo formulation (mixtures and combined toxicity studies are excluded), and
- Sufficient data on dosing the test substance (i.e. static, semi-static, flow through system), and

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[6] Non-target plants does NOT include crop plants. Under Commission Regulation (EU) No. 284/2013 (EU Commission, 2013), information on deleterious impacts on the crop plant itself is not relevant to either the environmental fate or ecotoxicology regulatory data packages for the product.

- Information that informs or partially informs data requirements, relating to ecotoxicology.

Monitoring studies

- Appropriate analyte (excluding salts or individual enantiomers), and
- Appropriate extraction/analysis method (e.g. pre-validated or scientifically rigorous), and
- Appropriate test species (i.e. a species able to inform with respect to ecotoxicology endpoints, including non-standard species if these can be used to provide supplementary information, and non-target plants[6]), and
- Appropriate environmental conditions representative of European geoclimate, and
- Appropriate sampling locations (i.e. areas containing arable cropping, or related to such areas), where substance use (i.e. application rates and timing) can be expected to be representative of those recommended under current intended uses, and
- Appropriate sampling strategy (i.e. scheduled sampling or event driven sampling, time of year, developmental stage, sampling campaign duration and monitoring programme duration), and
- Information that informs or partially informs data requirements, relating to ecotoxicology.

The following criteria for relevance were used in the selection of **environmental fate** and **environmental behaviour** studies for the LRR:

Experimental studies

- Well defined test substance (excluding salts and individual enantiomers), and
- Appropriate substrate (i.e. type of soil, collection site and history - a standard substrate, or a non-standard substrate if it would be applicable to a particular intended use), and
- Appropriate experimental conditions (i.e. temperature, duration etc.), and
- Appropriate extraction/analysis method (e.g. pre-validated or scientifically rigorous), and
- Application rates and/or substrate loads which are representative of those expected under current intended uses and (if applicable) appropriate associated endpoint derivation(s), and
- Information that informs or partially informs data requirements, relating to environmental fate/behaviour.

Monitoring studies

- Appropriate, analyte (i.e. active substance and/or metabolite(s)), and

- Appropriate extraction/analysis method (e.g. pre-validated or scientifically rigorous), and
- Appropriate matrix type (i.e. soil, sediment and water), relevant to environmental fate and behaviour assessments, and
- Appropriate environmental conditions representative of European geoclimate, and
- Appropriate sampling locations (i.e. areas containing arable cropping, or related to such areas), where substance use (i.e. application rates and timing) can be expected to be representative of those recommended under current intended uses, and
- Appropriate sampling strategy (i.e. scheduled sampling or event driven sampling, time of year, developmental stage, sampling campaign duration and monitoring programme duration), and
- Appropriate explanatory data and/or statistical analysis of analyte concentrations in relation to land use, weather, substance use (and combinations thereof), sufficient to provide information on sources, emissions and pathways, and
- Information that informs or partially informs data requirements, relating to ecotoxicology.

With respect to **residues** studies, a strategy was followed that is outlined in a report by the Austrian Agency for Health and Food Safety (AGES) and implies that residue studies in the open literature are unlikely to employ appropriate methodology:

"Studies dealing with analytical methods investigating residues in food of plant and animal origin are found in large numbers in scientific bibliographic databases. The results of analytical method studies are not directly connected to risk assessment. In fact, the methods have to be provided by the applicant in order to show that possible residues in food of plant and animal origin may be analysed using little effort so that they can be applied on a routine basis. Therefore it was concluded to not consider such studies relevant for the dossiers" (AGES, 2013).

Such studies were therefore not generally considered for inclusion in the LRR, unless the title and/or abstract contained information that suggested the use of pre-approved and/or established methodology.

CRITERIA FOR RELIABILITY

The reliability assessment for all relevant **toxicology** and **metabolism** studies was done according to the criteria outlined by Klimisch *et al.* (1997), below. However, it is noted that the criteria are broad, and the scores cannot always capture successfully the subtleties within publications (for example, they are not directly applicable to epidemiology studies and there is no clear score for cases where expert judgement of the data leads to a conclusion different to that presented by the investigators). In these cases, a "best fit" Klimisch score, with qualification, was employed.

Klimisch Score	Description	Details
1	Reliable without restriction	This includes studies or data from the literature or reports which were carried out or generated according to generally valid and/or internationally accepted testing guidelines (preferably performed according to Good Laboratory Practice (GLP)) or in which the test parameters documented are based on a specific (national) testing guideline (preferably performed according to GLP) or in which all parameters described are closely related/comparable to a guideline method.
2	Reliable with restriction	This includes studies or data from the literature or reports (mostly not performed according to GLP) in which the test parameters documented do not totally comply with the specific testing guideline, but are sufficient to accept the data or in which investigations are described which cannot be subsumed under a testing guideline, but which are nevertheless well documented and scientifically acceptable.
3	Not reliable	This includes studies or data from the literature or reports in which there are interferences between the measuring system and the test substance or in which organisms/test systems were used which are not relevant in relation to the exposure (e.g. unphysiologic pathways of application) or which were carried out or generated according to a method which is not acceptable, the documentation of which is not sufficient for an assessment and which is not convincing for an expert judgment. [This would include studies for which dose associated with the effects reported is neither calculable nor estimable.]
4	Not assignable	This includes studies or data from the literature which do not give sufficient experimental details and which are only listed in short abstracts or secondary literature (books, reviews etc.).

In addition, for **ecotoxicity**, **environmental fate** and **environmental behaviour** studies, a reliability indicator was employed taking into account the guidance of Mensink *et al.* (2008) and the "Criteria for Reporting and Evaluating ecotoxicity Data" (CRED) guidance of Moermond *et al.* (2016), which is itself adapted from Klimisch *et al.* (1997):

Reliability indicator[7]	Description	Definition
Ri 1	Reliable	The methodology and the description are in accordance with internationally accepted test guidelines and/or the instructions in the manual.
Ri 2	Less reliable	The methodology and/or the description are less in accordance with internationally accepted test guidelines and/or the instructions in the manual.
Ri 3	Not reliable	The methodology and/or description are not in accordance with internationally accepted test guidelines and/or the instructions in the manual.

SUMMARY OF RELEVANT AND RELIABLE PUBLICATIONS

Following detailed assessments of the publications of certain relevance identified within the open peer-reviewed literature, two relating to the ecotoxicity and environmental fate/ behaviour endpoints were considered to be reliable. These studies are summarised in Appendix 3. At the client's request, publications relating to mammalian toxicology were not evaluated for reliability or summarised.

Studies may be considered relevant either by informing the critical endpoint values presented in Appendix I of the current EFSA Scientific Report on metamitron (EFSA, 2008[8]), or as a result of addressing an endpoint that has not previously been considered. Studies may be considered relevant by informing any endpoints relating to toxicity, metabolism ecotoxicity, environmental fate, environmental behaviour or residues. Reliability is evaluated from a methodological perspective.

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[7] In the absence of an Ri 4, ecotoxicity and environmental fate and behaviour studies for which the reliability was deemed unassignable (generally due to an absence of primary data) have been classed as not relevant in Appendix 2.

[8] Appendix II of the current EU data package on metamitron was not available to [redacted] at the time of writing.

REFERENCES

AGES (2013). Austrian Agency for Health & Food Safety, Institute for Plant Protection Products. External scientific report. Case studies for the application of the Guidance of EFSA on Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009, using substances for which dossiers are submitted under Regulation (EU) No 1141/20101. EFSA supporting publication 2013, EN-511. https://www.efsa.europa.eu/en/supporting/pub/en-511

ECPA (2012). European Crop Protection Association. ECPA Technical Guidance Paper No: 2012/4[9]. Technical guidance on the application of the EFSA Guidance Document "Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009". https://croplifeeurope.eu/wp-content/uploads/2021/02/21679_ECPA_TGP_on_applying_EFSA_guidance_on_open_literature.pdf

EFSA (2008). European Food Safety Authority. Conclusion on the peer review of metamitron. EFSA Scientific Report 185, 1-95. Conclusion regarding the peer review of the pesticide risk assessment of the active substance metamitron. Issued on 29 September 2008. http://www.efsa.europa.eu/sites/default/files/scientific_output/files/main_documents/185r.pdf

EU Commission (2013). Commission Regulation (EU) No. 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. Official Journal L93, 85-152. 3.4.2013. https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:093:0085:0152:EN:PDF%20

Klimisch HJ, Andreae E and Tillmann U (1997). A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Regulatory Toxicology and Pharmacology 25, 1-5.

Mensink BJWG, Smit CE and Montforts MHMM (2008). Netherlands National Institute for Public Health and the Environment (RIVM). Manual for summarising and evaluating environmental aspects of plant protection products. Report 601712004/2008. http://www.rivm.nl/bibliotheek/rapporten/601712004.pdf

Moermond CTA, Kase R, Korkaric M and Agerstrand M (2016). CRED: Criteria for reporting and evaluating ecotoxicity data. Environmental Toxicology and Chemistry 35, 1297-1309.

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[9] Previously designated 2012/2.

[redacted]

Appendix 1

Overview of the search process for the Literature Review Report (LRR) on metamitron and its metabolite desamino-metamitron

October 2023

Project number ADA23027

Prepared by:

[redacted]

[redacted]

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OVERVIEW OF DATABASE UTILISATION

DATABASES SEARCHED

The following databases were searched by [redacted] for information potentially relevant to the mammalian toxicity, metabolism, ecotoxicity, environmental fate, environmental behaviour or residues of metamitron and its metabolite desamino-metamitron:

ProQuest Dialog databases

For both substances:

AGRICOLA
Analytical Abstracts
BIOSIS® Toxicology
CAB ABSTRACTS
Embase®
Environment Abstracts
MEDLINE®
ToxFile®
Toxicology Abstracts
TOXLINE

U.S. National Library of Medicine database (US NLM)

For both substances:

PubMed®

It has previously been noted that ProQuest Dialog cannot be relied upon to return all the relevant publications that might be identified through TOXLINE (discontinued). TOXLINE content is now only available embedded within PubMed®, and so this additional search is included routinely via the US NLM directly. It is possibly unnecessary due to the inclusion of MEDLINE® in the ProQuest Dialog databases consulted (PubMed® being itself a subset of MEDLINE®).

Bibra database

For all substances:

TRACE

JUSTIFICATION FOR DATABASE UTILISATION

AGRICOLA

AGRICOLA (ProQuest dialog) consists of worldwide literature citations for journal articles, monographs, proceedings, theses, patents, translations, audiovisual materials, computer software, and technical reports pertaining to all aspects of agriculture and related fields.

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[1] Disclaimer: searches are valid and complete as of the date of searching. [redacted] accepts no responsibility for the accuracy, completeness or sufficiency of any databases or searching platforms employed.

[redacted]

This database is updated monthly.

Subject coverage:

- Agriculture (general)
- Agriculture (products; engineering; information systems)
- Animal sciences
- Biotechnology
- Botany
- Chemistry conservation
- Cytology
- Agricultural economics, energy, entomology and history
- Farm management
- Feed science
- Fertilizers
- Fibers and textiles
- Food and nutrition
- Forestry
- Horticulture
- Human ecology
- Human nutrition
- Hydrology
- Hydroponics
- Microbiology
- Natural history
- Natural resources
- Pesticides
- Physiology
- Plant sciences
- Pollution
- Public health
- Rural sociology
- Soil sciences
- Veterinary medicine
- Water quality
- Weather and climate
- Wildlife
- Zoology

Analytical Abstracts

Analytical Abstracts (ProQuest Dialog) covers all aspects of analytical chemistry in a wide variety of areas including general applications, biochemistry and clinical chemistry, industrial and applied science, environmental science, agriculture and food, pharmaceuticals and instrumentation.

This database is updated weekly.

Subject coverage, all fields of analytical chemistry, including

- General
- Inorganic
- Organic
- Industrial
- Biochemical
- Pharmaceutical
- Food
- Agricultural and environmental
- Computer handling of analytical data
- Instrumentation

BIOSIS® Toxicology

BIOSIS® Toxicology (ProQuest Dialog) is a subset of BIOSIS® Previews, with a focus on toxicology and related topics. Records are drawn from journal articles, conference papers, monographs and book chapters, notes, letters, and reports, as well as original research. U.S. patent records are also included.

This database is updated weekly.

Subject coverage, all aspects of toxicology, relating to:

- Agriculture
- Bacteriology
- Biochemistry
- Biophysics
- Biotechnology
- Botany
- Cell biology
- Clinical medicine
- Drugs
- Environmental biology
- Environmental science
- Experimental medicine
- Genetics
- Immunology
- Microbiology
- Nutrition
- Occupational health
- Parasitology
- Pathology
- Pharmacology
- Physiology
- Public health
- Radiation biology
- Systematic biology

- Veterinary science
- Virology

CAB ABSTRACTS

CAB ABSTRACTS (ProQuest Dialog) provides comprehensive coverage of the worldwide literature on agriculture and allied fields, including veterinary medicine, human nutrition, horticulture, forestry, leisure, recreation, recreation and tourism, crop sciences, crop protection, breeding and genetics, animal production, animal nutrition, parasitology, soils, land use, agricultural engineering, agricultural economics and biotechnology. Publication types are journals, monographic series, theses, technical reports, conferences, selected patents, books and annual reports.

This database is updated weekly.

Subject coverage:

- Agricultural biotechnology
- Agricultural economics and rural sociology
- Agricultural engineering
- Animal health and veterinary medicine
- Animal production and genetics
- Biodeterioration and biodegradation
- Crop production
- Crop protection
- Dairy science
- Environmental degradation, conservation and amelioration
- Forestry
- Genetic resources
- Horticulture
- Human nutrition and diet-related disorders
- Human parasitic diseases
- Leisure, recreation and tourism
- Plant breeding and genetics
- Postharvest science
- Rural development
- Soil science
- Sugar industry

Embase®

Embase® (ProQuest Dialog) provides comprehensive bibliographic coverage of the literature on drugs and pharmacology and of all other aspects of human medicine and related disciplines. Embase is a key resource for biomedical evidence, from published, peer-reviewed literature, in-press publications and conference abstracts.

This database is updated daily.

Subject coverage:

- Drug research
- Pharmacology
- Pharmacoeconomics
- Pharmaceutics
- Toxicology
- Human medicine
- Basic biological research
- Health policy and management
- Public, occupational and environmental health
- Substance dependence and abuse
- Psychiatry
- Forensic science
- Biomedical engineering and instrumentation
- Medical devices

Environment Abstracts

Environment Abstracts (ProQuest Dialog) encompasses all aspects of the impact of people and technology on the environment and the effectiveness of remedial policies and technologies. The database covers journals, conference papers and proceedings, special reports from international agencies, non-governmental organizations, universities, associations and private corporations. Other materials selectively indexed include significant monographs, government studies and newsletters.

This database is updated monthly.

Subject coverage:

- Agriculture
- Air pollution
- Control technologies
- Endangered species
- Energy
- Environmental design
- Environmental education
- Environmental law and policy
- Environmental safety
- Geophysical and climate chance
- Global warming
- International environmental policy
- Land use and pollution
- Marine pollution
- Noise pollution
- Population
- Population studies
- Radiological contamination

- Resource management
- Solid and toxic waste
- Sustainable development
- Toxicological effects
- Transportation
- Waste management
- Water pollution
- Wildlife / biodiversity

MEDLINE®

MEDLINE® (ProQuest Dialog) is the US National Library of Medicine (NLM) premier bibliographic database. It contains references to journal articles in life sciences with a concentration on biomedicine and health. This is broadly defined to encompass those areas of the life sciences, behavioural sciences, chemical sciences, and bioengineering needed by health professionals and others engaged in basic research and clinical care, public health, health policy development, or related educational activities. Medline also covers life sciences vital to biomedical practitioners, researchers, and educators, including aspects of biology, environmental science, marine biology, plant and animal science as well as biophysics and chemistry.

This database is updated daily.

Subject coverage, biomedicine, including but not limited to:

- Clinical and preclinical medicine
- Dentistry
- Nursing
- Population and reproductive biology
- Pharmacology and pharmaceutics
- Psychiatry and psychology
- Environmental, public and occupational health
- Veterinary medicine
- Nutrition
- Pathology
- Anatomy and physiology
- Toxicology
- Genetics
- Microbiology
- Pathology
- Biomedical technology
- Health planning and administration
- Space life science

ToxFile®

ToxFile® (ProQuest Dialog) covers the toxicological, pharmacological, biochemical and physiological effects of drugs, pesticides and other chemicals. Typical areas of coverage include adverse drug reactions, chemically induced diseases, carcinogenesis, mutagenesis, teratogenesis, environmental pollution, waste disposal, radiation, and food contamination.

This database is updated daily.

Subject coverage:

- Adverse drug reactions
- Air pollution
- Animal venom
- Antidotes
- Carcinogenesis via chemicals
- Chemically induced diseases
- Drug evaluation
- Environmental pollution
- Food contamination
- Mutagenesis
- Occupation
- Pesticides
- Radiation
- Teratogenesis
- Toxicology
- Waste disposal

Toxicology Abstracts

Toxicology Abstracts (ProQuest Dialog) covers issues from social poisons and substance abuse to natural toxins, from legislation and recommended standards to environmental issues.

This database is updated monthly.

Subject coverage:

- Pharmaceuticals
- Food, additives and contaminants
- Agrochemicals
- Cosmetics, toiletries and household products
- Industrial chemicals
- Metals
- Toxins and other natural substances
- Social poisons and drug abuse
- Polycyclic hydrocarbons
- Nitrosamines and related compounds
- Radiation and radioactive materials
- Methodology
- Legislation and recommended standards

TOXLINE

TOXLINE (ProQuest Dialog) is a toxicology reference database that provides bibliographic information for journal articles on the effects of drugs and other chemicals.

According to ProQuest Dialog, this database is updated monthly. As of December 2019 it was discontinued as a standalone database, but its content continues to be available via PubMed®.

Subject coverage:

- Biochemistry
- Pharmacology
- Physiology
- Toxicology

PubMed®

PubMed® (US NLM) comprises more than 35 million citations for biomedical literature from MEDLINE®, life science journals, and online books. Citations may include links to full-text content from PubMed Central® and publisher web sites.

This database is updated daily.

TRACE

TRACE (bibra) includes information from peer-reviewed toxicology and nutrition journals as well as secondary sources and websites.

This database is updated daily.

Subject coverage:

- Chemical toxicology

SEARCH PROCESS FOR METAMITRON

TOP-UP SEARCHES – JULY 2023

Database[2]	**Latest database update**[3]	**Date of search**	**Search dates**	**Search strategy**	**Total number of records**
AGRICOLA	06 June 2023 or later [updated monthly]	06 July 2023	01 October 2019 – 30 June 2023	41394-05-2 OR Metamitron OR Goltix OR "3-Methyl-4-amino-6-phenyl-1,2,4-triazin(4H)-on" OR "4-Amino-3-methyl-6-phenyl-1,2,4-triazin-5(4H)-one" OR "4-Amino-4,5-dihydro-3-methyl-6-phenyl-1,2,4-triazin-5-one" OR "BRN 0613129" OR "DRW 1139" OR Herbrak OR Metamitrone OR Methiamitron OR "H69RGO1QO6" OR ("Triazin-5(4H)-one" AND "4-Amino-3-methyl-6-phenyl") OR "4-Amino-3-methyl-6-phenyl-1,2,4-triazin-5-one" OR Metomat OR Danagan OR Goldbeet OR Metamitrex OR "Gold Beet" OR Betix OR Metafol OR Beetix OR Bettix OR Tradiametron OR "Stef-Metron" OR Glotron OR Celmitron OR Modipur OR Bettatronex OR Metaliq OR Fitobiet OR "AGH 210" OR "Betaherb"	**156**[4]
Analytical Abstracts	29 June 2023 or later [updated weekly]				
BIOSIS® Toxicology	29 June 2023 or later [updated weekly]				
CAB ABSTRACTS	29 June 2023 or later [updated weekly]				
Embase®	05 July 2023 [updated daily]				
Environment Abstracts	06 June 2023 or later [updated monthly]				
MEDLINE®	05 July 2023 [updated daily]				
ToxFile®	05 July 2023 [updated daily]				
Toxicology Abstracts	06 June 2023 or later [updated monthly]				
TOXLINE	06 June 2023 or later [updated monthly]				

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[2] See DATABASES SEARCHED section above for service providers and JUSTIFICATION FOR DATABASE UTILISATION section for subject coverage.

[3] The specific date on which the database was updated is not known; the date shown is the earliest possible date for the last update.

[4] AGRICOLA, Analytical Abstracts, BIOSIS® Toxicology, CAB Abstracts, Embase®, Environment Abstracts, MEDLINE®, ToxFile®, Toxicology Abstracts and TOXLINE were searched simultaneously in ProQuest Dialog, with automatic de-duplication.

Database[2]	Latest database update[3]	Date of search	Search dates	Search strategy	Total number of records
PubMed®	04 July 2023 [updated daily]	05 July 2023	01 October 2019 – 30 June 2023	("41394 05 2"[EC/RN Number] OR Metamitron OR Goltix OR Metamitrone OR "H69RGO1QO6" OR ("Triazin-5(4H)-one" AND "4-Amino-3-methyl-6-phenyl"))	**0**[5]
TRACE	04 July 2023 [updated daily]	05 July 2023	2019 – 2023	41394-05-2	**8**
Total number of summary records retrieved:					**164**
Number of summary records excluded from the search results after rapid assessment:					**114**
Total number of summary records remaining after filtering out those of clear irrelevance (and de-duplicating):					**50**
Total number of full-text documents assessed:					**14**
Number of publications excluded from further consideration after assessment for relevance and/or reliability:					**12**
Number of publications considered relevant and reliable, and summarised in the Appendix 3 of the LRR:					**2**

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[5] All of the papers identified through PubMed had already been identified through ProQuest searches.

SEARCH PROCESS FOR DESAMINO-METAMITRON

TOP-UP SEARCHES – JULY 2023

Database[2]	Latest database update[3]	Date of search	Search dates	Search strategy	Total number of records
AGRICOLA	06 June 2023 or later [updated monthly]	06 July 2023	01 October 2019 – 30 June 2023	“36993-94-9” or ((“Desamino” or “deamino” or “deaminated”) and “Metamitron”) or (“dihydro” and “methyl” and “phenyl” and “triazin-5-on”) or (“methyl” and “phenyl” and “triazin-5-one”)	5[4]
Analytical Abstracts	29 June 2023 or later [updated weekly]				
BIOSIS® Toxicology	29 June 2023 or later [updated weekly]				
CAB ABSTRACTS	29 June 2023 or later [updated weekly]				
Embase®	05 July 2023 [updated daily]				
Environment Abstracts	06 June 2023 or later [updated monthly]				
MEDLINE®	05 July 2023 [updated daily]				
ToxFile®	05 July 2023 [updated daily]				
Toxicology Abstracts	06 June 2023 or later [updated monthly]				
TOXLINE	06 June 2023 or later [updated monthly]				
PubMed®	04 July 2023 [updated daily]	05 July 2023	01 October 2019 – 30 June 2023	("Desamino" OR "deamino" OR "deaminated") AND "Metamitron"	0
TRACE	04 July 2023 [updated daily]	05 July 2023	2019 – 2023	36993-94-9	2

Database[2]	Latest database update[3]	Date of search	Search dates	Search strategy	Total number of records
Total number of summary records retrieved:					**7**
Number of summary records excluded from the search results after rapid assessment:					**6**
Total number of summary records remaining after filtering out those of clear irrelevance (and de-duplicating):					**1**
Total number of full-text documents assessed:					**0**
Number of publications excluded from further consideration after assessment for relevance and/or reliability:					**1**
Number of publications considered relevant and reliable, and summarised in the Appendix 3 of the LRR:					**0**

Appendix 2
Literature search results and documentation of study selection from potentially relevant references for the Literature
Review Report (LRR) on
Metamitron and its metabolite desamino-metamitron.
August 2023
Project number: ADA23027

Covering search dates October 2019 to June 2023

Metamitron – for search results for desamino–metamitron, see separate tab.

Authors	Year	Title	Reference	Meet relevance criteria (Y; N)?	Justification for relevance assessment	Meet reliability criteria (Y;N;N/A)	Justification for reliability assessment (Klimisch Score or CRED guidance reliability indicator)	Publication abstract
Daramola, Ifeoluwa O.; Ojemaye, Mike O.; Okoh, Anthony I.; Okoh, Omobola O.	2023	Occurrence of herbicides in the aquatic environment and their removal using advanced oxidation processes: a critical review	Environmental Geochemistry and Health, 45(5): 1231-1260	N	Contaminant removal studies are not within the scope of the current submission	N/A	N/A	Herbicides are chemicals used globally to kill unwanted plants so as to obtain high agricultural yields and good agricultural products. Herbicides are sometimes transported from the farmlands into water bodies mainly through runoffs. These chemicals are recalcitrant, and their accumulation is hazardous to abiotic and biotic components of the ecosystem. At present, the best alternative technology for elimination of herbicides in water is the usage of advanced oxidation processes (AOPs). The AOPs, which are performed homogeneously or heterogeneously, are capable of breaking down complex pollutants in water into carbon dioxide and mineral compounds. In these processes, · OH is produced and used for degradation process. It is recommended that the total organic carbon (TOC) produced during degradation reaction be monitored because the · OH produced or generated can react to form intermediates before complete mineralisation is achieved. Different kinds of AOPs for degradation of herbicides have their specific advantages as well as limitations. This report shows that AOPs are excellent techniques for degradation of herbicides in aqueous solutions, and the mechanisms showed that herbicides were mineralised. The amount and type of photocatalysts, pH of the medium, surface characteristics of the photocatalysts, doping of the photocatalysts, temperature of the medium, concentration of herbicides, presence of competing ions, intensity and irradiation period, and type of oxidants have great influence on the degradation of herbicides in water. Overall, this report showed that most AOPs could not completely degrade herbicides in water and complete degradation can be achieved by developing novel and robust AOPs that will completely mineralise herbicides in water—this will pave way for water and environmental safety.
N'dohou, Ehounoud Hermann Narcisse; Gervais, N.'zi Konan; Paul, Gnonsoro Urbain; Marius, Kamelan Tanoh; Marcellin, Yao Koffi; Paul, Kouamélan Essetchi	2023	Spatial and seasonal distribution of pesticides in the waters of Azagny area (Grand Lahou, Cote d'Ivoire)	Environmental Monitoring and Assessment, 195(5): 626	N	Test conditions not representative of European geoclimatic conditions	N/A	N/A	This study provides comprehensive data on the seasonal variation and distribution of pesticides in the waters bordering Azagny National Park (ANP). Forty-six (46) samples of water from the Azagny area were analyzed using high-performance liquid chromatography (HPLC) coupled with a UV/visible detector to assess the level of thirty-one pesticide molecules divided into six families. These include triazines, phenylureas, organophosphates, carbamates, chloroacetanilides, dicarboximides, and crimidine, which are regularly used in this area. The respective average concentrations of pesticides are 54.54 μg//L, 20.93 μg/L, 18.24 μg/L, 3.06 μg/L, and 16.52 μg/L in the Bandama, Azagny Canal, ANP, mangroves, and estuarine environment. The analyses also showed that herbicides were the most abundant pesticides in the three waters, Bandama, Azagny Canal, and Azagny Park, with levels of 100%, 63%, and 59%, respectively, followed by insecticides with a levels of 0%, 37%, and 41%, respectively. However, rodenticides (76%) were more frequently detected than herbicides (24% in the mangroves). Regarding seasonal variation, high levels of pesticides were detected in the Bandama River, the Azagny Canal, and the mangroves during the dry season, while multiple pesticide residues were detected during the rainy season. The waters bordering Azagny National Park (ANP) are contaminated with pesticide residues (triazines, phenylureas, organophosphates, carbamates, and chloroacetanilides). As a result, policymakers should implement measures to regularly monitor pesticide levels in plantations surrounding the Azagny region's waters in order to better preserve biodiversity.
Reymond, Naomi; Glanzmann, Vick; Huisman, Sofie; Plagellat, Cécile; Weyermann, Céline; Estoppey, Nicolas	2023	An improved Chemcatcher-based method for the integrative passive sampling of 44 hydrophilic micropollutants in surface water – Part B: Field implementation and comparison with automated active sampling	Science of the Total Environment, 871	N	Method development is not within the scope of the current submission	N/A	N/A	Integrative passive sampling is particularly useful in the monitoring of hydrophilic contaminants in surface water, but the impact of hydrodynamics on contaminant uptake still needs to be better considered. In part A (Glanzmann et al., 2023), Chemcatcher-like hydrophilic samplers (i.e., SDB-RPS extraction disks covered by PES microporous membranes) were calibrated to determine the sampling rates R S of 44 hydrophilic contaminants (pesticides, pharmaceuticals, industrial products) taking into account the hydrodynamic conditions. In this study, Chemcatcher-like passive sampling devices that allowed co-deploying hydrophilic samplers and performance reference compounds (PRC)-spiked silicone disks were tested in a Swiss river with intermediate water velocities (5–50 cm s −1 , 23 cm s −1 on average) during 11 consecutive 14-day periods. The PRC dissipation from silicone disks – combined with the calibration data from part A – allowed to determine in-situ R S that took into account hydrodynamic conditions. The obtained aqueous time-weighted average (TWA) concentrations were found to be robust with good concordance between duplicates (mean quotient of 1.16 between the duplicates). For most measurements (76 %), TWA concentrations showed no major difference (<factor 2) from concentrations obtained with automated sampling (14-day composite samples). This observation was also valid for TWA concentrations calculated with extrapolated R S at infinite water velocity (R S,MAX), revealing that the added value of using in-situ R S compared to R S,MAX is limited above intermediate water velocities (>20 cm s −1). R S from the literature (R S,LIT) – obtained at water velocities between 8 and 37 cm s −1 – were also shown to provide comparable TWA concentrations in the studied hydrodynamic conditions (average water velocity of 24 cm s −1). The estimated errors due to the use of R S,MAX or R S,LIT rather than in-situ R S are given as a function of the water velocity to determine in which conditions the developed method is required (or not) in monitoring programs.
Aslantas, Sule; Golge, Ozgur; González-Curbelo, Miguel Ángel; Kabak, Bulent	2023	Determination of 355 Pesticides in Lemon and Lemon Juice by LC-MS/MS and GC-MS/MS	Foods (Basel, Switzerland), 12(9)	N	Residue concentrations in the crop plant are not within the scope of the current submission	N/A	N/A	While pesticides have become a primary tool in modern agriculture, these compounds remain a high priority on the list of consumer concerns regarding food safety. The use of pesticides in the production and post-harvesting of lemon fruits is widely used to ensure agricultural yield and fruit quality. Therefore, monitoring studies on citrus fruits to enforce regulatory compliance and ensure food safety is in great demand. The aim of this study was to monitor multi-class pesticide residues in lemon fruits commercialized in Turkey. The transmission of residues that existed on the outer surface of the fruit into its juice was also studied. Whole fruits and lemon juice samples were prepared using the quick, easy, cheap, effective, rugged and safe (QuEChERS) methodology prior to analysis. For the screening and quantification of 355 pesticide residues, liquid chromatography-tandem mass spectrometry (LC-MS/MS) and gas chromatography-tandem mass spectrometry (GC-MS/MS) were used. The analytical method has been shown to have a sufficiently low limit of quantification with respect to current maximum residue limits (MRLs) for all target analytes. The obtained recovery and precision parameters fulfilled the requirements in DG SANTE guidelines. The in-house validated analytical method was then applied for the determination of 355 pesticide substances in 100 whole fruit samples and their juices. Sixteen different residues were detected in 43% of lemon fruits, whereas 57 lemon samples were pesticide-free. The MRLs exceedances were recorded in 29 lemon samples. The most frequently detected (17%) pesticide in lemon fruits was chlorpyrifos-methyl, with a range of 0.013-0.098 mg kg-1. A lower frequency was detected for metamitron (10%, 0.027-0.118 mg kg-1), buprofezin (9%, 0.023-0.076 mg kg-1), pyriproxyfen (9%, 0.021-0.102 mg kg-1) and malathion (7%, 0.100-0.482 mg kg-1) in whole fruits. However, none of the pesticide residues were detected in lemon juice samples. These results showed that target analytes are unable to penetrate the lemon exocarp and/or endocarp.
Zheng, Siheng; Sheng, Feng; Gu, Cheng; Li, Yanying; Fang, Zhou; Luo, Jun	2023	DGT method for the in situ measurement of triazines and the desorption kinetics of atrazine in soil	Environmental Science and Pollution Research, 30(17): 51061-51074	N	Method development is not within the scope of the current submission	N/A	N/A	Triazines are frequently detected in nature water and agricultural soils worldwide. They are considered harmful to plants, animals, and the human health. In this study, diffusive gradients in thin films (DGT) method was developed for the assessment of several triazines. DGT device was used for the in situ measurement of atrazine in a pesticide factory and obtained reliable data. The atrazine concentrations measured by DGT, and solvent extraction method was in a constant ratio. The DIFS model was coupled with DGT technique to study the desorption kinetics of atrazine in four kinds of different soils. The yellow–brown soil was more inclined to adsorb atrazine than other three soils. 2_D DIFS model was used to obtain the partition coefficient for labile atrazine (K dl), the values of the response time (T c), and desorption/adsorption rates (k 1 and k −1). The yellow–brown soil has a larger labile pool size, and a faster resupply speed of atrazine. The 1_D DIFS model was used to simulate the profiles of atrazine concentrations in soil solution and solid phase. The results show that the desorption of atrazine in soil was limited by kinetic limitation at short time, and was limited by the solid phase reservoir at long time.

Rodríguez-Ramos, Ruth; Santana-Mayor, Álvaro; Socas-Rodríguez, Bárbara; Herrera-Herrera, Antonio V.; Rodríguez-Delgado, Miguel Ángel	2023	Assessment of pesticide residues contamination in cereals and pseudo-cereals marketed in the Canary Islands	Food Chemistry, 400	N	Analytical methodology development is not within the scope of the current submission	N/A	N/A	In this work, the development of an analytical method for the evaluation of a wide variety of pesticide residues in cereals and pseudo-cereals widely consumed has been carried out. A QuEChERS method was used as extraction and clean-up procedure prior to separation and quantification of the target analytes by ultra-high performance liquid chromatography coupled to mass spectrometry using a single quadrupole-time-of-flight analyser. The methodology was validated for oat, rye, spelt, barley and quinoa matrices, following the European Commission guidelines (SANTE/11312/2021), achieving good absolute recovery values in the range 60–124% with relative standard deviation values lower than 20% and providing limits of quantification of the method in the low mg/kg range, in accordance with the maximum residue limits established by European policies. Finally, considering the importance of cereals in general population diet, the analysis of 60 samples was carried out in order to assure their safe consumption.
Aldas-Vargas, Andrea; Poursat, Baptiste A J; Sutton, Nora B	2022	Potential and limitations for monitoring of pesticide biodegradation at trace concentrations in water and soil.	World journal of microbiology & biotechnology, 38(12): 240	N	Method development is not within the scope of the current submission	N/A	N/A	Pesticides application on agricultural fields results in pesticides being released into the environment, reaching soil, surface water and groundwater. Pesticides fate and transformation in the environment depend on environmental conditions as well as physical, chemical and biological degradation processes. Monitoring pesticides biodegradation in the environment is challenging, considering that traditional indicators, such as changes in pesticides concentration or identification of pesticide metabolites, are not suitable for many pesticides in anaerobic environments. Furthermore, those indicators cannot distinguish between biotic and abiotic pesticide degradation processes. For that reason, the use of molecular tools is important to monitor pesticide biodegradation-related genes or microorganisms in the environment. The development of targeted molecular (e.g., qPCR) tools, although laborious, allowed biodegradation monitoring by targeting the presence and expression of known catabolic genes of popular pesticides. Explorative molecular tools (i.e., metagenomics & metatranscriptomics), while requiring extensive data analysis, proved to have potential for screening the biodegradation potential and activity of more than one compound at the time. The application of molecular tools developed in laboratory and validated under controlled environments, face challenges when applied in the field due to the heterogeneity in pesticides distribution as well as natural environmental differences. However, for monitoring pesticides biodegradation in the field, the use of molecular tools combined with metadata is an important tool for understanding fate and transformation of the different pesticides present in the environment.
Degrendele, Céline; Prokeš, Roman; Šenk, Petr; Jílková, Simona Rozárka; Kohoutek, Jiří; Melymuk, Lisa; Přibylová, Petra; Dalvie, Mohamed Aqiel; Röösli, Martin; Klánová, Jana; Fuhrimann, Samuel	2022	Human Exposure to Pesticides in Dust from Two Agricultural Sites in South Africa	Toxics, 10(10)	N	Human exposure only	N/A	N/A	Over the last decades, concern has arisen worldwide about the negative impacts of pesticides on the environment and human health. Exposure via dust ingestion is important for many chemicals but poorly characterized for pesticides, particularly in Africa. We investigated the spatial and temporal variations of 30 pesticides in dust and estimated the human exposure via dust ingestion, which was compared to inhalation and soil ingestion. Indoor dust samples were collected from thirty-eight households and two schools located in two agricultural regions in South Africa and were analyzed using high-performance liquid chromatography coupled to tandem mass spectrometry. We found 10 pesticides in dust, with chlorpyrifos, terbuthylazine, carbaryl, diazinon, carbendazim, and tebuconazole quantified in >50% of the samples. Over seven days, no significant temporal variations in the dust levels of individual pesticides were found. Significant spatial variations were observed for some pesticides, highlighting the importance of proximity to agricultural fields or of indoor pesticide use. For five out of the nineteen pesticides quantified in dust, air, or soil (i.e., carbendazim, chlorpyrifos, diazinon, diuron and propiconazole), human intake via dust ingestion was important (>10%) compared to inhalation or soil ingestion. Dust ingestion should therefore be considered in future human exposure assessment to pesticides.
Park, Byung Kyu; Jung, Seung Hye; Kwon, Sung Hee; Kim, Sun Hoi; Yeo, Eun Young; Yeom, Mi Sook; Seo, Soon Jae; Joo, Kwang Sig; Heo, Myung Je; Hong, Geun Pyo	2022	Health risk associated with pesticide residues in vegetables from Incheon region of Korea	Environmental Science and Pollution Research, 29(43): 65860-65872	N	Test conditions not representative of European geoclimatic conditions	N/A	N/A	Abstract This study was conducted to investigate the pesticide residue concentrations and assess potential human health risks from vegetable consumption in Incheon. A total of 960 samples were collected from the Incheon areas of Korea in 2019. The pesticide residues were analyzed by the multi-residue method of the Korean Food Code for 373 different pesticides using GC–MS/MS, LC–MS/MS, GC-ECD/NPD, and HPLC-UVD. Among the vegetable samples, 869 samples (90.5%) were free from detectable residues, while 91 samples (9.5%) contained residues, and 16 samples (1.7%) had residues exceeding the Korean maximum residue limit (MRLs). A total of 33 different pesticide residues were found, and 11 residues exceeded MRLs. The most frequently detected pesticide residues were chlorfenapyr, fludioxonil, pyridalyl, hexaconazole, and procymidone. Samples exceeding the MRLs were found in aster scaber, coastal hog fennel, lettuce (leaves), mustard green, mustard leaf, perilla leaves, Pimpinella brachycarpa , radish leaves, shepherd' purse, spinach, and winter-grown cabbage. The potential health risk assessment of pesticides was estimated by calculating the estimated daily intake (EDI) and the acceptable daily intake (ADI). The range of HQs was 0.002–90.621%, which was below 100%. Therefore, the results of this study show that the detected pesticide could not be considered a serious public health problem through the consumption of vegetables.
Goel, Vikrant; Pandey, Deepika; Shukla, Sudeep	2022	Multiresidue analysis and probabilistic dietary risk assessment of 241 pesticides in wheatgrass (Triticum sp.) using LC–MS/MS in combination with QuEChERS extraction	Biomedical Chromatography, 36(8)	N	Analytical methodology development is not within the scope of the current submission	N/A	N/A	Wheatgrass is consumed as an important nutritious herbal food supplement across the globe; however, limited studies have been reported analyzing multiclass pesticides in this complex, nutrient-rich natural product. An analytical method was developed for the estimation of 241 pesticides in random wheatgrass samples collected from Delhi Northern Capital Region (Delhi-NCR). Extraction was performed by QuEChERS, cleaning was performed by dispersive solid-phase extraction and the extracts were analyzed using triple quadrupole liquid chromatography mass spectrometry. The limit of quantification was 0.5 μg/kg, which is well below the European Union Maximum Residue Level. The coefficient of determination was >0.991 across a calibration range of 0.5–100 μg/kg. The relative standard deviation values for 231 pesticides based on 10 replicates of samples spiked at 10 μg/kg were <5%. Among random samples, 54% confirmed the presence of at least one pesticide. The results indicated the presence of eight different pesticides among 38% of the total population with metribuzin at 299.7 μg/kg and carfentrazone-ethyl at 19.47 μg/kg exceeding the permissible limits among 6% of the total estimated population. The chronic and acute risk quotients as calculated were <1, indicating nonsignificant dietary risk to consumers. However, the presence of pesticides above the permissible limit is likely to result in adverse health effects to the consumers of herbal supplements from an urban population and incorporating measures would be useful to ensure the quality and safety of wheatgrass consumption.
Yıldırım, İsmet; Çiftçi, Uğur	2022	Monitoring of pesticide residues in peppers from Çanakkale (Turkey) public market using QuEChERS method and LC–MS/MS and GC–MS/MS detection	Environmental Monitoring and Assessment, 194(8)	N	Residue levels in food products are not within the scope of the current submission	N/A	N/A	Residue analyses were conducted for 283 pesticide active ingredients on pepper samples collected from the local markets (between April and November) of Çanakkale province of Turkey by using QuEChERS method and LC–MS/MS and GC–MS/MS devices. In present pepper samples, 35 different pesticide residues were detected. About 25.0% (27 samples) of present samples had single residue and 43.5% (47 samples) had multiple residues. Of the detected pesticides, acetamiprid, triadimenol, imidacloprid, boscalid, pirimiphos-methyl, tebuconazole, and metalaxyl were the most common ones, while carbendazim/benomyl, fenpropathrin, and thiram were the banned ones. Moreover, 24 of the pesticide residues detected were above the MRL values, 19 pesticides were in the "moderately hazardous (II)," and two pesticides were in the "extremely hazardous (Ib)" class (WHO). Present findings revealed that consumer health may be in danger despite all legal measures by the Ministry of Agriculture and Forestry of Turkey, thus greater emphasis should be put on monitoring of pesticide use and residues.

Malla, Muneer Ahmad; Dubey, Anamika; Kumar, Ashwani; Yadav, Shweta	2022	Metagenomic analysis displays the potential predictive biodegradation pathways of the persistent pesticides in agricultural soil with a long record of pesticide usage	Microbiological research, 261, 127081	N	Bioremediation is not within the scope of the current submission	N/A	N/A	Microbes are crucial in removing various xenobiotics, including pesticides, from the environment, specifically by mineralizing these hazardous pollutants. However, the specific procedure of microbe-mediated pesticide degradation and its consequence on the environment remain elusive owing to limitations in culturing techniques. Therefore, in this study, we have investigated i) the physicochemical and elemental compositions of PCAS (pesticide-contaminated agricultural soils) and NS (natural soils); ii) the bacterial communities and degradation pathways, as well as some novel biodegradation genes (BDGs) and pesticide degradation genes (PDGs) across two different landscapes (PCAS and NS) by applying high-throughput sequencing. The chemical and elemental composition analyses showed that all nutrients (P, K, N, S, Mn, B, and Zn) were significantly higher in PCAS than in NS ($p \leq 0.05$). The results of the 16S rRNA amplicon sequencing analysis of pesticide-contaminated (PCAS-1, PCAS-2, PCAS-3, PCAS-4) samples showed that the relative abundance of the phylum Proteobacteria (30-36%) > Actinobacteria (15-20%) > Firmicutes (13-14%) > Bacteroidetes (7-13%), were higher compared to the natural soil (NS-1, NS2). Consistent with this, a phylogenetic shift was observed with (alpha, beta, and gamma Proteobacteria) being abundant in PCAS, whereas delta and epsilon groups were more prevalent in NS. The functional characterization of the PCAS and NS by PICRUSt2 revealed that bacterial communities play a significant role in pesticide metabolism. Predictive metagenome analysis of contaminated soils showed the role of core degrading genes in membrane transport, stress response, regulatory genes, resource transport, and environmental sensing. Furthermore, 14 BDGs and 30 PDGs were examined, with a relative abundance of 0.081-1.029 % and 0.107-0.8903 % in each PCAS, respectively. The major BDGs and PDGs, with the compounds they hydrolyze, include ppo (polyphenol oxidase and laccase), CYP (cytochrome p450 protein), lip gene (lignin peroxidase), similarly, among the PDGs mhel (carbendazim), opd (organophosphate), mpd (methyl parathion), atzA, atzB, atzD, atzF and trzN (atrazine), chd (chlorothalonil), hdx (metamitron), hdl-1 (isoproturon) and fmo (nicosulfuron). Overall, our findings demonstrated the significance of utilizing metagenomic methods to predict microbial aided degradation in the ecology of contaminated environments.
Larras, Floriane; Charles, Sandrine; Chaumot, Arnaud; Pelosi, Céline; Le Gall, Morgane; Mamy, Laure; Beaudouin, Rémy	2022	A critical review of effect modeling for ecological risk assessment of plant protection products	Environmental Science and Pollution Research, 29(29): 43448-43500	N/A	N/A	N	Klimisch 4 Contains no primary data	A wide diversity of plant protection products (PPP) is used for crop protection leading to the contamination of soil, water, and air, which can have ecotoxicological impacts on living organisms. It is inconceivable to study the effects of each compound on each species from each compartment, experimental studies being time consuming and cost prohibitive, and animal testing having to be avoided. Therefore, numerous models are developed to assess PPP ecotoxicological effects. Our objective was to provide an overview of the modeling approaches enabling the assessment of PPP effects (including biopesticides) on the biota. Six categories of models were inventoried: (Q)SAR, DR and TKTD, population, multi-species, landscape, and mixture models. They were developed for various species (terrestrial and aquatic vertebrates and invertebrates, primary producers, micro-organisms) belonging to diverse environmental compartments, to address different goals (e.g., species sensitivity or PPP bioaccumulation assessment, ecosystem services protection). Among them, mechanistic models are increasingly recognized by EFSA for PPP regulatory risk assessment but, to date, remain not considered in notified guidance documents. The strengths and limits of the reviewed models are discussed together with improvement avenues (multigenerational effects, multiple biotic and abiotic stressors). This review also underlines a lack of model testing by means of field data and of sensitivity and uncertainty analyses. Accurate and robust modeling of PPP effects and other stressors on living organisms, from their application in the field to their functional consequences on the ecosystems at different scales of time and space, would help going toward a more sustainable management of the environment.
Schönenberger, Urs T.; Beck, Birgit; Dax, Anne; Vogler, Bernadette; Stamm, Christian	2022	Pesticide concentrations in agricultural storm drainage inlets of a small Swiss catchment	Environmental Science and Pollution Research, 29(29): 43966-43983	Y	Relevant to environmental fate/behaviour - monitoring study	Y	Ri 1 Reliable study conducted to a standard equivalent to GLP test guidelines	Agricultural pesticides transported to surface waters pose a major risk for aquatic ecosystems. Modelling studies indicate that the inlets of agricultural storm drainage systems can considerably increase the connectivity of surface runoff and pesticides to surface waters. These model results have however not yet been validated with field measurements. In this study, we measured discharge and concentrations of 51 pesticides in four out of 158 storm drainage inlets of a small Swiss agricultural catchment (2.8 km 2) and in the receiving stream. For this, we performed an event-triggered sampling during 19 rain events and collected plot-specific pesticide application data. Our results show that agricultural storm drainage inlets strongly influence surface runoff and pesticide transport in the study catchment. The concentrations of single pesticides in inlets amounted up to 62 µg/L. During some rain events, transport through single inlets caused more than 10% of the stream load of certain pesticides. An extrapolation to the entire catchment suggests that during selected events on average 30 to 70% of the load in the stream was transported through inlets. Pesticide applications on fields with surface runoff or spray drift potential to inlets led to increased concentrations in the corresponding inlets. Overall, this study corroborates the relevance of such inlets for pesticide transport by establishing a connectivity between fields and surface waters, and by their potential to deliver substantial pesticide loads to surface waters.
Meng, Xiaodi; Song, Wei; Xiao, Yu; Zheng, Ping; Cui, Chuanjian; Gao, Wanjun; Hou, Ruyan	2022	Rapid determination of 134 pesticides in tea through multi-functional filter cleanup followed by UPLC-QTOF-MS	Food Chemistry, 370	N	Analytical methodology development is not within the scope of the current submission	N/A	N/A	Ensuring the safety of tea requires effective methods for the simultaneous analysis of pesticide residues in the product. A sensitive and reliable method to scan for 134 pesticide residues in tea was developed that employs a novel Multi-Functional Filter (MFF) based on d-SPE extraction and ultra-high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry. The adsorption material was developed by porous polyvinylpolypyrrolidone (PVPP) for the removal of polyphenols. Acetonitrile extraction was passed through a syringe and then detected by UPLC-Q-TOF-MS. Method validation revealed satisfactory linearity with correlation coefficients higher than 0.985 for all pesticides. All limits of quantification were below 10 µg/kg. The matrix effects of 133 of the pesticides were nearly negligible (<20%), except for Sebutylazine (=22%). The recoveries at two spiked levels (50, 100 µg/kg) were 66.83–118.33%, and the Relative standard deviation (RSD) was lower than 20%, indicating accuracy and precision of the new method.
Romniou, Styliani E; Dasenaki, Marilena; Komaitis, Efstratios; Proestos, Charalampos	2022	Development and Validation of Pesticide Residues Determination Method in Fruits and Vegetables through Liquid and Gas Chromatography Tandem Mass Spectrometry (LC-MS/MS and GC-MS/MS) Employing Modified QuEChERS Method and a Centrifugal Vacuum Concentrator	Agriculture, 12(11)	N	Analytical methodology development is not within the scope of the current submission	N/A	N/A	Pesticides are used for controlling organisms, weeds and animals, causing damage to plants. Although the use of pesticides is a prerequisite for producing safe food, their accumulation makes their rapid determination necessary to avoid negative impacts on human health. The aim of this study was to develop reliable and robust analytical methods for the determination of pesticide residues in fruits and vegetables, validated according to SANTE/12682/2019 guidance. Five different categories of fruits and vegetables were selected (apple, orange, onion, lettuce, tomato). The sample preparation was based on QuEChERS methodology, slightly modified in the clean-up step, and appropriate d-SPE reagents were selected for each commodity. A Multi-Tube Vortexer was used for better agitation. In the final step, the extract was split in two: one part was acidified and injected in LC-MS/MS and the other part was evaporated in a centrifugal vacuum concentrator, and reconstituted and injected in GC-MS/MS. With the centrifugal vacuum concentrator used instead of nitrogen stream, more pesticides were determined, while sensitivity and repeatability increased. Validation results satisfied the SANTE/12682/2019 guidelines for approximately 220 analytes for each commodity. LOQ was set at 0.010 mg/kg for all analytes. Successful external quality assessment (proficiency testing) proved that the methods are fit for purpose.
Glowacka, A; Flis-Olszewsk, E	2022	The biodiversity of weed communities of dent maize, narrow-leaved lupin and oat in relation to cropping system and weed control.	Agronomy Science, 77(3): 123-137	N	Contains no primary data	N/A	N/A	The aim of the experiment was to assess the effect of cropping system and as well as various methods of weed control on the biodiversity of the weed community of dent maize, narrow-leaved lupine and spring oat. The data used in the study came from a three year field experiment carried out at the Experimental Station in south-eastern Poland (50°42'N, 23°16'E). The following factors were studied: 1. Cropping system - sole cropping and strip intercropping; 2. Weed control - mechanical and chemical. Changes in the diversity of the segetal flora are analysed using the species richness index (S), the Shannon-Wiener diversity index (H '), the Margalef index (R), the Simpson dominance index (D) and Pielou's evenness index (J '). The use of chemical weed control increased the diversity of the weed community in all species tested compared to mechanical weed regulation. Chemical weed regulation significantly decreased the value of Simpson dominance index due to the limitation of the occurrence of dominant weed species. Strip intercropping increased weed biodiversity, however, the influence of cropping systems depended on the crop species and the weed controlmethod used.

Wang, Yuanyuan; Meng, Zhijuan; Su, Chunyan; Fan, Sufang; Li, Yan; Liu, Haiye; Zhang, Xuan; Chen, Pingping; Geng, Yunyun; Li, Qiang	2022	Rapid Screening of 352 Pesticide Residues in Chrysanthemum Flower by Gas Chromatography Coupled to Quadrupole-Orbitrap Mass Spectrometry with Sin-QuEChERS Nanocolumn Extraction	Journal of Analytical Methods in Chemistry, 2022	N	Analytical methodology development is not within the scope of the current submission	N/A	N/A	To analyze pesticide residues, GC coupled with quadrupole-Orbitrap MS (GC-Orbitrap-MS) has become a powerful tool because of its unique characteristics of accurate mass full-spectrum acquisition, high resolution, fast acquisition rates, and overcoming matrix interference. This paper presents an efficiency evaluation of GC-Orbitrap-MS for identification and quantitation in the 352 pesticide residues analysis of chrysanthemum flowers in full-scan mode. A streamlined pretreatment approach using one-step extraction and dilution was used, which provided high-throughput processing and excellent recovery. The samples were extracted using acetonitrile. The extracted solution was purified by a Sin-QuEChERS Nano column to suppress the matrix in chrysanthemum flowers and determined by GC-Orbitrap-MS. The calibration curves for the 352 pesticides obtained by GC-Orbitrap-MS were linear in the range of 0.5-200 μg·kg-1, with the correlation coefficients higher than 0.99. The limits of detection (LODs) and the limits of quantification (LOQs) for the 352 pesticide residues were 0.3-3.0 μg·kg-1 and 1.0-10.0 μg·kg-1, respectively. The average recoveries in chrysanthemum flower at three levels were 95.2%, 88.6%, and 95.7%, respectively, with relative standard deviations (RSDs) of 7.1%, 7.5%, and 7.2%, respectively. Lastly, the validated method and retrospective analysis was applied to a total of 200 chrysanthemum flower samples bought in local pharmacies. The proposed method can simultaneously detect multipesticide residues with a good performance in qualitative and quantitative detection.
Česnik, Helena Baša; Radeka, Sanja; Lisjak, Klemen	2022	Pesticide Residues and Heavy Metals in Vineyard Soils of the Karst and Istria	Land, 11(12)	N	Metamitron was not detected in the soils	N/A	N/A	Pesticide residues and heavy metal concentrations were determined in two depths (0–20 and 20–40 cm) of Chromic Cambisol in 69 vineyards in the Slovenian winegrowing region of the Karst. Similarly, pesticide residues and heavy metal concentrations were also determined in two depths of Calcaric Cambisol in 11 vineyards in the other Slovenian and Croatian winegrowing regions of Istria. The topsoil (0–20 cm) was analysed for the presence of 176 different pesticidal active substances using two multiresidue analytical methods: (a) gas chromatography coupled with mass spectrometry (GC/MS) and (b) liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS). Seven active substances (five fungicides and two insecticides) were detected in the soil samples. Their concentrations were compared with the maximum concentrations observed in the vineyards of the winegrowing regions of France, Italy, and Spain. In addition to pesticides, the soil samples were analysed for the presence of nine heavy metals commonly detected in vineyard soils. The concentrations of arsenic, cadmium, cobalt, chromium, copper, molybdenum, nickel, lead, and zinc were below the critical thresholds set by Slovenian legislation, with the exception of one soil sample in which the Cu concentration exceeded the critical threshold. Compared with the maximum concentrations measured in other vineyard soils in Spain, Italy, and France, the heavy metal concentrations in the vineyard soils of Karst and Istria were lower. Both the heavy metal concentrations and the residual concentrations of pesticidal active substances in the vineyard soils of the Karst and Istria regions were significantly lower than the concentrations that are occasionally discussed in the literature.
Tóth, Š	2022	Sowthistles Sonchus L. spp. and sugar beet.	Listy Cukrovarnické a Reparské, 138(5/6): 192-196	N	Metamitron was not evaluated	N/A	N/A	In this paper we describe the biological properties of three species of weeds from the genus Sonchus L., the occurrence and economic importance of which has been on the increase in Slovakia, as well as the possibilities of their herbicide regulation. These are the perennial milkweed, Sonchus arvensis L., and the annual to biennial species of herbaceous milkweed, Sonchus oleraceus L., and rough milkweed, Sonchus asper (L.) Hill. Milkweeds are mainly found in broad-row crops and compete even in areas with a limited choice of effective herbicides. Sugar beet is a crop in whose stands milkweed control requires increased care and attention, starting with pre-crop selection. Soil tillage as well as pre-sowing preparation should aim at creating high-quality seedbed for the earliest and most uniform crop emergence and canopy closure. Considering the trio of frequent broad-spectrum mixed herbicide partners of phenmediphane, desmediphane and ethofumesate especially milkweed is resistant from the germinating leaf stage onwards, and on the contrary, rough milkweed is the most sensitive and only reliably sensitive at the germinating leaf stage. In contrast to metamitron, to which field sowthistle is sensitive in the stage of leaf emergence in PRE use and within POST, field sowthistle is tolerant to chloridazon from the very early growth phases. Higher doses of clopyralid and triflusulfuron-methyl are effective against the most problematic field sowthistle, at their higher dose registered applied usually by divided application for the purpose of avoiding undesired phytotoxicity. For the same reason of phytotoxicity if possible, especially in the case of spot occurrence of field sowthistle, the use of more effective doses by spot application may be preferable.
Tadmor, Yuval; Raz, Amir; Reikin-Barak, Shira; Ambastha, Vivek; Shemesh, Eli; Leshem, Yehoram; Crane, Omer; Stern, Raphael A; Goldway, Martin; Tchernov, Dan; Liran, Oded	2021	Metamitron, a Photosynthetic Electron Transport Chain Inhibitor, Modulates the Photoprotective Mechanism of Apple Trees	Plants (Basel, Switzerland), 10(12)	N	Effects in the crop plant are not within the scope of the current submission	N/A	N/A	Chemical thinning of apple fruitlets is an important practice as it reduces the natural fruit load and, therefore, increases the size of the final fruit for commercial markets. In apples, one chemical thinner used is Metamitron, which is sold as the commercial product Brevis ® (Adama, Ashdod, Israel). This thinner inhibits the electron transfer between Photosystem II and Quinone-b within light reactions of photosynthesis. In this study, we investigated the responses of two apple cultivars-Golden Delicious and Top Red-and photosynthetic light reactions after administration of Brevis®. The analysis revealed that the presence of the inhibitor affects both cultivars' energetic status. The kinetics of the photoprotective mechanism's sub-processes are attenuated in both cultivars, but this seems more severe in the Top Red cultivar. State transitions of the antenna and Photosystem II repair cycle are decreased substantially when the Metamitron concentration is above 0.6% in the Top Red cultivar but not in the Golden Delicious cultivar. These attenuations result from a biased absorbed energy distribution between photochemistry and photoprotection pathways in the two cultivars. We suggest that Metamitron inadvertently interacts with photoprotective mechanism-related enzymes in chloroplasts of apple tree leaves. Specifically, we hypothesize that it may interact with the kinases responsible for the induction of state transitions and the Photosystem II repair cycle.
Vuaille, Jeanne; Daraghmeh, Omar; Abrahamsen, Per; Jensen, Signe M.; Nielsen, Soren Kirkegaard; Munkholm, Lars J.; Green, Ole; Petersen, Carsten T.	2021	Wheel track loosening can reduce the risk of pesticide leaching to surface waters	Soil Use and Management, 37(4)	N	Contains no primary data	N/A	N/A	Wheel tracks can lower topsoil infiltrability and increase water ponding in agricultural fields. A seedbed harrow mounted with two goosefeet tine points, the eradicators, was used to investigate track loosening at different depths on a sandy loam soil as a way of mitigating compaction effects and reducing the risk of pesticide transport to surface waters. Loosening strongly affected air permeability and steady-state infiltration. The agro-ecological system model Daisy was used to simulate the effects of soil structural and hydraulic changes on pesticide leaching to subsurface drain lines over a 332-year period. Measured properties of the topsoil were combined with a representative subsoil and weather series and with realistic management scenarios. The loads of pesticide in the drains for 3 months after loosening were calculated for each year, and the risk was defined as the 90th percentile of the load. We focused on three different herbicides used in sugar beet cultivation in spring: glyphosate, metamitron and phenmedipham. Our simulations showed that for all pesticides loosening could lower the risk by 10% on average for a 3-m working width, and the tracks contribution to the risk by 34%, for all drain spacing and working width settings. Wheeling did not affect the risk but this result was sensitive to the parameterization of the hydraulic conductivity in the compacted soil layer, showing potentially higher risk under certain conditions. These results showed that wheel track loosening is an effective strategy for reducing the risk of surface water contamination from pesticides used in agriculture.

Taylor, Adam C.; Mills, Graham A.; Gravell, Anthony; Kerwick, Mark; Fones, Gary R.	2021	Passive sampling with suspect screening of polar pesticides and multivariate analysis in river catchments: Informing environmental risk assessments and designing future monitoring programmes	Science of the Total Environment, 787	N	Insufficient information to contribute to the environmental fate and behaviour data package	Ri 1 Reliable study conducted to a standard equivalent to GLP test guidelines	Y	Pollution of surface water by polar pesticides is a major environmental risk, particularly in river catchments where potable water supplies are abstracted. In these cases, there is a need to understand pesticide sources, occurrence and fate. Hence, we developed a novel strategy to improve water quality management at the catchment scale using passive sampling coupled to suspect screening and multivariate analysis. Chemcatcher® passive sampling devices were deployed (14 days) over a 12 month period at eight sites (including a water supply works abstraction site) in the Western Rother, a river catchment in South East England. Sample extracts (n = 197) were analysed using high-resolution liquid chromatography-quadrupole-time-of-flight mass spectrometry and compounds identified against a commercially available database. A total of 128 pesticides from different classes were found. Statistical analysis of the qualitative screening data was used to identify clusters of pesticides with similar spatiotemporal pollution patterns. This enabled pesticide sources and fate to be identified. At the water supply works abstraction site, spot sampling and passive sampling were found to be complementary, however, the passive sampling method in conjunction with suspect screening detected 50 pesticides missed by spot sampling combined with targeted analysis. Geospatial data describing pesticide application rates was found to be poorly correlated to their detection frequency using the Chemcatcher®. Our analysis prioritised 61 pesticides for inclusion in a future water quality risk assessment at the abstraction site. It was also possible to design a seasonal monitoring programme to effectively characterise the spatiotemporal pesticide profiles within the catchment. A work flow of how to incorporate passive sampling coupled to suspect screening into existing regulatory monitoring is proposed. Our novel approach will enable water quality managers to target the mitigation (non-engineered actions) of pesticide pollution within the catchment and hence, to better inform drinking water treatment processes and save on operational costs.
Halbach, Katharina; Möder, Monika; Schrader, Steffi; Liebmann, Liana; Schäfer, Ralf B; Schneeweiss, Anke; Schreiner, Verena C; Vormeier, Philipp; Weisner, Oliver; Liess, Matthias; Reemtsma, Thorsten	2021	Small streams-large concentrations? Pesticide monitoring in small agricultural streams in Germany during dry weather and rainfall	Water research, 203	N	Insufficient information to contribute to the environmental fate and behaviour data package	N/A	N/A	Few studies have examined the exposure of small streams (< 30 km2 catchment size) to agriculturally used pesticides, compared to large rivers. A total of 105 sites in 103 small agricultural streams were investigated for 76 pesticides (insecticides, herbicides, fungicides) and 32 pesticide metabolites in spring and summer over two years (2018 and 2019) during dry weather and rainfall using event-driven sampling. The median total concentration of the 76 pesticides was 0.18 µg/L, with 9 pesticides per sample on average (n = 815). This is significantly higher than monitoring data for larger streams, reflecting the close proximity to agricultural fields and the limited dilution by non-agricultural waters. The frequency of detection of all pesticides correlated with sales quantity and half-lives in water. Terbuthylazine, MCPA, boscalid, and tebuconazole showed the highest median concentrations. The median of the total concentration of the 32 metabolites exceeded the pesticide concentration by more than an order of magnitude. During dry weather, the median total concentration of the 76 pesticides was 0.07 µg/L, with 5 pesticides per sample on average. Rainfall events increased the median total pesticide concentration by a factor of 10 (to 0.7 µg/L), and the average number of pesticides per sample to 14 (with up to 41 in single samples). The concentration increase was particularly strong for 2,4-D, MCPA, terbuthylazine, and nicosulfuron (75 percentile). Metabolite concentrations were generally less responsive to rainfall, except for those of terbuthylazine, flufenacet, metamitron, and prothioconazole. The frequent and widespread exceedance of the regulatory acceptable concentrations (RAC) of the 76 pesticides during both, dry weather and rainfall, suggests that current plant protection product authorization and risk mitigation methods are not sufficient to protect small streams.
Roingeard Camille, Monnereau Alain, Goujon Stéphanie, Orazio Sébastien, Bouvier Ghislaine, Vacquier Blandine	2021	Passive environmental residential exposure to agricultural pesticides and hematological malignancies in the general population: a systematic review	Environmental Science and Pollution Research, 28(320): 43190-43216	N/A	N/A	N	Klimisch 4 Contains no primary data	Incidence rates of hematological malignancies have been constantly increasing over the past 40 years. In parallel, an expanding use of agricultural pesticides has been observed. Only a limited number of studies investigated the link between hematological malignancies risk and passive environmental residential exposure to agricultural pesticides in the general population. The purpose of our review was to summarize the current state of knowledge on that question. A systematic literature search was conducted using PubMed and Scopus databases. We built a scoring scale to appraise relevance of each selected articles. We included 23 publications: 13 ecological studies, 9 case-control studies and a cohort study. Positive associations were reported between hematological malignancies and individual pesticides, pesticide groups, all pesticides without distinction, or some crop types. Relevance score was highly various across studies regardless of their design. Children studies were the majority and had overall higher relevance scores. The effect of passive environmental residential exposure to agricultural pesticides on hematological malignancies risk is suggested by the literature. The main limitation of the literature available is the high heterogeneity across studies, especially in terms of exposure assessment approach. Further studies with high methodological relevance should be conducted.
Ulrich, Uta	2021	Omnipresent distribution of herbicides and their transformation products in all water body types of an agricultural landscape in the North German Lowland	Environmental Science and Pollution Research, 28(32): 44183-44199	N	Metamitron was not evaluated	N/A	N/A	The research of the environmental fate of pesticides has demonstrated that applied compounds are altered in their molecular structure over time and are distributed within the environment. To assess the risk for contamination by transformation products (TP) of the herbicides flufenacet and metazachlor, the following four water body types were sampled in a small-scale catchment of 50 km 2 in 2015/2016: tile drainage water, stream water, shallow groundwater, and drinking water of private wells. The TP were omnipresent in every type of water body, more frequently and in concentrations up to 10 times higher than their parent compounds. Especially metazachlor sulfonic acid, metazachlor oxalic acid, and flufenacet oxalic acid were detected in almost every drainage and stream sample. The transformation process leads to more mobile and more persistent molecules resulting in higher detection frequencies and concentrations, which can even occur a year or more after the application of the parent compound. The vulnerability of shallow groundwater and private drinking water wells to leaching compounds is proved by numerous positives of metazachlor-TP with maximum concentrations of 0.7 µg L −1 (drinking water) and 20 µg L −1 (shallow groundwater) of metazachlor sulfonic acid. Rainfall events during the application period cause high discharge of the parent compound and lower release of TP. Later rainfall events lead to high displacement of TP. For an integrated risk assessment of water bodies, the environmental behavior of pesticide-TP has to be included into regular state-of-the-art water quality monitoring.
Creusot, Nicolas; Garoche, Clémentine; Grimaldi, Marina; Boulahtouf, Abdelhay; Chiavarina, Barbara; Bourguet, William; Balaguer, Patrick	2021	A Comparative Study of Human and Zebrafish Pregnane X Receptor Activities of Pesticides and Steroids Using In Vitro Reporter Gene Assays	Frontiers in Endocrinology, 12	N	*In vitro* gene expression assays do not provide key endpoint data	N/A	N/A	The nuclear receptor pregnane X receptor (PXR) is a ligand-dependent transcription factor that regulates genes involved in xenobiotic metabolism in mammals. Many studies suggest that PXR may play a similar role in fish. The interaction of human PXR (hPXR) with a variety of structurally diverse endogenous and exogenous chemicals is well described. In contrast, little is known about the zebrafish PXR (zfPXR). In order to compare the effects of these chemicals on the PXR of these two species, we established reporter cell lines expressing either hPXR or zfPXR. Using these cellular models, we tested the hPXR and zfPXR activity of various steroids and pesticides. We provide evidence that steroids were generally stronger activators of zfPXR while pesticides were more potent on hPXR. In addition, some chemicals (econazole nitrate, mifepristone, cypermethrin) showed an antagonist effect on zfPXR, whereas no antagonist chemical has been identified for hPXR. These results confirm significant differences in the ability of chemicals to modulate zfPXR in comparison to hPXR and point out that zfPXR assays should be used instead of hPXR assays for evaluating the potential risks of chemicals on aquatic species.
Grodtke, Mara; Paschke, Albrecht; Harzdorf, Julia; Krauss, Martin; Schüürmann, Gerrit	2021	Calibration and field application of the Atlantic HLB Disk containing Chemcatcher® passive sampler - Quantitative monitoring of herbicides, other pesticides, and transformation products in German streams	Journal of hazardous materials, 410, 124538	N	Insufficient information to contribute to the environmental fate and behaviour data package	N/A	N/A	The Chemcatcher® (CC) passive sampler containing an Atlantic HLB-L Disk (AD) was calibrated in a laboratory-based flow-through tank over 21 days under stirring for 38 polar organic pesticides with log Kow ranging from -1.7 to 3.8. The resultant sampling rates Rs range from 0.025 to 0.068 L/d. In 2018, field trials were conducted in the German rivers Mulde and Havel, as well as in 7 agricultural streams in Lower Saxony and Saxony-Anhalt. For 36 detected pesticides, the overall low concentrations were 0.2 to 49.4 ng/L. The determined pesticide profiles reflect agricultural use and were dominated by triazine herbicides including transformation products, by neonicotinoid insecticides, and by the herbicide mecoprop. Additional single hot spots were provided by the herbicides metamitron, isoproturon, and MCPA (showing the overall largest value of 49.4 ng/L). Notably, the detected waterborne pesticides include banned herbicides and associated transformation products in concentration ratios suggesting also recent input. This concerns in particular atrazine and its transformation products 2-OH-atrazine, deethylatrazine and deisopropylatrazine. An extended target screening of AD-CC extracts from the river Havel revealed the additional presence of other organic micropollutants including biocides, surfactants and industrial chemicals, and demonstrated the AD-CC applicability up to log Kow of 4.5.

da Silva, Karlo Alves; Nicola, Vitoria Beltrame; Dudas, Rafaela Tavares; Demetrio, Wilian Carlo; Maia, Lilianne Dos Santos; Cunha, Luis; Bartz, Marie Luise Carolina; Brown, George Gardner; Pasini, Amarildo; Kille, Peter; Ferreira, Nuno G C; de Oliveira, Cíntia Mara Ribas	2021	Pesticides in a case study on no-tillage farming systems and surrounding forest patches in Brazil.	Scientific reports, 11(1): 9839	N	Test conditions not representative of European geoclimatic conditions	N/A	N/A	With the growing global concern on pesticide management, the relationship between its environmental recalcitrance, food security and human health has never been more relevant. Pesticides residues are known to cause significant environmental contamination. Here, we present a case study on long-term no-tillage farming systems in Brazil, where Glyphosate (GLY) has been applied for more than 35 years. GLY and its main breakdown product, aminomethylphosphonic acid (AMPA) were determined in topsoil (0-10 cm) samples from no-tillage fields and nearby subtropical secondary forests by high-performance liquid chromatography coupled with a fluorescence detector. In addition, the presence of carbamates, organochlorines, organophosphates and triazines were also screened for. GLY and AMPA were present in all soil samples, reaching values higher than those described for soils so far in the literature. A significant decrease for AMPA was observed only between the secondary forest and the farm's middle slope for site B. GLY and AMPA were observed respectively at peak concentrations of 66.38 and 26.03 mg/kg soil. GLY was strongly associated with forest soil properties, while AMPA associated more with no-tillage soil properties. Soil texture was a significant factor contributing to discrimination of the results as clay and sand contents affect GLY and AMPA retention in soils. This was the first study to report DDT and metabolites in consolidated no-tillage soils in Brazil (a pesticide fully banned since 2009). Based on human risk assessment conducted herein and the potential risk of GLY to local soil communities, this study offers a baseline for future studies on potential adverse effects on soil biota, and mechanistic studies.
Tefide, Kizildeniz	2021	Pesticide residues and health risk appraisal of tomato cultivated in greenhouse from the Mediterranean region of Turkey	Environmental Science and Pollution Research, 28(18): 22551-22562	N	Residue levels in food products are not within the scope of the current submission	N/A	N/A	This research aims at assessing the health risks associated with pesticide residues in greenhouse grown tomato production in the Mediterranean Region of Turkey. A multiresidue method based on modified QuEChERS (quick, easy, cheap, effective, rugged, and safe) was used for sample preparation that is applied for pesticide detection from extraction of tomato samples in the methodology generated by The Association of Official Analytical Chemists (AOAC) Official Method. The restrain of the quantification varied from 0.002 to 0.009 mg kg −1 . The validated data exposed both adequate recoveries, repeatability and reproducibility, including accomplished all other requirements of the European DG SANTE/12682/2019 Guideline. This study divulges that tomatoes cultivated in greenhouse demonstrate 61.5% of samples with one or various pesticide residues. The maximum permitted residue level of above the EU DG Guideline was in 12.2% of the samples. The main determined pesticide residues on the tomatoes cultivated in greenhouse were identified as chlorpyrifos methyl, cyfluthrin, deltamethrin, and acetamiprid. Chlorpyrifos methyl (9.5%), cyfluthrin (6.6%), deltamethrin (5.5%), and acetamiprid (3.2%) were recognized as the most conducing residues to the hazard index (HI). The HI was 9.5% for adults and 11.02% for children (3 to <10 years). The major contributor of the HI was chlorpyrifos in both.
Peng, Jie; Gan, Jinhua; Ju, Xiaoqian; Liu, Ting; Chen, Jianwu; He, Li	2021	Analysis of triazine herbicides in fish and seafood using a modified QuEChERS method followed by UHPLC-MS/MS	Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences, 1171	N	Analytical methodology development is not within the scope of the current submission	N/A	N/A	A widely applicable method was established and validated for the qualitative and quantitative analysis of twenty-six triazine herbicides in multiple fish and seafood using ultra-high-performance liquid chromatography tandem mass spectrometry (UHPLC-MS/MS). New convenient sample preparation approach based on modified QuEChERs was proposed by adding EMR-lipid to the traditional QuEChERS purification agents. Good separation was obtained after gradient elution through a C 18 column. Target compounds were detected with electrospray ionization in positive ion mode and quantified in selective reaction monitoring (SRM) mode. Under this effective method, satisfactory results of linearity, sensitivity, accuracy, precision and matrix effect were achieved. Good linearities of the calibration curves yielded the correlation coefficients higher than 0.996 for all herbicides. The LOQs of 26 triazine herbicides ranged from 0.5 to 1.0 ng g −1 . Good accuracy and precision were shown with the recoveries at the concentration of 1.0, 5.0 and 20.0 ng g −1 from 70.1% to 111.7% and the precisions of intra- and inter-day less than 12%. The matrix effects (-21.8–27.6%) were almost negligible. Finally the method was applied to the analysis of 72 crayfish samples from breeding bases of Hubei and Hunan provinces (China).
Wang, S; Miltner, A; Muskus, A M; Nowak, K M	2021	Microbial activity and metamitron degrading microbial communities differ between soil and water-sediment systems	Journal of hazardous materials, 408, 124293	Y	Relevant to environmental fate/behaviour	N	Ri 3 Study not reliable	The herbicide metamitron is frequently detected in the environment, and its degradation in soil differs from that in aquatic sediments In this study, we applied 13C6-metamitron to investigate the differences in microbial activity, metamitron mineralization and metamitron degrading microbial communities between soil and water-sediment systems. Metamitron increased soil respiration, whereas it suppressed respiration in the water-sediment system as compared to controls. Metamitron was mineralized two-fold faster in soil than in the water-sediment. Incorporation of 13C from 13C6-metamitron into Phospholipid fatty acids (PLFAs) was higher in soil than in sediment, suggesting higher activity of metamitron-degrading microorganisms in soil. During the accelerated mineralization of metamitron, biomarkers for Gram-negative, Gram-positive bacteria and actinobacteria dominated within the 13C-PLFAs in soil. Gram-negative bacteria dominated among the metamitron degraders in sediment throughout the incubation period. Actinobacteria, and actinobacteria and fungi were the main consumers of necromass of primary degraders in soil and water-sediment, respectively. This study clearly showed that microbial groups involved in metamitron degradation depend on the system (soil vs. water-sediment) and on time. It also indicated that the turnover of organic chemicals in complex environments is driven by different groups of synthropic degraders (primary degraders and necromass degraders) rather than by a single degrader.
Adriaanse, P I; Jacobs, C M J; Griethuysen, C van	2021	Estimation of photochemical degradation rates of pesticides in outdoor cosm water: guidance for inclusion in higher tier exposure assessments of the registration procedure in The Netherlands or at EU level, using the TOXSWA model.	Wageningen Environmental Research rapport, 3084	N	Contains no primary data	N/A	N/A	Estimation of the degradation rate of plant protection products in water under realistic conditions may be important for correct estimation of exposure concentrations for regulatory purposes. Standardized tests for degradation in water and in water-sediment systems in the laboratory exist, but these do not reflect degradation under field conditions. This is especially true for studies on photolytic degradation; therefore, generally photolytic degradation is not accounted for in the lower tiers of the exposure assessment. The aim of this study is to develop a procedure for the estimation of photochemical degradation rates from outdoor cosm experiments for use in the higher tiers of the exposure assessment. Observations in outdoor ponds or cosms are regularly used as a higher-tier risk assessment to evaluate the ecotoxicological effects on the aquatic ecosystem in a more realistic way. By means of inverse modelling of the behaviour of the compound in the cosm we determined the degradation rate in water, DegT50, for three compounds which are known to degrade photolytically. We did so by coupling the fate model TOXSWA to the optimisation tool PEST and determined the DegT50 for a daily reference UV radiation, weighed with a vitamin-D action spectrum, assuming that the degradation rate was directly proportional to the amount of weighed UV radiation. The UV radiation data were derived from satellite-based observations accounting for the effects of the thickness of the ozone layer and the cloud cover. For cosm studies with metribuzin, imidacloprid and metamitron we obtained satisfactory estimates of DegT50 values. After correcting these for effects of water depth, coverage of water surface by plants and the skyview factor on the UV radiation in the water, the variation between the DegT50 values of metribuzin and imidacloprid was smaller than the variation between DegT50 values derived (in an earlier study) by assuming that the degradation rate depended on water temperature and not on UV radiation. This indicates that for photolabile compounds assuming a radiation-dependent degradation rate will probably lead to a more realistic exposure in the regulatory surface water scenarios.
Wang, Xiaochun; Liu, Qinglong	2020	Spatial and Temporal Distribution Characteristics of Triazine Herbicides in Typical Agricultural Regions of Liaoning, China	Bulletin of Environmental Contamination and Toxicology, 105(6): 899-905	N	Test conditions not representative of European geoclimatic conditions.	N/A	N/A	The aim of the current study was to track the composition, spatial and temporal distribution charactistics of triazine herbicides in arable soils and corns in typical agricultural regions of Liaoning Province, China. All samples were analyzed using high performance liquid chromatography-tandem mass spectrometry (HPLC-MS/MS). Twelve kinds of triazine herbicides were found including atrazine, simazine, prometryn, propazine, ametryn, metribuzin, simetryn, aziprotryne, cyanizine, atrazine-desethyl, atrazine-desisopropyl and atrazine-desethyl-desisopropyl in the soil samples, of which atrazine, simazine, prometryn, atrazine-desethyl and atrazine-desethyl-desisopropyl were proved to be the predominant species with a high incidence though relatively low contamination level. The maximum concentration of atrazine in the soils was 73.80 µg·kg −1 . Five kinds of triazine herbicides were found in corns in the region including atrazine, simazine, prometryn, atrazine-desethyl and atrazine-desethyl-desisopropyl with the detection rate 96.4%, 17.8%, 14.3%, 60.7% and 46.4%, respectively. The maximum contaminant level of atrazine in corns was 12.52 µg·kg −1 , which is lower than that regulated in the National Standard of the People’s Republic of China (GB2763-2012).

Fuhrimann, Samuel; Klánová, Jana; Přibylová, Petra; Kohoutek, Jiři; Dalvie, Mohamed Aqiel; Röösli, Martin; Degrendele, Céline	2020	Qualitative assessment of 27 current-use pesticides in air at 20 sampling sites across Africa	Chemosphere, 258	N	Test conditions not representative of European geoclimatic conditions	N/A	N/A	Increasing use of current-use pesticides (CUPs) in Africa raises environmental and public health concerns. But there is a large uncertainty about their occurrence and the composition of pesticide mixtures on this continent. This paper investigates the presence of 27 CUPs in air across 20 sampling sites in Africa. 166 passive air samples, consisting of polyurethane foam (PUF), were collected in 12 African countries between 2010 and 2018. Samples were extracted with methanol and analyzed via high-performance liquid chromatography coupled with tandem mass spectrometry. The detection frequencies of CUPs per site were compared to land use patterns and sampling years, while their similarities were assessed using hierarchical cluster analysis. Overall, 24 CUPs were detected at least once. In 93% of all samples, at least one CUP was detected, while 78% of the samples had mixtures of two or more CUPs (median 3, interquartile range 5). Atrazine and chlorpyrifos were detected in 19 out of 20 sampling sites. Carbaryl, metazachlor, simazine, tebuconazole and terbuthylazine had the highest detection frequencies at sampling sites dominated by croplands. Across all the sampling years, 16 CUPs were present. Seven CUPs were newly detected from 2016 onwards (azinfos-methyl, dimetachlor, chlorsulfuron, chlortoluron, isoproturon, prochloraz and pyrazon), while metamitron was only present before 2012. Sites within a radius of about 200 km showed similarities in detected CUP mixtures across all samples. Our results show the presence of CUP mixtures across multiple agricultural and urban locations in Africa which requires further investigation of related environmental and human health risks.
Diamanti, Konstantina S; Alygizakis, Nikiforos A; Maria-Christina, Nika; Oswald, Peter; Thomaidis, Nikolaos S	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): 4893-4907	N	Insufficient information to contribute to the environmental fate and behaviour data package	N/A	N/A	The quality of the Dniester River Basin has been seriously impacted by the chemicals released by agriculture, industry, and wastewater discharges. To assess its current chemical pollution status, a transboundary monitoring campaign was conducted in May 2019. Thirteen surface water, 13 sediment, and three biota samples were collected and analyzed using generic sample preparation methods for the determination of organic substances by liquid chromatography high-resolution mass spectrometry (LC-HRMS) and metals by inductively coupled plasma mass spectrometry (ICP-MS). Wide-scope target and suspect screening resulted in detection of Water Framework Directive (WFD) priority substances and emerging contaminants, whereas the raw data were stored in NORMAN Digital Sample Freezing Platform (DSFP) for future retrospective screening. Furthermore, risk assessment was performed to prioritize detected substances and propose a draft list of river basin–specific pollutants. All studied metals (As, Hg, Zn, Cu, Cr, Cd, Pb, Ni) were detected in the surface water and sediments. In total, 139 organic contaminants belonging to various chemical classes (pesticides, pharmaceuticals, drugs of abuse, stimulants, sweeteners, industrial chemicals, and their transformation products) were detected. The highest cumulative concentration of contaminants was observed in surface water from the Byk River, a tributary of the Dniester (Moldova). Concentrations of WFD priority substances diuron and mercury and EU Watch List neonicotinoid compounds imidacloprid and thiamethoxam exceeded their environmental quality standards (EQS), whereas concentrations of 23 emerging substances exceeded their predicted no-effect concentration (PNEC) at minimum one site. Emerging contaminants telmisartan, metolachlor, terbuthylazine, and 4-acetamidoantipyrine were prioritized as potential river basin–specific pollutants.
Belsky, Joseph; Joshi, Neelendra K	2020	Effects of Fungicide and Herbicide Chemical Exposure on Apis and Non-Apis Bees in Agricultural Landscape	Frontiers in Environmental Science	Y	Relevant to ecotoxicity	N	Klimisch 4 Contains no primary data	Fungicide and herbicide chemistries are commonly applied in agricultural production systems and other agricultural landscapes during flowering periods which are concurrent with the timing of bee-dependent pollination services in many plant species. As a result, bees can be exposed to these pesticides while foraging crops and other flowering plants in the landscape where they have been administered. Laboratory and semi-field studies simulating these pesticide exposure scenarios have demonstrated lethal and sub-lethal impacts to both Apis and non-Apis species of domesticated bees. Exposure to fungicides and herbicides has also been attributed to bee genetic and molecular level changes in some cases. Herbicides can also indirectly impact bees as a result of decreasing weeds and other flowering plants that serve as nutrient resources for foraging bees. We analyze a series of recent studies concerning the toxicity of fungicides and herbicides to Apis and non-Apis bees as a basis for forming our views on key priorities regarding the direction of future research initiatives in this area. Exploring impacts of agricultural pesticides beyond insecticides to bees is timely given documented bee declines in the last decade and resulting widescale interest in identifying different drivers of these declines among the biological and ecological scientific communities.
Richard, Claire	2020	Study of the dissolved organic matter (DOM) of the Auzon cut-off meander (Allier River, France) by spectral and photoreactivity approaches	Environmental Science and Pollution Research, 27(21): 26385-26394	N	Metamitron was not evaluated	N/A	N/A	Wetlands are recognized for the importance of their hydrological function and biodiversity, and there is now a consensus to protect and restore them as well as to complete the knowledge on their functioning. Here, we studied the dissolved organic matter (DOM) of a wetland composed of the Auzon cut-off meander, the Allier River, the alluvial fluvial flow, and watershed aquifer. Water was sampled at different locations, in spring, summer, and autumn. For each sample, DOM was characterized for its chemical and optical properties and its photooxidant capacity through its ability to generate DOM triplet excited states (3 DOM*) and singlet oxygen upon simulated solar light exposure. UV-visible and fluorescence indices revealed that DOM was mainly microbial-derived whatever the sampling sites with spatial and temporal variations in terms of aromaticity (5.5–22%), specific UV absorbance at 254 nm (0.28–2.82 L m −1 mgC −1), ratio of the absorbance at 254 and 365 nm (4.6–10.8), fluorescence index (1.35–166), and biological index (0.812–2.25). All the samples generated 3 DOM* and singlet oxygen, rates of formation of which showed parallel variations. Using principal component analysis (PCA), we found positive correlations between the sensitizing properties of DOM samples and parameters associated to the abundance of low molecular weight and low absorbing chromophores. Moreover, the parameter variation across the wetland reinforced the hydrological movements observed in a previous study, suggesting that these parameters could be used as water connection tracers.
Bighiu, Maria Alexandra; Gottschalk, Steffi; Arrhenius, Åsa; Goedkoop, Willem	2020	Pesticide Mixtures Cause Short-Term, Reversible Effects on the Function of Autotrophic Periphyton Assemblages	Environmental Toxicology and Chemistry, 39(7): 1367-1374	N	Metamitron not evaluated in isolation	N/A	N/A	In a laboratory experiment we investigated the effects of pesticide mixtures on the structure and function of freshwater biofilms, with focus on their photoautotrophic component. We identified 6 herbicides and 1 fungicide commonly found in Swedish streams at relatively high concentrations and created 3 ternary mixtures that were tested in concentration series ranging from observed environmental concentrations to up to 100 times higher. Biofilms were exposed to these pesticide mixtures for 8 d and then allowed to recover for another 12 d. Our results show a rapid and consistent inhibition of photosynthesis after just 24-h exposure to the highest test concentration of pesticides, as well as in some treatments with lower concentrations (i.e., 10 times the environmental level), on exposure. Interestingly, the observed effects were reversible because biofilm photosynthesis recovered rapidly and completely in clean media in all but one treatment. In contrast to the functional response, no effects were observed on the algal assemblage structure, as assessed by diagnostic pigments. We conclude that the pesticide mixtures induce a rapid but reversible inhibition of photosynthesis, without short-term effects on biofilm structure. Environ Toxicol Chem 2020;39:1367–1374. © 2020 The Authors. Environmental Toxicology and Chemistry published by Wiley Periodicals LLC on behalf of SETAC.
Berho, Catherine; Samuel, Robert	2020	Estimating 42 pesticide sampling rates by POCIS and POCIS-MIP samplers for groundwater monitoring: a pilot-scale calibration	Environmental Science and Pollution Research, 27(15): 18565-18576	N	Method development is not within the scope of the current submission	N/A	N/A	Pesticides occur in groundwater as a result of agricultural activity. Their monitoring under the Water Framework Directive is based on only a few spot-sampling measurements per year despite their temporal variability. Passive sampling, which was successfully tested in surface water to provide a more representative assessment of contamination, could be applied to groundwater for a better definition of its contamination. However, few reliable calibration data under low water flow are available. The objective of our study thus consisted in determining sampling rates by two types of passive samplers, a POCIS (polar organic chemical integrative sampler) for polar pesticides, and a POCIS-MIP sampler based on a receiving phase of molecular imprinted polymers, specific for AMPA and glyphosate under low flow conditions as exist in groundwater. To our knowledge, this is the first time that sampling rates (sampling rate represents the volume of water from which the analyte is quantitatively extracted by the sampler per unit time) are estimated for groundwater applications. Our calibrations took place in an experimental pilot filled with groundwater and with low water flow (a few metres per day). Pesticide uptake in POCIS showed good linearity, with up to 28 days before reaching equilibrium. Two types of accumulation in POCIS were noted (a linear pattern up to 28 days, and after a time lag of 7 to 14 days). Sampling rates for 38 compounds were calculated and compared with those available in the literature or obtained previously under laboratory conditions. The values obtained were lower by a factor 1 to 14 than those estimated under stirring conditions in the literature, whereas water flow velocity (m s −1) differed by a factor of 2000 to 10,000.

Martin, Caroline; Gonzalez, Patrice	2020	An environmentally realistic pesticide and copper mixture impacts embryonic development and DNA integrity of the Pacific oyster, Crassostrea gigas	Environmental Science and Pollution Research, 27(4): 3600-3611	N	Metamitron not evaluated in isolation	N/A	N/A	Frequent occurrences of pesticides in the environment have raised concerns that combined exposure to these chemicals may result in enhanced toxicity through additive or synergistic interaction between compounds. Spermatozoa and embryos of the Pacific oyster, Crassostrea gigas , were exposed to different concentrations of a pesticide mixture with and without copper, mimicking the cocktail of pollutants occurring in the oyster culture area of Arcachon Bay. For the 1× exposure condition, measured concentration corresponds to a total concentration of 1.083 μg L −1 for the mixture of 14 pesticides and to 6.330 μg L −1 for copper (Cu). Several endpoints including larval abnormalities, DNA damage to spermatozoa and embryo and gene expression in D-larvae were investigated. Results demonstrated that pesticide mixtures in combination with or without copper induced a dose-dependent increase in embryotoxic and genotoxic effects on D-larvae from the lowest tested dose of 0.1×. Transcription of genes involved in anti-oxidative stress (cat), respiratory chain (coxI), metal detoxification (mt1 and mt2), and cell cycle arrest and apoptosis (p53) was found to be significantly downregulated while the xenobiotic biotransformation gene gst was significantly upregulated in embryos exposed to pesticide mixture with and without Cu. These findings raise the question of the possible impacts of mixtures of pesticides and metals on wild or farmed oyster populations from polluted coastal marine areas.
Kowalska, Grażyna	2020	Pesticide Residues in Some Polish Herbs	Agriculture, 10(5)	N	Residue levels in food products are not within the scope of the current submission	N/A	N/A	In the presented study a total of 104 samples of herbal material (herbage of thyme, savory, sage, rock rose, marjoram, horsetail, oregano, basil; seeds of flax; roots of liquorice, valerian and lovage, flowers of coneflower and camomile and fruits of fennel and caraway) were analysed for the content of 250 pesticides. Residues of 16 pesticides were identified in 72.1% of the analysed herbal samples. In 11 of the analysed samples of thyme herbage and in one sample of basil herbage concentrations exceeding the maximum allowable levels were demonstrated. Residues of the identified substances were detected most frequently in samples of thyme (66.34%), compared to the other groups of analysed herbal material where the percentage share of samples containing the compounds sought was at the level of approximately 20%.
Astaykina, Angelika; Streletskii, Rostislav; Maslov, Mikhail; Kazantseva, Svetlana; Karavanova, Elizabeth; Gorbatov, Victor	2020	Novel Pesticide Risk Indicators for Aquatic Organisms and Earthworms	Agronomy, 10(8)	N	Contains no primary data	N/A	N/A	There are many approaches of pesticide risk assessment. Despite their variation in difficulty and information complexity, all of them are intended to predict the actual pesticide risk as accurately as possible, i.e., to predict the behavior and hazard of a pesticide in the environment with high precision. The aim of this study was to develop a risk indicator of pesticide’s negative impact on soil and aquatic organisms. The developed pesticide risk indicator constitutes the sum of points of acute toxicity exposure ratio, long-term toxicity exposure ratio, and the bioconcentration factor. To develop the indicator, mathematical models were used; the input data included the soil and climate conditions of a specific region. Combining the data of pesticide toxicity in the environment allowed for a more accurate risk assessment in terms of using plant protection products. The toxicity and behavior in soil and water of 200 widespread pesticides were studied. It could be concluded that a mathematical model, PEARL 4.4.4, calibrated for region-specific soil-climate conditions, provides a relevant description of the natural translocation and decomposition of pesticides in soils. In addition, the output data of this model can be applied to calculate the risk indicators. The combination of these parameters with pesticide toxicity for non-target groups of organisms allows the risk indicator to be a universal tool for predicting the negative impact of pesticides on the environment at the regional level.
Pinheiro, Lara A; Dáder, Beatriz; Wanumen, Andrea C; Pereira, José Alberto; Santos, Sónia A P; Medina, Pilar	2020	Side Effects of Pesticides on the Olive Fruit Fly Parasitoid Psyttalia concolor (Szépligeti): A Review	Agronomy, 10(11)	N/A	N/A	N/A	Klimisch 4 Contains no primary data	Pesticide applications in olive orchards could alter the biological control of parasitoid Psyttalia concolor Szépligeti (Hymenoptera: Braconidae) on the key pest Bactrocera oleae Rossi (Diptera: Tephritidae). Psyttalia concolor adults can be contaminated by exposure to spray droplets, contact with treated surfaces or oral uptake from contaminated food sources. Pesticides impact both pest and parasitoid populations when they coexist in time and space, as they reduce pest numbers available for parasitoids and might cause toxic effects to parasitoids from which they need to recover. Therefore, the appropriate timing and application of selective chemical treatments provides the opportunity to incorporate this parasitoid in the IPM of B. oleae . This manuscript reviews the current literature on lethal and sublethal effects of insecticides, fungicides, herbicides, and biopesticides on P. concolor . Insecticides were generally more toxic, particularly organophosphates and pyrethroids, while herbicides and biopesticides had less effects on mortality and reproductive parameters. Some fungicides were quite harmful. Most of the studies were conducted in laboratory conditions, focused on reproduction as the only sublethal effect, exclusively considered the effect of a single pesticide and persistence was hardly explored. Field studies, currently quite scarce, are absolutely needed to satisfactorily assess the impact of pesticides on P. concolor .
Martinello, Marianna; Manzinello, Chiara; Borin, Alice; Avram, Larisa Elena; Dainese, Nicoletta; Giuliato, Ilenia; Gallina, Albino	2020	A Survey from 2015 to 2019 to Investigate the Occurrence of Pesticide Residues in Dead Honeybees and Other Matrices Related to Honeybee Mortality Incidents in Italy	Diversity, 12(1): 15	Y	Relevant to ecotoxicity - monitoring study	Y	Ri 1 Reliable study conducted to a standard equivalent to GLP test guidelines	Honeybee health can be compromised not only by infectious and infesting diseases, but also by the acute or chronic action of certain pesticides. In recent years, there have been numerous reports of colony mortality by Italian beekeepers, but the investigations of these losses have been inconsistent, both in relation to the type of personnel involved (beekeepers, official veterinarians, members of the police force, etc.) and the procedures utilized. It was therefore deemed necessary to draw up national guidelines with the aim of standardizing sampling active ties. In this paper, we present the results of a survey carried out in Italy from 2015 to 2019, following these guidelines. Residues of 150 pesticides in 696 samples were analyzed by LC-MS/MS and GC-MS/MS. On average, 50% of the honeybee samples were positive for one or more pesticides with an average of 2 different pesticides per sample and a maximum of seven active ingredients, some of which had been banned in Europe or were not authorized in Italy. Insecticides were the most frequently detected, mainly belonging to the pyrethroid group (49%, above all tau-fluvalinate), followed by organophosphates (chlorpyrifos, 18%) and neonicotinoids (imidacloprid, 7%). This work provides further evidence of the possible relationship between complex pesticide exposure and honeybee mortality and/or depopulation of hives.
Dereumeaux, Clémentine; Fillol, Clémence; Quenel, Philippe; Denys, Sébastien	2020	Pesticide exposures for residents living close to agricultural lands: A review	Environment International, 134, 105210	N/A	N/A	N	Klimisch 4 Contains no primary data	Background: Residents living close to agricultural lands might be exposed to pesticides through non-occupational pathways including spray drift and volatilization of pesticides beyond the treated area. Objective: This review aimed to identify and analyze scientific literature measuring pesticide exposure in non-farmworker residents living close to agricultural lands, and to suggest practical implications and needs for future studies. Methods: A review was performed using inclusion criteria to identify original articles of interest published between 2003 and 2018. Results: From the 29 articles selected in this review, 2 belonged to the same study and were grouped, resulting in a total of 27 studies. Seven studies assessed exposure to pesticides using environmental samples, 13 collected biological samples and 7 analyzed both. Nine studies included a reference group of residents living far from agricultural lands while 11 assessed the influence of the spraying season or spray events on pesticide exposures. Studies included in this review provide evidence that residents living near to agricultural lands are exposed to higher levels of pesticides than residents living further away. Discussion and conclusion: This review highlights that the following study design characteristics may be more appropriate than others to measure pesticide spray drift exposure in non-farmworker residents living close to agricultural lands: inclusion of a non-agricultural control group, collection of both biological and environmental samples with repeated sampling, measurements at different periods of the year, selection of numerous study sites related to one specific crop group, and measurements of pesticides which are specific to agricultural use. However, few studies to date incorporate all these characteristics. Additional studies are needed to comprehensively measure non-occupational pesticide exposures in this population in order to evaluate health risks, and to develop appropriate prevention strategies.
Nayek, A; Khan, M; Manna, S K; Chakraborty, A K; Mandal, T K	2020	Toxicological assessment of oral Metamitron in goats.	Online Journal of Veterinary Research, 24(11): 659-664	Y	Repeated-dose oral toxicity	?	Client does not require summaries of studies on mammalian toxicity for this 2023 update	A toxicological assessment was performed in goats following repeated oral administration of metamitron. Groups of black Bengal male adult goats were dosed 10 ml of 1% carboxy methyl cellulose (controls), injected subcutaneous 2.25 mg/kg levamisole and 30 mg metamitron in 10 ml Carboxy methyl cellulose daily for 35 days. Jugular blood was taken before administration and every 7 days after treatment. Metamitron did not alter the immune status but pre-scapular lymph nodes and spleen revealed proliferation of lymphoid follicles with moderate lymphocytosis. The changes did not correlate with changes in white blood cells.

Kienle, Cornelia; Vermeirssen, Etiënne L.M.; Schifferli, Andrea; Singer, Heinz; Stamm, Christian; Werner, Inge	2019	Effects of treated wastewater on the ecotoxicity of small streams - Unravelling the contribution of chemicals causing effects	PLoS ONE, 14(12)	N	Metamitron not evaluated in isolation	N/A	N/A	Wastewater treatment plant effluents are important point sources of micropollutants. To assess how the discharge of treated wastewater affects the ecotoxicity of small to medium-sized streams we collected water samples up- and downstream of 24 wastewater treatment plants across the Swiss Plateau and the Jura regions of Switzerland. We investigated estrogenicity, inhibition of algal photosynthetic activity (photosystem II, PSII) and growth, and acetylcholinesterase (AChE) inhibition. At four sites, we measured feeding activity of amphipods (Gammarus fossarum) in situ as well as water flea (Ceriodaphnia dubia) reproduction in water samples. Ecotoxicological endpoints were compared with results from analyses of general water quality parameters as well as a target screening of a wide range of organic micropollutants with a focus on pesticides and pharmaceuticals using liquid chromatography high-resolution tandem mass spectrometry. Measured ecotoxicological effects in stream water varied substantially among sites: 17β-estradiol equivalent concentrations (EEQ bio , indicating the degree of estrogenicity) were relatively low and ranged from 0.04 to 0.85 ng/L, never exceeding a proposed effect-based trigger (EBT) value of 0.88 ng/L. Diuron equivalent (DEQ bio) concentrations (indicating the degree of photosystem II inhibition in algae) ranged from 2.4 to 1576 ng/L and exceeded the EBT value (70 ng/L) in one third of the rivers studied, sometimes even upstream of the WWTP. Parathion equivalent (PtEQ bio) concentrations (indicating the degree of AChE inhibition) reached relatively high values (37 to 1278 ng/L) mostly exceeding the corresponding EBT (196 ng/L PtEQ bio). Decreased feeding activity by amphipods or decreased water flea reproduction downstream compared to the upstream site was observed at one of four investigated sites only. Results of the combined algae assay (PSII inhibition) correlated best with results of chemical analysis for PSII inhibiting herbicides. Estrogenicity was partly and AChE inhibition strongly underestimated based on measured steroidal estrogens respectively organophosphate and carbamate insecticides. An impact of dissolved organic carbon on results of the AChE inhibition assay was obvious. For this assay more work is required to further explore the missing correlation of bioassay data with chemical analytical data. Overall, the discharge of WWTP effluent led to increased estrogenicity, PSII and AChE inhibition downstream, irrespective of upstream land use.
Kyselová, K; Náměstek, J; Laňar, L; Mészáros, M	2019	Efficacy and crop safety of soil herbicides in the fruit nursery.	Acta Universitatis Agriculturae et Silviculturae Mendelianae Brunensis, 67(1): 101-110	N	Effects in the crop plant are not within the scope of the current submission	N/A	N/A	The research was conducted in the fruit nursery of the Research and Breeding Institute of Pomology (RBIP) Holovousy, Czech Republic in 2015, 2016 and 2017. The efficacy and potential phytotoxic effect of soil herbicides were assessed in spring-planted and summer-budded rootstocks M9, MA, Gisela 5 and St. Julien A in seven treatments with the following herbicides: linuron, metazachlor, metamitron, chlorotoluron, dimethenamid-P, pendimethalin, and combination of pendimethalin and dimethenamid-P in one product. The effects of the surfactant and simulated rainfall in combination with the pendimethalin + dimethenamid-P treatment were also assessed. Herbicides were applied twice a season, i.e. in spring after planting and in autumn to control weeds emerging during the season. The efficacy of the herbicide combining both pendimethalin and dimethenamid-P was the highest in all three seasons. Metazachlor, pendimethalin and dimethenamid-P provided satisfactory efficacy with adequate soil moisture. Pre-emergent efficacy of metamitron, linuron and chlorotoluron was not satisfactory, especially in dryer conditions. The synergistic effect of the surfactant and rainfall on the efficacy of pendimethalin in combination with dimethenamid-P was proved in the dry year only. None of the tested herbicides had a negative effect either on the growth and health status of planted rootstocks or subsequently on budded plants in the following year.
Moxon M, Strupp C, Aggarwal M, Odum J, Lewis R, Zedet S and Mehta J	2020	An analysis of the setting of the acute reference dose (ARfD) for pesticides in Europe.	Regulatory Toxicology and Pharmacology, 113, 104638	N/A	N/A	N	Klimisch 4 Contains no primary data	To protect human health, acute reference values have been established for pesticides which have the potential to cause a toxic effect after acute human exposure. These values are used to identify exposure levels below which there is no appreciable risk. Comprehensive reference documents, including OECD criteria, are available to aid identification of relevant toxicological endpoints. Within Europe, there is a concern that the identification process is inconsistent and unnecessarily conservative such that safe products with no established human health risk are being restricted. For this reason, the basis for the setting of an acute reference dose (ARfD) has been investigated for 130 pesticides to better understand how the toxicological endpoints are selected. The investigation has shown that most ARfDs are derived from repeat dose studies and that there is an over-representation of prenatal developmental toxicity studies. There is clear evidence that ARfDs derived from rabbit developmental toxicity studies are set over conservatively with regard to acute maternal effects and often inappropriately. To facilitate an improved system, refinements to the existing process are recommended, the use of maternal data in the rabbit as the basis for deriving an ARfD is critically evaluated and a new, more pragmatic approach to ARfD derivation is proposed.

[redacted]

Appendix 3b

Open literature on the environmental fate/behaviour and ecotoxicology of metamitron and desamino metamitron

Project Code: 3670259

Report Number: E2023-25

Date:

September 2023 (Final)

Report for:

[redacted]

Authors:

[redacted]

[redacted]

[redacted]

[redacted]

Study Author and Project Manager

I/We, the undersigned, hereby declare that the calculations used in this study are as referenced in this report, and that this study provides a true and accurate account of the results obtained.

[redacted]

Environmental Fate Modeller / Risk Assessor

Technical Reviewer

I/We the undersigned, hereby declare that this report and work it describes have been checked in accordance with the relevant [redacted] Quality Assurance procedures.

[redacted]

Senior Risk Assessor / Ecotoxicologist

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1 Background

[redacted] has requested the assistance of [redacted] in conducting reliability and relevance scoring for publications in the open literature that consider ecotoxicology or environmental fate/behaviour aspects of metamitron or its metabolite desamino-metamitron. This work forms part of a Literature Review Report (LRR) on metamitron and twelve metabolites, and has been undertaken to comply with data requirements under Regulation (EC) No 1107/2009.

This work extends the open literature reliability and relevance reviews performed in 2016 (RA0568, Report No. E2016-36) and 2019 (RA1046, Report No. E2016-36 update).

The specific tasks requested by [redacted] are as follows:

- To judge relevance of studies provided on the basis of title and abstract
- To judge relevance and reliability of studies provided on basis of full text
- To summarise studies considered relevant and reliable.

2 Introduction

A series of publications provided by [redacted] have been evaluated for their relevance and reliability following the guidance outlined by EFSA (EFSA, 2011), on submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009.

*Relevanc*e indicates whether a study is appropriate for informing the current regulatory data package on the active substance or metabolite concerned. The criteria used for this purpose in relation to publications on the ecotoxicology and/or environmental fate/behaviour of metamitron or desamino metamitron are summarised in Table 1.

Table 1. Criteria used to assess the relevance of studies in the open literature.

Ecotoxicology	Environmental fate and behaviour
Information that informs the existing regulatory data package, either as - Test delivers the endpoint required for risk assessment, or - Data valuable as supplementary information for risk assessment (e.g. potentially useful for refined risk assessment). - A report of monitoring data concerning adverse effects of the active substance to non-target organisms.	Information that informs the existing regulatory data package, either as - Test delivers the endpoint required for risk assessment, or - Data valuable as supplementary information for risk assessment (e.g. potentially useful for refined risk assessment). - A report of monitoring data concerning fate and behaviour of the active substance and relevant metabolites, breakdown and reaction products in soil, groundwater, surface water, sediment and air.
Experimental studies	
Appropriate test substance (excluding salts or individual enantiomers).	Appropriate test substance (excluding salts or individual enantiomers).
Appropriate test species (i.e. a species able to inform with respect to ecotoxicology endpoints, including non-standard species if these can be used to provide supplementary information, and non-target plants).	Appropriate substrate (i.e. type of soil, collection site and history - a standard substrate, or a non-standard substrate if it would be applicable to a particular intended use).
Appropriate number of individuals tested.	Appropriate experimental conditions (i.e. temperature, duration, etc.).
Test conditions representative of European geoclimatic conditions.	Appropriate (e.g. a pre-validated or scientifically rigorous) extraction/analysis method.
Sufficient data on dosing the test substance (i.e. static, semi-static, flow through system).	Application rates and/or substrate loads which are representative of those expected under current intended uses and (if applicable) appropriate associated endpoint derivation(s).

Monitoring studies	
Appropriate analyte (excluding salts or individual enantiomers).	Appropriate analyte (i.e. active substance and/or metabolites).
Appropriate (e.g. a pre-validated or scientifically rigorous) extraction/analysis method.	Appropriate (e.g. a pre-validated or scientifically rigorous) extraction/analysis method.
Appropriate test species (i.e. a species able to inform with respect to ecotoxicology endpoints, including non-standard species if these can be used to provide supplementary information, and non-target plants).	Appropriate matrix type (i.e. soil, sediment and water), relevant to environmental fate and behaviour assessments.
Appropriate environmental conditions representative of European geoclimate.	Appropriate environmental conditions representative of European geoclimate.
Appropriate sampling locations (i.e. areas containing arable cropping, or related to such areas), where substance use (i.e. application rates and timing) can be expected to be representative of those recommended under current intended uses.	Appropriate sampling locations (i.e. areas containing arable cropping, or related to such areas), where substance use (i.e. application rates and timing) can be expected to be representative of those recommended under current intended uses.
Appropriate sampling strategy (i.e. scheduled sampling or event driven sampling, time of year, developmental stage, sampling campaign duration and monitoring programme duration).	Appropriate sampling strategy (i.e. scheduled sampling or event driven sampling, time of year, sampling campaign duration and monitoring programme duration).
	Appropriate explanatory data and/or statistical analysis of analyte concentrations in relation to land use, weather, substance use (and combinations thereof), sufficient to provide information on sources, emissions and pathways.

Reliability pertains to the intrinsic, scientific value of an individual study, determined by the set-up, performance, evaluation and reporting of the experiment (RIVM, 2008). The reliability indicator used in this assessment for qualifying the public literature is based on the RIVM Manual for summarising and evaluating environmental aspects of plant protection products (RIVM, 2008). The RIVM guidance provides summary tables which guide evaluation, and these form the basis of each respective reliability assessment. The final indicator definitions for reliability are summarised in Table 2.

Table 2. Indicators used to describe reliability of studies from the open literature (RIVM, 2008).

Reliability indicator	Description	Definition
Ri 1	Reliable	The methodology and the description are in accordance with internationally accepted test guidelines and/or the instructions in the manual.
Ri 2	Less Reliable	The methodology and/or the description are less in accordance with internationally accepted test guidelines and/or the instructions in the manual.
Ri 3	Not Reliable	The methodology and/or description are not in accordance with internationally accepted test guidelines and/or the instructions in the manual.

It is noted that public literature does not necessarily comply with the data requirements for pesticide registration. The studies are also not necessarily in accordance with GLP and raw data are generally not available. This means that for the evaluation of pesticides within the context of most European MS authorisation procedures, these studies will at the most receive a Ri 2.

The results from the reliability and relevance assessment of the potentially relevant publications are summarised below. The studies have been categorised under ‘Fate and behaviour in the environment’ and ‘Ecotoxicology’.

3 Environmental fate and behaviour

3.1 Metamitron

Schönenberger, U.T.; Beck, B.; Dax, A.; Vogler, B.; Stamm, C. 2022. Pesticide concentrations in agricultural storm drainage inlets of a small Swiss catchment. Environmental Science and Pollution Research 29, 43966–43983.

The following table has been adapted for use in evaluating surface water monitoring studies from the tables included in RIVM, 2003 and 2008.

Key to notes: E=expert judgement, Y=reliability is lower, Q3 = item is not reported. Empty sections under notes have not been evaluated as review was stopped, once found to be not reliable or relevant.

Items	**Notes**	**Reliability Lower**
Description		
Substances targeted	The target list included 51 substances that were either pesticides known to be applied in the catchment (45 substances) or their transformation products (6 substances).	
Water body	Catchment outlet stream and storm drainage inlets.	
Area description and history: Main agricultural use/ crops grown in area, other potential sources of exposure, layout of surrounding area	The study catchment is located in a rural area in the Swiss midlands (canton of Bern, outlet: 47°07′12.570″N 7°30′48.926″E). It occupies 2.8 km^2, has an average slope of 5.0% and is covered by arable land (38%), forests (32%), agricultural areas with very little or no pesticide use (18%) (e.g. meadows, pasture, ecological compensation areas) and other/undefined agricultural areas (4%). Settlements, farmyards, roads and farm tracks mainly cover the remaining area (8%). On arable land, the predominant crop types during the study year were grains, potatoes, and sugar beet. The conditions in the study catchment (soils, topography, climate, storm drainage system) are quite typical for the Swiss Plateau such that key findings can be generalised to a larger area. The agricultural area is heavily drained by artificial structures by tile drains in the soils and by storm drains along the road network. In total, 158 storm drainage inlets were identified along or on agricultural areas. Most of them are located along farm tracks (111), or concrete roads (33). The remaining fourteen are located directly on fields. All of these inlets are drained to the stream at the catchment outlet. In addition, 84% of the agricultural area is tile drained. Modelling was used to estimate the surface runoff connectivity of the sampling sites. Around 76% of the agricultural area in the catchment has a surface runoff connectivity to the stream. From this area, 25% is directly connected to the stream, and 75% is indirectly connected via inlets. The four sampled inlets drain around 5.7% of the agricultural area connected to inlets in the study catchment and 2.9% of the roads connected to inlets. The collector shaft drains around half of the agricultural and road area in the catchment that is connected to inlets. The remaining agricultural area (24%) is connected to sink areas.	
Temperature & precipitation	The average annual rainfall equals 1075 ± 163 mm/year (MeteoSwiss, 2018)	
Plant protection product applications	Plot-specific crop and pesticide application data for 96% of the agricultural areas in the catchment for the period January to October of the study year 2019 was provided by most of the 26 farmers in the catchment. The pesticide application data were recorded using a crop management system and included the day of application, product, amount applied, crop, plot size and a georeferenced polygon of the plot. From the substances analysed in this study, 96% of the total active ingredient mass applied in 2019 was applied within the study period.	

Sampling: Strategy (i.e. scheduled sampling or event driven sampling, time of year, sampling campaign duration and monitoring programme duration).	There were six sampling sites in the catchment, four were located at storm drainage inlets (I1–I4), one at a collector shaft (CS) and one at the outlet stream (ST) for the catchment. Out of the 158 inlets in the catchment, inlets I1–I4 were selected because they fulfilled two criteria: First, the dimensions of the inlet permitted the installation of measuring equipment. Second, only surface runoff entered the inlet through the lid; all inlets with inflow pipes from tile drains were excluded. From the ten inlets fulfilling these criteria, four were selected because they represented different terrain and cropping conditions. All were located at the border of a field and a gravel farm track. While I1, I2 and I4 lay directly next to the farm track, I3 was separated from the farm track by a grass strip of approximately 0.5-m width. During dry periods, there is no discharge transported through the four inlets, and in I1, I2 and I4 the water stagnates at the height of the outlet pipe. In contrast, during dry periods, the water level in I3 falls to a lower level due to seepage through the shaft bottom. The collector shaft collects water from 64 inlets (including I3 and I4), and from a large part of the tile drainage system in the catchment. In central Europe, most pesticides are applied in spring and summer, seasons when rainfall intensities are higher and the greatest pesticide concentrations in surface waters are usually measured. The study period (1 April to 20 August 2019) was chosen to cover most of this high-risk period. Since water only flows through the inlets during rain events, event-based sampling was performed. There were two types of event — rainfall and sampling events. Measured rainfall was classified into a rainfall event if the total rainfall exceeded 1 mm within 8 h. Subsequent rainfall was assigned to the same event if there was no dry period of at least 8 h in between. After dry periods of more than 8 h, a new rainfall event was defined. Sampling events were defined as rainfall events during which water samples were taken. Overall, 423 samples were collected, 193 were selected as the most relevant ones for further analysis. All inlet samples were analysed. Collector shaft and stream samples for six out of the top ten event samples with the largest sum concentrations in the sampled inlets were analysed, these samples cover the range of rain intensities observed. Inlet water samples were analysed for 19 of 37 rain events, covering 80% of the total discharge transported through the sampled inlets during the study period. In the remaining events, either discharge was too small to trigger sampling (15 events), or no sampling bottles were installed (3 events). Additionally, for six of these events, water samples from the collector shaft and the stream were analysed.	
Sampling: Method of sampling, measures to avoid cross contamination, number of individual samples if combined samples, number of replicates	Inlets (I1–I4): discharge was measured by installing a weir with a calibrated rating curve in front of the outlet pipe. The water level was measured using a capacitive pressure sensor (DWL compact, UIT, Germany) coupled to a data logger equipped with a GPRS module (LogTransfield, UIT, Germany). For water sampling, we installed an event-based, water-level proportional sampler. Collector shaft (CS): the water level was measured using the same sensors as in the inlets. Water samples were taken using an automatic sampler (TP5C portable sampler, MAXX GmbH, Germany) coupled to a GPRS module. Stream (ST): discharge was measured by the cantonal authorities using an ultrasonic sensor (POA-V2XXK, NIVUS AG, Germany). Water samples were taken with the same sampler type as in the collector shaft.	

	Rain gauge (R): Rainfall data (resolution: 1 min, accuracy: 0.1 mm) was provided by the cantonal authorities from a rain gauge at the southern catchment edge. In the inlets, the water-level proportional samplers started sampling at a defined water level threshold above the bottom of the weir (2 cm for inlets with little runoff, 3 cm for inlets with larger runoff), corresponding to a discharge of approximately 1.7 and 5 L/min. This resulted in one composite sample per event for each inlet exceeding the water level threshold. Rain events that were too small to exceed the water level threshold in an inlet were not sampled. When the water level threshold was exceeded in at least two inlets, the automatic samplers at the collector shaft and the stream were triggered via the GPRS module to start sampling. In the collector shaft, time proportional samples (50 mL) were taken every 2 to 3 min and pooled together into one composite sample per 20 to 30 min, depending on the event (details in Table A6). Depending on the event duration, the total sampling duration was 4 to 8 h. In the stream, time proportional sampling was performed with the same frequency during the discharge peak. Before and after the peak, samples were pooled over a period of up to 2 h. Depending on the event duration, the total sampling duration was 10 to 12 h. If no composite samples were taken in an inlet during an event (due to lack of sufficient discharge, or due to malfunctioning of the sampler), we took a grab sample from the stagnant water during sample collection.	
Sample conservation: Stability of sample during transport and storage	All samples were kept in glass bottles and protected from sunlight. At sites CS and ST, the samples were cooled by the automatic samplers (4 °C), and at sites I1–I4 by the stagnating water around the bottle (average temperature: 13.5 °C). They were collected on average 1.3 days after sampling and frozen at −20 °C until analysis.	
Extraction method and sample preparation	Dissolved phase pesticide concentrations were determined using direct injection liquid chromatography coupled to high-resolution mass spectrometry (LCHRMS). The particulate phase was not analysed. The target list comprised 51 substances that were either pesticides known to be applied in the catchment (45 substances, including metamitron), or their transformation products (6 substances, including desamino metamitron). Samples were thawed and centrifuged for 5 min at 2000 g. The supernatant was transferred and isotope-labelled internal standard (ISTD) was added. Randomly selected samples were spiked with a standard solution in order to assess relative recovery of the compounds. Centrifugation, transfer, spiking of ISTD and standard solution were fully automated. Laboratory blanks and blinds, and field blinds, were included in the measurement sequence to monitor instrument carry-over and contamination.	
Analytical method: Recovery (%), limit of detection/quantitation, precision of method (<25% RSD)	Chromatographic separation was performed on a reversed-phase C18 column (Atlantis T3, 3-µm particle size, 3.0 × 150 mm inner diameter, Waters), applying a water–methanol gradient (both containing 0.1% formic acid). The measurements were performed on a hybrid quadrupole-orbitrap mass spectrometer (Lumos Fusion, Thermo Scientific) equipped with an electrospray ionisation source. Quantification of the target compounds was performed using TraceFinder 5.1 (Thermo Scientific). For 95% of the compounds, relative recovery was in the range of 80–120%. For 80% of the compounds, the limit of quantification (LOQ) was 20 ng/L or lower. Further details on the chemical analysis (such as the gradient, the ionisation, processed sample volumes) are given in Section A1.2 of the paper.	
Results		
Climate conditions: temperature, precipitation (in study, long term averages)	During the study period, 37 rain events were recorded, duration ranged between 1 and 41 h (median: 9 h). During 34 rain events, discharge was measured in at least one of the inlets. The discharge formation in the inlets depended on the total rainfall sum of the respective rain event, but not on	

	the rainfall intensity. The rainfall needed to trigger discharge differed between the inlets. The minimal rainfall sum needed was 1.3–1.5 mm for I1, I2 and I4, while I3 was only getting active with 3.6 mm. This can be explained by the grass strip separating I3 from the adjacent road. Additionally, due to the seepage through the shaft bottom of I3 during dry periods, surface runoff entering the inlet first had to fill the shaft, before being transported through the outlet pipe. Similarly, the measured discharge differed strongly between the four inlets, being much higher in I1 and I2 than in I3 and I4.	
Surface water measurements: Sampling dates or intervals, no. measurements, range, average concentrations, confidence intervals	Measured concentrations of pesticides differed considerably between sampling sites. Metamitron was the substance with the greatest concentration in I1 and I2 (7900 ng/L and 920 ng/L, respectively). Metamitron and metamitron-desamino were persistently measured in successive samplings for I1 and I2 at concentrations greater than 100 ng/L between May and August. Site and date-based concentration data for metamitron and metamitron-desamino are provided as supplementary information.	
Reliability score	The study is well designed and expertly conducted. The methods are reported in excellent detail.	**Ri 1**
Relevance score	*-Information that informs the existing regulatory data package:* Yes. Monitoring studies may not be a data requirement but may be submitted as part of a refined risk assessment. *-Appropriate test substance:* Yes. *-Appropriate substrate:* Yes. Stream water and drain data from agricultural areas. *-Appropriate experimental conditions:* Yes. *-Appropriate extraction/analysis method*: Yes. *-Application rates and/or substrate loads which are representative of those expected under current intended uses*: Yes With time and effort a lot of information about the real-world fate of metamitron and metamitron-desamino could be extracted from this paper.	**Relevant**

Vuaille, J.; Daraghmeh, O.; Abrahamsen, P.; Jensen, S.M.; Kirkegaard Nielsen, S.; Munkholm, L.J.; Green, O.; Petersen, C.T. 2021. Wheel track loosening can reduce the risk of pesticide leaching to surface waters. Soil Use and Management 37, 906‑920.

Relevance score	*-Information that informs the existing regulatory data package:* No. In this paper the impact of compaction mitigations on the risk of pesticide transport to surface waters were investigated. Field measurements of the effect of track loosening and seedbed preparation methods on different soil structure and hydraulic properties of a sandy loam textured soil were used to parameterise soil scenarios in ‘DAISY’, a mechanistic model which simulates agro-ecological systems. ‘DAISY’ modelling focussed on sugar beet cultivation and herbicide application in spring. Metamitron (and the metabolite desamino-metamitron) was one of five herbicide treatments modelled. No primary data (*i.e.* measured concentrations of metamitron in environmental matrices) are reported in this publication, only modelled data (metamitron and desamino-metamitron transport to the vadose zone) are reported.	**Not relevant**

Taylor, A.C.; Mills, G.A.; Gravell, A.; Kerwick, M.; Fones, G.R. 2021. Passive sampling with suspect screening of polar pesticides and multivariate analysis in river catchments: Informing environmental risk assessments and designing future monitoring programmes. Science of the Total Environment 787, 147519, 16 pp.

The following table has been adapted for use in evaluating surface water monitoring studies from the tables included in RIVM, 2003 and 2008.

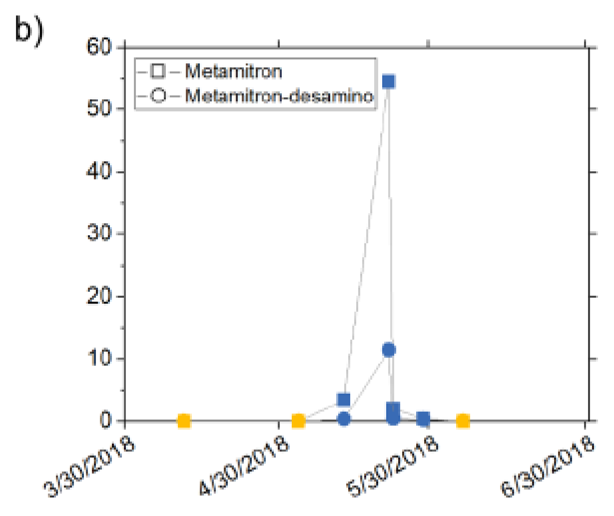
Key to notes: E=expert judgement, Y=reliability is lower, Q3 = item is not reported. Empty sections under notes have not been evaluated as review was stopped, once found to be not reliable or relevant.

Items	**Notes**	**Reliability Lower**
Description		
Substances detected	128 substances covering the following categories: fungicide, herbicide, insecticide, molluscicide, plant growth regulator, repellent, rodenticide, safener, synergist and transformation product. Metamitron was detected.	
Water body	Main river channel and feeder streams.	
Area description and history: Main agricultural use/ crops grown in area, other potential sources of exposure, layout of surrounding area	The trial was undertaken in the Western Rother river catchment (draining 350 km^2) in South East England. Land use within the catchment is primarily arable (28%) or pasture (47%), with scattered urban conurbations (e.g. Horsham, Petersfield, Midhurst and Pulborough), industry, woodland, meadow and amenity grassland. This catchment is used as a source for potable water supplies. The abstraction point on the Western Rother is located before the confluence with the River Arun at Pulborough. Four sampling sites were located on the main river Rother between the source and the abstraction point. The four other sites were located on tributaries within the catchment. These were strategically chosen based on the contribution of point sources such as waste water treatment works (WWTW) and diffuse sources originating from agriculture, woodland, the built environment, and animal husbandry. Further details of sampling sites are provided in the supplementary information (Table S1).	
Temperature & precipitation	The catchment scale or regional climate is not described, no weather data are reported.	Q3
Application if study is edge of field scale	-	
Sampling: Strategy (i.e. scheduled sampling or event driven sampling, time of year, sampling campaign duration and monitoring programme duration).	Scheduled sampling occurred over a year to ensure data were inclusive of any seasonal variation effecting pesticide fate, e.g. climatic conditions, pesticide usage, local hydrology and physiochemical status of the water body. Chemcatcher devices were deployed consecutively for two week periods over 12 months (25 individual deployments) at 8 sites, totalling 200 deployments (= samples).	
Sampling: Method of sampling, measures to avoid cross contamination, number of individual samples if combined samples, number of replicates	Duplicate Chemcatcher devices were placed in deployment apparatus and lowered into the middle of the channel and secured to a location on the bank with a chain. A buoy supported the deployment apparatus in the water column, this ensured the sampling surface of the PSD was orientated parallel to river flow. Three samples were lost in the field and the remaining 197 samples were retrieved and analysed. Further information on the sampling devices and their deployment are provided as supplementary information.	
Sample conservation: Stability of sample during transport and storage	After deployment Chemcatcher® samplers were removed from the deployment apparatus, wrapped in aluminium foil and placed in a labelled zip lock bag and transported to the laboratory in a cool box. In the laboratory Chemcatcher® samplers (deployed and field blank) were immediately disassembled. The PES membrane was discarded and the	

	HLB-L disk was then removed, wrapped in aluminium foil and stored at ~−18 °C until extraction (within a week). During each deployment and retrieval operation two new PSD were exposed to serve as field blanks.	
Extraction method and sample preparation	Prior to extraction, HLB-L disks were allowed to reach room temperature and then dried (~24 h) in a laminar flow cabinet. Disks were then placed in an extraction manifold and eluted into glass vials (60 mL) under gravity with MeOH (40 mL). One millilitre of HPLC grade water was added to the glass vials containing the eluent to prevent the extract from going dry during evaporation. Extracts were evaporated to ~0.5 mL in a Genevac EZ-2 centrifugal rotary evaporator (Genevac Ltd., Ipswich, UK) set at 40 °C. Extracts were then transferred to 2 mL deactivated (silanized) vials (Agilent, Santa Clara, USA), adjusted to 1 mL with MeOH, weighed, then stored at −18 °C prior to instrumental analysis (typically within one month).	
Analytical method: Recovery (%), limit of detection/quantitation, precision of method (<25% RSD)	Sample extracts were analysed using high-resolution liquid chromatography-quadrupole-time-of-flight mass spectrometry and compounds identified against a commercially available database. Triplicate sample extracts were analysed by liquid chromatography coupled with time-of-flight mass spectrometry (LC-Q-TOF). Reference standards were periodically analysed to confirm the stability of the instrument and as a check on mass accuracy. A Dionex Ultimate 3000 UHPLC system comprising a Dionex AcclaimRSLC 120 C_{18} analytical column (2.1 i.d. × 100 mm length, 2.2 µm particle size), (Thermo Fisher Scientific, Bremen, Germany) and a VanGuard, Acquity UPLC BEH C_{18} guard column (1.7 µm particle size), (Waters, Dublin, Ireland) was used to achieve chromatographic separation. A Bruker Maxis Impact II electrospray high resolution time-of-flight tandem mass spectrometer (Q-TOF-MS) (Bruker Daltonics, Bremen, Germany) was used (capillary voltage, 2500 V; end plate offset, 500 V; nebulizer pressure, 2 bar (N_2); drying gas, 8 L min^{-1} (N_2); drying temperature, 200 °C). The resolution of the instrument was 30,000 at m/z 150–200. HyStar software (rev. 3.2) and Target Analysis for Screening and Quantification (TASQ®) 1.4 software (Bruker Daltonics, Bremen, Germany), were used for data acquisition and interpretation, respectively; and optimised for Bruker's Pesticide Screener™ (2.1) database against which samples were screened. Gradient separation was achieved with mobile phases: A, water containing 10% of MeOH, 5 mM ammonium formate and 0.01% v/v formic acid and B, MeOH with 5mMammonium formate and 0.01% v/v formic acid. Extracts were diluted (1:9 v/v) in mobile phase A and 20 µL was then injected into the column, which was maintained at 30 °C. The gradient and flow elution programme was 0 min, 1% B, 0.2 mL min^{-1}; 3 min, 39% B, 0.2 mL min^{-1}; 14 min, 99.9% B, 0.4 mL min^{-1}; 16 min, 99.9% B, 0.48 mL min^{-1}; 16.1 min, 1% B, 0.48 mL min^{-1}; 19.1 min, 1% B, 0.2 mL min^{-1}; and 20 min, 1% B, 0.2 mL min^{-1}. Automatic mass axis calibration was undertaken with a calibrant solution (1mM sodium formate in water/isopropanol/formic acid (1:1:0.01 v/v/v)) prior to each analytical run. Data were acquired in positive ionisation mode, between 0.8 and 15 min using the broadband collision-induced dissociation (bbCID) acquisition mode of the Q-TOF-MS. The scan rate was 2 Hz and spectra were recorded between m/z 30–1000. In bbCID full scan and MS/MS spectra were generated by alternating between low (MS) and high (MS/MS) collision energies of 6 eV and 30 eV ± 6 eV. TASQ® performed an automatic comparison of extracted ion chromatograms with a signal to noise ratio < 3 against theoretical mass accuracy (±5 ppm) and retention time (±0.5 min), to produce an initial list of identified analytes in the Chemcatcher® extracts. Manual verification of this initial list was performed to remove false positives, using the following criteria; isotopic fit <250mSigma, a peak abundance>5000 and presence of diagnostic qualifier ions. Any analytes present in the mobile phase were removed from the list of analytes found in the Chemcatcher® extracts. Analytes present in the field blank were also removed if the response was <three	

	times those of the field exposed samplers. Following filtering a final list of identified analytes was compiled.	
Results		
Climate conditions: temperature, precipitation (in study, long term averages)	Data for monitoring period not reported	Q3
Surface water measurements: Sampling dates or intervals, no. measurements, range, average concentrations, confidence intervals	No reported data on metamitron in the main text, but in the supplementary information metamitron was detected at three sites: Site 1: 4% of samples. Site 1 is the main channel, 2 km downstream of the groundwater source (*i.e.* in receipt of limited diffuse pollution), the surrounding area is rural (fields and woodland). Site 5: 8 % of samples. Site 5 is a tributary in a rural location, receiving diffuse pollution from woodland and animals. Site 7: 4 % of samples. Site 7 is a tributary in a rural location with significant agricultural activity from which it receives diffuse pollution. Metamitron detections were seasonal: Spring: Not detected Summer: 2 % of samples Autumn: 4 % of samples Winter: 2 % of samples. Minimum and maximum concentrations, and confidence limits are not reported.	Q3
Reliability score	For the purposes of demonstrating the utility of the passive sampling device the study is well designed and expertly conducted. The methods are reported in excellent detail.	**Ri 1**
Relevance score	*-Information that informs the existing regulatory data package:* Yes. Monitoring studies may not be a data requirement but may be submitted as part of a refined risk assessment. *-Appropriate test substance:* Yes. *-Appropriate substrate:* Yes. Stream water from agricultural areas. *-Appropriate experimental conditions:* Yes. *-Appropriate extraction/analysis method*: Yes. *-Application rates and/or substrate loads which are representative of those expected under current intended uses*: Estimated based on Government statistics. It is reasonable to infer that the metamitron detections do result from metamitron use in the agricultural areas, particularly given the large scope of the study. However, the results for metamitron are reported in insufficient detail (detection frequencies rather than actual measured concentrations) to be able to make a meaningful contribution to the environmental fate and behaviour data package.	**Not relevant**

Halbach, K.; Möder, M.; Schrader, S.; Liebmann, L.; Schäfer, R.B.; Schneeweiss, A.; Schreiner, V.C.; Vormeier, P.; Weisner, O.; Liess, M.; Reemtsma, T. 2014. Small streams–large concentrations? Pesticide monitoring in small agricultural streams in Germany during dry weather and rainfall. Water Research 203, 117535, 10 pp.

Relevance score	A relationship between rainfall (blue markers) and the presence of metamitron (square markers) and metamitron-desamino (circle markers) is reported for an unspecified selected site in a small agricultural stream (Figure 6b).  *-Appropriate sampling strategy (i.e. triggers, season, campaign and programme duration.)*: No. Samples were taken in small agricultural streams in spring and summer (April to July) of 2018 and 2019, covering the application period of intensive pesticide use. The sampling strategy comprised regular grab water sampling (every third week) according to WFD approach, and event-driven sampling to cover rain events. Of the regularly taken 551 samples, only 480 samples are included in this study. Samples were categorized as 'DRY' were taken during dry weather (<10 mm rainfall reported on the day of sampling and no rainfall event noted on this day or the day before). Event-driven sampling was triggered by a rise of water level in the respective stream that corresponded to precipitation > 10 mm/day in the respective catchment ('RAIN', 335 samples). The data presented in Figure 6b are essentially 'snap-shot' concentrations – a single year of data collected over a very short period. Without data from other years it is not possible to determine if the data are 'unusual', or can be considered representative and therefore informative for environmental risk assessment purposes. - *Appropriate explanatory data and/or statistical analysis of analyte concentrations in relation to land use, weather, substance use*: No. No information about the land use, cropping and spatial relationship with other sampling sites is provided for the site providing the data presented in Figure 6b, or any of the sites is provided in this paper. Further information on sampling and site characteristics are provided in a previous publication (Liess et al., 2021). The supplementary information provides sufficient information on the analytical method, calibration and validation, but does not contain site-based pesticide concentrations for each sampling event. Thus, this paper contains no useable data for environmental risk assessment.	**Not relevant**

Grodtke, M.; Paschke, A.; Harzdorf,J.; Krauss, M.; Schüürmann, G. 2021. Calibration and field application of the Atlantic HLB Disk containing Chemcatcher® passive sampler – Quantitative monitoring of herbicides, other pesticides, and transformation products in German streams. Journal of Hazardous Materials 410, 124538, 10 pp.

Relevance score	*-Appropriate sampling strategy (i.e. triggers, season, campaign and programme duration.)*: No. Passive samplers were analysed after 18-22 days' exposure to surface water during June 2018 in the German rivers Mulde and Havel, as well as in 7 agricultural streams in Lower Saxony and Saxony-Anhalt. The sampling strategy consists of a single 'snap-shot' sampling event, without data from other years or months or seasons it is not possible to determine if the data are 'unusual', or can be considered representative and therefore informative for environmental risk assessment purposes. *- Appropriate explanatory data and/or statistical analysis of analyte concentrations in relation to land use, weather, substance use*: No. The supplementary information provides sufficient information on the analytical method, calibration and validation, sampler construction and positioning in the environment, but does not contain site-based pesticide concentrations for each sampling event. Insufficient information about the land use, cropping and spatial relationship with other sampling sites is provided for the sampling sites. Thus, this paper contains no useable data for environmental risk assessment.	**Not relevant**

Wang, S.; Miltner, A.; Muskus, A.M.; Nowak, K.M. 2021. Microbial activity and metamitron degrading microbial communities differ between soil and water-sediment systems. Journal of Hazardous Materials 408, 124293, 11 pp.

The study by Wang *et al*., 2021 contains data on aerobic degradation in soil and degradation in water-sediment systems each of which is evaluated for relevance and reliability separately.

The **aerobic degradation in soil** component is assessed in the following table adapted from the laboratory soil degradation study table in RIVM, 2008. The article states the test was conducted according to OECD No. 307 (OECD, 2002a).

Key to notes: E=expert judgement, Y=reliability is lower, Q3 = item is not reported. **Y [→ Ri 3]** = core item is unreliable, test therefore considered unreliable. Empty sections under notes have not been evaluated as review was stopped, once found to be not reliable or relevant.

Items	**Notes**	**Reliability Lower**
Description		
Test substance	$^{13}C_6$-metamitron from Delta Bio Research Chemicals Ltd. (Vaughan, Ontario, Canada). The isotopic purity of $^{13}C_6$-metamitron was 99 at% and the chemical purity was 98%.	
Vehicle	Not reported	**Q3**
Soil	The soil was a Haplic Chernozem sampled from the topsoil of the Static Fertilization Experiment in Bad Lauchstädt (Saxony-Anhalt, Germany), a long-term agricultural experiment. The particle size distribution was: clay, 21 ± 0.4%; silt, 68 ± 2.0%; sand, 11 ± 0.5%. Total nitrogen, 0.17 ± 0.01%; total organic carbon (TOC), 2.1 ± 0.1%; pH, 6.6 ± 0.05 and maximum water holding capacity (WHCmax), 37.5 ± 1%. Prior to the incubation experiments the soil was passed through a 2 mm sieve.	

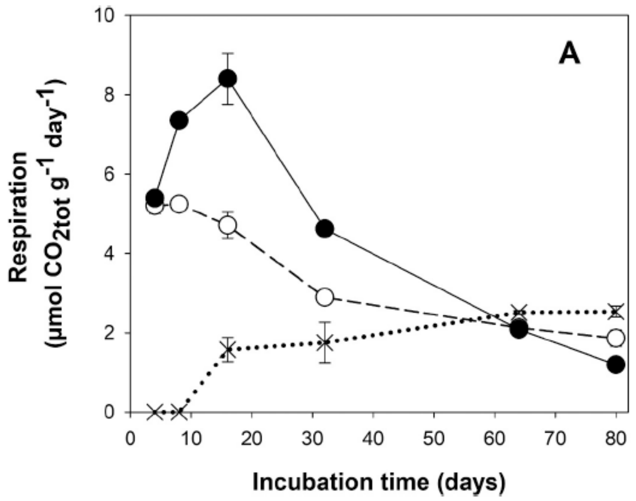
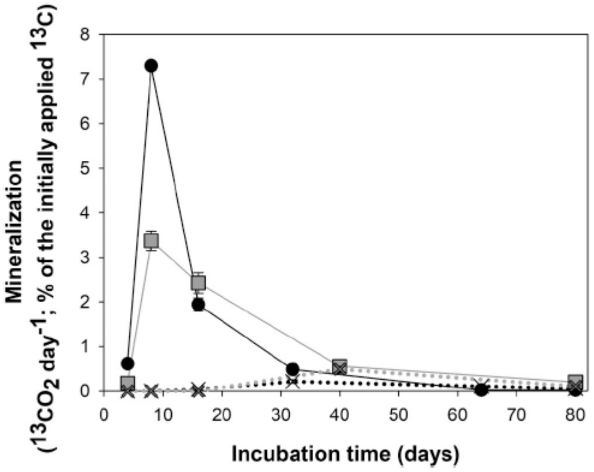
	The cultivation history of the soils has been published in another paper: Wang *et al*. (2017b). It was stated that the soil used for the experiment had received the Goltix WG formulation, which contains metamitron, for at least 10 years. Further details being available in Wang *et al*. (2017b). [Compounds that may have led to adapted micro-organisms had probably been used in the previous five years]	**Y [→Ri 3]**
Experimental design	Two controls (blank and unlabelled metamitron) were used to correct for ^{13}C natural abundance in both incubations. Sterilized soil (autoclaved three times for 20 min at 120 °C and microwave heating for 10 min at 600 W) treatments were included to differentiate between the microbial and abiotic degradation of metamitron.	
Experimental conditions	The incubations were carried out in the dark and at 20 °C for 80 days. [The mass of soil incubated in each vessel and vessel volume are not reported, see Wang *et al*., 2017a]	**Q3**
Application	Soil was spiked with 55 mg kg^{-1} metamitron. The form of metamitron addition (dry powder or solution) is not reported. The initial concentration of metamitron in soil was eleven-fold higher than the recommended application field rate (of 5 mg kg^{-1}) in order to obtain reliable isotopic enrichment results for microbial phospholipid fatty acids against the ^{13}C background. [The application rate is more than two times greater than the recommended field rate: inhibition (or stimulation) of the soil organisms is possible, leading to a higher (lower) DT$_{50}$]	**Q3** **Y [→Ri 3]**
Moisture content	The water content of soil was adjusted to 60% of the WHCmax., whereas	
Sampling frequency	Soil samples (two controls and $^{13}C_6$-metamitron) were taken on day 4, 8, 16, 32, 64 and 80 and analyzed for extractable metamitron.	
Extraction/analysis method	$^{13}CO_2$ evolved during metamitron mineralisation was trapped in 10 mL of 2 M sodium hydroxide solution, which was replaced regularly. The total concentration of CO_2 (respiration) was determined at each sampling date using a total organic carbon analyzer (Shimadzu TOC-5050, Duisburg, Germany). The isotopic composition ($^{12}C/^{13}C$ atom%) of CO_2 was measured by gas chromatography-combustion-isotope ratio-mass spectrometry (GC-C-irMS) after separation on a BPX-5 column (50 m × 0.32 m × 5 µm). The temperature program for GC-C-irMS was described previously in Girardi *et al*. (2013). [Metamitron recovery is not reported]	**Q3**
Results		
Soil respiration		

	Fig. 1. Respiration (µmol CO_2tot g^{-1} day^{-1}) of soil (A). Control without metamitron (open circles), Labelled metamitron (closed circles), Abiotic control (×). The respiration rate the in control soil without metamitron was nearly constant in the first 16 days (4.7 ± 0.3–5.2 ± 0.04 µmol g^{-1} CO_2 tot g^{-1} day^{-1}, $p > 0.05$; Fig. 1A); then it decreased quickly reaching a rate of 1.9 ± 0.2 µmol g^{-1} CO_2 tot g^{-1} day^{-1} after 80 days. Metamitron changed soil respiration as reflected in the increased respiration rates during 8–32 days (4.6 ± 0.2 – 8.4 ± 0.6 µmol CO_2 tot g^{-1} day^{-1}1; $p < 0.05$). Respiration in the abiotic soil system increased after an 8 day lag-phase. On day 16, it was two times lower (1.6 ± 0.3 µmol CO_2 tot g^{-1} day^{-1}; $p < 0.05$) than its biotic counterpart. On days 64 and 80, abiotic respiration rates were higher (2.5 ± 0.1 µmol CO_2 tot g^{-1} day^{-1}; $p < 0.05$) than in the control soil (1.9 ± 0.2–2.1 ± 0.2 µmol CO_2 tot g^{-1} day^{-1}) and amended with $^{13}C_6$-metamitron (1.2 ± 0.1–2.1 ± 0.1 µmol CO_2 tot g^{-1} day^{-1}). [Microbial activity persisted throughout the duration of the experiment]	
Concentrations in soil	 **Fig. 3.** Mineralization of $^{13}C_6$-metamitron (day^{-1}, % of the initially applied ^{13}C) over 80 days of incubation in soil and water-sediment. *Soil*: Biotic ((●)), Abiotic soil (×). *Water-sediment*: Biotic ((□)), Abiotic water-sediment ((⊠)). The mineralization rate in soil increased rapidly reaching a maximum on day 8 (7.3 ± 0.09% of $^{13}C_6$-metamitron equivalents per day; $p < 0.05$); then it decreased strongly to 0.03 ± 0.004% day^{-1} after 80 days. Cumulative mineralization of $^{13}C_6$-metamitron in soil on day 80 was (60 ± 0.7%; see Wang *et al.*, 2017a for further details). Only minimal conversion of $^{13}C_6$-metamitron to $^{13}CO_2$ was observed in abiotic soil with a maximum rate of 0.2 ± 0.04% of $^{13}C_6$-metamitron equivalents on day 32.	
DT_{50} of active substance	Not reported.	**Ri 3**
Reliability score	There are significant limitations regarding the reliability of this study, specifically regarding the metamitron application rate relative to typical commercial use. According to RIVM (2008), information on the application rate constitutes one of the core items, if this aspect is not reliable, the test must be tagged with Ri 3 (unreliable). Overall, this study is therefore considered unreliable.	**Ri 3**
Relevance score	*-Information that informs the existing regulatory data package:* Yes. Although the data presented here are not suitable for derivation of a DT_{50} due to the adaptation of the microbial community, the study	**Relevant (supplementary only)**

	could be valuable as supplementary information on the persistence of metamitron in arable soils. -*Appropriate test substance*: Yes. -*Appropriate substrate*: Yes. -*Appropriate experimental conditions* (i.e. temperature, duration, etc.): Yes. -*Appropriate (e.g. a pre-validated or scientifically rigorous) extraction/analysis method*: Yes. -*Application rates and/or substrate loads which are representative of those expected under current intended uses*: No.	

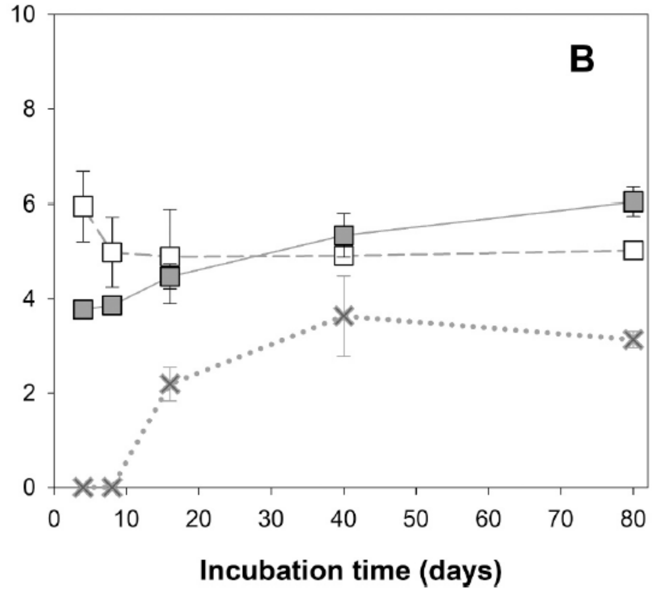
Wang, S.; Miltner, A.; Muskus, A.M.; Nowak, K.M. 2021. Microbial activity and metamitron degrading microbial communities differ between soil and water-sediment systems. Journal of Hazardous Materials 408, 124293, 11 pp.

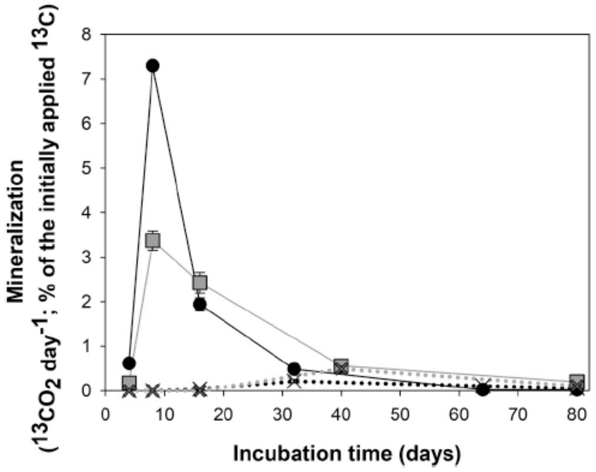
The study by Wang *et al*., 2021 contains data on aerobic degradation in soil and degradation in water-sediment systems each of which is evaluated for relevance and reliability separately.

The **aerobic transformation in aquatic sediment systems** component is assessed in the following table adapted from the laboratory soil degradation study table in RIVM, 2008. The article states the test was conducted according to OECD No. 308 (OECD, 2002b).

Key to notes: E=expert judgement, Y=reliability is lower, Q3 = item is not reported. **Y [→ Ri 3]** = core item is unreliable, test therefore considered unreliable. Empty sections under notes have not been evaluated as review was stopped, once found to be not reliable or relevant.

Items	**Notes**	**Reliability Lower**
Description		
Test substance	$^{13}C_6$-metamitron from Delta Bio Research Chemicals Ltd. (Vaughan, Ontario, Canada). The isotopic purity of $^{13}C_6$-metamitron was 99 at% and the chemical purity was 98%.	
Vehicle	Not reported	**Q3**
Sediment and water	Sediment and water were obtained from the Getel creek in the northeastern rim of the Harz Mountains (Saxony-Anhalt, Germany, 51º45′ 25.02 ºN, 11º17′ 50.25ºE). The sediment and water characteristics were described in detail in a previous study (Wang *et al*., 2016). Briefly, the sediment contained 37.7 ± 2% of sand, 62.3 ± 1.1% of silt + clay, 8.5 ± 0.05% of TOC, and 1.5 ± 0.05% of total nitrogen. The pH of the sediment was 7.1 ± 0.1. Prior to the incubation experiments the sediment was passed through a 2 mm sieve. Thes creek is surrounded by agricultural lowlands with continuous crop rotation and pesticide application. [Sediment is likely to have been contaminated with the test substance or its structural analogues within the previous 4 years.]	**Y [→Ri 3]**
Experimental design	Two controls (blank and unlabelled metamitron) were used to correct for ^{13}C natural abundance in both incubations. Sterilized sediment (autoclaved three times for 20 min at 120 °C and microwave heating for 10 min at 600 W) treatments were included to differentiate between the microbial and abiotic degradation of metamitron.	
Experimental conditions	The incubations were carried out in the dark and at 20 °C for 80 days. [The mass of sediment and the volume of water incubated in each vessel and vessel volume are not reported, see Wang *et al*., 2017b]	**Q3**
Application	The water phase of the water-sediment system was spiked with 55 mg L^{-1} metamitron (corresponding to 90 mg kg^{-1} sediment assuming	

	100% partitioning into the solid phase). The form of metamitron addition (dry powder or solution) is not reported. The initial concentration in water-sediment was at least forty-fold greater than the metamitron concentrations found in rivers (0.05–1.5 mg L^{-1}, Moschet et al., 2015) in order to obtain reliable isotopic enrichment results for microbial phospholipid fatty acids against the ^{13}C background. Furthermore, the content of TOC of sediment (8.5%) was four times higher than that of soil (2.1%); therefore, at least twice higher amount of $^{13}C_6$-metamitron as compared with soil was needed to obtain reliable results for the isotopic enrichment. [The application rate is more than two times greater than the concentrations found in rivers: inhibition (or stimulation) of microorganisms is possible, leading to a higher (lower) DT_{50}. The amount applied does not exceed the water solubility of metamitron]	**Q3** **Y [→Ri 3]**
Sampling frequency	Water-sediment systems (unlabelled metamitron and $^{13}C_6$-metamitron) were destructively sampled on day 4, 8, 16, 40 and 80. Due to the high number of samples yielding from all incubations and the workload associated with that, the control water-sediment system was sampled only on day 80, whereas the abiotic set-ups were sampled on day 16, 32, 64 and 80 for soil, and on day 16, 40 and 80 for water-sediment.	
Extraction/analysis method	$^{13}CO_2$ evolved during metamitron mineralisation was trapped in 10 mL of 2 M sodium hydroxide solution, which was replaced regularly. The total concentration of CO_2 (respiration) was determined at each sampling date using a total organic carbon analyzer (Shimadzu TOC-5050, Duisburg, Germany). The isotopic composition ($^{12}C/^{13}C$ atom%) of CO_2 was measured by gas chromatography-combustion-isotope ratio-mass spectrometry (GC-C-irMS) after separation on a BPX-5 column (50 m × 0.32 m × 5 µm). The temperature program for GC-C-irMS was described previously in Girardi *et al*. (2013). [Metamitron recovery is not reported]	**Q3**
Results		
Respiration in the water-sediment system	 Fig. 1. Respiration (y-axis: µmol CO_2tot g^{-1} day^{-1}) of water-sediment system (B). Control without metamitron (open squres), Labelled metamitron (closed squares), Abiotic control (×). Respiration in the control water-sediment system was nearly constant throughout the incubation period (5 ± 0.01–6 ± 1.0 µmol CO_2 tot g^{-1} day^{-1}). Addition of metamitron to water reduced the CO_2 respiration rate on day 4 and 8 (4 ± 0.03 µmol CO_2 tot g^{-1} day^{-1}, $p < 0.05$; Fig. 1B). Thereafter, the respiration in the water-sediment system containing the herbicide was similar to the control by day 40.	

	Respiration of the abiotic control was only 1.2-fold lower by the end than in the biotic counterpart (2 ± 0.4–3.6 ± 0.9 µmol CO$_2$ tot g^{-1} day^{-1}). Identically to the abiotic soil system, no CO$_2$ respiration was Detected before day 16. CO$_2$ respiration increased until day 32 and then remained constant until day 80. [Microbial activity persisted throughout the duration of the experiment]	
Concentrations in water and sediment	 **Fig. 3.** Mineralization of ^{13}C$_6$-metamitron (day^{-1}, % of the initially applied ^{13}C) over 80 days of incubation in soil and water-sediment. *Soil*: Biotic (●), Abiotic soil (×). *Water-sediment*: Biotic (□), Abiotic water-sediment (✖). ^{13}CO$_2$ mineralization rates in water-sediment system followed a similar trend as in soil (Fig. 3). Maximum ^{13}CO$_2$ mineralisation was measured on day 8 (3.3 ± 0.2% of ^{13}C$_6$-metamitron equivalents per day; $p < 0.05$). Thereafter, it dropped progressively towards the end reaching 0.2 ± 0.02% day^{-1} after 80 days. Cumulative mineralization of ^{13}C$_6$-metamitron in the water-sediment system was 49 ± 4.7% (Wang *et al*., 2017b).	
DT$_{50}$ of active substance	Not reported.	**Ri3**
Reliability score	There are significant limitations regarding the reliability of this study, specifically regarding the metamitron application rate relative to typical commercial use. According to RIVM (2008), information on the application rate constitutes one of the core items, if this aspect is not reliable, the test must be tagged with Ri 3 (unreliable). Overall, this study is therefore considered unreliable.	**Ri 3**
Relevance score	-*Information that informs the existing regulatory data package:* Yes. Although the data presented here are not suitable for derivation of a DT$_{50}$ due to the potential adaptation of the microbial community, the study could be valuable as supplementary information on the persistence of metamitron in water-sediment systems. -*Appropriate test substance*: Yes. -*Appropriate substrate*: Yes. -*Appropriate experimental conditions* (i.e. temperature, duration, etc.): Yes. -*Appropriate (e.g. a pre-validated or scientifically rigorous) extraction/analysis method*: Yes. -*Application rates and/or substrate loads which are representative of those expected under current intended uses*: No.	**Relevant (supplementary only)**

Adriaanse, P.I.; Boesten, J.J.T.I.; ter Horst, M.M.S.; Jacobs, C.M.J.; van Griethuysen, C. 2021. Estimation of photochemical degradation rates of pesticides in outdoor cosm water; Guidance for inclusion in higher tier exposure assessments of the registration procedure in The Netherlands or at EU level, using the TOXSWA model. Wageningen Environmental Research report. Report No. 3084, 188 pp.

Relevance score	*-Information that informs the existing regulatory data package:* No. This report describes the development of a procedure for the estimation of photochemical degradation rates in outdoor cosm systems for use in the higher tiers of the exposure assessment. The fate model TOXSWA was coupled to the PEST optimisation tool and $DegT_{50}$ was predicted by inverse modelling for daily referenced UV radiation data, weighted according to a vitamin-D action spectrum. UV radiation data were derived from satellite-based observations. The proposed methodology was tested using cosm data for three compounds including metamitron (viz. Wendt-Rasch et al., 2004; Brock et al., 2004 and Van Wijngaarden et al., 2004). No primary data (*i.e.* measured concentrations of metamitron in environmental matrices) are reported in this publication, only modelled data (photolytic $DegT_{50}$) are reported.	**Not relevant**

Diamanti, K.S.; Alygizakis, N.A.; Nika, M-C.; Oswaldova,M.; Oswald, P.; Thomaidis, N.S.; Slobodnik, J. 2021. Assessment of the chemical pollution status of the Dniester River Basin by wide-scope target and suspect screening using mass spectrometric techniques. Journal of Hazardous Materials 410, 124538, 10 pp.

Relevance score	*-Appropriate sampling strategy (i.e. triggers, season, campaign and programme duration.)*: No. Thirteen surface water, 13 river sediment, and three biota samples were collected from different sampling sites along the Dniester River between 25 and 28 May 2019. Sampling sites were selected throughout the entire basin, including inflowing tributaries and the estuary to reflect a variety of anthropogenic pressures (e.g., agricultural sites, industrial areas, wastewater outlets, reservoirs). The sampling period covered the spring season, when there was an increased use of herbicides in agriculture. Only slight rainfall and surface runoff were recorded prior to and during the sampling. The sampling strategy consists of a single ‘snap-shot’ sampling event, without data from other years or months or seasons it is not possible to determine if the data are ‘unusual’, or can be considered representative and therefore informative for environmental risk assessment purposes. *- Appropriate explanatory data and/or statistical analysis of analyte concentrations in relation to land use, weather, substance use*: No. The main text provides sufficient information on the analytical method, calibration and validation, but insufficient information is provided about the land use, cropping and spatial relationship with other sampling sites is provided for the sampling sites. No information is provided on site-based pesticide concentrations for each sampling event. Thus, this paper contains no useable data for environmental risk assessment.	**Not relevant**

4 Ecotoxicology

4.1 Metamitron

Aslantas, S.; Golge, O.; González-Curbelo, M. A.; Kabak, B. 2023. Determination of 355 Pesticides in Lemon and Lemon Juice by LC-MS/MS and GC-MS/MS. Foods 12, 1812. 12 pp.

Relevance score	*-Information that informs the existing regulatory data package:* No. This paper reports the screening and quantification of 355 pesticides in 100 whole lemon fruits and their juices, obtained from the commercial market in Turkey. Whole fruit and juice samples were prepared using the quick, easy, cheap, effective, rugged and safe (QuEChERS) methodology prior to analysis by liquid chromatography-tandem mass spectrometry (LC-MS/MS) and gas chromatography-tandem mass spectrometry (GC-MS/MS). The analytical method was validated in-house and had a sufficiently low limit of quantification with respect to current maximum residue limits (MRLs) for all target analytes. The obtained recovery and precision parameters fulfilled the requirements in DG SANTE guidelines. Sixteen different residues were detected in 43% of lemon fruits, whereas 57 lemon samples were pesticide-free. The MRLs exceedances were recorded in 29 lemon samples. Metamitron was one of 16 different pesticides detected above the LOQ, and was the second most frequently detected pesticides being present in 10% of lemon fruits at concentrations ranging between 0.027 and 0.118 mg kg^{-1}. None of the pesticide residues were detected in lemon juice samples. These results showed that target analytes are unable to penetrate the lemon exocarp and/or endocarp. In recent years, metamitron has been used as a chemical fruit-thinning agent for several fruits, including apple, pear and citrus fruits. Under Commission Regulation No. 284/2013 information on residue concentrations in the crop plant itself, and harvestable components thereof, is not relevant to either the environmental fate (Section 9) or ecotoxicology regulatory data packages (Section 10) for the product.	**Not relevant**

Głowacka, A.; Flis-Olszewska, E. 2022. The biodiversity of weed communities of dent maize, narrow-leaved lupin and oat in relation to cropping system and weed control. Agronomy Science 77, 1-16.

Relevance score	*-Information that informs the existing regulatory data package:* No. In this paper the effects of weed control (chemical and mechanical) and cropping system (sole and strip intercropping) on the biodiversity of weed communities was determined for three crops : dent maize, narrow-leaved lupine and spring oats. Metamitron was the chemical control treatment applied to narrow-leaved lupin (2,800 g/ha, BBCH 12/13). The underlying data came from a field study performed in Poland between 2008 and 2010. Detailed information of the conditions of the study and agrotechnical procedures is not reported in this paper, but an earlier paper : Głowacka (2014). No primary data (*i.e.* species-level information on weeds) are reported in this publication, only derived data (diversity metrics) are reported. Changes in the number and weight of weeds is presented and discussed in Głowacka (2013), which may also contain information on specific weed species. Information on weed species has relevance for product efficacy, but not ecotoxicity.	**Not relevant**

Astaykina, A.; Streletskii, R.; Maslov, M.; Kazantseva, S.; Karavanova,E.; Gorbatov,V. 2020. Novel pesticide risk indicators for aquatic organisms and earthworms. Agronomy 10, 1070, 18 pp.

Relevance score	*-Information that informs the existing regulatory data package:* No. The aim of this study was to develop a risk indicator based on the sum of points of acute toxicity exposure ratio, long-term toxicity exposure ratio, and the bioconcentration factor (BCF). These negative impacts of pesticides on soil and aquatic organisms were calculated by combining predicted environmental concentrations in soil and surface water with data on pesticide toxicity in the environment. A field column experiment with metribuzin (low sorption capacity (K_{OC} = 38), high solubility (~5 g/L) was performed to calibrate chromatographic flow model PEARL 4.4.4 for soddy–podzolic soils under the climate conditions of the Moscow region. PEARL 4.4.4 was used to predict pesticide concentrations in soil. The FOCUS STEP 1–2 model was used to predict the pesticide concentrations in surface water bodies that considered factors such as pesticide interception by crop, deposition of spray drift to the surface of the water body and its migration into the water body due to surface runoff and drainage from soil.. Data on the physicochemical and eco-toxicological properties of 200 active substances of pesticides (herbicides, fungicides, and insecticides) were obtained from the international database PPDB (Pesticide Property Data Base). Metamitron was predicted to be present in high concentrations in surface waters, as well as in the plough layer of soddy-podzolic soil. Metamitron was amongst the 20 most toxic pesticides for earthworms based on acute (LC_{50}) and chronic (NOEC) toxicity data, but not amongst the 20 most toxic pesticides for aquatic organisms based on minimum LC_{50}/EC_{50} and NOEC data. Metamitron had a one of the highest risk indicator values corresponding to a low risk of negative impacts on earthworms. No primary data (*i.e.* species-level information on earthworms or aquatic organisms) are reported in this publication, only secondary data and derived data (risk indicator values) are reported.	**Not relevant**

Martinello, M.; Manzinello, C.; Borin, A.; Avram, L.E.; Dainese, N.; Giuliato, I.; Gallina, A.; Mutinelli, F. 2020. A Survey from 2015 to 2019 to investigate the occurrence of pesticide residues in dead honeybees and other matrices related to honeybee mortality incidents in Italy. Diversity 12, 15. 16 pp.

The following table has been adapted for use in evaluating honey bee monitoring studies from the tables included in RIVM, 2003 and 2008.

Key to notes: E=expert judgement, Y=reliability is lower, Q3 = item is not reported. Empty sections under notes have not been evaluated as review was stopped, once found to be not reliable or relevant.

Items	**Notes**	**Reliability Lower**
Description		
Substances studied	150 substances covering the following categories: acaricide, bactericide, fungicide, herbicide, insecticide, molluscicide, nematicide, plant growth regulator, repellent, synergist and a few relevant metabolites. Substances studied includes metamitron.	
Species	Honeybee.	
Area description and history: Main agricultural use/ crops grown in area, other potential sources of exposure, layout of surrounding area	Samples were collected at locations throughout Italy. The geographical distribution of the honeybee death events coincides with the areas in Italy in which intensive agriculture is mainly practiced (such as apple and citrus orchards and vineyards mainly other than maize cultivations.).	
Sampling: Strategy (i.e. scheduled sampling or event driven sampling, time of year, sampling campaign duration and monitoring programme duration).	Event driven. Samples were collected between 2015 and 2019 in response to reports from beekeepers of colony mortality and depopulation events attributed to the use of PPPs.	
Sampling: Method of sampling, measures to avoid cross contamination, number of individual samples if combined samples, number of replicates	Samples of 250 – 1000 dead honeybees were collected from hive entrances or the ground in front of the hive. In addition, samples of bee bread and honey from combs and samples of vegetable matrices were also collected in the immediate vicinity of the hive, or from nearby crops treated with pesticides. All samples were collected by official veterinarians of the Local Health Service. The samples were individually packed in plastic sampling bags to avoid cross contamination. 507 samples of bees and 187 samples of other matrices were analysed.	
Sample conservation: Stability of sample during transport and storage	After collection samples were stored at -20 °C until delivery to the analytical laboratory.	
Extraction method and sample preparation	Duplicate samples were prepared following the QuEChERS (Quick Easy Cheap Effective Rugged Safe) approach using the slightly modified method reported by Anastassiades et al. [17]. Samples were homogenised prior to extraction by pulverising with a crushing mill (A11 basic IKA-Werke GmbH & Co. KG, Staufen, Germany) cooled with liquid nitrogen. One gram of pollen and vegetable matrices, two grams of bees and wax or 5 g of honey were extracted by vortexing in 10 mL of water for 5 min, acetonitrile with 0.1% acetic acid (10 mL) was added and vortexed for 20 min before cooling at -20 °C for 15 min. The QuEChERS salts EN method was used for partitioning. Sodium citrate 1 g, sodium hydrogen citrate sesquihydrate 0.5 g, magnesium sulphate 4 g and sodium chloride 1 g were added and vigorously shaken up and down for 1 min. The mixture was centrifuged and 7 mL of supernatant was transferred to a tube containing purification dispersive SPE Fatty Samples EN salts (magnesium sulphate 900 mg, PSA 150 mg and C18 150 mg). The solution was vortexed for 1 min and centrifuged, and 4 mL of the	

	supernatant was transferred to a clean tube and evaporated to dryness under vacuum at 45 °C. The residue was dissolved in 0.5 mL of reconstitution solution prior to analysis.	
Analytical method: Recovery (%), limit of detection/quantitation, precision of method (<25% RSD)	LC-MS/MS analysis The analysis was performed using a Shimadzu LCMS-8040 (Kyoto, Japan), with a tandem quadrupole analyser, in MRM spectrum mode using an electron spray ionization source in both positive and negative ionization modes. The chromatography was performed on a Raptor (Restek Corporation, Bellefonte, PA, USA) biphenyl column (10 cm × 2.1 mm, 2.7 μm-particles) thermostated at 35 °C. The mobile phase solvents were 5 mM ammonium formiate in water with 0.1% formic acid and 5 mM ammonium formiate in methanol with 0.1% formic acid. The chromatographic eluting conditions were optimized as follows: from 3% to 10% B (0–1 min), from 10% to 55% B (1–3 min), from 55% to 100% B (3–10.5 min), 100% B maintained for 2.5 min, from 100% to 3% B in 0.01 min), followed by re-equilibration to 3% B for a further 3 min. The total analysis run time was 15 min. The flow rate was 0.4 mL/min and the injection volume was 2 μL. Quantitative and qualitative analyses were performed with LabSolution Insight software based on the two most intensive fragment ion transitions. GC-MS/MS Analysis The analysis was performed on a Shimadzu GC-MS TQ8040 equipped with Phenomenex ZB-Semivolatiles columns (30 m, 0.25 mm ID, 0.25 μm) and a tandem mass spectrometry detector. A sample volume of 1 μl was injected in the splitless mode at an injector temperature of 270 °C. The oven temperature was programmed as follows: initial temperature 60 °C (held for 2 min) increased by 70 °C/min to 200 °C; increased by 6 °C/min to 300 °C (held for 2 min). The ion source and interface temperature were held at 230 °C and 280 °C, respectively. The total analysis run time was 23 min. Quantitative and qualitative analyses were performed with LabSolution Insight software based on the two most intensive fragment ion transitions. For all substances studied: LOQ = 10 μg kg^{-1}	
Results		
Detections in honeybees	Metamitron was not amongst the substances detected in honeybee samples analysed in the five years of monitoring.	
Detections in other samples	Metamitron was not amongst the substances detected in the other samples analysed in the five years of monitoring.	
Reliability score	The study is based on a well-designed national monitoring programme and expertly conducted. The methods are reported in excellent detail.	**Ri 1**
Relevance score	-*Information that informs the existing regulatory data package:* Yes. Monitoring studies may not be a data requirement but may be submitted as part of a refined risk assessment. -*Appropriate test substance:* Yes. -*Appropriate substrate:* Yes. -*Appropriate experimental conditions:* Yes. -*Appropriate extraction/analysis method*: Yes. -*Application rates and/or substrate loads which are representative of those expected under current intended uses*: Unknown, but given the wide geographical coverage, it is likely that metamitron will have been applied to crops in Italy. It is reasonable to conclude that the absence of metamitron detections in honeybees is probably due to metamitron application to crops that are not attractive to honeybees and/or applications are made when honeybees are not active; rather than metamitron is not applied to crops in Italy.	**Relevant**

	Although this paper does not provide a 'real life' endpoint, the duration and geographical range of the study means it has value in weight of evidence argumentation.	

5 Summaries of relevant and reliable studies

Schönenberger, U.T.; Beck, B.; Dax, A.; Vogler, B.; Stamm, C. 2022. Pesticide concentrations in agricultural storm drainage inlets of a small Swiss catchment. Environmental Science and Pollution Research 29, 43966–43983.

Note: For transparency, the numbering system under which figures and tables were originally published has been maintained. Their consideration in this study summary is not necessarily sequential and nor are all figures and/or tables presented in the open literature study reproduced in this document.

Background

In contrast to other countries, roads and adjacent fields in Switzerland are less often drained to ditches, but to inlet and maintenance shafts of storm and tile drainage systems. Model-based studies at the national level indicate that around half of surface runoff from fields and the related pesticide load is expected to be transported to surface waters through such shafts. Similarly, wash-off of spray drift deposited on roads through such shafts to surface waters has been predicted as being a major pesticide transport pathway. However, there is a lack of empirical data to validate these findings. To address this data gap runoff and pesticide transport through inlet shafts (hereafter inlets) was measured in an agricultural storm drainage system. The measurements were performed in a catchment in which considerable high pesticide transport through hydraulic shortcuts was expected (i.e. an intensively used agricultural catchment with a high shortcut density and little direct surface connectivity to the stream).

Methods

Study catchment

The study catchment is located in a rural area in the Swiss midlands (canton of Bern, outlet: 47°07′12.570″N 7°30′48.926″E). The average annual rainfall equals 1075 ± 163 mm/year (MeteoSwiss, 2018). It occupies 2.8 km^2, has an average slope of 5.0% and is covered by arable land (38%), forests (32%), agricultural areas with very little or no pesticide use (18%) (e.g. meadows, pasture, ecological compensation areas) and other/undefined agricultural areas (4%). Settlements, farmyards, roads and farm tracks mainly cover the remaining area (8%). On arable land, the predominant crop types during the study year were grains, potatoes, and sugar beet. The conditions in the study catchment (soils, topography, climate, storm drainage system) are quite typical for the Swiss Plateau such that key findings can be generalised to a larger area.

The agricultural area is heavily drained by artificial structures by tile drains in the soils and by storm drains along the road network. In total, 158 storm drainage inlets were identified along or on agricultural areas. Most of them are located along farm tracks (111), or concrete roads (33). The remaining fourteen are located directly on fields. All of these inlets are drained to the stream at the catchment outlet. In addition, 84% of the agricultural area is tile drained (Figure 2).

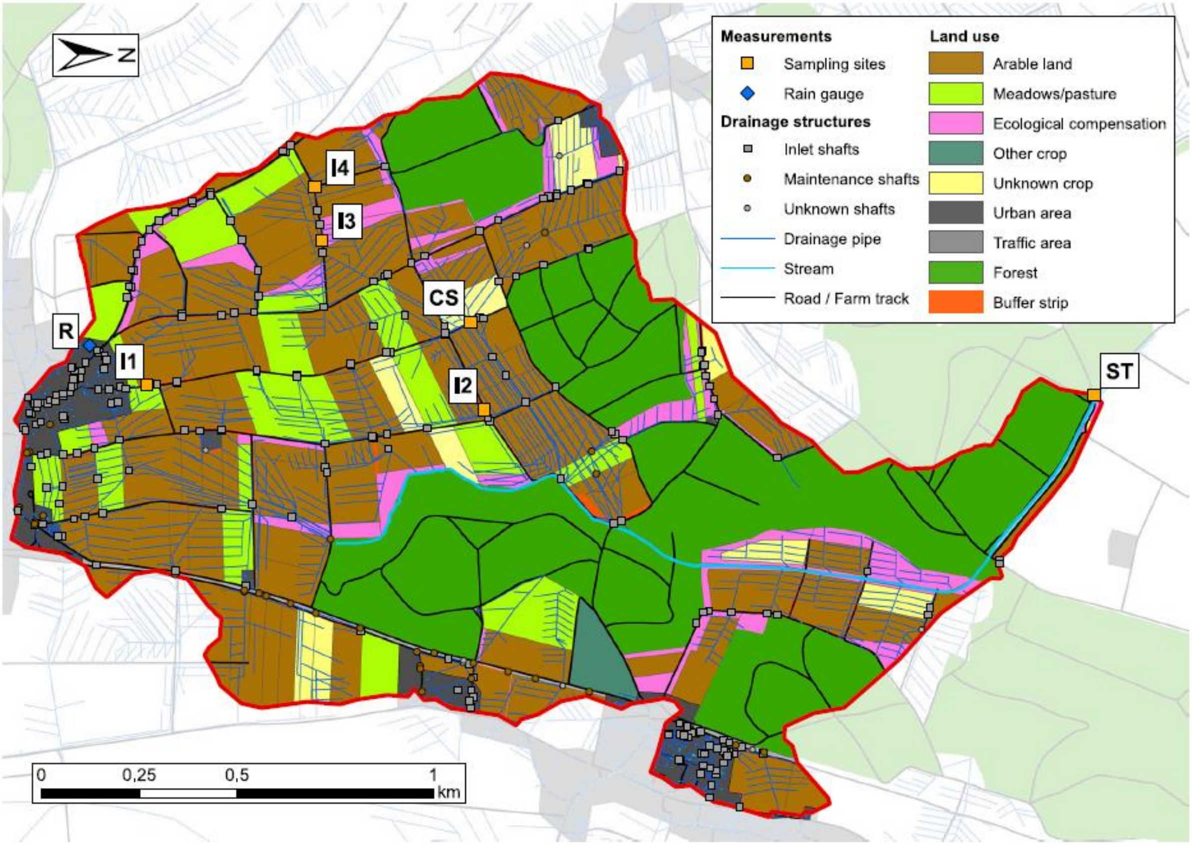


Fig. 2 Map of the study catchment. Yellow squares show the sampling sites (I1–I4: inlets; CS: collector shaft; ST: stream) and the blue diamond shows the rain gauge (R)

Modelling was used to estimate the surface runoff connectivity of the sampling sites. Around 76% of the agricultural area in the catchment has a surface runoff connectivity to the stream. From this area, 25% is directly connected to the stream, and 75% is indirectly connected via inlets. The four sampled inlets drain around 5.7% of the agricultural area connected to inlets in the study catchment and 2.9% of the roads connected to inlets. The collector shaft drains around half of the agricultural and road area in the catchment that is connected to inlets. The remaining agricultural area (24%) is connected to sink areas.

Pesticide usage

Plot-specific crop and pesticide application data for 96% of the agricultural areas in the catchment for the period January to October of the study year 2019 was provided by most of the 26 farmers in the catchment. The pesticide application data were recorded using a crop management system and included the day of application, product, amount applied, crop, plot size and a georeferenced polygon of the plot. From the substances analysed in this study, 96% of the total active ingredient mass applied in 2019 was applied within the study period.

Sampling sites

There were six sampling sites in the catchment, four were located at storm drainage inlets (I1–I4) (Figure 1a), one at a collector shaft (CS) and one at the outlet stream (ST) for the catchment (Figure 2).

Out of the 158 inlets in the catchment, inlets I1–I4 were selected because they fulfilled two criteria: First, the dimensions of the inlet permitted the installation of measuring equipment. Second, only surface runoff entered the inlet through the lid; all inlets with inflow pipes from tile drains were excluded. From the ten inlets fulfilling these criteria, four were selected because they represented different terrain and cropping conditions. All were located at the border of a field and a gravel farm track. While I1, I2 and I4 lay directly next to the farm track, I3 was separated from the farm track by a grass strip of approximately 0.5-m width. During dry periods, there is no discharge transported through the four inlets, and in I1, I2 and I4 the water stagnates at the height of the outlet pipe. In contrast, during dry periods, the water level in I3 falls to a lower level due to seepage through the shaft bottom.

The collector shaft collects water from 64 inlets (including I3 and I4), and from a large part of the tile drainage system in the catchment (Figure 1b).

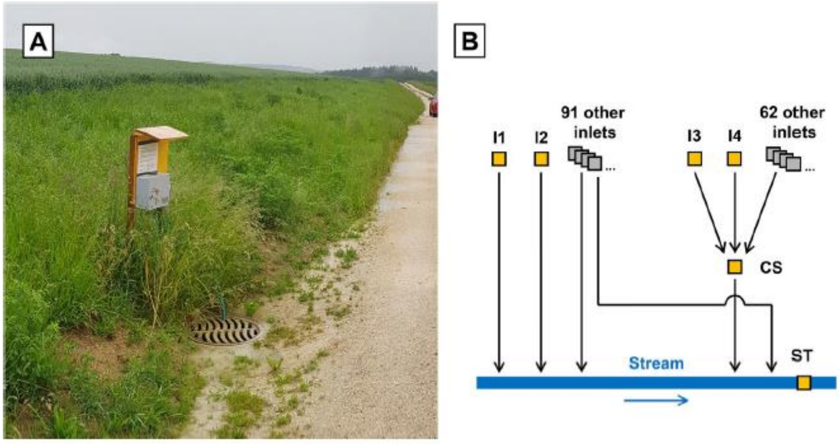


Fig. 1 **A** Example picture of a storm drainage inlet in the study catchment taken during the study period. The depicted inlet (I1) is one of the four inlets sampled and is situated between a farm track and a wheat field. A larger picture of the situation around the inlet is shown in Figure A1. **B** Schematic representation of the storm drainage network in the catchment (black lines: pipes, grey squares: inlets) and of the sampling locations (yellow squares). I1–I4: inlets; CS: collector shaft; ST: stream

Sampling strategy

In central Europe, most pesticides are applied in spring and summer, seasons when rainfall intensities are higher and the greatest pesticide concentrations in surface waters are usually measured. The study period (1 April to 20 August 2019) was chosen to cover most of this high-risk period.

Since water only flows through the inlets during rain events, event-based sampling was performed. There were two types of event — rainfall and sampling events. Measured rainfall was classified into a rainfall event if the total rainfall exceeded 1 mm within 8 h. Subsequent rainfall was assigned to the same event if there was no dry period of at least 8 h in between. After dry periods of more than 8 h, a new rainfall event was defined. Sampling events were defined as rainfall events during which water samples were taken.

Overall, 423 samples were collected, 193 were selected as the most relevant ones for further analysis. All inlet samples were analysed. Collector shaft and stream samples for six out of the top ten event samples with the largest sum concentrations in the sampled inlets were analysed, these samples cover the range of rain intensities observed.

Inlet water samples were analysed for 19 of 37 rain events, covering 80% of the total discharge transported through the sampled inlets during the study period. In the remaining events, either discharge was too small to trigger sampling (15 events), or no sampling bottles were installed (3 events). Additionally, for six of these events, water samples from the collector shaft and the stream were analysed.

In situ measurements, and sample collection and storage

- Inlets (I1–I4): discharge was measured by installing a weir with a calibrated rating curve in front of the outlet pipe. The water level was measured using a capacitive pressure sensor (DWL compact, UIT, Germany) coupled to a data logger equipped with a GPRS module (LogTransfield, UIT, Germany). For water sampling, we installed an event-based, water-level proportional sampler.

- Collector shaft (CS): the water level was measured using the same sensors as in the inlets. Water samples were taken using an automatic sampler (TP5C portable sampler, MAXX GmbH, Germany) coupled to a GPRS module.

- Stream (ST): discharge was measured by the cantonal authorities using an ultrasonic sensor (POA-V2XXK, NIVUS AG, Germany). Water samples were taken with the same sampler type as in the collector shaft.

- Rain gauge (R): Rainfall data (resolution: 1 min, accuracy: 0.1 mm) was provided by the cantonal authorities from a rain gauge at the southern catchment edge.

In the inlets, the water-level proportional samplers started sampling at a defined water level threshold above the bottom of the weir (2 cm for inlets with little runoff, 3 cm for inlets with larger runoff), corresponding to a discharge of approximately 1.7 and 5 L/min. This resulted in one composite sample per event for each inlet exceeding the water level threshold. Rain events that were too small to exceed the water level threshold in an inlet were not sampled. When the water level threshold was exceeded in at least two inlets, the automatic samplers at the collector shaft and the stream were triggered via the GPRS module to start sampling.

In the collector shaft, time proportional samples (50 mL) were taken every 2 to 3 min and pooled together into one composite sample per 20 to 30 min, depending on the event (details in Table A6). Depending on the event duration, the total sampling duration was 4 to 8 h.

In the stream, time proportional sampling was performed with the same frequency during the discharge peak. Before and after the peak, samples were pooled over a period of up to 2 h. Depending on the event duration, the total sampling duration was 10 to 12 h.

If no composite samples were taken in an inlet during an event (due to lack of sufficient discharge, or due to malfunctioning of the sampler), we took a grab sample from the stagnant water during sample collection.

All samples were kept in glass bottles and protected from sunlight. At sites CS and ST, the samples were cooled by the automatic samplers (4 °C), and at sites I1–I4 by the stagnating water around the bottle (average temperature: 13.5 °C). They were collected on average 1.3 days after sampling and frozen at −20 °C until analysis.

Sample preparation and analysis

Dissolved phase pesticide concentrations were determined using direct injection liquid chromatography coupled to high-resolution mass spectrometry (LCHRMS). The particulate phase was not analysed. The target list comprised 51 substances that were either pesticides known to be applied in the catchment (45 substances, including metamitron), or their transformation products (6 substances, including desamino metamitron).

Samples were thawed and centrifuged for 5 min at 2000 g. The supernatant was transferred, and isotope-labelled internal standard (ISTD) was added. Randomly selected samples were spiked with a standard solution in order to assess relative recovery of the compounds. Centrifugation, transfer, spiking of ISTD and standard solution were fully automated. Laboratory blanks and blinds, and field blinds, were included in the measurement sequence to monitor instrument carry-over and contamination.

Chromatographic separation was performed on a reversed-phase C18 column (Atlantis T3, 3-µm particle size, 3.0 × 150 mm inner diameter, Waters), applying a water–methanol gradient (both containing 0.1% formic acid). The measurements were performed on a hybrid quadrupole-orbitrap mass spectrometer (Lumos Fusion, Thermo Scientific) equipped with an electrospray ionisation source. Quantification of the target compounds was performed using TraceFinder 5.1 (Thermo Scientific). For

95% of the compounds, relative recovery was in the range of 80–120%. For 80% of the compounds, the limit of quantification (LOQ) was 20 ng/L or lower. Further details on the chemical analysis (such as the gradient, the ionisation, processed sample volumes) are given in Section A1.2 of the paper.

Results

Rain events

During the study period, 37 rain events were recorded, duration ranged between 1 and 41 h (median: 9 h) (Figure 4). During 34 rain events, discharge was measured in at least one of the inlets. The discharge formation in the inlets depended on the total rainfall sum of the respective rain event, but not on the rainfall intensity. The rainfall needed to trigger discharge differed between the inlets. The minimal rainfall sum needed was 1.3–1.5 mm for I1, I2 and I4, while I3 was only getting active with 3.6 mm. This can be explained by the grass strip separating I3 from the adjacent road. Additionally, due to the seepage through the shaft bottom of I3 during dry periods, surface runoff entering the inlet first had to fill the shaft, before being transported through the outlet pipe. Similarly, the measured discharge differed strongly between the four inlets, being much higher in I1 and I2 than in I3 and I4.

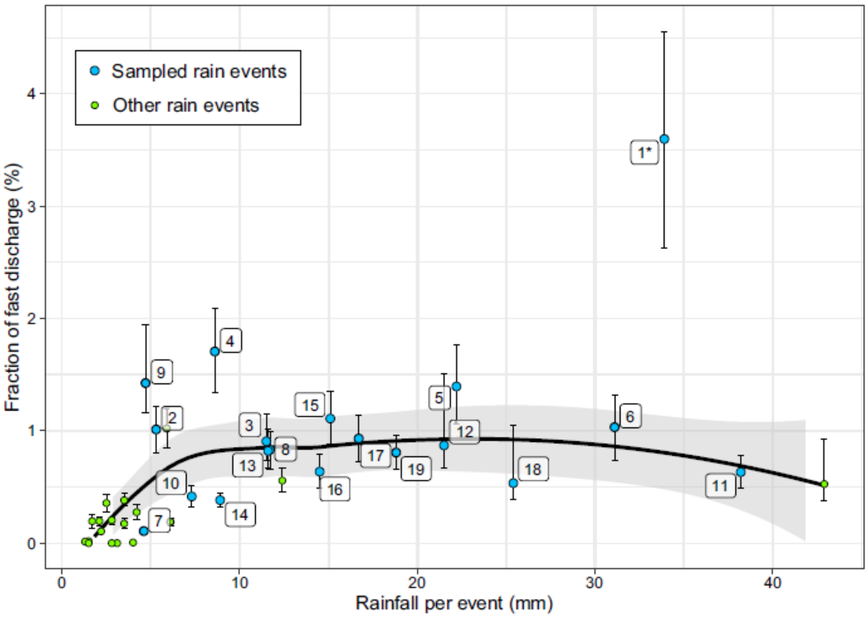


Fig. 4 Ratio between the discharge sum in the four inlets and the fast discharge in the stream $r_{Q,\mathrm{fast}}$. Points correspond to the moderate estimates ($r_{Q,\mathrm{fast,mod}}$), error bars to the minimum and high estimates ($r_{Q,\mathrm{fast,min}}$ and $r_{Q,\mathrm{fast,high}}$). Sampling event numbers are indicated with white boxes. The numbers represent the events in ascending order of time. The black line represents a smoothed conditional mean of $r_{Q,\mathrm{fast,mod}}$, obtained by a locally weighted scatterplot smoothing (LOESS) using the R package ggplot2 (version 3.3.3, function geom_smooth). The grey area represents the corresponding 95% confidence interval. Event 1 was a snowmelt event and was therefore excluded from the analysis

Metamitron concentrations

Measured concentrations of pesticides differed considerably between sampling sites. Metamitron was the substance with the greatest concentration in I1 and I2 (7900 ng/L and 920 ng/L, respectively) (Table 1).

Table 1 Overview over the pesticide concentrations measured at the different sampling sites. Due to the uncertainty caused by the limit of quantification (LOQ), a range is provided for the mean concentrations. For calculating the lower limit of this range, we replaced the concentrations below the LOQ by 0. For calculating the upper limit, we replaced them by the LOQ. An overview over the measured transformation product concentrations are provided in Table A7. I1–I4: inlets; CS: collector shaft; ST: stream

Site	I1	I2	I3	I4	CS	ST
Number of substances above LOQ	33	26	22	25	33	42
Mean pesticide concentration (ng/L)	92–124	9–40	11–43	291–322	51–65	190–201
Maximal pesticide concentration (ng/L)	7900	920	500	62,000	7900	35,000
Pesticide with highest concentration	Metamitron	Metamitron	Diflufenican	Terbuthylazine	Terbuthylazine	Propamocarb

Metamitron and metamitron-desamino were persistently measured in successive samplings for I1 and I2 at concentrations greater than 100 ng/L between May and August.

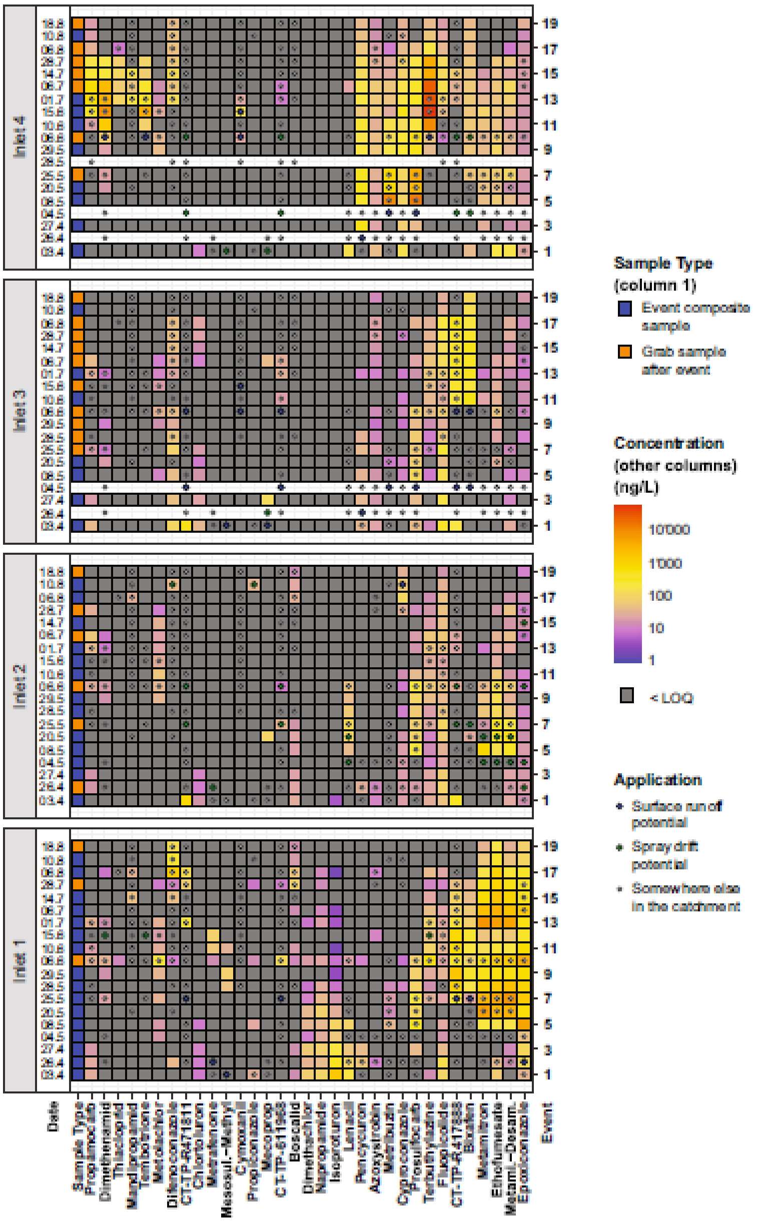


Fig. 5 Concentrations c (ng/L) measured in inlets for events 1 (3 April 2019) to 19 (18 August 2019). Only substances found at least twice in concentrations > 25 ng/L are shown. White rows indicate that no sample was taken. In the first column, the sample type is indicated. In the remaining columns, substances are clustered by the concentrations measured. Coloured dots indicate that the particular substance was applied in the period between the respective and the previous event. Dot colours specify the potential transport processes

Discussion

The authors attributed high pesticide concentrations in the inlets to prior applications on fields with surface runoff or spray drift potential to the corresponding inlet. However, also applications on fields without the potential for these processes to occur led to high concentrations in inlets of up to 7900 ng/L (e.g. metamitron and ethofumesate at I1, propamocarb at I4). These results show that other mechanisms besides surface runoff and spray drift also contributed to high concentrations in inlets. These mechanisms may involve droplet losses, accidental spills, residual wash off from applications in previous years, unreported applications, applications outside the study catchment, or (only in case of I1) farmyard runoff. The highest concentrations related to applications on fields without surface runoff or spray drift potential were measured in I1 (metamitron and ethofumesate). By rechecking with the farmers, unreported applications could be excluded. Additionally, metamitron and ethofumesate have a rather fast degradability (DT_{50}, soil: 19 and 22 days; DT_{50}, water: 11 and 20 days) and were not applied in the contributing area of the inlet in the year before this study, thus, wash off of residuals as a source is unlikely. However, I1 is located close to a village at a farm track often used by farmers for accessing their fields in or outside the study catchment. In contrast, the other inlets are located along farm tracks less often used. This indicates that droplet losses from leaking spraying equipment or accidental spills on the farm track could be responsible for the increased concentrations in I1.

[Reviewer’s additional notes: Site and date-based concentration data for metamitron and metamitron-desamino are provided as supplementary information.]

Martinello, M.; Manzinello, C.; Borin, A.; Avram, L.E.; Dainese, N.; Giuliato, I.; Gallina, A.; Mutinelli, F. 2020. A Survey from 2015 to 2019 to investigate the occurrence of pesticide residues in dead honeybees and other matrices related to honeybee mortality incidents in Italy. Diversity 12, 15. 16 pp.

Note: For transparency, the numbering system under which figures and tables were originally published has been maintained. Their consideration in this study summary is not necessarily sequential and nor are all figures and/or tables presented in the open literature study reproduced in this document.

Background

In 2014, the Italian Ministry of Health established a monitoring programme to verify the real exposure of honeybees to the neonicotinoids clothianidin, thiamethoxam, fipronil and imidacloprid in areas extensively used by bees for foraging or by beekeepers. A systematic approach was adopted covering the management (notification to the competent authority, epidemiological and clinical investigation in the apiary, sampling, laboratory investigation) of bee mortality incidents where pesticide poisoning was suspected. On 31 July 2014 the General Directorate of Animal Health and Veterinary Medicinal Products of the Italian Ministry of Health, issued the "Linee guida per la gestione delle segnalazioni di moria o spopolamento degli alveari connesse all'utilizzo di agrofarmaci" (Guidelines for the management of reports of death or depopulation of bee colonies related to the use of plant protection products). These guidelines provide operational directives for managing these events with respect to gathering information on the possible causes of death and/or depopulation of beehives, standardizing investigations in terms of the procedures adopted both in the field and at the laboratories responsible for analysing the sampled dead bees.

Methods

Sampling

Between 2015 and 2019, in response to reports from beekeepers of colony mortality and depopulation events attributed to the use of PPPs, samples of 250 – 1000 dead honeybees were collected from hive entrances or the ground in front of the hive. In addition, samples of bee bread and honey from combs and samples of vegetable matrices (most frequently leaves, corn seedlings, maize) were also collected in the immediate vicinity of the hive, or from nearby crops treated with pesticides. All samples were collected by official veterinarians of the Local Health Service and were individually packed in plastic sampling bags to avoid cross contamination. After collection samples were stored at -20 °C until delivery to the analytical laboratory.

Sample preparation

Duplicate samples were prepared following the QuEChERS (Quick Easy Cheap Effective Rugged Safe) approach using the slightly modified method reported by Anastassiades et al. [17]. Samples were homogenised prior to extraction by pulverising with a crushing mill (A11 basic IKA-Werke GmbH & Co. KG, Staufen, Germany) cooled with liquid nitrogen.

One gram of pollen and vegetable matrices, two grams of bees and wax or 5 g of honey were extracted by vortexing in 10 mL of water for 5 min, acetonitrile with 0.1% acetic acid (10 mL) was added and vortexed for 20 min before cooling at -20 °C for 15 min. The QuEChERS salts EN method was used for partitioning. Sodium citrate 1 g, sodium hydrogen citrate sesquihydrate 0.5 g, magnesium sulphate 4 g and sodium chloride 1 g were added and vigorously shaken up and down for 1 min. The mixture was centrifuged and 7 mL of supernatant was transferred to a tube containing purification dispersive SPE Fatty Samples EN salts (magnesium sulphate 900 mg, PSA 150 mg and C18 150 mg). The solution was vortexed for 1 min and centrifuged, and 4 mL of the supernatant was transferred to a clean tube and evaporated to dryness under vacuum at 45 °C. The residue was dissolved in 0.5 mL of reconstitution solution prior to analysis. UPLC-MS/MS (Ultra Pressure Liquid Chromatography coupled with tandem mass spectrometry) reconstitution solution consisted of 5mM ammonium formiate in water with 0.1% formic acid and 5 mM ammonium formiate in methanol with 0.1% formic acid (1:1 v/v), and PTFE filtered (0.45 µm pore size). Samples analysed using GC-MS/MS were reconstituted with 0.5 mL of heptane and PTFE filtered (0.45 µm pore size).

LC-MS/MS analysis
The analysis was performed using a Shimadzu LCMS-8040 (Kyoto, Japan), with a tandem quadrupole analyser, in MRM spectrum mode using an electron spray ionization source in both positive and negative ionization modes. The chromatography was performed on a Raptor (Restek Corporation, Bellefonte, PA, USA) biphenyl column (10 cm × 2.1 mm, 2.7 µm-particles) thermostated at 35 °C. The mobile phase solvents were 5 mM ammonium formiate in water with 0.1% formic acid and 5 mM ammonium formiate in methanol with 0.1% formic acid. The chromatographic eluting conditions were optimized as follows: from 3% to 10% B (0–1 min), from 10% to 55% B (1–3 min), from 55% to 100% B (3–10.5 min), 100% B maintained for 2.5 min, from 100% to 3% B in 0.01 min), followed by re-equilibration to 3% B for a further 3 min. The total analysis run time was 15 min. The flow rate was 0.4 mL/min and the injection volume was 2 µL.

GC-MS/MS Analysis
The analysis was performed on a Shimadzu GC-MS TQ8040 equipped with Phenomenex ZB-Semivolatiles columns (30 m, 0.25 mm ID, 0.25 µm) and a tandem mass spectrometry detector. A sample volume of 1 µl was injected in the splitless mode at an injector temperature of 270 °C. The oven temperature was programmed as follows: initial temperature 60 °C (held for 2 min) increased by 70 °C/min to 200 °C; increased by 6 °C/min to 300 °C (held for 2 min). The ion source and interface temperature were held at 230 °C and 280 °C, respectively. The total analysis run time was 23 min.

Quantitative and qualitative analysis
Analytical-grade (98–99.9% purity) standards of 150 substances (including metamitron) covering the following plant protection categories: acaricide, bactericide, fungicide, herbicide, insecticide, molluscicide, nematicide, plant growth regulator, repellent, synergist and a few relevant metabolites were obtained from Sigma-Aldrich (Steinheim, Germany). Pesticide-grade solvents, Supel^{TM} QuE Citrate Extraction Tubes and Supel^{TM} QuE PSA/C18 (EN) Cleanup Tubes were used to extract and purify samples. High purity water was prepared using a Milli-Q water purification system (Millipore, Milford, MA, USA). Single standard solutions were prepared in methanol at a concentration of 1000 mg/L. The working standard solutions were prepared by mixing the appropriate amounts of single standard solutions and diluting with methanol to a final concentration of 10 and 1 mg/L. All solutions were stored in the dark in 10 mL amber bottles at -20 °C.

Both instruments were programmed in MRM (multiple reaction monitor) mode with two selected transitions per molecule. Matrix matched standards were used for calibration and quantification, prepared by analysing blank (negative) samples spiked with pesticides after the extraction and purification steps. Quantitative and qualitative analyses were performed with LabSolution Insight software based on the two most intensive fragment ion transitions. The LOQ for all substances studied was 10 µg kg^{-1}.

Results

Sampling locations
Samples were collected at locations throughout Italy (Figure 1). The geographical distribution of the honeybee death events coincides with the areas in Italy in which intensive agriculture is mainly practiced (such as apple and citrus orchards and vineyards mainly other than maize cultivations. Five hundred and seven samples of bees and 187 samples of other matrices were analysed.


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Figure 1. Location of positive and negative samples for each officially reported honeybee mortality event in Italy from 2015 to 2019.

Substances detected

In total, 63 different active ingredients were found in honeybee samples, with concentrations ranging from 0.1 to 134,665 ng/bee, and 51 different active ingredients in the other analysed matrices (beeswax, bee bread, honey and vegetable matrices), ranging from 0.01 to 359.5mg/kg. Most investigated samples were positive for at least one active ingredient (53%) and contaminated by more than one residue: 53% of the samples were contaminated by at least two different residues, 32% by at least three, while as many as nine active ingredients were detected in one extreme case, coming from Udine province (North-Eastern Italy).

Insecticides were the most frequently detected active substances (49.2%) in honeybees, the most prevalent being the acaricide tau-fluvalinate (38.2%). Pyrethroid permethrin, the second most frequently found active substance, had a prevalence of 13.3%. Chlorpyrifos was the third most commonly determined pesticide (12.9%). Globally, most of the other matrices analyzed (67%) were positive for at least one active ingredient. Again, the acaricide tau-fluvalinate was the most commonly found active ingredient, with a prevalence of 53.4%, followed by the insecticide methiocarb with a prevalence of 13.6% (also considering the metabolite methiocarb sulfoxide), and the synergist piperonyl butoxide (11.0%).

Metamitron was not amongst the substances detected in honeybee samples analysed in the five years of monitoring (2015 – 2019).

Reviewer's Conclusion

Authorised plant protection products containing metamitron have on the Italian market for more than ten years. It is reasonable to conclude that the absence of metamitron detections in honeybees is probably due to metamitron application to crops that are not attractive to honeybees and/or applications are made when honeybees are not active; rather than metamitron is not applied to crops in Italy.

6 Additional references

Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market (OJ L 93, 3.4.2013, p. 84) https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0283&from=EN

Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market (OJ L 93, 3.4.2013, p. 68) https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:093:0085:0152:EN:PDF%20

EFSA, 2008. European Food Safety Authority. Conclusion regarding the peer review of the pesticide risk assessment of the active substance metamitron. EFSA Scientific Report 2008; 185:1-95.

EFSA, 2011. European Food Safety Authority. 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.

EFSA, 2014. European Food Safety Authority. EFSA Guidance Document for evaluating laboratory and field dissipation studies to obtain DegT50 values of active substances of plant protection products and transformation products of these active substances in soil. EFSA Journal 2014; 12(5):3662.

FOCUS, 2014. Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration. Version: 1.1, 18 December 2014.

OECD, 2000. Organisation for Economic Co-operation and Development. Test No. 106: Adsorption - Desorption Using a Batch Equilibrium Method. OECD Guidelines for the Testing of Chemicals, Section 1, OECD Publishing, Paris.

OECD, 2002a. Organisation for Economic Co-operation and Development. Test No. 307: Aerobic and Anaerobic Transformation in Soil. OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris.

OECD, 2002b. Organisation for Economic Co-operation and Development. Test No. 308: Aerobic and Anaerobic Transformation in Aquatic Sediment Systems. OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris.

OECD, 2004. Organisation for Economic Co-operation and Development. Test No. 312: Leaching in Soil Columns. OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris.

OECD, 2006. Organisation for Economic Co-operation and Development. Test No. 227: Terrestrial Plant Test: Vegetative Vigour Test. OECD Guidelines for the Testing of Chemicals, Section 3, OECD Publishing, Paris.

RIVM, 2001. Netherlands National Institute for Public Health and the Environment. Evaluation of pesticide leaching in lysimeter and field studies. Parent substances. RIVM report 601506 007/2001. Verschoor, A.J., Boesten, J.J.T.T., Leistra, M., van der Linden, A.M.A., Linders, J.B.H.J., Pol, J.W.

RIVM, 2003. Netherlands National Institute for Public Health and the Environment. Monitoring data in pesticide registration. RIVM report 601450015/2003. Cornelese, A.A., Boesten, J.J.T.I., Leistra, M., van der Linden, A.M.A., Linders, J.B.H.J.L., Pol, J.W.W., Verschoor, A.J.

RIVM, 2006. Netherlands National Institute for Public Health and the Environment. A guidance document of the Dutch Platform for the Assessment of Higher Tier Studies. Guidance for summarising earthworm field studies. RIVM report number 601506006/2006. De Jong, F.M.W., van Beelen, P., Montforts, M.H.M.M.

RIVM, 2008. Netherlands National Institute for Public Health and the Environment. Manual for summarising and evaluating environmental aspects of plant protection products. Report 601712004/2008. Mensink, B.J.W.G., Smit, C.E., Montforts, M.H.M.

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