Water Quality Criteria Report for Clothianidin

Phase III: Application of the pesticide water quality criteria methodology

Prepared for the Central Coast Regional Water Quality Control Board

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October 2020

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Funding for this project was provided by the State of California Central Coast Regional Water Quality Control Board (CCRWQCB). The contents of this document do not necessarily reflect the views and policies of the CCRWQCB, nor does mention of trade names or commercial products constitute endorsement or recommendation for use.

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List of acronyms and abbreviations

ACR	Acute-to-Chronic Ratio
AF	Assessment factor
APHA	American Public Health Association
ASTM	American Society for Testing and Materials
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BMF	Biomagnification Factor
CAS	Chemical Abstract Service
CDFW	California Department of Fish and Wildlife
CSIRO	Commonwealth Scientific and Industrial Research Organization, Australia
CVRWQCB	Central Valley Regional Water Quality Control Board
CCRWQCB	Central Coast Regional Water Quality Control Board
DPR	Department of Pesticide Regulation
EC_x	Concentration that affects x% of exposed organisms
FDA	Food and Drug Administration
FT	Flow-through test
IC_x	Inhibition concentration; concentration causing *x*% inhibition
ICE	Interspecies Correlation Estimation
IUPAC	International Union of Pure and Applied Chemistry
K	Interaction Coefficient
K_H	Henry's law constant
K_{ow}	Octanol-Water partition coefficient
K_p or K_d	Solid-Water partition coefficient
LC_x	Concentration lethal to *x*% of exposed organisms
LD_x	Dose lethal to *x*% of exposed organisms
LL	Less relevant, Less reliable study
LOEC	Lowest-Observed Effect Concentration
LR	Less relevant, Reliable study
MATC	Maximum Acceptable Toxicant Concentration
MDL	Method Detection Limit
N	Not relevant or Not reliable study
n/a	Not applicable
NOEC	No-Observed Effect Concentration
NR	Not reported
OECD	Organization for Economic Co-operation and Development
pK_a	Acid dissociation constant
RL	Relevant, Less reliable study
RR	Relevant and Reliable study
S	Static test
SMACR	Species Mean Acute-to-Chronic Ratio
SMAV	Species Mean Acute Value

SR	Static renewal test
SSD	Species Sensitivity Distribution
TES	Threatened and Endangered Species
US	United States
USEPA	United States Environmental Protection Agency

Introduction

1.1 Introduction to clothianidin

This criteria report for clothianidin describes, section by section, the procedures used to derive aquatic toxicity criteria according to the UC Davis methodology (see Section 1.2). References are included to specific sections of the methodology so that the reader can refer to the report for further details.

In the environment, clothianidin transforms into several degradates that are more or less stable. Degradates are formed through aquatic photolysis as well as aerobic metabolism in soil and/or water (Figure 2). Clothianidin is itself a degradation product of the neonicotinoid thiamethoxam. This criteria report includes toxicity data for clothianidin degradates when available. Some sections do not mention a particular degradate due to a dearth of data for that particular chemical species. The data tables containing degradate data are color coded to assist the reader in separating each of the degradate from the parent compound clothianidin.

1.2 Method background

A methodology for deriving freshwater water quality criteria for the protection of aquatic life was developed by the University of California - Davis (TenBrook et al. 2009a). The need for a methodology was identified by the California Central Valley Regional Water Quality Control Board (CVRWQCB 2006) and findings from a review of existing methodologies (TenBrook & Tjeerdema 2006, TenBrook et al. 2009b). The UC Davis methodology has been used to derive aquatic life criteria for several pesticides of particular concern in the Sacramento River and San Joaquin River watersheds. It is now being used to derive aquatic life criteria for the watersheds under the jurisdiction of the Central Coast Regional Water Quality Control Board (CCRWQCB). The methodology report (TenBrook et al. 2009a) contains an introduction (Chapter 1); the rationale of the selection of specific methods (Chapter 2); detailed procedure for criteria derivation (Chapter 3); and a criteria report for a specific pesticide (Chapter 4). In 2014 a sediment methodology was developed by University of California - Davis (Fojut et al. 2014), which contains some updated parameters that are relevant for calculating freshwater water quality criteria. These include Assessment Factor and Acute-to-Chronic Ratio parameters (AF and ACR, respectively). Sections 3-3.3 (AF) and 3-4.2.3 (ACR) of the aquatic method state that these parameters can be recalculated and updated if additional relevant data become available (TenBrook et al. 2009a). Unless otherwise specified, mentions of the methodology refer to the aquatic method (TenBrook et al. 2009a). The sediment method will be specifically referenced for clarity (Fojut et al. 2014).

1.3 Interim Criteria

The toxicity data sets for the neonicotinoids thiamethoxam and clothianidin both posed challenges for deriving aquatic life criteria using the UC Davis Method. These pesticides appear to be toxic to a narrower range of organisms compared to most other broad spectrum insecticides that have been evaluated using the UC Davis Method, as demonstrated by non-definitive or censored toxicity values for a number of key taxa from otherwise relevant and reliable studies. At a minimum, the UC Davis Method requires an acceptable definitive toxicity value from the family Daphniidae in the genus *Daphnia, Ceriodaphnia*, or *Simocephalus* to calculate an acute criterion. For clothianidin, acute tests were performed on *Daphnia magna* and *Ceriodaphnia dubia*, but the tests did not result in definitive toxicity values for these species. The concentrations tested in these studies were well below solubility because thiamethoxam and clothianidin are very water soluble, so it may be possible to determine definitive toxicity values for these species, but they would likely be well-above environmentally relevant concentrations. Two other key taxa used in the UC Davis Method – a warmwater fish and a species in the family Salmonidae – also were tested, but the tests did not result in definitive toxicity values because the species were so tolerant of thiamethoxam and clothianidin.

Because the thiamethoxam and clothianidin datasets were both rich in other sensitive invertebrates, and the taxa missing from the final datasets appear to be very insensitive to these pesticides, the authors derived what are termed Interim Acute and Chronic Criteria for these pesticides. The term “interim” was chosen because if definitive toxicity data became available for several key taxa, it would be possible to calculate definitive aquatic life criteria for these pesticides and to denote that the calculation of these criteria deviates from the existing UC Davis Method. Interim Acute and Chronic Criteria were derived in recognition that performing additional acute toxicity tests with the required taxa lacking definitive toxicity values aimed at resulting in definitive, rather than censored (>), toxicity values may not be a good use of resources because it has already been demonstrated that these species are not sensitive to these pesticides at environmentally relevant concentrations.

The Interim Acute Criteria were derived using the Assessment Factor procedure, in which the lowest toxicity value in the final acute dataset was divided by a factor and the magnitude of the factor is based on the number of toxicity values in the dataset that fulfilled the five taxa requirements of the UC Davis Method. To derive the Interim Acute Criteria for these two pesticides, the AF was chosen based on having all five required taxa in the dataset, even though the toxicity values for three of the five required taxa are censored values; this approach deviates from the UC Davis Method guidance in two ways. The two deviations are that (1) censored toxicity values are excluded according to the UC Davis Method and (2) acute criteria are not derived without a definitive toxicity value from the family Daphniidae in the genus *Daphnia, Ceriodaphnia*, or *Simocephalus*. There are two reasons a toxicity value from the family Daphniidae in the genus *Daphnia, Ceriodaphnia*, or *Simocephalus* is required to calculate an acute criterion by the UC Davis Method: (1) testing a daphnid is always required when registering a pesticide with the US EPA, so it was expected that data for this taxon would always be available and (2) daphnids are invertebrates, which are expected to be relatively more sensitive than the other taxa required to register a pesticide (typically fish species). The goal in requiring a daphnid toxicity value is to avoid underestimating the toxicity of the pesticide to aquatic ecosystems by only using data for less sensitive species. It also gave a point of reference for calculating the AFs used to calculate criteria when the five required taxa for calculating the acute criterion using a species sensitivity distribution are not all available. In the case of thiamethoxam and clothianidin, daphnids and fish are relatively insensitive, but the acute datasets demonstrate that there are many invertebrates that are sensitive to thiamethoxam and clothianidin toxicity. Thus, deriving Interim Criteria for these pesticides without definitive daphnid data is unlikely to underestimate the toxicity of them on aquatic ecosystems. Conversely, excluding the nondefinitive data and using an AF based on only two of the five required taxa would likely result in overly conservative criteria because the missing taxa are all very insensitive to these pesticides. The UC Davis Method was developed with a goal of being able to derive water quality criteria for pesticides even when only small datasets are available but did not consider how these requirements may affect criteria calculation for pesticides that have a more narrow spectrum of toxicity. The Interim Acute and Chronic Criteria for thiamethoxam and clothianidin provide one potential procedure for deriving criteria for pesticides with limited toxicity to some of the required taxa.

The Interim Chronic Criteria for thiamethoxam and clothianidin were derived by using an ACR following the guidance of the UC Davis Method.

Statistical uncertainty cannot be directly quantified when criteria are calculated using AFs and ACRs. However, because these are Interim Criteria, the authors chose to present additional values to provide a lower and upper range of levels that may also be protective of aquatic ecosystems. The lower acute limits were calculated using the AF procedure of the UC Davis Method based on only the number of definitive toxicity values in the final acute datasets, which was two of the five required taxa for both pesticides. The upper acute limits were calculated by dividing the lowest toxicity value in the acute dataset by a factor of 2, which is how US EPA Acute Aquatic Life Benchmarks are derived. The lower and upper chronic limits were calculated using the Acute-to-Chronic ratio procedure with the respective acute values.

These Interim Criteria were derived with the goal of providing guidance to environmental managers on protective levels of thiamethoxam and clothianidin. In addition, it is also a proposal for an alternate procedure that may be appropriate to add to the UC Davis Method for deriving criteria with a narrow spectrum of toxicity. The main aspect of this new procedure is to allow the use of censored data in deriving acute criteria when the toxicity level is above the highest concentration tested, the highest concentration is well-above concentrations detected in the environment or is approaching or exceeding solubility, and the test is otherwise relevant and reliable as scored in the UC Davis Method. Censored data are only proposed to be used with the assessment factor procedure for deriving acute criteria because in this procedure they serve to fulfill taxa requirements, but the censored values themselves are not used for calculations. They demonstrate that sensitive taxa are not being overlooked due to a lack of testing, but that some taxa were tested and are particularly insensitive to the pesticide of interest. Censored data are not proposed to be used in species sensitivity distributions because the values themselves are not meaningful and should not be combined with uncensored data in a statistical distribution. Censored data may be off by orders of magnitude compared to the true toxic level for that species, and such different values could significantly affect the fit of the statistical distribution, thus significantly affecting the resulting criteria. The assessment factor procedure is a more appropriate use for censored data, as it is intended to be a method to derive criteria when insufficient information is available to fit a species sensitivity distribution, as is the case when censored data are the only data available for a given taxa.

Basic information

Clothianidin is a nitroguanidine-substituted neonicotinoid insecticide that is applied to agricultural crops, soils, and seeds as well as turf, landscaping plants, and some animal husbandry structures (USEPA 2017). It is a systemic insecticide that translocates throughout living plant tissue via xylem and phloem so that insects may come into contact with the insecticide when affected tissue is bitten, chewed, or otherwise consumed. The mode of action is disruption of the insect central nervous system by outcompeting acetylcholine for binding sites on nicotinic acetylcholine receptors (USEPA 2017). Clothianidin is a soil metabolite of thiamethoxam.

Chemical: Clothianidin (Fig. 1)
CAS: [*C*(*E*)-*N*[(2-chloro-5-thiazolyl)methyl]-*N*-methyl-*N*-nitroguanidine
CAS Numbers:

1. 210880-92-5 (current)
   (Fontaine 2001, USEPA 2017)
2. 205510-53-8 (former)
   (Fontaine 2001, USEPA 2017)

USEPA PC Code: 044309
CA DPR Chem Code: 5792
IUPAC: (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine
Chemical Formula: $C_6H_8ClN_5O_2S$

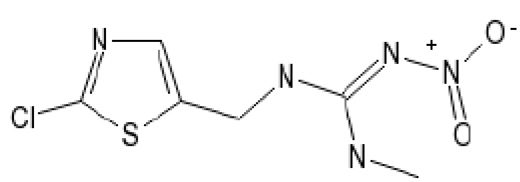

Figure 1 Structures of clothianidin

(USEPA 2017)

Trade names: Poncho 600, TI 435, HSDB 7281, Titan, Arena, UNII-2V9906ABKQ, SumiShield, Telsta, Dantotsu

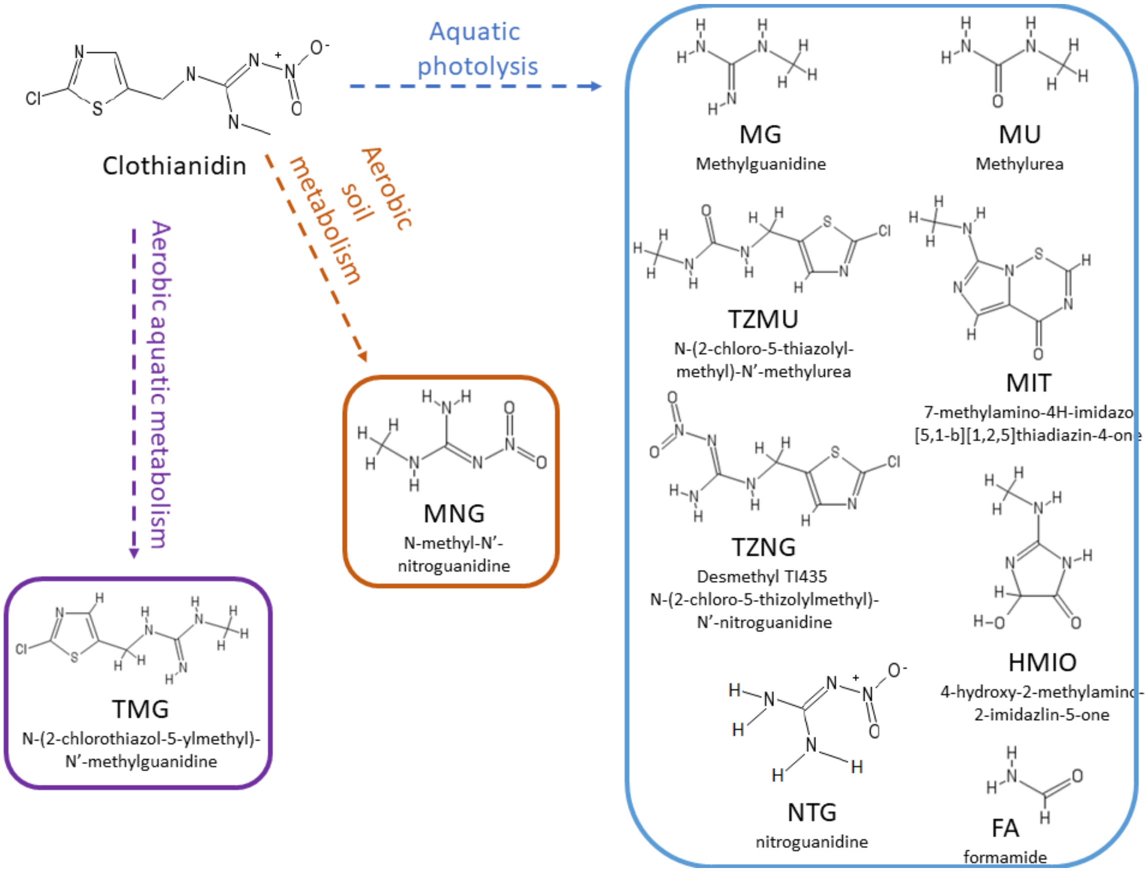

Figure 2 Identified major and minor degradates of clothianidin.

Toxicity data was not available for all degradation products (adapted from USEPA 2017).

Physical-chemical data, Bioconcentration, and Fate

Molecular Weight
249.7 g/mole (PPDB 2016)

Density
1.16 g/mL (PPDB 2016)

Water Solubility
307 mg/L at unknown temperature (pH 4 & 10) (MacBean 2010)
340 mg/L at 20ºC (PPDB 2016)
327 mg/L at 25ºC (Fontaine 2001)
327 mg/L at 20°C (Fontaine 2001)
327 mg/L at 20ºC (Morrissey 2000)
Geometric mean: 325 mg/L

Melting Point
176.8°C (Fontaine 2001)
146.49°C (EPI Suite, USEPA 2015)
176.8°C (PPDB 2016)
176.8°C (MacBean 2010)
Geometric mean: 168.7°C

Vapor Pressure
$1.3x10^{\wedge-7}$ Pa at 25°C (Fontaine 2001)
$3.8x10^{-8}$ mPa at 20°C (Fontaine 2001)
$1.7x10^{-10}$ mPa at unknown temperature (Fontaine 2001)
0.481 mPa at 25°C (EPI Suite, USEPA 2015)
0.482 mPa at 25°C (EPI Suite, USEPA 2015)
$2.8x10^{-8}$ mPa at unknown temperature (EPI Suite, USEPA 2015)
Geometric mean: $4.2x10^{-6}$ mPa = 0.0042 μPa

pKa
11.1 (Fontaine 2001)
11.09 at 25°C (PPDB 2016)
11.09 at 20°C (MacBean 2010)
Geometric mean: 11.09

Henry's constant (K_H)
$9.33x10^{-11}$ Pa m^3 mol^{-1} at unknown temperature (EPI Suite, USEPA 2015)
$1.798x10^{-5}$ Pa m^3 mol^{-1} at unknown temperature (EPI Suite, USEPA 2015)
$2.9x10^{-11}$ Pa m^3 mol^{-1} at 25°C (PPDB 2016)
$2.9x10^{-11}$ Pa m^3 mol^{-1} at 20°C (Fontaine 2001)
Geometric mean: $1.1x10^{-9}$ Pa m^3 mol^{-1}

Organic Carbon Sorption Partition Coefficients (log K_{OC})

Clothianidin:

3.196	(EPI Suite, USEPA 2015)
1.433	(EPI Suite, USEPA 2015)
2.11	(Lewis 2000)
2.538	(Lewis 2000)
2.090	(Lewis 2000)
1.924	(Lewis 2000)
2.076	(Lewis 2000)
2.21	(Stupp 2001)
3.181	(EPI Suite, USEPA 2015)

Geometric mean: 2.24
Arithmetic mean: 2.31

MNG: (Dorn 2000a)

1.4 sandy loam
0.7 sand
1.2 silt loam
1.53 sandy loam
1.32 sand

Geometric mean: 17
Arithmetic mean: 20

TZNG: (Mondel 2000)

2.41 sandy loam
0.78 sand
2.84 silt loam
4.71 sandy loam
0.63 sand

Geometric mean: 1.7
Arithmetic mean: 2.3

TZMU: (Dorn 2000b)

1.76 sandy loam
1.66 sand
1.75 silt loam
1.98 sandy loam
1.72 sand

Geometric mean: 59
Arithmetic mean: 61

TMG: (Dorn 2000c)

2.72 sandy loam
2.81 sand
3.13 silt loam
3.56 sandy loam
3.79 sand

Geometric mean: 1589
Arithmetic mean: 2459

All degradates geometric mean: 23
All degradates arithmetic mean: 509

Log K_{ow}
0.70 (Fontaine 2001)
0.7 (MacBean 2010)
0.64 (EPI Suite, USEPA 2015)
0.905 (PPDB 2016)
Geometric mean: 0.73

Bioconcentration Factor

Table 1 Bioconcentration factors (BCF) for clothianidin, NR is for not reported

Species	BCF	Exposure	Reference
NR	"Low risk" no value because LogP<3	NR	PPDB 2016
NR	3.162	NR	EPI Suite, USEPA 2015 (regression method)
NR	1.005	NR	EPI Suite, USEPA 2015 (Arnot-Gobas method)

BCF geometric mean: 1.8

Environmental Fate

Table 2 Clothianidin hydrolysis and photolysis and other degradation, NR is for not reported

Reaction type	Half-life (h or d)	Water or soil	Temp (°C)	pH	Reference
Hydrolysis	1.004×10^{12} h Stable	NR; model river	NR	NR	EPI Suite, USEPA 2015
Hydrolysis	1.096×10^{13} h Stable	NR; model lake	NR	NR	EPI Suite, USEPA 2015
Hydrolysis	Stable	Various (sand, silt, loam)	20	NR	Lewis 2000
Aqueous Photolysis	0.6 d	Aqueous buffer solution	NR	NR	Babezinski 2000

Aqueous Photolysis	0.6 d	Aqueous buffer solution	NR	NR	Schad 2000a
Aqueous Photolysis	0.6 d	NR	NR	NR	Hellpointer 1999
Aqueous Photolysis	1.10-131 d depending on season/latitude	Pure water at 0-5 cm	Ambient	NR	Hellpointer 1999
Aqueous Photolysis	>1-290 d depending on season	Pure water at 0-5 cm	Ambient	NR	Hellpointer 1999
Biodegradation (aerobic)	143 d	Silt	20	NR	Gilges 2000
Biodegradation (aerobic)	227 d	Silt Loam	20	NR	Gilges 2000
Biodegradation (aerobic)	490 d	Loamy sand	20	NR	Gilges 2000
Biodegradation (aerobic)	1001 d	Sandy loam	20	NR	Gilges 2000
Biodegradation (aerobic)	541 d	Silt loam	20	NR	Schad 2000b
Biodegradation (aerobic)	1328 d	Loam	20	NR	Schad 2000b
Biodegradation (aerobic)	549 d	Loamy sand	20	NR	Schad 2000b
Biodegradation (aerobic)	533 d	Sand	20	NR	Schad 2000b
Biodegradation (aerobic)	808 d	Silt loam	20	NR	Schad 2000b
Biodegradation (aerobic)	170 d	Pond water & sediment (loam)	20	7.2	Ripperger 2006
Biodegradation (aerobic)	55 d	Pond water	20	7.2	Ripperger 2006
Biodegradation (aerobic)	51 d	Pond sediment (loam)	20	7.2	Ripperger 2006
Biodegradation (aerobic)	7.6 d	Water layer of cropped rice plot	Ambient	NR	Greenland 2011
Biodegradation (aerobic)	Pre-irrigation: 2.04 d Post-irrigation: 5.66 d	Cropped rice plot	Ambient	NR	Greenland 2011

Biodegradation (aerobic)	Pre-irrigation: 1.41 d Post-irrigation: 8.58 d	Unplanted rice plot	Ambient	NR	Greenland 2011
Biodegradation (aerobic)	14.7 d	0-5 cm soil in cropped rice plot	Ambient	NR	Greenland 2011
Biodegradation (aerobic)	13.7 d	0-5 cm soil in unplanted rice plot	Ambient	NR	Greenland 2011
Biodegradation (aerobic)	Pre-irrigation: 2.24 d Post-irrigation: 2.32 d	Cropped rice plot	Ambient	NR	Greenland 2010
Biodegradation (aerobic)	Pre-irrigation: 2.06 d Post-irrigation: 2.62 d	Unplanted rice plot	Ambient	NR	Greenland 2010
Biodegradation (anaerobic)	21 d	Pond water & sediment	20	4.7-5.0	Reddemann 2000
Biodegradation (anaerobic)	4 d	Pond water	20	4.7-5.0	Reddemann 2000

Human and wildlife dietary values

There are no FDA action levels for clothianidin in food (USFDA 2000) and there are no EPA pesticide tolerances set for any aquatic species (USEPA 2012).

Wildlife LC_{50} values (dietary) for animals with significant food sources in water

The US EPA Proposed Interim Registration Review Decision for Clothianidin and Thiamethoxam contains information for clothianidin on bobwhite quail only. It states that birds show moderate acute toxicity to clothianidin based on oral exposure and practically no subacute toxicity based on dietary exposure (USEPA 2020).

An acute dietary study of *Anas platyrhynchos* (mallard duck) by Johnson 1998 reported an LC_{50} value of >5,200 mg/kg after 8 days of exposure. If additional highly rated measured data for mallard duck become available in the future, they should be examined to determine the potential risk to wildlife.

Wildlife dietary NOEC values for animals with significant food sources in water

A 21-week dietary exposure study on the reproductive effects on mallard duck (*Anas platyrhynchos*) resulted in a NOEC value of 500 mg/kg (Gallagher 2000). An acute dietary study of *A. platyrhynchos* by Johnson 1998 reported a NOEC of 650 mg/kg after 8 days of exposure. No other NOEC data was available for wildlife species with significant food sources in water during the present report preparation. If additional highly rated measured data for mallard duck become available in the future, they should be examined to determine the potential risk to wildlife.

Ecotoxicity data

Approximately 40 original studies on the effects of clothianidin on aquatic life were identified and reviewed. In the review process, many parameters were rated for documentation and acceptability for each study, including, but not limited to: organism source and care, control description and response, chemical purity, concentrations tested, water quality conditions, and statistical methods (see Tables 3.6, 3.7, 3.8 in TenBrook et al. 2009a). Single-species effects studies that were rated as relevant (R) or less relevant (L) according to the method (Table 3.6) were summarized in data summary sheets. Information in these summaries was used to evaluate each study for reliability, using the rating systems described in the methodology (Tables 3.7 and 3.8, section 3-2.2, TenBrook et al. 2009a), to give a reliability rating of reliable (R), less reliable (L), or not reliable (N).

Studies of the effects of clothianidin on mallard ducks were rated for reliability using the terrestrial wildlife evaluation. Mallard studies rated as reliable (R) or less reliable (L) were used to consider bioaccumulation. Two studies for mallard duck rating R were located in the literature and are summarized in Section 4.

Copies of completed summaries for all aquatic studies are included in the Appendix of this report. All data rated as acceptable (RR) or supplemental (RL, LR, LL) for criteria derivation are summarized in Tables 3 - 10, found at the end of this report. Acceptable studies rated as RR are used for numeric criteria derivation, while supplemental studies rated as RL, LR or LL are used for evaluation of the criteria to check that they are protective of particularly sensitive species and threatened and endangered species. These considerations are reviewed in section 10.1 and 10.3 of this report, respectively. Studies that were rated not relevant (N) or not reliable (RN or LN) were not used for criteria derivation.

Six mesocosm studies were identified and reviewed. One study was rated L and five studies rated R. The studies are listed in Appendices A3 and A6. They are used as supporting data in Section 10.2 to evaluate the derived criteria to ensure that they are protective of ecosystems.

<u>Evaluation of aquatic animal data</u>

Using the data evaluation criteria (section 3-2.2, TenBrook et al. 2009a), five acute studies yielding 33 toxicity values from 20 taxa were judged reliable and relevant for acute criterion derivation (Tables 3-4). One acute toxicity animal value was rated reliable and relevant for the clothianidin degradate TMG and two acute values were rated reliable and relevant for the degradate TZNG. Twenty-eight acute toxicity animal values for 20 taxa from 17 studies were rated RL, LL, or LR and were used as supplemental information for evaluation of the derived acute criteria in the Sensitive Species section 10.1 (Table 5). Two acute toxicity animal values for one species from one study were rated RL, LL, or LR for the clothianidin degradate TZMU (Table 5). Eight acute toxicity animal values for three species from four studies were rated RL, LL, or LR for the clothianidin degradate MNG (Table 5). Two acute toxicity animal values for two species from two studies were rated RL, LL, or LR for the clothianidin degradate TMG (Table 5). Two acute toxicity animal values for two species from two studies were rated RL, LL, or LR for the clothianidin degradate TZNG (Table 5). Twenty-five chronic animal toxicity values from 11 studies were rated RR (Tables 7-8). Forty-eight chronic toxicity animal values from 12 studies were rated RL, LL, or LR (Table 10).

Evaluation of aquatic plant data

All plant studies were considered chronic because the typical endpoints of growth or reproduction are inherently chronic. Two studies yielding two plant toxicity values for the parent compound of clothianidin and one study yielding a single plant toxicity value for the metabolite TMG were rated RR (Table 6).

Plant studies are more difficult to interpret than animal data because a variety of endpoints may be used, but the significance of each one is less clear. In this methodology, only endpoints of growth or reproduction (measured by biomass) and tests lasting at least 24-h had the potential to be rated highly and used for criteria calculation, which is in accordance with standard methods (ASTM 2007a, 2007b; USEPA 1996). The plant studies were rated for quality using the data evaluation criteria described in the methodology (section 3-2.2, TenBrook et al. 2009a).

Data reduction

Multiple toxicity values for clothianidin for the same species were reduced down to one species mean acute value (SMAV) or one species mean chronic value (SMCV) according to procedures described in the methodology (section 3-2.4, TenBrook et al. 2009a). Twelve toxicity values from three studies were reduced from the final acute data set (Table 4). Twenty-four toxicity values from nine studies were reduced from the final chronic data set (Table 8).

Acute criterion calculation

The acute criterion is calculated with acute animal toxicity data only, because plant toxicity tests are always considered chronic (section 3-2.1.1.1, TenBrook et al. 2009a). A final acute criterion could not be calculated for clothianidin due to a lack of highly rated studies that meet the methodology requirements. Only two of the five taxa requirements were met. The dataset does not contain data for a warm water fish, a salmonid, or a daphnid species. Section 3-3.3 requires that at least one of the available, acceptable data must be from the family Daphniidae in the genus *Daphnia*, *Ceriodaphnia*, or *Simocephalus*, or a criterion cannot be calculated. The highly rated clothianidin dataset does not contain values for any daphnid species. Therefore, a final acute criterion could not be calculated.

As invertebrates, daphnids are generally a relatively sensitive species to aquatic pesticide exposures compared to vertebrates, and the USEPA requires data from this family for pesticide registration in order to ensure adequate protection of invertebrates. The UC Davis Method requires a daphnid value for the same reason. However, species from the Daphnidae family and fish have been shown to be relatively insensitive to neonicotinoids, such as clothianidin. These species were tested as part of the USPEA registration process but resulted in non-definitive values (> or <) that are not used in the UC Davis Method calculations. However, it is reasonable to calculate an interim acute criterion for clothianidin, despite the lack of such data because there are other sensitive species in the dataset that will ensure protection of species that are most sensitive to this pesticide. Further discussion on the rationale for deriving an interim acute criterion is given in section 1.3 of this report.

To provide information to environmental decision makers, an interim acute criterion was calculated for clothianidin utilizing available acute animal toxicity data. Since acceptable acute toxicity values were not available from the five required taxa for a species sensitivity distribution, an interim acute criterion was calculated using the AF procedure (section 3-3.3, TenBrook et al. 2009a). The acute dataset was missing definitive toxicity values for a daphnid, salmonid, and a warm water fish. Clothianidin is an organic pesticide, and the AFs given in the methodology (Table 3.13, TenBrook et al. 2009a) are the most specific AFs available for organic pesticides. The methodology points out that the AFs are limited in that they are based on organochlorine, organophosphate, and pyrethroid pesticides, which are neurotoxic insecticides. Clothianidin is a neurotoxic insecticide, thus, it is reasonable to use the AF procedure for clothianidin.

Sections 3-3.3 of the aquatic method state that AFs can be recalculated and updated if additional relevant data become available (TenBrook et al. 2009a). The AFs for the aquatic criteria calculations were updated in 2014 after additional data became available for recalculation. These updated AF values are included in the sediment method (Fojut et al. 2014). The AFs given in the methodologies will be used for clothianidin with the understanding that AFs based on measured pesticide toxicity data are likely more accurate than choosing an arbitrary AF. The methodology points out that AFs are recognized as a conservative approach for dealing with uncertainty in assessing risks posed by chemicals (section 2-3.2, TenBrook et al. 2009a). Using an AF to calculate a criterion always involves a high degree of uncertainty and there is potential for under- or over-protection, which is strongly dependent on the representation of sensitive species in the available data set. The methodology instructs that the derived criterion should be compared to all available ecotoxicity data to ensure that it will be protective of all species (section 3-6.0, TenBrook et al. 2009a).

An AF was used to derive an interim criterion, by dividing the lowest value in the acute dataset by a predetermined factor. The factors were first given in Table 3.13 of the water method and were then updated in the sediment method in Table 18. Definitive toxicity values were available for three (benthic crustacean, insect, and daphnid) of the five required taxa. Censored toxicity values were available for the remaining three required taxa (warmwater fish and Salmonidae) and each one would be an acceptable test except for the fact that the species was insensitive to the tested concentrations and thus a definitive toxicity value could not be calculated.

The interim acute value was calculated using the AF of 5.1, which is used when all five required taxa are available in the dataset, as discussed in section 1.3.

The acute value calculated using the AF represents an estimate of the median 5th percentile value of the SSD, which is the recommended acute value. The recommended acute value is divided by a factor of two to calculate the acute criterion (section 3-3.3, TenBrook et al. 2009a). Because the toxicity data used to calculate the interim criterion reported two significant figures, the criterion is rounded to two significant figures (section 3-3.2.6, TenBrook et al. 2009a). The clothianidin acute criterion is termed an interim acute criterion to acknowledge that the procedure used to derive the criterion deviates from the UC Davis Method and that it may be possible to obtain definitive toxicity values for the taxa missing definitive values, at which time a final acute criterion could be derived.

An interim acute criterion was calculated using the lowest value in the data set. Raby 2018c reported an immobility EC_{50} value for *Neocoleon triangulifer* of 3.5 µg/L:

Interim acute value = lowest value in data set ÷ AF
= estimated 5th percentile
= 3.5 µg/L ÷ 5.1
= 0.6863 µg/L

Interim acute criterion = acute value ÷ 2
= 0.6863 µg/L ÷ 2
= 0.3431 µg/L

Interim acute criterion = 0.34 µg/L

To provide some quantification of the uncertainty in the interim acute criterion, lower and upper estimates were calculated based on more or less conservative procedures for deriving aquatic life thresholds. The lower estimate was derived using the AF procedure, but using an AF based on only the definitive toxicity values in the dataset, which represent three of the five required taxa. The lower estimate is a relatively conservative value because the missing taxa are all known to be relatively insensitive, and the AF is designed to account for missing taxa that may possibly be more sensitive than the species available in the dataset. The lower estimate was calculated using an AF of 12.

Lower estimate acute value = lowest value in data set ÷ AF
= estimated 5th percentile
= 3.5 µg/L ÷ 12
= 0.29167 µg/L

Lower estimate of the acute criterion = lower estimate acute value ÷ 2

= 0.29167 µg/L ÷ 2
= 0.16667 µg/L
= 0.17 µg/L

The upper estimate was derived in the same manner as USEPA Office of Pesticide Program's aquatic life benchmarks, in which the lowest acute toxicity value is divided by two:

Upper estimate acute value: 3.5 µg/L

Upper estimate of the acute criterion = upper estimate acute value ÷ 2
= 3.5 µg/L÷ 2
= 1.75 µg/L

Chronic criterion calculation

Acceptable chronic values were not available for five different species, so a distribution could not be fit to the available toxicity data (section 3-4.1, TenBrook et al. 2009a). The chronic dataset was missing toxicity values for all of the required taxa except for a daphnid. The methodology instructs that in the absence of acceptable data to fit a distribution, the chronic criterion is calculated using an acute-to-chronic ratio (ACR) (section 3-4.2, TenBrook et al. 2009a). Additionally, the ACR procedure requires paired acute and chronic data from organisms in at least three different families including a fish, an invertebrate, and at least one other acutely sensitive species (section 3-4.2.1, TenBrook et al. 2009a). Highly rated paired acute and chronic studies were not available for a fish; therefore, a default ACR value was used in its place. The default value is 11.4 as updated in the sediment method for both aquatic and sediment ACR calculations (table 19, Fojut et al., 2014).

Highly rated acute and chronic studies were available for *Chironomus dilutus* to meet the invertebrate requirement. There were several highly rated acute *C. dilutus* values available in the final acute dataset, but the values originated from several different studies performed in different laboratories. Section 3-4.2.1 of the methodology instructs that if there are multiple acute tests that are equally appropriate, then the geometric mean must be used and that the acute test(s) should be part of the same study and use the same dilution water as the chronic test. Therefore, paired acute and chronic values for *C. dilutus* from Phillips 2019 were used to calculate the *C. dilutus* species mean acute-to-chronic ratio (SMACR). An acute geometric mean based on mortality of 4.85 µg/L was calculated using two acute toxicity values, both from Phillips 2019. The final chronic dataset contained two *C. dilutus* MATC values based on mortality with a geometric mean of 1.36 µg/L, both from Phillips 2019. These acute and chronic geometric mean toxicity values were used to calculate the SMACR for *C. dilutus.*

SMACR = acute toxicity value ÷ chronic toxicity value

C. dilutus SMACR = 4.85 µg/L ÷ 1.36 µg/L
= 3.57

The method instructs that if not enough freshwater data are available to fulfill the ACR data requirements, that saltwater species may be used. These studies are included in the acute and chronic supplemental datasets. Drottar tested the toxicity of clothianidin to *Americamysis bahia* in two different studies performed in the same laboratory and reported an acute LC_{50} value of 53 µg/L based on mortality after 96 hours (2000a) and an MATC value of 14 µg/L (2000b) based on reproduction over 39 days. This allowed for calculation of a species mean acute-to-chronic ratio (SMACR) for *A. bahia:*

SMACR = acute toxicity value ÷ chronic toxicity value

A. bahia SMACR = 53 µg/L ÷ 14 µg/L
= 3.8

Final multispecies ACR = geometric mean of *C. dilutus* SMACR, *A. bahia* SMACR, and one default ACR for lack of fish SMACR
Final multispecies ACR = geomean(3.57, 3.8, 11.4)
= 5.37
= 5.4

Because the chronic criterion is calculated based on the acute value, and only an interim acute value is available for clothianidin, the chronic criterion will also be termed an interim value. The interim chronic criterion was calculated using the final multispecies ACR of 5.4 was as follows:

Interim chronic criterion = interim acute value ÷ final multispecies ACR
= 0.6863 µg/L ÷ 5.4
= 0.1271 µg/L

Interim chronic criterion = 0.13 µg/L
= 130 ng/L

Until either all the required chronic data are available for clothianidin to calculate a chronic criterion using a species sensitivity distribution or a final acute value is available (rather than an interim value), a definitive chronic criterion cannot be calculated. The lower and upper estimates of the chronic criterion were also calculated based on the lower and upper estimates of the acute value.

Lower estimate of the chronic criterion = lower estimate acute value ÷ final multispecies ACR
= 0.29167 µg/L ÷ 5.4
= 0.0540 µg/L
= 0.05 µg /L

Upper estimate of the chronic criterion = lowest final acute value ÷ final multispecies ACR

$$= 3.5\ \mu g/L \div 5.4$$
$$= 0.6481\ \mu g/L$$
$$= 0.65\ \mu g/L$$

Water quality effects

1.4 Bioavailability

There were no studies found concerning the bioavailability of clothianidin in the water column that differentiates between tissue type. No studies were found concerning the bioavailability of clothianidin in the water column that differentiates when these compounds are sorbed to solids, sorbed to dissolved solids, or freely dissolved. Until there is more information that discusses the bioavailability of these three phases, it is recommended that compliance is based on the total concentration of clothianidin in water (section 3-5.1, TenBrook et al. 2009a).

1.5 Mixtures

The concentration addition model and the non-additive interaction model are the only predictive mixture models recommended by the methodology (section 3-5.2, TenBrook et al. 2009a), so other models found in the literature will not be considered for compliance. The concentration addition model predicts that the toxicity of a pesticide mixture will behave as directly additive, in other words the mixture toxicity is predicted by directly summing the component concentrations as toxic equivalents. Mixtures eliciting greater-than-additive effects are termed synergistic and those eliciting less-than-additive effects are termed antagonistic when compared to the toxic effect of each individual mixture component in single compound exposures. Clothianidin can occur in the environment with other pesticides of similar or different modes of action. Clothianidin is a nitroguanidine-substituted neonicotinoid insecticide acts as a nervous system disrupter.

Two studies were available that demonstrated clothianidin mixtures adhering to the concentration addition model. Maloney 2018a performed in-situ wetland limnocorral studies for 28 and 56 days with single-pesticide concentrations of imidacloprid, clothianidin, or thiamethoxam as well as binary mixtures (clothianidin-imidacloprid, clothianidin-thiamethoxam, and thiamethoxam-imidacloprid). Environmental populations of aquatic invertebrates were exposed to 0.71 μg/L of clothianidin alone and binary mixtures with 0.36 μg/L clothianidin. This study demonstrated that binary mixtures were not more toxic to these invertebrate mesocosms than single compounds under semi-controlled field settings. This is in contrast to laboratory-based experiments, which have shown greater-than-additive toxicity of binary mixtures of neonicotinoid in single species exposures. At 28 days, the clothianidin-thiamethoxam exposure resulted in an approximately 44% lowered cumulative emergence of in-situ Chrinomidae compared to laboratory-based exposures. At 56 days, effects on cumulative emergence and biomass of Chironomidae were significant for the clothianidin-thiamethoxam mixture but not for the imidacloprid-clothianidin mixture. However, both clothianidin-thiamethoxam and imidacloprid-clothianidin mixtures were shown to display concentration addition effects.

Rico 2018 also demonstrated concentration addition for clothianidin mixtures with other neonicotinoids. This study used outdoor constructed mesocosms inoculated with field-collected macrophytes and invertebrates to assess toxicity to an equimolar mixture of five neonicotinoids with individual nominal concentrations of 0, 0.2, 1, 5, 25, and 250 µg/L. The neonicotinoids were imidacloprid, acetamiprid, thiacloprid, thiamethoxam and clothianidin. Additive toxicity was demonstrated in this single exposure, ten-day, equimolar study.

Two studies were available that demonstrated other toxicity mixture effects of clothianidin on aquatic species. Maloney et al. (2017) studied a mixture of three neonicotinoids with similar modes of action with *Chironomus dilutus*. The mixtures were composed of imidacloprid and clothianidin and/or thiamethoxam in binary or ternary combinations. It was found that all mixture toxicities were best predicted with some form of response-additive synergism. In combination with clothianidin, the model demonstrated dose level dependency. The ternary mixture displayed a standard response-additive model.

A later study by Maloney (2018b) and its corrigendum publication in 2019 exposed *Chironomus dilutus* to mixtures of imidacloprid with neonicotinoids clothianidin and thiamethoxam. Thiamethoxam-clothianidin mixtures adhered to the concentration addition model in this chronic, 28-day laboratory study. It was shown that toxicities of binary mixtures of imidacloprid-clothianidin and imidacloprid-thiamethoxam were dose-ratio dependent with synergism at higher concentrations of clothianidin and thiamethoxam, respectively. However, ternary mixtures of all three neonicotinoids displayed weak antagonism at all concentration ratios and dose levels.

The literature review demonstrates that the toxicities of these neonicotinoid pesticide mixtures are generally predicted by the concentration addition model and should be considered additively. Deviations from this model are possible, indicating that toxicity of neonicotinoid mixtures are nuanced and complex. It is recommended that all neonicotinoid mixtures be considered additively. In order for mixtures to be considered in compliance, the methodology requires that each pesticide considered in an accepted mixture model must have a numeric water quality criterion for calculation of a toxic unit or a relative potency factor for a particular body of water. Water quality criteria exist for imidacloprid and thiamethoxam. It is up to regulators to choose which calculation is most appropriate for any given body of water (Section 3-5.2, TenBrook et al. 2009a).

1.6 Temperature, pH, and other water quality effects

Temperature, pH, and other water quality effects on the toxicity of clothianidin were examined to determine if any effects are described well enough in the literature to incorporate into criteria compliance (section 3-5.3, TenBrook et al. 2009a). There were no highly rated studies available designed explicitly to test the effects of temperature or pH on clothianidin. Rico 2018 indicates that some aquatic invertebrates may be more sensitive to some neonicotinoids under increased temperatures. Additional studies

would need to be available in order to incorporate temperature effects into criteria compliance.
Clothianidin has a large dissociation constant of 11 (Fontaine 2001, MacBean 2010, PPDB 2016), indicating that pH could have an effect on the chemical structure in the range of conditions found in natural freshwater environments.

Comparison of ecotoxicity data to derived criteria

1.7 Sensitive species

The derived criteria were compared to toxicity values for the most sensitive species in both the acceptable (RR) and supplemental (RL, LR, LL) data sets to ensure that these species will be adequately protected (section 3-6.1, TenBrook et al. 2009a).

The lowest acute value in the data sets rated RR, RL, LR, or LL (Tables 3, 4, and 5) was the RR rated 96-hour EC_{50} of 3.5 µg/L based on immobility of the mayfly *Neocloeon triangulifer* (Raby 2018c). The next lowest acute value rated RR, RL, LR, or LL was the 96-hour MATC of 2.65 µg/L based on mortality for the chrionomid *Chironomus dilutus* (Phillips 2017). This toxicity value was supplemental because MATC values are not used not used for acute criterion calculation in the UC Davis Method. The upper estimate of the acute criterion (1.75 µg/L) would be protective of all acutely sensitive species in the data sets.

The chronic animal data set shows that aquatic animals are more sensitive to clothianidin than plants. The interim chronic criterion (0.13 ng/L) was calculated to be protective of animals and is several orders of magnitude lower than the single chronic plant MATC of 10,500 µg/L for *Navicula pelliculosa*. The upper estimate of the chronic criterion (0.65 µg/L) is more than 16,000 times lower than the *N. pelliculosa* value. The upper estimate of the chronic criterion is more than twice as greater than the lowest chronic animal EC_{50} of 0.28 µg/L based on emergence of *Chironomus dilutus*. This value was considered supplemental because EC_{50} values are not used for chronic criterion calculations in the UC Davis Method. However, the lower estimate of the chronic criterion (0.05 µg/L) is an order of magnitude lower than the *C. dilutus* value of 0.28 µg/L. The interim chronic criterion (0.13 µg/L) is a factor of two times greater than the *C. dilutus* value. It is worth noting that this value was obtained from a study with an unusually high percentage of control emergence for *C. dilutus* as compared with other studies from the same lab (Maloney 2017 and 2018) and other laboratories (Raby 2018b and Phillips 2019). These later studies were not able to replicate a chronic toxicity value based on any life cycle endpoint such as emergence in this range, nor has the high control emergence been repeated. This calls into question the reliability of this value. The next lowest value in the chronic animal dataset is also for *C. dilutus* from Cavallaro 2017 at 0.46 µg/L based on sex ratio. This value is nearly four times higher than the interim chronic criterion. The interim chronic criterion (0.13 µg/L) is two times greater than this *C. dilutus* value. Raby 2018b reported the third- and fourth-lowest values for in the dataset with 0.54 µg/L for the number of eggs per egg mass and 0.68 µg/L for percent complete emergence for *C. dilutus*. These values are over four and five times greater than the interim chronic criterion, respectively. The upper estimate of the chronic criterion (0.65 µg/L) is 1.2 times lower and 0.03 µg/L than these Raby 2018b *C. dilutus* values, respspectively. It appears that *C. dilutus* is a particularly sensitive species to clothianidin exposure. Adequate protection will be attained for these sensitive species if water concentrations do not exceed the interim acute and interim chronic criteria values.

1.8 Ecosystem and other studies

The derived criteria are compared to acceptable laboratory, field, or semi-field multispecies studies (rated R or L) to determine if the criteria will be protective of ecosystems (section 3-6.2, TenBrook et al. 2009a).

Six studies describing effects of clothianidin on mesocosm, microcosm and model ecosystems were identified and rated for reliability according to the UCDM (Table 3.9, TenBrook et al. 2009a). Five studies were rated as reliable (R; Cavallaro 2018, Miles 2017, Rico 2018, Robinson 2019, and Maloney 2018) and are described below. One study was rated as less reliable (L; Basley 2018).

Basley 2018 exposed invertebrates to single clothianidin contamination events at levels of 0-15 g/L in constructed outdoor ephemeral ponds for 33-38 days. Plastic buckets were filled with tap water and environmental/uncontaminated soil containing naturally occurring ostracod eggs and left open to be colonized by flying insects. The effects on colonization and abundance were studied. Chironomids and ostracods were negatively affected whereas *Culex* larvae were not. There was not a clear dose response for clothianidin with some taxa appearing in greater abundance at higher clothianidin concentrations than at lower concentrations. Toxicity values for individual species or the community were not reported.

Cavallaro 2018 performed a nine-week *in situ* wetland limnocorral experiment with exposures of 0.0, 0.05, or 0.5µg/L followed by a six-week recovery period. During the dosing period, community structure was not statistically different from controls but rebound effects were observed during the recovery period with changes in the highest treatment, which indicates that clothianidin may cause delayed reproduction effects for some species. Toxicity values for individual species or the community were not reported.

Maloney 2018 also performed an in-situ wetland limnocorral studies for 28 and 56 days with single-pesticide concentrations of imidacloprid, clothianidin, or thiamethoxam as well as binary mixtures. Environmental populations of aquatic invertebrates were exposed to 0.71 µg/L of clothianidin alone and binary mixtures of 0.36 µg/L clothianidin. Total insect emergence and cumulative chironomid emergence and chironomid biomass were assessed. Community composition effects were subtle and nuanced. For example, the mean proportions of Trichoptera and Odonata emergence increased in all treatments but the cumulative abundances of these taxa were not significantly different from controls. Cumulative chironomid emergence and biomass were not significantly different between the pesticide treatments and the controls although there was a significant effect of time, indicating that these pesticides can have extended toxic effects. Clothianidin significantly shifted sex-ratios of chironomids towards female-dominated populations by day 56. Toxicity values for individual species or the community were not reported.

Miles 2017 constructed outdoor mesocosms stocked with two-level trophic populations consisting of herbivores and predators to test the direct effects of predator survival/behavior with indirect effects on herbivore survival and growth. A commercial formulation of clothianidin was used at nominal concentrations of 0, 10, and 50 µg/L. It was noted that the majority of the control water contained trace amounts of the neonicotinoids imidacloprid and thiamethoxam as well as clothianidin. Field-collected and laboratory-reared organisms were used. All predator species experienced increased mortality compared to controls at highest exposure. Overall prey mortality decreased with clothianidin exposure except for one amphibian species. This study indicated that clothianidin can affect community structure through the food chain in systems dominated by invertebrate predators. Toxicity values from the mesocosm tests for individual species and the community were not reported.

Rico 2018 used outdoor constructed mesocosms inoculated with field-collected macrophytes and invertebrates to assess toxicity to an equimolar mixture of five neonicotinoids with individual nominal concentrations of 0, 0.2, 1, 5, 25, 250 µg/L. The neonicotinoids were imidacloprid, acetamiprid, thiacloprid, thiamethoxam and clothianidin. NOEC values for most taxa in the mesocosm were determined to be >250 µg/L, which is at least three orders of magnitude greater than even the upper estimate of the chronic criterion for clothianidin. There was not a uniform dose-response relationship for the entire population.

Robinson 2019 dosed artificial pond mesocosms with 2.5 and 250 µg/L of a commercial formulation of clothianidin to observe effect on amphibian larval development through metamorphosis. No differences were measured between the pesticide and the controls.

The mesocosm data for clothianidin indicate that the interim chronic criterion of 0.13 µg/L would be protective of all trophic levels tested in these studies.

1.9 Threatened and endangered species

The derived criteria are compared to measured toxicity values for threatened and endangered species (TES), as well as to predicted toxicity values for TES, to ensure that they will be protective of these species (section 3-6.3, TenBrook et al. 2009a). Current lists of state and federally listed threatened and endangered plant and animal species in California were obtained from the California Department of Fish and Wildlife (CDFW, formerly the California Department of Fish and Game) website (CDFW 2015). One listed animal species is represented in the dataset with two toxicity values. Five Evolutionarily Significant Units of *Oncorhynchus mykiss* are listed as federally threatened or endangered throughout California. The acute dataset contains one *O. mykiss* study rated as supplemental due to a non-definitive LC50 of >104.2 µg/L (Wilhelmy 1998). This value indicates that the upper estimate of the acute criterion of 1.75 µg/L would be protective of this species.

The USEPA interspecies correlation estimation (Web-ICE v. 3.2.1; Raimondo et al. 2013) software was used to estimate toxicity values for the listed animals or plants represented in the acute data set by members of the same family or genus. Table 11 summarizes the results of the ICE analyses. The estimated toxicity values in Table 11 range from 78.42 µg/L for Apache trout, 113.08 µg/L for Cutthroat trout, 150.55 µg/L for Chinook salmon, 152.02 µg/L for Coho salmon, and 311.73 µg/L for Sockeye salmon.

No plant studies used in the criteria derivation were of state or federal endangered, threatened or rare species. There are no aquatic plants listed as state or federal endangered, threatened or rare species so they could not be considered in this section.

Based on the available data and estimated values for animals, there is no evidence that the derived acute or chronic criteria will be underprotective of threatened and endangered species.

Harmonization with other environmental media

1.10 Bioaccumulation

Bioaccumulation was assessed to ensure that the derived criteria will not lead to unacceptable levels of clothianidin in food items (section 3-7.1, TenBrook et al. 2009a). Clothianidin has a log K_{ow} of 0.73 (Section 3), a K_d of 0.52-4.14 depending on soil type (Lewis 2000), and a molecular weight of 249.7 g/mole, which does not indicate a strong bioaccumulative potential. There are no FDA action levels for clothianidin in food (USFDA 2000), however, the EPA has established pesticide tolerances for residues of clothianidin but not in any aquatic animal species. The only product that is grown in water for which a pesticide toleranace exists is rice at 0.01 ppm or mg/kg (USEPA 2019). Bioconcentration of clothianidin has been measured by only a few researchers (Table 1).

To check that these criteria are protective of humans that may consume aquatic organisms, a bioaccumulation factor (BAF) was used to estimate the water concentration that would roughly equate to a reported tolerance for residues in food of aquatic origin for humans (pesticide tolerance, $_{human}$), in this case for rice. These calculations are further described in section 3-7.1 of the methodology (TenBrook et al. 2009a). The BAF of a given chemical is the product of the BCF and a biomagnification factor (BMF), such that BAF=BCF*BMF. No BMF value was found for clothianidin. A BCF of 1.8 L/kg (Table 1) was used as an example estimation of bioaccumulation in the environment. No BMF value was available in the literature so it was estimated two ways according to the methodology (a value of 1 both when as approximated from log K_{ow} and as approximated from BCF as in section 3-7.1 and Table 3.15 in TenBrook et al. 2009a).

$$NOEC_{water} = \frac{Pesticide\ tolerance_{human}}{BCF_{food\_item} \cdot BMF_{food\_item}}$$

Human:

$$NOEC_{water} = \frac{0.01\ ^{mg}/_{kg}}{1.8^{L}/_{kg}*1} = 0.006\ ^{mg}/_{L} = 6\ ^{\mu g}/_{L}$$

In this example, the interim chronic criterion (0.13 μg/L) is a factor of two below the estimated $NOEC_{water}$ value for humans. The upper estimate of the chronic criterion (0.65 μg/L) is one order of magnitude lower than the $NOEC_{water}$ value for humans. In both cases, the interim chronic criterion and upper estimate are not expected to cause adverse effects due to bioaccumulation.

To check that these criteria are protective of terrestrial wildlife that may consume aquatic organisms, a bioaccumulation factor (BAF) was used to estimate the water concentration that would roughly equate to a reported toxicity value for such terrestrial wildlife ($NOEC_{,\ oral\ predator}$). These calculations are further described in section 3-7.1 of the methodology (TenBrook et al. 2009a). The BAF of a given chemical is the product of the BCF and a biomagnification factor (BMF), such that BAF=BCF*BMF. No BMF value was found for clothianidin. Chronic dietary toxicity values are preferred for this calculation. There were two highly rated studies available for *Anas platyrhynchos* that reported NOEC values. A 21-week dietary exposure study on the reproductive effects on mallard duck (*Anas platyrhynchos*) resulted in a NOEC value of 500 mg/kg (Gallagher 2000). An acute dietary study of *A. platyrhynchos* by Johnson 1998 reported a NOEC of 650 mg/kg after 8 days of exposure. The geometric mean of these NOEC values was 570 mg/kg. A BCF of 1.8 L/kg (Table 1) was used as an example estimation of bioaccumulation in the environment. No BMF value was available in the literature so it was estimated two ways according to the methodology (a value of 1 both when as approximated from log K_{ow} and as approximated from BCF as in section 3-7.1 and Table 3.15 in TenBrook et al. 2009a).

$$NOEC_{water} = \frac{NOEC_{oral\ predator}}{BCF_{food\ item} \cdot BMF_{food\ item}}$$

Mallard:

$$NOEC_{water} = \frac{570\ ^{mg}/_{kg}}{1.8^{L}/_{kg}*1} = 317\ ^{mg}/_{L} = 317{,}000\ ^{\mu g}/_{L}$$

In this example, the interim chronic criterion (0.13 μg/L) and the upper estimate of the chronic criterion (0.65 μg/L) are each six orders of magnitude below the estimated $NOEC_{water}$ value for wildlife and are not expected to cause adverse effects due to bioaccumulation.

1.11 Harmonization with air and sediment criteria

This section addresses how the maximum allowable concentration of clothianidin might impact life in other environmental compartments through partitioning (section 3-7.2, TenBrook et al. 2009a). Clothianidin is not listed as a hazardous air pollutant or toxic air contaminant by the California Air Resources Board (CCR 2016). There are no other federal or state sediment or air quality standards for clothianidin (CARB 2008; CDWR 1995), nor is clothianidin mentioned in the NOAA sediment quality guidelines (NOAA 1999). For biota, the limited data on bioconcentration or biomagnification of clothianidin is addressed in section 15.

Clothianidin criteria summary

1.12 Limitations, assumptions, and uncertainties

The assumptions, limitations and uncertainties involved in criteria generation are available to inform environmental managers of the accuracy and confidence in criteria (section 3-8.0, TenBrook et al. 2009a). Chapter 2 of the methodology (TenBrook et al. 2009a) discusses these points for each section as different procedures were chosen, such as the list of assumptions associated with using an SSD (section 2-3.1.5.1), and reviews them in section 2-7.0. This section summarizes any data limitations that affected the procedure used to determine the final clothianidin criteria.

Overall, there was a lack of highly rated aquatic plant and animal toxicity data for clothianidin. Both the acute and chronic data sets lacked the full complement of five required taxa to fit a distribution for criteria derivation. The acute data set was missing data for warm water fish and Salmonidae. The chronic data set was missing values for Salmonidae, benthic crustacean, insect, and warm water fish. Final acute and chronic criteria could not be calculated due to these limitations in the datasets. Instead, interim criteria were derived using a proprosed procedure that would be an update to the existing UC Davis Method (see Section 1.3 for futher discussion). One limitation of the proposed procedure of using censored data when pesticides have a narrow spectrum of toxicity is that it has not undergone peer review as part of the original UC Davis Method, and may warrant revisions following additional peer review.

The AF procedure was used to calculate an interim acute criterion using the lowest definitive value in the acute dataset and an AF representing toxicity values being available for all five required taxa, even though the toxicity values for two of these taxa are censored values, which would not typically be used. This procedure is proposed because both missing taxa were tested and were so insensitive to clothianidin that definitive toxicity values could not be determined, and concentrations were tested that are well above those found in the environment. The goal in proposing this new procedure and deriving an interim acute criterion was to continue building on the concepts developed in the UC Davis Method for deriving criteria for pesticides when limited toxicity data are available. This procedure is proposed to avoid deriving overly conservative criteria by not using data for taxa that are very insensitive to clothianidin. Because this is a new procedure, lower and upper estimates of acute criteria are also presented based on more and less conservative calculations to provide some range of uncertainty around the interim acute criterion.

ACR calculations were used to determine an interim chronic criterion. The interim chronic criterion was derived with a minimum amount of data according to the methodology (section 3-4.2.3, TenBrook et al. 2009a) using three highly rated SMACRs and one default ACR value. The chronic criterion is also termed an interim value because it is calculated based on an interim acute value, but the procedure for calculing the interim chronic criterion does not otherwise deviate from the UC Davis Method. Plant studies are always considered chronic (Section 3-2.1.1.1, TenBrook et al. 2009a) and therefore could not be used in the ACR calculations because there was no associated acute data. As a result, the interim chronic criterion does not incorporate plant toxicity.

Other limitations include the lack of studies on the effects of water quality on clothianidin toxicity, such as pH and temperature. There was a derth of sediment, bioavailability, and wildlife studies. There were no sediment or bioavailability studies available although clothianidin has a moderately high solubility and therefore retention on sediment surfaces is not expected to be significant. Additional high-quality mallard duck studies could be useful although the demonstrated lack of definitive toxicity values indicates that this species is not sensitive to clothianidin.

1.13 Comparison to national standard methods

This section is provided as a comparison between the UC-Davis methodology for criteria calculation (TenBrook et al. 2009a) and the current USEPA (1985) national standard. The following example clothianidin criteria were generated using the USEPA (1985) methodology with the data set generated in this clothianidin criteria report.

The acute dataset is missing three of the five taxa requirements of the UC-Davis methodolgy. The UC-Davis methodology does not utilize non-definitive values (> or < values), however the USEPA method allows for these values (section IV.E.5., USEPA 1985). The first missing taxa is for a planktonic crustacean, of which one must be in the family Daphniidae in the genus *Ceriodaphnia*, *Daphnia*, or *Simocephalus*. However, this requirement could be met with with the supplemental value of >100,000 µg/L for *Ceriodaphnia dubia* in the Daphnidae family. The second missing taxa requirement is for a salmonidae and the supplemental value for *Oncorhynchus mykiss* of >104,200 µg/L can be used for this requirement. The third missing taxa requirement is for a warm water fish. The supplemental value of >117,000 µg/L for *Lepomis macrochirus* meets this taxa requirement.

The USEPA acute methods have three additional taxa requirements beyond the five required by the SSD procedure of the UC-Davis methodology (section 3-3.1, TenBrook et al. 2009a). They are:

1. A third family in the phylum Chordata (e.g., fish, amphibian);
2. A family in a phylum other than Arthropoda or Chordata (e.g., Rotifera, Annelida, Mollusca);
3. A family in any order of insect or any phylum not already represented.

The first additional requirement could not be met with RR rated or supplemental data because the USEPA method requires freshwater species only. The second additional requirement could be met by *Lumbriculus variegatus* in the Annelida phylum. *Trichocorixa* in the Corixidae family could satisfy the third additional requirement. However, it is reasonable to calculate an interim USEPA criterion for clothianidin, despite the lack data for a third freshwater family in the phylum Chordata because there are other more sensitive species in the dataset that will ensure protection of species that are most sensitive to this pesticide. The California Department of Fish and Game has derived criteria using the USEPA (1985) SSD method with fewer than the eight required families, using professional judgment to determine that species in the missing categories were relatively insensitive and their addition would not lower the criteria (Menconi & Beckman 1996; Siepmann & Jones 1998).

The acute dataset contains 18 values, including a species mean acute value from five *Chironomus dilutus* values. The USEPA method utilizes genus mean acute values so a geometric mean was calculated for these five *C. dilutus* values as well as one *C. riparius* value. Therefore, 18 acute values were combined with the three supplemental values above as well as a supplemental *Daphnia magna* value for a total of 22 values to calculate a USEPA acute criterion. The values were ranked, and a Final Acute Value was determined using the four lowest values. Because the lowest number of significant figures reported in the toxicity dataset used to calculate the criterion was one, the criterion is rounded to one significant figure. For clothianidin the Final Acute Value (estimate of the 5th percentile) was determined to be 4 µg/L according to USEPA 1985 caclulation, and the Final Acute Criterion is 2 µg/L. This Final Acute Criterion is an order of magnitude greater than the UC Davis methodology interim acute criterion of 0.34 µg/L and very similar to the acute reference value of 1.75 µg/L. Details of the calculations can be found in Appendix B.

USEPA Final Acute Value = 4 µg/L (see Appendix B)

USEPA Final Acute Criterion = Final Acute Value ÷ 2

= 4 µg/L ÷ 2

= 2 µg/L

According to the USEPA (1985) methodology, the chronic criterion is equal to the lowest of the Final Chronic Value, the Final Plant Value, and the Final Residue Value.

To calculate the Final Chronic Value, animal data are used and the same taxa requirements must be met as in the calculation of the acute criterion (section III B USEPA 1985). Only two of the eight taxa requirements are available in the RR chronic animal data set with *Chironomus riparius*, and *Daphnia magna* (Table 7). The missing taxa are as follows:

1. A warm water fish
2. A Salmonidae
3. A benthic crustacean
4. An insect
5. A third family in the phylum Chordata (e.g., fish, amphibian)
6. A family in a phylum other than Arthropoda or Chordata (e.g., Rotifera, Annelida, Mollusca)

The California Department of Fish and Wildlife has derived criteria using the USEPA (1985) SSD method with fewer than the eight required families, using professional judgment to determine that species in the missing categories were relatively insensitive and their addition would not lower the criteria (Menconi & Beckman 1996; Siepmann & Jones 1998). However, in this case, there are too many missing taxa values to derive a Final Chronic Value in this way.

The Final Plant Value is calculated as the lowest result from a 96-hour test conducted with an important plant species in which the concentrations of test material were measured and the endpoint was biologically important. The final chronic plant dataset for clothianidin does not contain a value from a 96-hour test (Table 6). The lowest value is from a 72-hour microalgae test of *Raphidocelis subcaptitata* with an NOEC of 7,300 g/L to serve as the chronic criterion. Therefore, a Final Plant Value cannot be derived for clothianidin.

The Final Residue Value is calculated by dividing the maximum permissible tissue concentration by an appropriate bioconcentration or bioaccumulation factor. A maximum allowable tissue concentration is either (a) a FDA action level for fish oil or for the edible portion of fish or shellfish, or (b) a maximum acceptable dietary intake based on observations on survival, growth, or reproduction in a chronic wildlife feeding study or long-term wildlife field study. There are no FDA action levels for clothianidin in food (USFDA 2000), however, the EPA has established pesticide tolerances for residues of clothianidin but not in any aquatic animal species. The only product that is grown in water for which a pesticide toleranace exists is rice at 0.01 ppm or mg/kg (USEPA 2019). There were two highly rated studies that report NOEC values available for wildlife that result in a geometric mean of 570 mg/kg. A BCF of 1.8 (Table 1) was used to calculate the Final Residue Value.

$$
\begin{aligned}
\text{Final Residue Value}_{\text{human}} &= \text{maximum acceptable dietary intake} \div \text{BCF}\\
&= 0.01\ \text{mg/kg} \div 1.8\ \text{L/kg}\\
&= 0.006\ \text{mg/L}\\
&= 6\ \mu\text{g/L}
\end{aligned}
$$

$$
\begin{aligned}
\text{Final Residue Value}_{\text{wildlife}} &= \text{maximum acceptable dietary intake} \div \text{BCF}\\
&= 570\ \text{mg/kg} \div 1.8\ \text{L/kg}\\
&= 317\ \text{mg/L}\\
&= 317{,}000\ \mu\text{g/L}
\end{aligned}
$$

A Final Chronic Value cannot be calculated. A Final Plant Value cannot be calculated. The Final Residue Value for humans is the lowest value and therefore the chronic criterion by the USEPA (1985) methodology for clothianidin would be 6 g/L. The example chronic criterion is two orders of magnitude higher than the interim chronic criterion recommended by the UC-Davis methodology.

1.14 Environmental Monitoring Data

A review of the available data from the Surface Water Database (SURF 2019) indicates that clothianidin has been detected in some freshwater systems within the Central Coast Regional Water Quality Control Board (CCRWQCB) jurisdiction. Its geographic area encompasses some or all of nine counties. The data for the following counties was included in the SURF data anaylsis for this report because they fully reside within this waterboard's jurisdiction: Santa Cruz, San Benito, Monterey, San Luis Obispo, and Santa Barbara. Data was available for 2014-2018.

Clothianidin concentrations were detected in 20 of 105 reported samples between 2014-2018. The values ranged from 0.0382 to 1.35 parts per billion (ppb, equivalent to µg/L) in Monterey and San Luis Obispo Counties, respectively. Two Santa Barbara County detections ranged from 0.0395-0.462 ppb. Eight detections were greater than the interim acute criterion of 0.34 µg/L, ranging from 0.008 to 1.01 µg/L greater. There were zero detections greater than the upper estimate of the interim acute criterion of 1.75 µg/L and there were seven detections lower than the lower estimate of the interim acute criterion (by 0.05 to 0.14 µg/L). There were thirteen detections greater than the interim chronic criterion of 0.13 µg/L, raning from 0.043 to 1.22 µg/L greater. Three detections were greater than the upper estimate of the interim chronic criterion and three that were lower than the lower estimate of the interim chronti criterion, by 0.534 to 0.7 µg/L and by 0.0038 to 0.0118 µg/L, respectively. Average detection concentations by county are Monterey: 0.32, San Luis Obispo: 1.3, Santa Barbara: 0.043 ppb. Santa Cruz and San Benito reported no detections.

The reported method detection limits (MDL) for these clothianidin have varied over time from 0.001 to 0.01 ppb, which have always been below both the acute and chronic criteria.

1.15 Final criteria statement

Interim criteria for clothianidin:

- Interim acute 0.34 µg/L
- Interim chronic 0.13 µg/L

Aquatic life in the watersheds of the CCRWQCB should not be affected unacceptably if the four-day average concentration of clothianidin does not exceed 0.13 µg/L more than once every three years on the average and if the one-hour average concentration does not exceed 0.34 µg/L more than once every three years on the average.

Application:

Although the intention of this report is to report clothianidin water quality criteria to be protective of aquatic life in the watersheds of the CCRWQCB, these interim criteria would be appropriate for any freshwater ecosystem in North America, unless species more sensitive than the species examined in the development of these criteria are likely to occur in those ecosystems.

Comparisons to other aquatic criteria:

There are no established water quality criteria for clothianidin with which to compare the criteria derived in this report. However, the interim acute criterion in this report can be compared to the acute criterion derived according to the USEPA (1985) method. The USEPA acute criterion of 2 ug/L is greater than the interim acute criterion by a factor of six.

The USEPA has several aquatic life benchmarks established for clothianidin, shown in Table 12, to which the derived criteria in this report can be compared with caution (USEPA 2016). According to the USEPA (2016), aquatic life benchmarks are not calculated following the same methodology used to calculate water quality criteria. Water quality criteria can be used to set water quality standards under the Clean Water Act, but aquatic life benchmarks may not be used for this purpose (USEPA 2016).

The derived interim acute criterion (0.34 µg/L) is below the acute fish benchmark by five orders of magnitude and is below the acute invertebrate benchmark by a factor of 32 (Table 12). The upper estimate of the acute criterion was calculated using the same procedure as acute benchmarks, and the upper estimate (1.75 µg/L) is below the acute fish benchmark by four orders of magnitude and is below the acute invertebrate benchmark by one order of magnitude (Table 12). The interim chronic criterion of this report (0.13 µg/L) is well below the chronic benchmarks for fish and acute nonvascular plants (both by at least five orders of magnitude). The interim chronic criterion of this report (0.13 µg/L) is greater the chronic invertebrate benchmark of 0.05 µg/L. The chronic invertebrate benchmark is equal to the lower estimate of the chronic criterion.

Acknowledgements

Special thanks to Water Board staff for valuable input, editing assistance, and the opportunity to research the effect of clothianidin on the aquatic environment: Peter Meertens, Mary Hamilton, Daniel McClure, and Tessa Fojut, Ph.D.

References

Ahmed, M.A.I. and Matsumura, F., 2014. Synergistic actions of formamidine insecticides on the activity of pyrethroids and neonicotinoids against Aedes aegypti (Diptera: Culicidae). Journal of medical entomology, 49(6), pp.1405-1410.

Babezinski, P., Bornatsch, W. 2000. Photolysis of (nitroimino-carbon 14)TI-435 and (thiozolyl-2-carbon 14) TI-435 in sterile aqueous buffer solution. Bayer AG. Laboratory project number: M 112 0884-4: M 112 0962-1: 110261. USEPA 45422318.

Banman, C.S., Howerton, J.H., Lam, C.V. 2012a. Toxicity of clothianidin to the blue-green algae Anabena flos-aquae. Bayer CropScience Ecotoxicology, Stilwell, Kansas. Laboratory project ID EBTIP057. Submitted to Bayer CropScience, Research Park Triangle, North Carolina. USEPA 48720601.

Banman, C.S., Howerton, J.H., Lam, C.V. 2012b. Toxicity of clothianidin technical to the freshwater diatom Navicula pelliculosa. Bayer CropScience Ecotoxicology, Stilwell, Kansas. Laboratory project ID EBTIP059. Submitted to Bayer CropScience, Research Park Triangle, North Carolina. USEPA 48720602.

Banman, C.S., Howerton, J.H., Lam, C.V. 2012c. Toxicity of clothianidin to the saltwater diatom Skeletonema costatum. Bayer CropScience, Stilwell, Kansas. Laboratory project ID EBTIP058. Submitted to Bayer CropScience, Research Triangle Park, North Carolina. USEPA 48720603.

Barbee, G.C. and Stout, M.J., 2009. Comparative acute toxicity of neonicotinoid and pyrethroid insecticides to non-target crayfish (Procambarus clarkii) associated with rice–crayfish crop rotations. Pest Management Science: formerly Pesticide Science, 65(11), pp.1250-1256.

Bartlett, A.J., Hedges, A.M., Intini, K.D., Brown, L.R., Maisonneuve, F.J., Robinson, S.A., Gillis, P.L. and de Solla, S.R., 2018. Lethal and sublethal toxicity of neonicotinoid and butenolide insecticides to the mayfly, Hexagenia spp. Environmental Pollution, 238, pp.63-75.

Bartlett, A.J., Hedges, A.M., Intini, K.D., Brown, L.R., Maisonneuve, F.J., Robinson, S.A., Gillis, P.L. and de Solla, S.R., 2019. Acute and chronic toxicity of neonicotinoid and butenolide insecticides to the freshwater amphipod, Hyalella azteca. Ecotoxicology and environmental safety, 175, pp.215-223.

Basley, K. and Goulson, D. 2018. Neonicotinoids thiamethoxam and clothianidin adversely affect the colonisation of invertebrate populations in aquatic microcosms. Environmental Science and Pollution Research, 25(10), pp.9593-9599.

CARB. 2008. California Ambient Air Quality Standards (CAAQS). California Air Resources Board, Sacramento, CA.
URL < https://www.arb.ca.gov/research/aaqs/caaqs/caaqs.htm>

Cavallaro, M.C., Morrissey, C.A., Headley, J.V., Peru, K.M. and Liber, K., 2017. Comparative chronic toxicity of imidacloprid, clothianidin, and thiamethoxam to Chironomus dilutus and estimation of toxic equivalency factors. Environmental toxicology and chemistry, 36(2), pp.372-382. USEPA 50344701.

CCR. 2016. California Code of Regulation, Title 17, § 93001. Hazardous Air Pollutants Identified as Toxic Air Contaminants. URL < http://www.arb.ca.gov/toxics/id/taclist.htm>

CDFW (2015) State and federally listed threatened and endangered plant and animal species in California. URL <http://www.dfg.ca.gov/wildlife/nongame/t_e_spp/ >

CDWR. 1995. Compilation of Sediment and Soil Standards, Criteria, and Guidelines. California Department of Water Resources, State of California, The Resources Agency, Sacramento, CA. URL < https://water.ca.gov/LegacyFiles/pubs/waterquality/municipal_wq_investigations/mwqi_technical_documents/compilation_of_soil_and_sediment_standards_criteria_and_guidelines/compilation_of_soil_and_sediment_standards_criteria_and_guidelines._february_1995.pdf>

Dorgerloh, M. 2000a. TI 435 – thiazolylmethylguanidine – acute toxicity (96 h) to rainbow trout (Oncorhynchus mykiss) in a static test (limit test). Bayer AG Crop Protection – Development, Leverkusen-Bayerswerk, Germany. Report number 110020. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422408.

Dorgerloh, M., Sommer, H. 2000b. N-methylnitroguanidine – acute toxicity (96 hours) to rainbow trout (Oncorhynchus mykiss) in a static test (limit test). Bayer AG Crop Protection-Development, Leverkusen, Germany. Report number 110063. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422409.

Dorgerloh, M. 2000c. TI 435 – thiazolylnitroguanidine – acute toxicity (96 h) to rainbow trout (Oncorhynchus mykiss) in a static test (limit test). Bayer AG Crop Protection – Development, Leverkusen-Bayerswerk, Germany. Report number 110019. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422410.

Dorgerloh, M. 2000d. TI-435-Thiazolylmethylguanidine-influence on the growth of the green alga, Selanastrum capricornatum. Bayer AG Crop Protection-Development, Leverkusen-Bayerwerk, Germany. Report number 110169. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422505.

Dorgerloh, M. 2000e. N-methylnitroguanidine-Influence on the growth of green alga, Selanastrum capricornatum. Bayer AG Crop Protection-Development, Leverkusen-Bayerwerk, Germany. Report number 110281. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422506.

Dorgerloh, M. 2000f. TI-435-thiazolylnitroguanidine-influence on the growth of the green alga, Selanastrum capricornatum. Bayer AG Crop Protection-Development, Leverkusen-Bayerwerk, Germany. Report number 110168. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422507.

Dorn, R., Hein, W. 2000a. Adsorption/desorption of ^{14}C-MNG, a degradate of TI-435, on five different soils. Staatliche Lehr-Und Forschungsandstalt fur Landwirtschaft, Germany. Report number 110256. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422313.

Dorn, R., Hein, W. 2000b. Adsorption/desorption of ^{14}C-TZMU, a degradate of TI-435, on five different soils. Staatliche Lehr-und Forschungsanstalt fur Landwirtschaft, Germany. Report number 110257. Submitted to Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422315.

Dorn, R., Hein, W. 2000c. Adsorption/desorption of ^{14}C-TMG, a degradate of TI-435, on five different soils. Staatliche Lehr-und Forschungsanstalt fur Landwirtschaft, Germany. Report number 110258. Submitted to Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422316.

Drottar, K.H., MacGregor, J.A., Krueger, H.O. 2000a. TI-435 technical: a 96-hour flow-through acute toxicity test with the saltwater myside (Mysidopsis bahia). Wildlife International, Ltd., Easton, Maryland. Report number 110058. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA MRID 45422403.

Drottar, K.H., MacGregor, J.A., Krueger, H.O. 2000b. TI-435 technical: a flow-through life-cycle toxicity test with the saltwater (Mysidopsis bahia). Wildlife International, Ltd., Easton, Maryland. Report number 110167. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA MRID 45422405.

Drottar, K.R., Krueger, H.O. 2000c. TI-435 technical: an early life-stage toxicity test with the fathead minnow (Pimephales promelas). Wildlife International, Ltd., Easton, Maryland. Report number 110163. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422413.

Fojut, T.L., Vasquez, M., Trunnelle, K.J., Tjeerdema, R.S. 2014. Draft UCD Report: Methodology for Derivation of Pesticide Sediment Quality Criteria for the Protection of Aquatic Life - Phase II: Methodology and Derivation of Bifenthrin Interim Criteria , Report prepared by the University of California Davis for the Central Valley Regional Water Quality Control Board. URL: <http://www.swrcb.ca.gov/rwqcb5/water_issues/tmdl/central_valley_projects/central_valley_pesticides/sediment_quality_criteria_method_development/index.shtml>

Fontaine, L.D. 2001. Product chemistry of clothianidin technical. Bayer Corporation, Kansas City, Missouri. CDPR 202797. USEPA 45422301.

Gallagher, S.P., Casey, C.S., Beavers, J.B., Jaber, M.J., Kendall, T.Z. 2000. TI-435 technical a reproduction study with the mallard (Anas platyrhynchos). Wildlife International, Ltd., Easton, Maryland. Report number 110053. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422422.

Gilges, M. 2000. Aerobic degradation and metabolism of TI-435 in four soils. Bayer AG, Leverkusen, Germany. Report number 109869. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422325.

Greenland, R.G. 2010. Clothianidin: aquatic field dissipation. Stewart Agricultural Research Services, Inc., Clarence, Missouri. Study number SARS-09-93. Submitted to Valent U.S.A. Corporation. CADPR 261648.

Greenland, R.G. 2011. Clothianidin: aquatic field dissipation. Stewart Agricultural Research Services, Inc., Clarence, Missouri. Study number SARS-08-92. Submitted to Valent U.S.A. Corporation. CADPR 261646.

Heimbach, F. 1998. Influence of TMG (tech.) on development and emergence of larvae of Chironomus riparius in a water-sediment system. Bayer AG Crop Protection-Development, Leverkusen-Bayerwerk, Germany. Report number 110179. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422510.

Hellpointer, E. 1999. Determination of the quantum yield and assessment of the environmental half-life of the direct photodegradation of TI-435 in water. Bayer AG. Laboratory Project Number: M 1430953-5: 110126: MR-360/99. USEPA 45422322.

Hendel, B. 2000a. Acute toxicity of TI 435-Thiazolylmethlguanidine (techn.) to water fleas (Daphnia magna). Bayer AG Crop Protection, Leverkusen, Germany. Report number 110021. USEPA MRID 45422339.

Hendel, B. 2000b. Acute toxicity of TI 435-Thiazolylmethlguanidine (techn.) to water fleas (Daphnia magna). Bayer AG Crop Protection, Leverkusen, Germany. Report number HDB/Dm 232. USEPA MRID 45422340.

Hendel, B. 2000c. Acute toxicity of TI 435-Thiazolylnitroguanidine (techn.) to water fleas (Daphnia magna). Bayer AG Crop Protection, Leverkusen, Germany. Report number 110022. USEPA MRID 45422401.

Johnson, A.J. 1998. TI-435 technical dietary LC50 to the mallard duck. Huntingdon Life Sciences Ltd., Huntingdon, Cambridgeshire, England. Report number 110051. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422420.

Lewis, C. 2000. (Carbon 14)TI-435: Adsorption/Desorption in Soil. Covance Laboratories, Ltd., North Yorkshire, England. Report number 110254. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422311.

Macaulay, S.J., Hageman, K.J., Alumbaugh, R.E., Lyons, S.M., Piggott, J.J. and Matthaei, C.D., 2019. Chronic Toxicities of Neonicotinoids to Nymphs of the Common New Zealand Mayfly Deleatidium spp. Environmental toxicology and chemistry.

MacBean C., ed; e-Pesticide Manual. 15th ed., ver. 5.1, Alton, UK: British Crop Protection Council. Clothianidin (210880-92-5) (2008-2010)

Maloney, E.M., Morrissey, C.A., Headley, J.V., Peru, K.M. and Liber, K., 2017. Cumulative toxicity of neonicotinoid insecticide mixtures to Chironomus dilutus under acute exposure scenarios. Environmental toxicology and chemistry, 36(11), pp.3091-3101.

Maloney, E.M., Liber, K., Headley, J.V., Peru, K.M. and Morrissey, C.A., 2018a. Neonicotinoid insecticide mixtures: Evaluation of laboratory-based toxicity predictions under semi-controlled field conditions. Environmental Pollution, 243, pp.1727-1739.

Maloney, E.M., Morrissey, C.A., Headley, J.V., Peru, K.M. and Liber, K., 2018b. Can chronic exposure to imidacloprid, clothianidin, and thiamethoxam mixtures exert greater than additive toxicity in Chironomus dilutus?. Ecotoxicology and environmental safety, 156, pp.354-365.

Maloney, E.M., Morrissey, C.A., Headley, J.V., Peru, K.M. and Liber, K., 2019. Corrigendum to" Can chronic exposure to imidacloprid, clothianidin, and thiamethoxam mixtures exert greater than additive toxicity in Chironomus dilutus?"[Ecotoxicol. Environ. Saf. 156C (2018) 354-365]. Ecotoxicology and environmental safety, 182, pp.109437-109437.

Mattock, S.D. 2001. TI-435: comparative acute toxicity of Chironomus riparius with TZMU, MU, TZNG, and MNG. Covance Laboratories Ltd., North Yorkshire,

England. Report number 110171. Submitted to Takeda Chemical Industries Ltd, Tokyo, Japan. USEPA 45422414
Mondel, M., Hein, W. 2000. Adsorption/desorption of ^{14}C-TZNG, a degradate of TI-435, on five different soils. Staatliche Lehr-und Forschungsanstalt fur Landwirtschaft, Germany. Report number 110255. Submitted to Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422314.
Morrissey, M.A., Kramer, H.T. 2000. Determination of dissociation constant and physical-chemical properties of TI-435 pure active ingredient (PAI) (density, solubility, octanol/water partition coefficient, and dissociation constant). Covance Laboratories, Inc., Madison, Wisconsin. Laboratory project identification: Covance 6155-122. Submitted to Takeda Chemical Industries, Ltd., Tokyo, Japan. CDPR 202795.
NOAA. 1999. Sediment Quality Guidelines Developed for the National Status and Trends Program. National Oceanographic and Atmospheric Agency Office of Response and Restoration, Department of Commerce. URL< http://www.coastalscience.noaa.gov/publications/handler.aspx?key=1527>
Noack, M., Geffke, T. 1998. TI 435 technical: Daphnia magna reproduction test (21 d). Dr. U. Noack Laboratory for Applied Biology, Sarstedt, Germany. Report number 110018. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422412.
Palmer, S.J., MacGregor, J.A., Krueger, H.O. 2000a. TI-435 technical: a 48-hour static acute toxicity test with the cladoceran (Daphnia magna). Wildlife International, Ltd., Easton, Maryland. Project number 149A-122. Bayer report number 11004. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA MRID 45422338.
Palmer, S.J., MacGregor, J., Krueger, H.O. 2000b. TI-435 technical: a 96-hour static acute toxicity test with the bluegill (Lepomis macrochirus). Wildlife International, Ltd., Easton, Maryland. Report number 110003. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422407.
Palmer S.J., MacGregor, J.A., Kreuger, H.O. 2000c. TI-435 technical: a 14-day static-renewal toxicity test with duckweed (Lemna gibba G3). Wildlife International, Ltd., Easton, Maryland. Report number 110005. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422503.
Phillips, B.M., Voorhees, J.P., Siegler, K. 2019. UC Davis neonicotinoid threshold assessment draft final report-clothianidin and thiamethoxam. Department of Environmental Toxicology-Marine Pollution Studies Laboratory, University of California, Davis. Unpublished report.
PPDB, The Pesticide Properties DataBase (2016), Agriculture & Environment Research Unit (AERU), University of Hertfordshire, 2006-2016. URL <https://sitem.herts.ac.uk/aeru/ppdb/en/Reports/171.htm> Accessed February 2020
Prosser, R.S., De Solla, S.R., Holman, E.A.M., Osborne, R., Robinson, S.A., Bartlett, A.J., Maisonneuve, F.J. and Gillis, P.L., 2016. Sensitivity of the early-life stages of freshwater mollusks to neonicotinoid and butenolide insecticides. Environmental pollution, 218, pp.428-435.

Raby, M., Zhao, X., Hao, C., Poirier, D.G. and Sibley, P.K., 2018a. Relative chronic sensitivity of neonicotinoid insecticides to Ceriodaphnia dubia and Daphnia magna. Ecotoxicology and environmental safety, 163, pp.238-244.

Raby, M., Zhao, X., Hao, C., Poirier, D.G. and Sibley, P.K., 2018b. Chronic toxicity of 6 neonicotinoid insecticides to Chironomus dilutus and Neocloeon triangulifer. Environmental toxicology and chemistry.

Raby, M., Nowierski, M., Perlov, D., Zhao, X., Hao, C., Poirier, D.G. and Sibley, P.K., 2018c. Acute toxicity of 6 neonicotinoid insecticides to freshwater invertebrates. Environmental toxicology and chemistry, 37(5), pp.1430-1445.

Reddemann, J. 2000. Anaerobic aquatic metabolism for the active ingredient TI-435. Bayer AG, Leverkusen, Germany. Report number 110253. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422330.

Ripperger, R.J. 2006. [Thiazolyl-2-^{14}C]-clothianidin: aerobic aquatic metabolism. Bayer CropScience, Stilwell, Kansas. Report number METIX052. Submitted to Sumitomo Chemical Takeda Agro Company, Ltd., Tokyo, Japan. USEPA 46826903.

Salerno, J., Bennett, C.J., Holman, E., Gillis, P.L., Sibley, P.K. and Prosser, R.S., 2018. Sensitivity of multiple life stages of 2 freshwater mussel species (Unionidae) to various pesticides detected in Ontario (Canada) surface waters. Environmental toxicology and chemistry, 37(11), pp.2871-2880.

Schad, T. 2000a. Calculation of half-lives of TI-435 and its main metabolites generated by photolysis in sterile aqueous buffer solution. Bayer AG. Laboratory project number: P668 00 6756: 110124: MR-121/00. USEPA 45422320.

Schad, T. 2000b. Aerobic degradation and metabolism of TI-435 in six soils. Bayer AG, Leverkusen, Germany. Report number 110252. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422326.

Scheerbaum D. 1999a. TI-435 technical: oyster, acute toxicity test (shell deposition), limit test, flow-through, 96 h. Dr. U. Noack Laboratory for Applied Biology, Sarstedt, Germany. Report number 110174. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA MRID 45422404.

Scheerbaum, D. 1999b. TI-435 technical: fish (sheepshead minnow) acute toxicity, limit test, 96h, semi-static. Dr. U. Noack Laboratory for Applied Biology, Sarstedt, Germany. Report number 110173. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422411.

Scheerbaum, D. 1999c. TI-435 technical aquatic plant toxicity test using Lemna gibba. Dr. U. Noack Labratorium, D31157 Sarstedt, Germany. Project number 980902TU. Submitted to Takeda Chemical Industries, Ltd., Tokyo, Japan. USEPA 49281301.

Stupp, H. 2001. Time Dependent Sorption of TI-435 in Two Different Soils. Bayer AG, Leverkusen, Germany. Report number 110121. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422312.

Sutherland, C.A., MacGregor, J.A., Kreuger, H.O. 2000. TI-435 technical: a 5-day toxicity test with the freshwater alga (Selenastrum capricornatum). Wildlife International, Ltd., Easton, Maryland. Report number 110164. Submitted to Takeda Chemical Industries, Ltd., Tokyo, Japan. USEPA 45422504.

SURF, Surface Water Database. 2019. California Department of Pesticide Regulation. URL < https://www.cdpr.ca.gov/docs/emon/surfwtr/surfdata.htm>

TenBrook, P.L., Tjeerdema, R.S. 2006. Methodology for derivation of pesticide water quality criteria for the protection of aquatic life in the Sacramento and San Joaquin River Basins. Phase I: Review of existing methodologies. Report prepared for the Central Valley Regional Water Quality Control Board, Rancho Cordova, CA

TenBrook, P.L., Palumbo, A.J., Fojut, T.L., Tjeerdema, R.S., Hann, P., Karkoski, J. 2009a. Methodology for Derivation of Pesticide Water Quality Criteria for the Protection of Aquatic Life in the Sacramento and San Joaquin River Basins. Phase II: Methodology Development and Derivation of Chlorpyrifos Criteria. Report prepared for the Central Valley Regional Water Quality Control Board, Rancho Cordova, CA.

TenBrook, P.L., Tjeerdema, R.S., Hann, P., Karkoski, J. 2009b. Methods for Deriving Pesticide Aquatic Life Criteria. Reviews of Environmental Contamination and Toxicology, 199, 19-109.

TenBrook, P.L., Palumbo, A.J., Fojut, T.L., Hann, P., Karkoski, J., Tjeerdema, R.S. 2010. The University of California-Davis methodology for deriving aquatic life pesticide water quality criteria. Rev Environ Contamin Toxicol 209:1-155

USEPA. 1985. Guidelines for deriving numerical national water quality criteria for the protection of aquatic organisms and their uses, PB-85-227049. United States 37 Environmental Protection Agency, National Technical Information Service, Springfield, VA. URL <https://www.epa.gov/sites/production/files/2016-02/documents/guidelines-water-quality-criteria.pdf>

USEPA. 2012. Index to Pesticide Chemical Names, Part 180 Tolerance Information, and Food and Feed Commodities (by Commodity). United States Environmental Protection Agency, Office of Pesticide Programs, Washington, DC, USA. URL < https://www.epa.gov/sites/production/files/2015-01/documents/tolerances-commodity.pdf>

USEPA 2013. Web-Based Interspecies Correlation Estimation for Acute Toxicity, v3.3. United States Environmental Protection Agency, Washingtong, DC, USA. URL <https://www3.epa.gov/ceampubl/fchain/webice/index.html>

USEPA. 2015. Estimation Programs Interface Suite™ for Microsoft® Windows, v 4.11. United States Environmental Protection Agency, Washington, DC, USA.

USEPA. 2016. Aquatic Life Benchmarks for Pesticide Registration. URL <http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/aquatic-life-benchmarks-pesticide-registration>

USEPA. 2017. Preliminary Aquatic and Non-Pollinatory Terrestrial Risk Assessment to Support the Registration Review of Clothianidin. URL <https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/aquatic-life-benchmarks-and-ecological-risk and https://www.regulations.gov/document?D=EPA-HQ-OPP-2011-0865-0242 >

USEPA. 2018. ECOTOX User Guide: ECOTOXicology Knowledgebase System. Version 5.0. URL <http:/www.epa.gov/ecotox/> Accessed July 2019.

USEPA. 2019. Clothianidin, Pesticide Tolerance. Federal Register, Docket # [EPA-HQ-OPP-2008-0771; FRL-10000-64] URL <

https://www.federalregister.gov/documents/2019/11/25/2019-25535/clothianidin-pesticide-tolerances or https://www.govinfo.gov/content/pkg/FR-2019-11-25/pdf/2019-25535.pdf >

USEPA. 2020. Proposed Interim Registration Review Decision (PID) for clothianidin and thiamethoxam. EPA Documents: EPA-HQ-OPP-2011-0865 and EPA-HQ-OPP-2011-0581 URL <https://www.epa.gov/sites/production/files/2020-01/documents/clothianidin_and_thiamethoxam_pid_final_1.pdf>

USFDA. 2000. Guidance for Industry: Action Levels for Poisonous or Deleterious Substances in Human Food and Animal Feed. URL https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-action-levels-poisonous-or-deleterious-substances-human-food-and-animal-feed

Whilhelmy, H., Geffke, T. 1998. TI-435 technical: fish (rainbow trout), acute toxicity test, 96 h, limit test. D. U. Noack Laboratory for Applied Biology, Sarstedt, Germany. Report number 110283. Submitted to Bayer Corporation Agriculture Division, Stilwell, Kansas. USEPA 45422406.

Yokoyama, A., Ohtsu, K., Iwafune, T., Nagai, T., Ishihara, S., Kobara, Y., Horio, T. and Endo, S., 2009. A useful new insecticide bioassay using first-instar larvae of a net-spinning caddisfly, Cheumatopsyche brevilineata (Iwata, 1927) (Trichoptera: Hydropsychidae). Journal of Pesticide Science, pp.0811140065-0811140065.