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CHEMINOVA'S COMMENTS ON EPA'S DIMETHOATE EFFECTS DETERMINATION FOR THE CALIFORNIA RED-LEGGED FROG

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This document is a response to EPA's Dimethoate Effects Determination for the California Red-legged Frog. As such, it is not required to comply with 40CFR Part 160.

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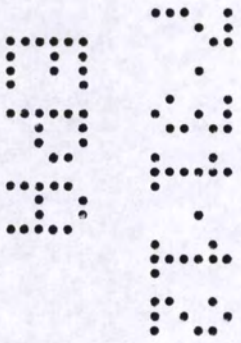

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CHEMINOVA'S COMMENTS OF EPA'S DIMETHOATE EFFECTS DETERMINATION FOR CALIFORNIA RED-LEGGED FROG

1.0 INTRODUCTION

The California red-legged frog (CRLF; *Rana draytonii*, formerly known as the subspecies *Rana aurora draytonii*) is endemic to the State of California and Baja California in Mexico (NDDB, 2001). The species has been extirpated from 70% of its former range and populations remain in approximately 256 streams and drainages in 27 counties in California (FWS, 2002; 2010). Given the reduction in CRLF numbers, the species was listed as threatened under the US *Endangered Species Act* (ESA) in 1996.

The following comments are in response to the CRLF effects determination that was issued for dimethoate by the U.S. Environmental Protection Agency (EPA, 2008a). The EPA (2008a) effects determination concluded that dimethoate was likely to adversely affect terrestrial-phase CRLF, CRLF prey, and CRLF habitat including aquatic and terrestrial designated critical habitats. The overall CRLF effects determination for dimethoate use was "likely to adversely affect" (EPA, 2008a). The Agency's effects determination for the CRLF and subsequent request for consultation with the U.S. Fish and Wildlife Service (FWS) were made pursuant to the October 20, 2006 Settlement Agreement in *Center for Biological Diversity (CBD) vs. EPA et al.* (US District Court, ND California, Case No. 02-1580-JSW(JL)).

Cheminova A/S is the primary registrant in the United States for the technical form of dimethoate (EPA Reg. 4787-7) and Cheminova, Inc. holds one registration of an end-use product containing dimethoate as the active ingredient. For purposes of the consultation process for dimethoate under Section 7 of the *Endangered Species Act*, Cheminova A/S and Cheminova Inc. (together "Cheminova") are considered "applicants" entitled to fully participate in the consultation process.

Cheminova has a number of concerns with regard to EPA's CRLF effects determination for dimethoate. Cheminova retained Intrinsik Environmental Sciences, Inc. (hereafter "Intrinsik") and Stone Environmental, Inc. (hereafter "Stone Environmental") to review and comment on the EPA dimethoate effects determination. The following report outlines these concerns. The report is organized into three sections: general comments (Section 2.0), specific comments (Section 3.0), and conclusions and recommendations (Section 4.0).

2.0 GENERAL COMMENTS

Some of the general comments about the effects determination stem from inaccuracies and incorrect/erroneous information used in the assessment. These issues are discussed herein.

2.1 Use Scenarios

Maximum application rates, application timing, and type of application influence estimated exposures for CRLFs, their prey and their critical habitat. Therefore, it is extremely important that the use patterns used by EPA in their effects determination be correct. Cheminova has compared the use patterns listed in EPA's effects determination with those included in Table 2-5 of Cheminova's refined effects determination (Intrinsik, 2012) and noted several inconsistencies. For example, the following crops are missing from EPA's use pattern: asparagus, cherries, Christmas trees, peas (not for use on field peas), soybeans and woody ornamentals. EPA assessed some crops that are not supported by California labels including Chinese cabbage and kohlrabi. Lastly, many of EPA's use patterns are wrong including alfalfa, Brussels sprouts, citrus, cottonwood grown for pulp, non-cropland areas adjacent to vineyards, pears, peas (succulent) and safflower. It is important that these issues be resolved before the Agency proceeds further with its consultation process with the FWS.

2.2 Initial Area of Concern

EPA considered all potential agricultural areas in California using land cover data to derive the initial area of concern and ultimately the action area for dimethoate. Dimethoate is not used on every field for the crops included on the labels. Many fields will not experience the pests for which dimethoate is effective. In addition, other pesticides may be used to treat pests. The approach by EPA considerably overestimates the extent of dimethoate use in California and, therefore, the action area extent. Rather than rely on land cover data to define the initial area of concern, EPA should use the California Pesticide Use Reporting Database (CA PUR) as the best available data to identify where dimethoate may be used in California.

To derive an appropriate Action Area if necessary, further spatial analysis would be required to account for off-field movement of dimethoate from fields in the refined area of initial concern via spray drift, flow of water and movement of contaminated prey items. The EPA developed an approach to determine the off-field movement of dimethoate and subsequently the extent of the action area. However, the analyses conducted by EPA to define off-field movement of dimethoate were in our opinion flawed. Details are provided in the discussion below.

2.3 Use of Spray Drift Models in Defining the Action Area

In EPA's dimethoate effects determination, AgDISP (Gaussian extension) was used to calculate exposure concentrations at distances up to approximately 3000 m from agricultural use areas. The predictions go an order of magnitude beyond any reasonable distance at which the model has been shown to be valid. Presented below are reasons why AgDISP and AgDRIFT should not be used to estimate deposition beyond 300 m downwind.

AgDRIFT 2.0.05® (regulatory version) is an EPA/OPP/EFED tool used to estimate off-field drift deposition of pesticides from aerial, orchard airblast and groundspray applications. For aerial, orchard airblast and groundspray applications, AgDRIFT 2.0.05® generates conservative Tier I screening estimates of off-field drift deposition. For aerial applications, AgDRIFT 2.0.05® can also be used to generate more realistic and less conservative Tier II and Tier III off-field drift deposition estimates.

AgDRIFT 2.0.05® is typically used to evaluate the impact of spray drift for pesticide use patterns and to account for setback distance when estimating EECs in water bodies near pesticide treated fields. AgDRIFT 2.0.05® allows the user to study the effects of many different application equipment conditions (e.g., nozzle- and sprayer setup), meteorological and tank mix variables on potential spray movements following application.

AgDRIFT 2.0.05® has been accepted for regulatory use in predicting drift deposition from aerial, orchard airblast, and groundspray applications onto near-field environments within approximately 300 m of the treated area (EPA, 2004a). In AgDRIFT 2.0.05®, groundspray deposition and orchard airblast deposition curves were empirically derived based on study results from the Spray Drift Task Force. Currently, there are only screening Tier I curves available for groundspray and orchard airblast which represent conservative estimates of drift deposition. The aerial algorithm in AgDRIFT 2.0.05® is based on the U.S. Forestry Services AgDISP aerial drift deposition model and can be used to predict pesticide deposition to a distance of 305 m from the point of release from aerial applications.

For distances in excess of 305 m, the AgDISP model itself must be used to estimate off-field deposition for aerial and groundspray applications. AgDISP is a single source, steady-state model that predicts aerial and groundspray drift from agricultural applications onto uniform, flat downwind environments under constant meteorological conditions. A Lagrangian algorithm is used in AgDISP to predict drift deposition up to 305 m of point of release. Deposition for distances beyond 305 m is estimated using a Gaussian far-field extension to the Lagrangian algorithm. AgDISP has been used by EPA to predict drift deposition at distances up to 3 kilometers for aerial and groundspray applications of pesticides. At distances beyond 305 m, results from the Gaussian extension have not been confirmed experimentally and due to the asymptotic behavior of the Gaussian curve at far distances, drift is likely overestimated at far field drift deposition.

Bird et al. (2002) compared the AgDISP aerial model predictions to experimental data from the Spray Drift Task Force studies and reported that the model overestimated deposition at the farthest sampling point (305 m) by a factor of two, and under highly evaporative conditions overestimated deposition by a factor of four. Similarly, Caldwell (2006) found that AgDISP over-predicted concentrations by factors of two to five at 305m downwind from a treated field for aerial applications with the over-prediction increasing as a function of distance from the treated field. At the CropLife America and Rise 2010 Spring Conference Meeting (April 15-16, 2010, Arlington, VA), Scott Jackson presented similar concerns about AgDISP and predicted concentrations for ground applications (Jackson, 2010). Scott Jackson's presentation showed that decrease in deposition for the field measured data declines more rapidly as a function of distance from the treated field than is predicted by the Gaussian extension to the Lagrangian algorithm in AgDISP (Jackson, 2010). Over prediction by AgDisp increases with increasing distance from the point of application. Basically, as distance increases from the treated area, the Gaussian extension to the Lagrangian algorithm flattens asymptotically and proceeds to a slow convergence to zero deposition. This may be the root cause of the increasing over-prediction as distance from the treated area increase.

Additionally, changes in wind direction, variable topography, and interception by crop canopies, structures, and vegetation are not considered by AgDISP. These factors will generally decrease predicted concentrations relative to current model predictions. The Gaussian extension to the Lagrangian algorithm is a recent addition to the AgDISP model. EPA has not evaluated nor accepted its use. AgDISP predicts dispersion under conditions of constant wind direction and speed and assumes a constant source. It does not account for variability in wind conditions that can be expected during the travel time over the distances that EPA has chosen to model.

Additionally, data from the Spray Drift Task Force used to develop the AgDRIFT 2.0.05® empirical drift curves for ground spray and orchard airblast were collected in 1992 and 1993. The nozzles and application equipment used in these studies now represent older technology. Nozzles and equipment have been improved to reduce drift in the last twenty years. This leads to the question of whether the empirical drift curves included in AgDRIFT 2.0.05® really represent current pesticide application methods.

For aerial applications, AgDRIFT 2.0.05® was developed in 2002 and the built-in equipment scenarios represent nozzles and equipment used 10 years ago. Again, this raises the question of whether or not this model truly represents current technology and practices.

Given the above findings, Cheminova is concerned that the use of the AgDISP model produces exaggerated over-predictions of drift for off-site movement of dimethoate spray droplets in air, especially beyond 300 m from the treated field. Several alternative methods are currently being investigated by researchers to improve estimation of drift deposition. These include both empirical and mechanistic models (for example, empirical curves fit to aerial and ground studies by Dr. Thomas Wolf and colleagues of Agricultural and Agri-Food Canada and Syngenta work with the Silsoe Spray Drift Ground Model). Because AgDRIFT makes use of the AgDISP

mechanistic model for aerial applications, both models should not be used in a regulatory context for estimating deposition outside the accepted range of 300 m downwind.
As a result, Cheminova recommends that EPA:

- Provide a complete accounting of all input parameters to the spray drift models. The input parameters used by EPA in the AgDISP modeling produced greater estimates of drift than what occurs in practice;
- Provide a discussion of the uncertainties and limitations of the drift models used;
- Explore the use of drift curves derived using field studies that involved more recent application methods and technology such as studies produced by Dr. Thomas Wolf and colleagues. Develop drift curves using best available data;
- If AgDRIFT or AgDISP are to be used, conduct the exposure assessment only at distances that have been verified using empirical data and are considered acceptable by EPA (2004a, 2005). Also apply a correction factor to the predicted deposition based on the known overestimation of AgDISP and AgDRIFT. Cheminova would like to see the predicted results from both Tier I and Tier II drift simulations included in the risk assessment along with equipment and meteorological parameters;
- Select model input parameters that reflect labeled use conditions and best management practices, instead of worst-case assumptions, and;
- Parameterize the model to represent current nozzle and equipment technology.

The lack of information on the model parameterization and the lack of appropriate use of EPA sanctioned models specific to spray drift is a shortcoming in the CRLF effects determination for dimethoate.

2.4 Effects Metrics

EPA selected some effects metrics that were deemed unacceptable by Cheminova based on a data quality assessment of supporting studies. Cheminova derived scoring criteria for toxicity studies for aquatic invertebrates, fish, amphibians, aquatic plants, birds and mammals to ensure that only high quality toxicity data would be considered in their effects determination. The screening criteria were used to categorize studies as acceptable, supplemental, or unacceptable. Each study rating was based on an evaluation of study design and execution, adherence to toxicity testing protocols, statistical analyses, and other key aspects of the study. The criteria and scoring results for aquatic invertebrates, aquatic vascular plant and avian dimethoate toxicity studies are presented in Appendix A (criteria), B, C, and D (study evaluations) of Cheminova's effects determination (Intrinsik, 2012). Scoring results for amphibians, freshwater fish, mammalian and algal toxicity studies are presented herein (Appendix A, B, C and D, respectively). Table 2-1 summarizes the effects metrics selected by EPA and Cheminova's proposed metrics.

Table 2-1 Summary of effects metrics used by EPA and those recommended by Cheminova for assessing the risk of adverse effects of dimethoate on CRLF

Assessment Endpoint	EPA's Effect Metrics			Cheminova's Recommended Effect Metrics		
	Species, Endpoint, Value	Reference/ MRID	Cheminova's Study Rating	Species, Endpoint, Value	Reference/ MRID	Cheminova's Study Rating
Measures of Direct Effects						
Acute toxicity to aquatic–phase CRLF	Rainbow trout (*Oncorhynchus mykiss*), 96 h LC50, 6.2 mg/L	Johnson and Finley 1980/ 40094602	Unacceptable	African clawed frog (*Xenopus laevis*), 96 h LC50, >98 mg/L	Schneider et al., 2011/ 48634201	Acceptable
Chronic toxicity to aquatic–phase CRLF	Rainbow trout (*Oncorhynchus mykiss*), 96 d NOEC (growth), 0.43 mg/L	Strawn and Muckerman 1994/ 43106301, 43106302, 43106303	Acceptable	African clawed frog (*Xenopus laevis*), 21 d NOEC (Development, growth, survival), ≥100 mg/L	Schneider et al., 2012	Acceptable
Acute toxicity to terrestrial–phase CRLF	Red-winged blackbird (*Agelaius phoeniceus*), gavage LD50, 5.4 mg/kg	Schafer 1972/ 00020560	Unacceptable	Northern bobwhite (*Colinus virginianus*), dietary 5 d LD50, 14.6 mg/kg bw/d (154 mg/kg diet)[a]	Zok, 2001/ 47769705	Acceptable
Sub-acute toxicity to terrestrial –phase CRLF	Ring-necked pheasant (*Phasianus colchicus*), dietary 5 d LC50, 332 mg/kg diet	Hill et al., 1975/ 00022923	Unacceptable			
Chronic toxicity to terrestrial–phase CRLF	Northern bobwhite (*Colinus virginianus*), dietary NOEL (Reduced egg production, survival of young), 4.0 mg/kg[b]	Gallagher et al., 1996/ 44049001	Acceptable	Northern bobwhite (*Colinus virginianus*), dietary NOEL (Adult body weight, feed consumption, egg production and hatchling survivorship), 1.09 mg/kg bw/d (10.1 mg/kg diet)[a]	Gallagher et al., 1996/ 44049001	Acceptable
Measures of Indirect Effects						
Toxicity to aquatic non-vascular plants	Blue-green algae (*Anabaena variabilis*), 15 d, EC50 0.084 mg/L[c]	Das and Adhikary 1996/MRID not available	Unacceptable	Freshwater algae (*Anabaena flos-aquae*), 72 h EC50 (Yield), 6.6 mg/L	Porch et al., 2011c/ 48572804	Acceptable
Toxicity to aquatic vascular plants	No data were available at the time of the EPA's effects determination.		NA	Duckweed (*Lemna gibba*) 7 d EC50 (frond number, biomass and growth) of >45.1 mg/L	Porch et al., 2009/ 47709703	Acceptable
Acute toxicity to aquatic invertebrates (prey)	Stone fly (*Pteronarcys californica*), 96 h LC50, 0.043 mg/L	Sanders and Cope 1968/MRID not available	Unacceptable	Water flea (*Daphnia magna*), 96 h EC50 (immobilization), 0.465 mg/L	Wüthrich, 1990/ 42864701	Acceptable
Chronic toxicity to aquatic invertebrates (prey)	Estimated acute-to-chronic ratio of 83 (48 h LC50 3.32 mg/L / 21 d	Song et al., 1997/MRID not available	Supplemental	*Daphnia magna* (water flea) NOEC (growth and reproduction) 0.04 mg/L	Wüthrich, 1990/ 42864701	Acceptable

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	Species, Endpoint, Value	Reference/ MRID	Cheminova's Study Rating	Species, Endpoint, Value	Reference/ MRID	Cheminova's Study Rating
	NOEC 0.04 mg/L using *Daphnia magna*) applied to the acute metric (0.043 mg/L; above) for an estimated NOEL of 0.0005 mg/L[d]	Wüthrich 1990/ 42864701	Acceptable			
Acute toxicity to fish (prey)	Rainbow trout (*Oncorhynchus mykiss*), 96 h LC50, 6.2 mg/L	Johnson and Finley 1980/ 40094602	Unacceptable	Rainbow trout (*Oncorhynchus mykiss*), 96 h LC50, 24 mg/L	Brougher et al., 2012/ MRID not available	Acceptable
Chronic toxicity to fish (prey)	Rainbow trout (*Oncorhynchus mykiss*), 96 d NOEC (growth), 0.43 mg/L	Strawn and Muckerman,1994/ 43106301, 43106302, 43106303	Acceptable	Rainbow trout (*Oncorhynchus mykiss*), 96 d NOEC (growth), 0.43 mg a.i./L[e]	Strawn and Muckerman,1994/ 43106301, 43106302, 43106303	Acceptable
Acute toxicity to terrestrial invertebrates (prey)	Honey bee (*Apis mellifera*), LD50, 0.05 µg a.i./bee	Fraser and Jenkins 1972/ 00026489	—	Honey bee (*Apis mellifera*), LD50 (contact and oral), 0.10 µg a.i./bee	Gough et al., 1994/ MRID not available	—[f]
Acute toxicity to mammals (prey)[g]	Laboratory rat (*Rattus norvegicus*t), gavage LD50, 358 mg/kg	Kynoch 1986/ 00164220	Acceptable	Laboratory rat (*Rattus norvegicus*t), gavage LD50 (males), 358 mg/kg bw	Kynoch, 1986/ 00164220	Acceptable
Chronic toxicity to mammals (prey)[g]	*Laboratory rat* (*Rattus norvegicus*), oral gavage NOEL (pup survival), 0.1 mg/kg bw[h]	Myers 2003/ 45529702, 45529703[i]	Supplemental	*Laboratory rat* (*Rattus norvegicus*), dietary NOEL (reproductive effects (decreased fertility, live pups per litter, pup body weight), 1.2 mg/kg bw/d	Brooker et al., 1992/ 42251501	Acceptable
Acute toxicity to frogs representing prey	Red-winged blackbird, (*Agelaius phoeniceus*), LD50, 5.4 mg/kg	Schafer 1972/ 00020560	Unacceptable	Northern bobwhite (*Colinus virginianus*), dietary 5 d LD50, 14.6 mg/kg bw/d (154 mg/kg diet)[b]	Zok, 2001/ 47769705	Acceptable
Sub-acute toxicity to frogs representing prey	Ring-necked pheasant (*Phasianus colchicus*), LC50, 332 mg/kg-diet	Hill et al., 1975/ 00022923	Unacceptable			

Table 2-1 Summary of effects metrics used by EPA and those recommended by Cheminova for assessing the risk of adverse effects of dimethoate on CRLF

Assessment Endpoint	EPA's Effect Metrics			Cheminova's Recommended Effect Metrics		
	Species, Endpoint, Value	Reference/ MRID	Cheminova's Study Rating	Species, Endpoint, Value	Reference/ MRID	Cheminova's Study Rating
Chronic toxicity to other species of frog (prey)	Northern bobwhite (*Colinus virginianus*), NOEL (Reduced egg production, survival of young), 4.0 mg/kg[b]	Gallagher et al., 1996/ 44049001	Acceptable	Northern bobwhite (*Colinus virginianus*), NOEL (adult body weight, feed consumption, egg production and hatchling survivorship), 1.09 mg/kg bw/d (10.1 mg/kg diet)[b]	Gallagher et al., 1996/ 44049001	Acceptable
Toxicity to monocot plants composing wetland and terrestrial habitat	No data were available at the time of the EPA's effects determination.		—	21 d NOEL of >1.5 lb a.i./A (seedling emergence, growth) for 10 different crops (monocots and dicots)	Porch et al., 2011a;b/ 47709701, 48628101, 47709702	—[f]
Toxicity to dicot plants composing wetland and terrestrial habitat			—	21 d NOEL of >1.5 lba.i./A (vegetative vigor, growth) for 10 different crops (monocots and dicots)		

[a] Cheminova converted to an average estimated daily dose using the body weights and food intake values reported in the study. The approach is presented in Cheminova's Effect Determination (Intrinsik, 2012).
[b] The reported NOEL from this study is actually 10.1 mg/kg a.i. diet.
[c] The study is unacceptable as it is a 15 day exposure, which is not a standard exposure duration for the test species. Also the test substance was not technical grade, and its source was not reported.
[d] Cheminova does not support the use of this ACR. See further discussion below.
[e] Cheminova is currently generating new data for this endpoint. Results to be determined (TBD).
[f] Cheminova has not developed criteria for bees and terrestrial plants. Cheminova determined this study to be the best available data.
[g] For reasons presented in Cheminova's effects determination (Intrinsik, 2012), Cheminova does not support the need for the assessment of risk to small mammals (for reduction in CRLF prey).
[h] In Myers (2003) the author notes that at the 0.5 mg/kg bw/d treatment level pup survival was within the normal range (i.e., within the range of control data from studies between October 2000 and September 2002 at the laboratory). The NOEL of 0.1 mg/kg bw was never reported by the study author, and also does not appear to be based on a statistically significant test result, but on the basis of one litter being lost at the 0.5 mg/kg bw/d treatment level. Myers (2001) demonstrates a NOEL for pup mortality (up to post natal day 11) of ≥ 3 mg/kg bw/d, which supports our conclusion that the NOEL of 0.1 mg/kg bw/d is erroneous. Further, results of oral gavage studies are inappropriate for direct comparison with dietary exposure estimates (i.e., residues on feed or total daily intake estimates), because they do not account for feeding behavior or the effects of the dietary matrices on toxicity.
[i] Two MRID numbers were provided in Table 23 of EPA (2008a), however, in the text EPA (2008a) clearly states that the effect metric of 0.1 mg/kg came from MRID 45529703 (i.e., Myers, 2003).

The acute-to-chronic ratio (ACR) used to convert the stonefly EC50 to a chronic NOEL was 83 based on toxicity data for *Daphnia magna*. This ACR was calculated using an acute 48-hour LC50 of 3.32 mg/L and a chronic 21-day NOEL of 0.04 mg/L for *Daphnia magna* because there were no chronic toxicity data available for the stonefly species. The source of these endpoints, however, was not explicitly reported in the ACR discussion. Based on the presented toxicity tables (EPA's effects determination, Table 27, page 78) the acute endpoint of 3.32 mg/L may be from Song et al. (1997). Song et al. (1997) is a supplemental study based on Intrinsik's study evaluation criteria (see Appendix A in Intrinsik, 2012). The chronic NOEL of 0.04 mg/L selected could be from Wüthrich (1990; MRID 42864701). This GLP study was evaluated and found to be acceptable based on Intrinsik's study evaluation criteria (See Appendix B in Intrinsik, 2012). The best practice for calculating an ACR is to use data from the same study, thus eliminating variability due to different procedures, environmental conditions, and sensitivity of the test populations. Therefore, a more appropriate ACR calculated by dividing the acute 96-hour EC50 for *Daphnia magna* (0.465 mg/L) (Wüthrich, 1990) by the chronic NOEL (0.04 mg/L) for *Daphnia magna* (Wüthrich, 1990) would be considered more appropriate. The resulting ACR is 11.6. Given this ACR results from acute and chronic effects evaluated in the same acceptable toxicity study, the accuracy of the daphnid ACR of 83 calculated by EPA is arguable. For such a critical piece of information, it is a serious shortcoming that EPA did not provide references for the daphnid-based ACR. However, Cheminova believes that an ACR was not required for this endpoint. Wüthrich (1990) reported a chronic NOEL of 0.04 mg/L for growth and reproduction of *daphnia magna*. This endpoint should have been used in the effects determination.

2.5 Effects to CRLF Prey

EPA used a conservative Tier 1 approach to assess the potential for indirect effects to the CRLF. The effects determination for indirect effects to prey relied on toxicity endpoints for direct effects on the most sensitive algae, invertebrates, birds and mammals. However, as documented by EPA in Section 2.5, adult CRLFs feed on a wide variety of prey and thus would not be expected to feed exclusively on prey items that are highly sensitive to dimethoate exposure. Further, EPA estimated risk to terrestrial prey assuming that such prey were on-field at the time of application. Given that adult CRLFs spend the vast majority of their time foraging in riparian vegetation it seems likely that most of their prey would be from riparian areas, not treated fields.

Cheminova does not support the assessment of indirect effects to terrestrial-phase CRLF via reduction in mammalian prey because available data suggests that:

1. Mammals are a minor portion of the CRLF diet, which is mostly comprised of invertebrates (Hayes and Tennant, 1985). Evidence of CRLF consuming mammalian prey is minimal, and is based on one of 35 individuals that had mouse remains in their digestive tract (Hayes and Tennant, 1985). Therefore, it is unlikely that mammalian species represent a large portion of the adult CRLF prey base; and,

2. The maximum home range radius estimated for the California mouse is 35 m (Appendix E). This mouse is prolific and is primarily associated with forested and chapparal habitat, not agricultural areas (Grinnell and Orr, 1934; Merritt, 1978)

Therefore, it is highly unlikely that any potential effects of dimethoate on mice will lead to significant indirect effects via reduction of mammalian prey populations for adult CRLF.

For plant food items, sufficient data are available to derive dimethoate-specific residue unit doses (RUDs; mg a.i./kg ww vegetation per lb a.i./A), rather than rely on the dated and highly conservative Hoerger-Kenaga nomogram values. EPA applies these lb/A nomogram values as RUDs (Table 2-2). Intrinsik (2012) derived dimethoate-specific RUDs values using the results of numerous field monitoring studies in Europe and United States conducted on behalf of Cheminova (Corden 2000, 2001, 2005; Goodband, 2003; Knäbe, 2004a; Pollman, 2006; Raufer, 2009a-d; Wilson, 2000, 2001a-l, 2002a-f, 2003 a,b). Results suggest that the use of the Hoerger-Kenaga nomograms in EPA's effects determination resulted in an overly conservative assessment of risks of indirect effects to CRLF. Using measured residues for dimethoate would result in a more realistic and defensible assessment of risks.

Table 2-2 Normalized dimethoate concentrations in various plant food items immediately after application

Value Used by EPA		Value from Intrinsik (2012)	
Food Item Category	**Upper Bound (mg a.i./kg ww per lb a.i./A)**	**Food Item Category**	**95th Percentile (mg a.i./kg ww per lb a.i./A)[a]**
Short grass	240	Short Grass	122.1
Forage/leafy crops (small insects)	135	Insects	66.6 (Crop Dwelling) 62.5 (Orchard Dwelling)
Small fruit and seeds	15	Small Fruit and Seeds	12.2

[a] 95th percentile of estimated lognormal distributions based on maximum likelihood estimates of distribution parameters. Data were tested for log normality (Shapiro-Wilks, p>0.05). See Intrinsik (2012) for details.

The Hoerger-Kenaga nomograms were derived using residues on vegetation. In EPA's effects determination it was assumed that the upper bound Hoerger-Kenaga nomograms for broadleaf plants (135 mg/kg per lb a.i./A) would apply to small insects. In fact, there is a significant amount of arthropod specific data that suggests that this is an overly conservative value (see Fischer and Bowers, 1997; Knäbe, 2004a,b; Barber et al., 2005). Cheminova applied these data in their effects determination, and found that the 95th percentile RUD estimates were less than half the presumed upper bound value of 135 mg/kg per lb a.i./A used by the EPA (Table 2-3). The EPA should consider current available arthropod pesticide residue data in their effects determination. In addition, EPA's use of maximum RUDs is overly conservative. Depending on the range of data being considered, using a maximum value may include extraneous outliers in the data, thus generating RUDs that are not realistic to be assuming as typical exposure residues.

Table 2-3 Estimated arthropod pesticide RUDs (mg a.i./kg ww per lb a.i./A)[a]		
Food Item Category	**Mean**	**95th Percentile[b]**
Orchard and vineyard dwelling arthropods	17.5	62.5
Leafy crop dwelling arthropods	16.7	66.6

[a] Data from Barber et al. (2005) and Knäbe (2004a,b). Maximum of Day 0 and Day 1 residue measurements. The approach to the data analysis is presented in Cheminova's effects determination (Intrinsik, 2012).

[b] 95th percentile of estimated lognormal distributions based on maximum likelihood estimates of distribution parameters. Data were tested for log normality (Shapiro-Wilks, p>0.05). See Intrinsik (2012) for details.

Because CRLFs are generalist feeders, the effects characterization should not be restricted to the most sensitive species. As long as overall productivity of prey species is protected, indirect effects to CRLFs are not expected. Available toxicity studies for dimethoate were evaluated based on Intrinsik's study evaluation criteria, which is provided in Appendix A to Cheminova's effects determination (Intrinsik, 2012). Acceptable and supplemental toxicity studies for aquatic invertebrates indicate that aquatic invertebrates have a wide range of sensitivities to dimethoate. Forty-eight and 96-hour EC/LC50s for freshwater invertebrates range from 0.249 mg/L for the midge (*Chironomus tentans*) to 6.41 mg/L for the yellow fever mosquito (*Aedes aegypti*). Thus, concentrations of dimethoate that only affect the most sensitive species are unlikely to have any significant effect on overall productivity of prey species in aquatic environments. The recommended approach for the effects characterization is to derive a species sensitivity distribution (SSD) for each prey group where data permit.

An SSD is a statistical distribution that captures the variation in toxicological sensitivity among a given set of species to a contaminant (Posthuma et al., 2002). We developed an acute SSD for aquatic invertebrates exposed to dimethoate. Only acceptable and supplemental study data were used to derive the SSD.

The number of acute toxicity studies available for freshwater invertebrates was limited. In the case of dimethoate, freshwater invertebrates and saltwater invertebrates appear to have similar sensitivity. The LC/EC50 range for freshwater invertebrate species is 0.249 to 6.41 mg/L and the corresponding LC/EC50 range for saltwater species is 0.031 to 303 mg/L (Intrinsik, 2012). These ranges are for acceptable and supplemental studies only. Therefore, acute toxicity studies for saltwater invertebrates were included in the acute SSD dataset.

The data points selected for the SSD are presented in Table 2-4. When multiple endpoint values were available for the same species, the average of these values was used to represent that species in the SSD. This calculation was required for *Daphnia magna* and the yellow fever mosquito. The exposure period for all freshwater endpoints was 48 hours. The exposure period for saltwater species was generally 48 hours except for the mysid (*Mysidopsis bahia*) and Eastern oyster (*Crassostrea monoceros*), which had exposure periods of 96 hours, and the rotifer (*Brachionus plicatilis*), which had an exposure period of 24 hours. Toxicity data were available for three different exposure periods (24, 48 and 72 hours) for brine shrimp (*Artemia salina*). The 48-hour toxicity value was selected for the SSD as this exposure duration is consistent with most other data.

Table 2-4 Acute toxicity data used to develop an acute SSD for dimethoate				
Common Name	**Scientific Name**	**EC/LC$_{50}$ (mg/L)**	**SSD Input Value (mg/L)**	**Reference**
Water flea	*Daphnia magna*	2	2.07	Hertl, 2002
		1.1		Andersen et al., 2006
		3.32		Song et al., 1997
		3.12		
		1.7		Beusen and Neven, 1989
		2		
		1.5		
		1.8		
Midge	*Chironomus tentans*	0.249	0.249	Anderson and Zhu, 2004; Andersen et al., 2006
Yellow fever mosquito	*Aedes aegypti*	5.04	5.73	Song et al., 1997; Song and Brown, 1998
		6.41		
Brine shrimp	*Artemia sp.*	15.7	15.7	
Black salt marsh mosquito	*Aedes taeniorhynchus*	0.031	0.031	
mysid	*Mysidopsis bahia*	22	22	Graves and Swigert, 1993a
Eastern oyster	*Crassostrea virginica*	113	113	Graves and Swigert, 1993b
Rotifer	*Brachionus plicatilis*	244	244	Guzzella et al., 1997

The acute SSD was generated using SSD Master v2.0 (Rodney et al., 2008), an Excel-based tool that fits five different cumulative distribution functions (normal, logistic, Gompertz, Weibull and Gumbel) in both log and arithmetic space. This software allows for the testing of model assumptions as well as model fit. The Gompertz model was the best-fitting model according to the Anderson-Darling (AD) goodness-of-fit test statistic (AD statistic = 0.129, $p>0.05$) and various graphical plots of model residuals (e.g., p-p and q-q plots). The Gompertz model equation is shown below (Equation 1).

$$f(x) = 1 - e^{-e^{\frac{(x-\mu)}{s}}} \qquad \text{Equation 1}$$

where x is concentration, and the functional response, f(x), is the proportion of species affected (i.e., the proportion of species whose LC50s are exceeded). The parameters, μ and s, are the location and scale parameters of the model. The scale parameter in the Gompertz model must always be positive. The fitted model parameters were: μ=4.342 and s=1.124 for acute toxicity data reported in μg/L. The SSD is shown in Figure 2-1.

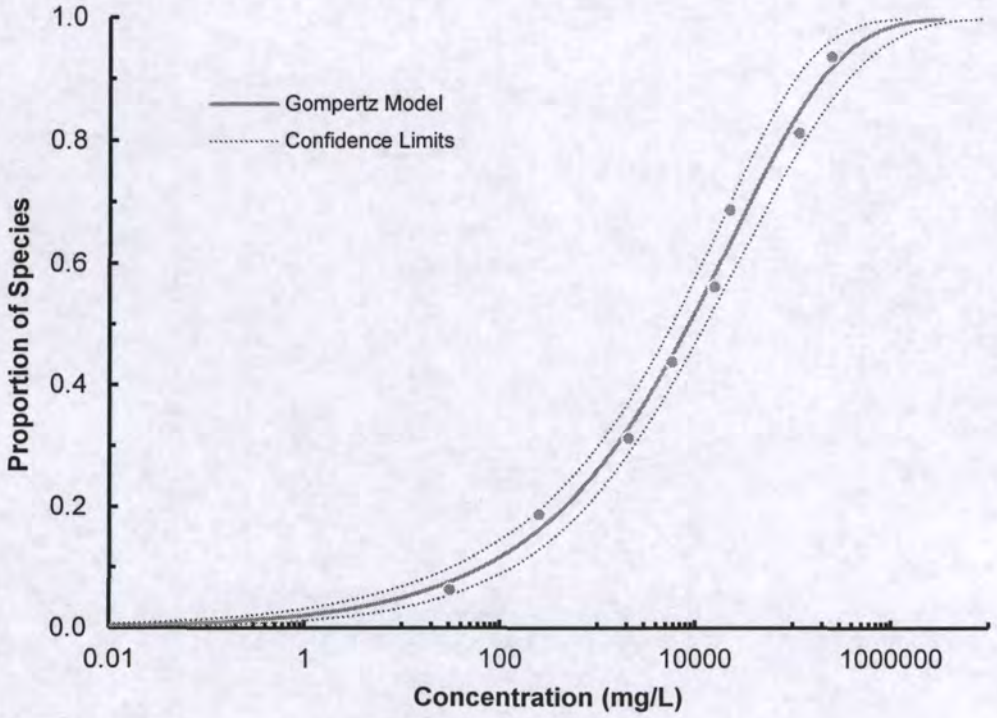

Figure 2-1 Acute SSD for aquatic invertebrate species exposed to dimethoate

Insufficient chronic toxicity data were available for aquatic invertebrates to derive a chronic SSD. In absence of an SSD derived with chronic toxicity data, the acute invertebrate SSD (Figure 2-1) can be divided by an acute-to-chronic ratio (ACR) to approximate a chronic SSD. The ACR was calculated by dividing the acute 96-hour EC50 for *Daphnia magna* (0.465 mg/L) (Wüthrich, 1990) by the chronic NOEL (0.04 mg/L) for *Daphnia magna* (Wüthrich, 1990). The Wüthrich (1990) study is an acceptable GLP study. The resulting ACR is 11.6. The best practice for calculating an ACR is to use data from the same study, thus eliminating variability due to different procedures, environmental conditions, and sensitivity of the test populations.

Rather than calculate conservative, deterministic risk quotients, risk curves should be derived by integrating the exposure and effects distributions (SSD or concentration-response curves). Risk curves and a description of how Cheminova characterizes risk in their refined effects determination are presented in Appendix F.

2.6 Dietary Exposure for CRLFs

EPA's estimation of risk to CRLF assumes that each prey group represents 100% of the diet (e.g., fish, aquatic invertebrates, frogs, mammals) of the CRLF. The available data, however, indicate that aquatic- and terrestrial-phase CRLFs have quite varied diets. The diet of CRLF larvae (i.e., tadpoles) has not been well studied, but they are primarily algal grazers (FWS, 2002). They also consume organic debris, plant tissue and minute organisms (NatureServe, 2006). Their anatomy enables them to filter and entrap suspended algae (Seale and Beckvar,

1980) and their mouthparts are designed for effective grazing of periphyton (Wassersug, 1984; Kupferberg et al., 1994; Kupferberg, 1997; Altig and McDiarmid, 1999). Some of the more common food items consumed by larvae include filamentous green algae (Dickman, 1968), filamentous blue-green algae (Pryor, 2003), epiphytic diatoms (Kupferberg, 1997) and detritus and various other algae (Jenssen, 1967). Larvae are also known to feed on algal species that are considered nuisance species or form blooms (Bold and Wynne, 1985).

Adult CRLFs consume a variety of invertebrate and vertebrate species found along the shoreline and close to the water surface. They will also forage several meters into dense riparian vegetation along the shoreline (FWS, 2002). A study examining the gut contents of 35 CRLFs reported prey from forty-two taxa (Hayes and Tennant, 1985). The prey groups observed most often included carabid and tenebrionid beetles, water striders, lycosid spiders, and larval neuropterans. The most commonly observed prey species were larval alderflies (*Sialis* cf. *californica*), pillbugs (*Armadillidrium vulgare*), and water striders (*Gerris sp.*). Prey were both terrestrial and aquatic. A preference for particular prey species was not observed in this study, and CRLFs appeared to select prey based on availability (Hayes and Tennant, 1985). The largest prey items consumed by large CRLFs (snout-vent length (SVL) >10 cm) were Pacific tree frogs (*Hyla regilla*) and California mice (*Peromyscus californicus*). Thus, adult frogs also have varied diets, with aquatic and terrestrial invertebrates being the most common prey.

Therefore, the CRLF has a varied diet at all life stages and based on the information above, can be considered both opportunistic and a generalist feeder. Therefore, when modeling CRLF dietary exposure, the model employed should account for the varied nature of the CRLF diet.

2.7 Estimated Exposure Concentrations

As typically done in screening-level assessments for pesticides, EPA (2008a) relied on the outputs of the PRZM3.12.2/EXAMS2.98.04 modeling efforts to estimate risk. The EPA standard pond scenario assumes that a pesticide applied to a 10 hectare field drains (from runoff and erosion) into a one hectare pond that is two meters deep. The model assumes no in- or out-flow from the EPA pond over the course of a 30-year simulation.

Provided below are reasons why the EPA pond is conservative and results in unrealistic estimates of dimethoate exposure:

- CRLF core areas represent a system of areas that, when protected and appropriately managed, should permit the long-term viability of CRLF populations and the re-establishment of populations within their historic range (FWS, 2002). Similarly, critical habitat is specific geographic area(s) that are essential for the conservation of a threatened or endangered species and that may require special management and protection. Critical habitat is designated by the Services under the ESA. Stone Environmental reported that 0.5 to 2% of the combined CRLF core areas and critical habitat consisted of agricultural land (Stone Environmental, 2012). Of the critical habitat

and core areas, only 0.16% and 0.74% are perennial ponds, intermittent ponds or swamps where CRLF are likely to be found, respctively. This shows that ponds are a very minor portion of habitat for the CRLF in core areas or critical habitat, and that CRLF prefer to inhabit flowing water bodies.

- Stagnant ponds are likely to have a far less diverse biota than other more common aquatic water bodies, such as natural ponds, lakes, and streams, due to little or no exchange of mass with other water bodies. Species that are entirely aquatic (e.g., fish, clams, mussels, non-emergent insects) would not be present in a stagnant pond. For refined aquatic assessments, a set of modelling scenarios that includes lakes and streams should be developed by the EPA/EFED. Such scenarios would produce more representative estimates of the concentrations of pesticides in water bodies that support functional aquatic communities.

- All runoff from the 10 hectare field is assumed to drain into the standard pond, a highly unrealistic assumption. Many farms would have runoff draining in several different directions.

- The wind is assumed to be blowing in the direction of the pond at the time of application, which is unlikely to occur during most applications of dimethoate.

In addition to the above concerns regarding EPA's standard pond scenario, the output from the PRZM3.12.2/EXAMS2.98.04 modeling is designed to be highly conservative. For example, EPA describes 1-in-10 year estimated environmental concentrations as "90th percentiles" (e.g., page 47 in EPA, 2008a). This designation is very misleading for the reasons described below:

- Before estimating a "90^{th} percentile", the PRZM3.12.2/EXAMS2.98.04 combined output is processed by first determining the highest daily pesticide concentration (or longer-term concentrations for non-acute exposures) for each year in a 30-year simulation period. The model then calculates the 90^{th} percentile from these 30 maximum annual values. For a 30 year period, EPA's "90^{th} percentile" is actually a concentration that would only be exceeded on three days in 30-years (or a 1-in-10 year event). On a daily basis, this estimate would actually be a 99.97^{th} percentile. In other words, the concentration estimated by EPA would be less for 99.97 percent of days in the pond, assuming that the other components of the modelling were accurate and unbiased (which they are not).

- To derive valid probabilistic exposure estimates (e.g., a 90th percentile), all key input variables must be modelled as distributions that reflect the range of plausible values for each variable. However, the only probabilistic variable in PRZM3.12.2/EXAMS2.98.04 is the meteorology (most importantly, rainfall). Conservative and sometimes implausible assumptions are made for almost all other key variables. The compounding effect of these conservative assumptions is an implausibly high exposure estimate.

The EPA has acknowledged that PRZM/EXAMS is highly conservative and does not produce realistic estimates of environmental concentrations. For example, Dr. Norman Birchfield, a Senior Biologist and Acting Risk Assessment Process Leader at the Environmental Fate and Effects Division (EFED) at EPA (in 2003), stated in his expert declaration in a lawsuit that EFED's models predict environmental concentrations that "are higher than most, if not all, analogous concentrations in the environment resulting from labelled uses" (Birchfield, 2003).

Concentrations of dimethoate in flowing water bodies as well as ponds and lakes with in- and out-flows are likely to be substantially lower than those estimated by PRZM/EXAMS for stagnant ponds. Immediately upon entering the water body, dimethoate will begin to disperse from the turbulence of the flow. For example, Bogen and Reiss (2011) applied the AgDrift Stream Assessment Tool to estimate pesticide concentrations in a slow-moving stream (e.g., side channel) over time. The key factor influencing concentration over time is stream velocity. For modeling purposes, a conservative stream depth of four inches and a stream velocity of 0.07 ft/sec were used (the lower 10^{th} percentile of mean velocities in side channels in the lower Moklumne river in Northern California). In addition, a conservative estimate of the riparian interception factor of 0.2 (20%) was accounted for. This factor is to account for drift interception by riparian vegetation (Bogen and Reiss, 2011). Aerial (medium droplet size) and ground (very fine droplet size) applications of 1.0 lb a.i./A (1.12 kg a.i./ha) were applied to the theoretical stream assuming the distance between application and the water body was 50, 100, 250, 500 and 1000 feet apart. Almost immediately after application, 100 feet away from the water body, the stream concentration increased to 50 µg/L. However the concentration quickly declined to below 10 µg/L after one hour and below 1 µg/L five hours after application (Bogen and Reiss, 2011; presentation to EPA and National Marine and Fisheries Service on October 23, 2009). In addition, Stone Environmental derived more realistic EECs for malathion in water bodies inhabited by CRLF (i.e., with realistic in-flow and out-flow, volume, and location characteristics) using SWAT (Soil and Water Assessment Tool) modeling. Peak EECs were 5 to 12 times greater for the PRZM3.12.2/EXAMS2.98.04 simulations (lettuce and strawberry, respectively) than they were for the most vulnerable water body in the SWAT simulation of the Watsonville watershed in California; Stone Environmental, 2012). For the 21-day duration, the EECs based on PRZM3.12/EXAMS2.98.04 were 20 to 50 times greater (lettuce and strawberry, respectively) than the SWAT simulation predictions. This comparison shows that the interpretation of risk is significantly reduced when EECs are based on modeling actual aquatic ecosystems (rather than highly conservative hypothetical ones in the case of PRZM3.12/EXAMS2.98.04), and when using a model that appropriately accounts for all hydrologic processes, such as SWAT (Intrinsik, In Prep; Stone Environmental, 2012). Not surprisingly, concentrations found in the relevant surface water monitoring studies show substantially lower concentrations than those predicted by PRZM-EXAMS (see Section 3 of Cheminova's effects determination (Intrinsik, 2012)).

As with any line of evidence, PRZM/EXAMS have their strengths and limitations. For example, the modelling system is use-pattern specific and can forecast relative changes in exposure given changes to an existing pesticide label. Exposure modelling, however, is limited in terms of environmental realism (e.g., stagnant pond is not representative of nearly all habitats for aquatic biota) and often relies on highly biased and conservative assumptions when data are limited.

For instance, EPA multiplies an aerobic biodegradation half-life by a factor of 3 if only one supporting degradation trial is available. Therefore, PRZM/EXAMS is most useful in identifying use patterns that potentially pose a risk to aquatic biota. However, for a more refined understanding of risk, it is important to consider refined exposure modeling and available monitoring data as lines of evidence in assessment of pesticide risks to aquatic biota. Although monitoring data have shortcomings (see below), they also have a number of strengths including: (1) they incorporate environmental realism and complexities that cannot be captured in exposure models (e.g., multiple applications that vary over space and time, variable crops, field sizes, slopes, soils, micro-climates, receiving environments, etc.), and (2) they can be used to corroborate the effectiveness of past management decisions.

2.8 Monitoring Data Warrant Consideration

In pesticide risk assessments, monitoring data are often cited by the EPA as having major shortcomings that reduce their utility for assessing risk to aquatic biota:

- The monitoring study protocols were not designed to capture peak pesticide exposure;
- Monitoring data reflect past use patterns and may not be representative of current and future use patterns; and,
- There is a lack of information on actual use to correlate with observed concentrations

Although there is uncertainty associated with using monitoring data to estimate exposure, Cheminova believes that EPA overstate uncertainties associated with use of monitoring data and, further, generally rely on modelling approaches that have greater uncertainties (i.e., PRZM/EXAMS, AgDRIFT). In this section, we discuss each of the potential shortcomings with regards to use of monitoring data in the refined aquatic effects determination for dimethoate.

2.9 Protocols Not Designed to Capture Peak Exposure

The EPA contends that monitoring studies, particularly those not targeted to agricultural areas at the time of pesticide application, will miss peak exposures. Peak exposures are often considered critical because the mode of action of dimethoate, acetylcholinesterase inhibition, occurs rapidly after initial exposure. However, the toxicity data to which monitoring results were compared in the risk characterization were based upon 48 or 96-hours exposures of freshwater invertebrates and fish, respectively. The effects metrics for organophosphate pesticides are strongly inversely correlated with exposure duration (i.e., as duration increases, LC50s and EC50s decrease; e.g., Eisler, 1969; Gupta, 1984; Mary et al., 1986; Mayer and Ellersieck, 1986; Parra et al., 2005). Völkl (1993) evaluated the degradation of dimethoate in water/sediment systems and found that dimethoate rapidly dissipated from the water phase by degradation to CO_2 and adsorption to the sediment. Thus, the absence of peak instantaneous concentrations in the monitoring datasets is beside the point. In addition, it is hard to accept the argument that peak exposure concentrations have been missed by the thousands of samples (N > 5,000) generated by all of the monitoring studies conducted to date in California (Intrinsik, 2012). Monitoring data sources examined include: USDA Pesticide Data Program (PDP) (2001-2009), the US Geological Survey (USGS) National Water Quality Assessment (NAWQA) Program

(2001-2011), California Department of Pesticide Regulation (DPR), and the California Environmental Data Exchange Network (CEDEN) (2001 – 2008). Although many monitoring studies were not targeted to the timing and location of dimethoate applications, many stations are located in agricultural and urban areas where pesticide use is high. Thus, it is inconceivable that exposure peaks meaningful to populations of aquatic invertebrates or fish over appropriate exposure durations (i.e., 48 or 96 hours) would have been missed in all of the available monitoring studies for dimethoate. The USGS NAWQA database was also queried for dimethoate in surface water across the United States. Dimethoate concentrations were all significantly lower than the peak concentrations detected in California (Intrinsik, 2012).

2.10 Monitoring Data Reflect Past Use Patterns Only

The number of approved use patterns, numbers of applications, and the application rates for remaining use patterns have declined in recent decades for dimethoate in the United States and Canada. Further, the labels for dimethoate now include a number of mitigation measures (e.g., use of larger droplet sizes, recommendation for vegetative filter strips, etc.) that were not included previously. As a result, past monitoring data likely overestimate current concentrations of dimethoate in North American surface waters. Thus, the risk estimates derived with monitoring data in Cheminova's CRLF effects determination (Section 3; Intrinsik, 2012) are likely overly conservative.

2.11 Data on Actual Use Patterns to Correlate with Monitoring Data

Rarely do surface water monitoring programs provide specific information on pesticide use on land parcels that could potentially influence monitoring results. Very few regulatory agencies in North America collect mandatory pesticide use data (e.g., a notable exception being the California Pesticide Use Database) that could be spatially and temporally correlated with sampling results. Use pattern data could help provide specific information on appropriate sample timing and provide some context to the concentrations detected. However, many pesticide monitoring programs are designed to sample potentially vulnerable water bodies during periods of heavy pesticide use. Thus, California monitoring data are thought to be reflective of ecologically-relevant dimethoate concentrations for CRLF.

EPA's effects determination noted that monitoring data were available for the San Joaquin River watershed and that the maximum concentration detected in the watershed was 0.0024 mg/L in 1991-1993. This reported peak concentration is notably well below Cheminova's lowest recommended aquatic effect metric of 0.04 mg/L (the chronic NOEL for *Daphnia magna* reported by Wüthrich (1990); See Table 2-1). What the effects determination failed to mention was that over 75% of the 35 positive samples had concentrations of <0.00036 mg/L. As a result, the California Department of Fish and Game (CDFG, 1996) concluded that, "dimethoate does not appear to present an acute or chronic hazard to aquatic organisms at this time." The Sacramento-San Joaquin river system drains an area of intense agriculture and high dimethoate usage. Thus, the monitoring data from this system should have been given more weight in the effects determination for characterizing risk.

Since the EPA's effects determination, monitoring data have been updated. A summary of currently available monitoring data is presented in Cheminova's effects determination (See Section 3; Intrinsik, 2012). Numerous additional sources of water quality data were also reviewed and summarized in the effects determination (Intrinsik, 2012). Data sources included the USDA Pesticide Data Program (PDP) (2001-2009), the US Geological Survey (USGS) National Water Quality Assessment (NAWQA) Program (2001-2011), California Department of Pesticide Regulation (DPR), and the California Environmental Data Exchange Network (CEDEN) (2001 – 2008). Dimethoate concentrations measured in surface water from each of the programs mentioned above are low. The maximum concentration reported in the PDP data was 0.004 µg/L for dimethoate. From the NAWQA program the maximum detected concentration was 0.494 µg/L. The maximum dimethoate concentration from the CEDEN database was 11.6 µg/L and from the DPR database was 11.6 µg/L. This maximum dimethoate concentration was found in the Grant Line Canal, CA which is a large man-made canal adjacent to a large agricultural area. The maximum concentration does not exceed the acute effects metric (LC50) for freshwater invertebrates of 465 µg/L (Wüthrich, 1990) nor the chronic effects metric (NOEL) for freshwater invertebrates (*Daphnia magna*, 40 µg/L; Wüthrich, 1990).

2.12 Omethoate Risks

On page 125 of the EPA's dimethoate effects determination, EPA makes the case that the risk estimates derived for terrestrial-phase CRLF and their amphibian and mammalian prey would be greater had the risks posed by omethoate, been factored into the calculations. Cheminova does not support the assessment of mammals for indirect effects to CRLF (this position was presented above).

With respect to CRLF and their amphibian prey, Cheminova is in agreement with the EPA that toxicity data suggest omethoate and dimethoate are equivalently toxic to the surrogate taxa (birds). However, Cheminova does not believe that predicted risks would be significantly higher for CRLF if omethoate were factored into a refined effects determination. Of CRLF and amphibian prey feed items, terrestrial arthropods are likely a significant portion of the diet (with aquatic invertebrates being of slightly more or less importance; Hayes and Tennant, 1985). Terrestrial arthropods are also expected to have the highest dimethoate residues (per wet weight unit; Intrinsik, 2012). In a GLP study conducted in a citrus orchard in Spain, Knäbe (2004a) investigated dimethoate and omethoate residues on crop dwelling arthropods. Results of the study show that omethoate concentrations are minor compared to peak dimethoate residues (≤14% of the dimethoate residue level). The study also reported an omethoate half-life of 0.33 d which is considerably shorter than the reported dimethoate half-life of 0.86 d (Knäbe, 2004a). Further, aquatic invertebrates may be an even more important feed item, particularly for the more sensitive juvenile CRLF. Laboratory studies and water monitoring data in California indicate that omethoate is not produced in aquatic environments (see Appendix F in Cheminova's effects determination (Intrinsik, 2012). Thus, aquatic invertebrates are unlikely to carry omethoate residues. As such, Cheminova believes it is unlikely that factoring omethoate into a refined effects determination would lead to a significant increase in predicted risk to CRLF.

3.0 SPECIFIC COMMENTS

Table 3. The source for the foliar dissipation half-life in this table is cited as "Table 5." Table 5 has no information on the foliar dissipation half-life.

Figure 7. It is not clear why ingestion of prey is considered an important pathway of exposure for terrestrial CRLFs, but not aquatic CRLFs. The text should provide justification for this apparent discrepancy.

Page 46. The text in the Analysis Plan notes that the likelihood of effects to individual organisms were estimated using the probit dose-response slope. This refinement to the risk quotient approach is laudable, but only addresses the effects portion of the risk quotient. The exposure estimate remains conservative and deterministic. The unfortunate outcome is probabilistic statements of risk (e.g., 1 in 180 chance of individual mortality) that are very misleading. For a number of uses, the text indicates a 1 in 1 chance of individual mortality. This statement implies absolute certainty of 100% mortality. In the case of adult CRLFs, there were a number of highly conservative assumptions in deriving the exposure estimates, e.g., that 100% of their prey would be from treated fields even though frogs rarely leave riparian areas. Thus, the 1 in 1 chance of individual mortality statement dramatically overstates risk and, potentially worse, misleads the reader into believing that the overstated risk is absolutely certain. Although we support the use of probabilistic risk assessment for the CRLF effects determination for dimethoate, use of such an approach must address both exposure and effects when estimating risk. Such assessments are routinely conducted for aquatic and wildlife receptors. For example, risks to prey of aquatic CRLF could be estimated by integrating the species sensitivity distribution for aquatic prey species with the exposure distribution derived using refined exposure modeling or surface water monitoring data. For direct effects to adult CRLF, the exposure distribution derived from a probabilistic total daily intake model could be integrated with the dose-response distribution derived on the appropriate surrogate species.

Page 47. The text in the first paragraph implies that volatilization could be an important route of atmospheric transport. However, given the very low Henry's Law constant for dimethoate and its limited persistence in the environment, it is highly unlikely that dimethoate is subject to atmospheric transport followed by wet and dry deposition.

Page 48. Here and elsewhere, it is unclear why T-REX v.1.3.1, which was developed to estimate risk to birds and mammals, was used to estimate risk to CRLFs. T-HERPS v.1.0 was specifically developed to estimate risk to amphibians and reptiles. Although the effects determination mentions use of T-HERPS v.1.0 in several places, the majority of the text focuses on risk results using T-REX v.1.3.1. We would expect risk to CRLFs to be overestimated with T-REX versus T-HERPS v.1.0 because CRLFs are poikilotherms and thus have a lower rate of metabolism than do homeotherms such as birds and mammals. The T-REX v.1.3.1 materials should be removed from the effects determination because they give misleading results.

Although T-HERPS v.1.0 corrects the considerable inaccuracy in using T-REX v.1.3.1 to estimate risks to amphibians, T-HERPS v.1.0 is still markedly flawed. T-HERPS v.1.0, like T-REX v.1.3.1, applies upper bound Hoerger-Kenaga nomograms which are overly conservative, outdated and based on vegetation residues only. T-HERPS applies these vegetation nomograms to terrestrial arthropod feed items. We demonstrated in Section 2.5 that these nomograms are significantly higher (over two times higher, in fact) than the 95th percentile RUDs estimated with actual arthropod pesticide residue data (see Table 2-3). Recently a new version of T-REX was release (T-REX v.1.5; EPA, 2012). In this latest version of T-REX arthropod-specific pesticide RUD estimates have been included. The EPA collected and screened arthropod pesticide residue data from registrant submitted studies and the open literature. These data are in close agreement with data presented in Barber et al. (2005). Residue data from these studies were used in simulation to estimate a 90th percentile residue value on the 90th percentile of fields. This new residue value, an upper bound value of 94 mg a.i./kg ww per lb a.i./A, is about 30% lower than the previous T-REX insect RUD based on residues on broadleaf vegetation. Inclusion of this new RUD in T-HERPS would clearly reduce EPA's risk estimates for CRLF consuming terrestrial arthropods.

Further, T-HERPS v.1.0 does not account for the variability in caloric density of feed items (i.e., gross energy) or feed item assimilation efficiencies. This is an important consideration because some food items have considerably more energy than others and may be assimilated more efficiently. Therefore, fewer items may be consumed to meet the daily energy requirements. Food intake rates in T-HERPS v.1.0 are based on a food ingestion allometric equation for iguanid lizards. Instead, total daily intake modeling should be based on the free metabolic rate, and account for any variability in caloric content or assimilation by the frog.

Table 10. As per EPA's Overview document (EPA, 2004), LOCs for listed species were applied in the assessment of indirect effects to CRLF via reductions in prey and/or degradation of habitat. We believe that these LOCs are overly conservative for indirect effects to generalist listed species. When species are generalist predators, like CRLF, they can consume a variety of dietary items, and are not restricted to only one species. Similarly, with respect to habitat, CRLF do not depend on particular aquatic or terrestrial plant species, but rather on particular plant communities that can provide cover and appropriate microenvironments. Thus, effects to the most sensitive prey or plant species do not automatically equate to indirect effects to generalist listed species. As such, Cheminova does not support the use of the exceedingly conservative listed species LOCs for indirect effects to listed species when such species are generalists with respect to diet and habitat.

Table 11. Table 11 indicates that CA lettuce is the scenario used for endive, lettuce and Swiss chard. It is unclear whether CA lettuce is a CRLF-specific scenario or an existing California crop scenario. The text in Section 3.1.2.1 does not mention this scenario.

The California Forestry PRZM scenario was used to estimate EECs for the application of dimethoate to cottonwood grown for pulp. This is a highly conservative scenario as this PRZM scenario uses a 40% slope, a slope that is much higher than most agricultural scenarios. Hybrid

poplar plantations should be modeled as an agricultural scenario, such as the PRZM Christmas tree scenario (4% slope), rather than a forestry setting (AAFC, 2012; Segal Ranch, 2012; NRCS, 2012). The use of the PRZM Forestry scenario is exceptionally conservative and produces overestimates of EECs for the cottonwood grown for pulp use pattern.

Table 12. The input values used in the PRZM/EXAMS modeling are highly conservative, often without any justification. For example, the measured aerobic soil metabolism half-life is arbitrarily multiplied by a factor of three. Similarly, the measured aerobic and anaerobic aquatic metabolism half-lives are arbitrarily multiplied by a factor of two. An upper 90th percentile is used for the foliar degradation rate for all use scenarios even though crop-specific values are available for many of the uses considered in the effects determination (see Table 4 in EPA effects determination). Finally, the K_d value is the lowest non-sand value. It would be more accurate to use the K_d values that most closely match the soil type for the crop under consideration. Collectively, the use of numerous conservative input values leads to compounded conservatism in the PRZM/EXAMS outputs. This approach is reasonable for a screening-level assessment, but should be considerably refined for use scenarios that indicate a potential risk to CRLFs. No such refinements were conducted as part of EPA's effects determination.

Moreover, EPA should not have used a K_d value. Per EPA OPP/EFED guidance, "Binding is correlated with organic carbon content if the coefficient of variation (*i.e.*, mean divided by the standard deviation) for K_{OC} values is less than that for K_d values. Use of the mean K_d may not be appropriate for certain chemicals with binding not correlated with organic carbon content, such as those that are ionic at environmental pH values. In these cases, the model user should document the rationale for the selected model input values. Additional guidance may be sought at the EFED WQTT." For dimethoate, sorption is correlated with percent organic carbon content. However, EPA used the K_d instead of the K_{OC} in their modeling. This inaccurately limited the modeled portion of dimethoate that sorbed to soils with high organic matter. The coefficient of variation was calculated for both the K_d and K_{OC} based on the laboratory adsorption/desorption studies and the K_{OC} had the lower coefficient of variation (Table 3-1). Therefore, the average K_{OC} of 22.3 should have been used for exposure modeling.

Table 3-1 Coefficient of variation for K_d and K_{OC} values for dimethoate

Soil Type	*K_d (L/kg)*	*% OC*	*K_{OC}*	*Reference*
Sand	0.06	0.9	6.67	Hawkins, 1986 [MRID 00164959]
Sandy Silt Loam	0.3	1.5	20	
Clay Loam	0.57	3.5	16.3	
Sandy Loam	0.74	7.4	10	
Sandy/loam Sand	0.25	0.48	51.9	Schanné, 1992 [MRID 47477301]
Sandy Loam	0.33	2.05	16.3	
Silt Loam	0.42	1.42	29.6	
Loam/silt Loam	0.42	1.4	30.2	
Sand	0.34	1.5	22.5	
Loam	0.37	1.9	19.5	
Summary Statistics				
Mean	0.44	-	22.3	-
Standard Deviation	0.21	-	16.2	-
Coefficient of Variation	2.05	-	1.49	-

Page 63. The T-REX modeling approach discussed here indicates that a foliar half-life of 2.88 days was used. It is unclear why this value was selected. On Page 21 it is stated, with respect to dimethoate, that "the mean foliar dissipation half-life was 2.8 days, and the upper 90% confidence bound on the mean was 2.9 days." Moreover, CRLF consume primarily invertebrates, and not vegetation. Knäbe (2004a) reported a dimethoate half-life on crop-dwelling arthropods of 0.86 days. There are no data suggesting that the half-life of dimethoate on the terrestrial prey of CRLF is even close to 2.88 days.

Page 63. The T-REX modeling approach discussed here indicates that the Mineau scaling factor of 1.15 was used to adjust toxicity values for tested birds to the bird size ranges of interest. The use of this adjustment factor has no scientific support because: (1) the scaling factor was derived for birds and there is no evidence suggesting that the factor can be extrapolated to amphibians, and (2) for most of the pesticides included in the Mineau study published in 1996, there was no relationship between toxicity and bird body size, indicating that the factor has limited support even for birds. It has also been suggested by several other authors that the Mineau scaling factor for birds applied in T-REX has a weak scientific basis (Gagne, 2009; Trask et al., 2010). EPA Region 1 of the Superfund Program has stopped using the Mineau scaling factor in their contaminated site assessments (Trask et al., 2010).

Page 65. Here it is stated that for modeling purposes the prey of the surrogate bird species is assumed to be small insects. Notably, the Hoerger-Kenaga nomogram value of 135 mg/kg per lb a.i./A in applied to small insects in T-REX v.1.3.1 is more than twice the estimated 95th percentile of measured normalized pesticide residues on crop dwelling arthropods (66.6 mg/kg per lb a.i./A) (Table 2-2 and Table 2-3; Knäbe, 2004a,b; Barber et al., 2005) (see Section 2.5 above for a discussion of why 95th percentiles should be used instead of maximum RUD values). There is no evidence to suggest that CRLF would ever be an obligate predator of terrestrial arthropods. In fact, available data suggest that CRLF are opportunistic predators feeding primarily on aquatic and terrestrial invertebrates, but also on frogs and occasionally mice (Hayes and Tennant, 1985). The supposition that CRLF consume only terrestrial arthropods leads to a risk characterization for only a worst-case, and in all likelihood, a fictitious exposure scenario. The effects determination should account for the variability observed in the CRLF diet.

Page 66. The results of the terrestrial CRLF exposure modeling results are provided here. However, the results are only provided for the T-REX modeling effort, which is an inappropriate model for the CRLF (see page 48 comment above). Results from the more appropriate T-HERPS modeling effort should be presented here.

Table 17. The results for the dose-based EECs for CRLFs are based on the assumption that the CRLF consumes its entire diet from treated fields, even though CRLFs are expected to forage almost exclusively in riparian areas.

Page 73. The text indicates that 48-hour EC50s for invertebrates range from 0.043 to 5.04 mg/L. Based on acceptable and supplemental studies that were evaluated by Intrinsik, 48 and 96-hour LC/EC50s for invertebrates ranged from 0.249 to 6.41 mg/L for dimethoate.

Page 77. The chronic NOEL of 0.1 mg/kg bw/d used in estimating risks to small mammal prey "was established based on observed decrease in pup deaths." How can a decrease in pup deaths be considered an adverse effect? More importantly, the chronic NOEL of 0.1 mg/kg bw/d was based on a flawed analysis of the data from a developmental neurotoxicity study (Myers, 2003 [MRID 45529703]) as has been noted in several peer-reviewed publications (Reiss and Gaylor, 2005; DeSesso et al., 2009). In Myers (2003) the author notes that at the 0.5 mg/kg bw/d treatment level pup survival was within the normal range (i.e., within the range of control data from studies between October 2000 and September 2002 at the laboratory). The NOEL of 0.1 mg/kg bw was never reported by the study author, and also does not appear to be based on a statistically significant test result, but on the basis of one litter being lost at the 0.5 mg/kg bw/d treatment level. A similar study conducted by the same laboratory, Myers (2001), demonstrates a NOEL for pup mortality (up to post natal day 11) of ≥ 3 mg/kg bw/d, which supports our conclusion that the NOEL of 0.1 mg/kg bw/d is erroneous. A meta-analysis of available rat developmental toxicity studies for dimethoate indicated a benchmark dose that would cause 1% mortality (BMD1) in one-day-old pups (the most sensitive endpoint for mortality) of 3.9 mg/kg bw/d. The corresponding 95% lower bound on the BMD1 (i.e., the BMDL1) was 2.4 mg/kg bw/d (Hauswirth et al., 2005). One percent mortality is likely an ecologically insignificant effect (see Appendix F) and would have negligible impact on prey availability for terrestrial-phase CRLFs, particularly given that most mammalian prey for the frogs would come from riparian areas rather than treated fields. Further, the oral gavage dosing used in the developmental neurotoxicity study is not relevant to how small mammals forage in the field. In the field, small mammals feed throughout the day. Thus, their exposure would be to a series of small doses in a food matrix, some of which would be metabolized between foraging events. This is not the case with the unrealistic oral gavage method of dosing, resulting in an overestimate of the toxicity of dimethoate to small mammals. The more relevant studies from an ecological perspective would be to use the rodent multiple-generation dietary reproduction studies that have been conducted with dimethoate. Clearly, EPA is being hyperconservative in using a chronic NOEL of 0.1 mg/kg bw/d as the basis for assessing risk due to reduction in availability of mammalian prey for terrestrial CRLFs. The more appropriate metric would be the chronic NOEL of 1.2 mg/kg bw/d from the Brooker et al. (1992) two-generation rat study (See Table 2-1). That said, as noted in Section 2.5 of this report, Cheminova does not support the assessment of direct effects to mammals.

Page 82. On page 82, EPA states, "No data are available to assess the risks of dimethoate to vascular aquatic plants. Given the lack of data, RQ values could not be derived to represent the risks of dimethoate exposure to vascular aquatic plants." On behalf of the registrant, Porch et al. (2009) recently conducted a 7-day static renewal toxicity test on duckweed (*Lemna gibba*) exposed to dimethoate. The results for the technical product indicated EC50 values for frond number and biomass that were >41.5 mg a.i./L, the highest concentration treatment included in the test. The same results were observed with the formulation product (Dimethoate 400). Given

the concentrations observed in monitoring studies and predicted with PRZM/EXAMS, it is clear that dimethoate poses no risk to aquatic vascular plants.

Page 84. Again, only T-REX risk estimates are provided here, rather than the results from the more appropriate T-HERPS model.

Table 34. Finally, the risk outputs from T-HERPS are presented to the reader. Again, there is no reason to include the T-REX results in the CRLF effects determination for dimethoate. As expected, the RQs are much lower than those from T-REX, generally by several orders of magnitude depending on the prey item and size of the CRLF assumed. We would expect that RQs would be even lower if more accurate and appropriate residue data were used and if the variability in the CRLF diet were accounted for.

Table 35. It is not clear why diets of "Small Herbivore Mammals", "Small Insectivore Mammals" and "Small Terrestrial-phase Amphibians" were selected for a 37 g CRLF. Available data suggests that a CRLF of this size is unlikely to consume prey > 20 mm (Hayes and Tennant, 1985). Further, there is no description of the ingestion rates of these prey. The T-HERPS v.1.0 user manual suggests that the consumption of an entire small mammal is modeled, and that herbivorous small mammals are assumed to eat exclusively short grass, while insectivorous mammals are assumed to eat exclusively large insects. Small herbivorous mammals do not only consume short grass. The California mouse (*Peromyscus californicus*), a prey of CRLF (Hayes and Tennant, 1985), consumes a varied diet consisting predominantly of seeds (Merritt, 1974). Residues on seeds are considerably lower, and would certainly lead to lower and more realistic estimates of exposure. T-HERPS assumes that a small mammal has reached its full total daily intake when consumed by the CRLF, an assumption that is very conservative (EPA, 2008b). Further, T-HERPS does not account for rates of metabolism and excretion of dimethoate. Data are available that suggest that ≥59% of dimethoate administered orally is excreted by rats within 6 hours (Kirkpatrick et al., 1995), suggesting that a TDI estimate for mice could considerably over estimate residues in these prey. Although it is possible that CRLF consume small insectivorous mammals, there are no data to support this claim.

Page 95. The approach of using drift estimates to establish distances from edge of field where LOCs are not exceeded is misleading, in that it does not account for any intra-field and off-field variability in residues (i.e., upper bound RUDs are still applied). Further, it does not account for spatial-averaging that would occur within the foraging range of both CRLF and their prey.

Page 96. The likelihood of individual mortality estimates derived from the dose-based CRLF risk estimates were based on a "probit dose-response of 2.54." It is not clear whether this is a typical probit slope value for birds or a conservative one. Although values are available for other bird species, they are not discussed in the text or provided in tables. The text indicates that the probit slope value of 2.54 comes from a study by Schafer et al. (1973). This study is of dubious quality as it involved wild caught birds and very low numbers of birds per treatment level. Schafer et al (1973) was rated as unacceptable based on Cheminova's study evaluation criteria.

Cheminova has recommended that Zok (2001 [MRID 47769705]) be used to assess acute risks to birds (See Table 2-1).

"...if a medium sized CRLF consumes a mouse that was present on a dimethoate treatment site, it would be expected to die due to dimethoate exposure." Again, to our knowledge there is no data supporting the assumption that a medium sized (37 g) CRLF would be capable of consuming a mouse. Notably, the T-HERPS v.1.0 small herbivorous mammal weighs 35 g. The model assumption is that a CRLF is consuming a mammal that is its same size. This is unrealistic. Hayes and Tennant (1985) report that only large CRLF (snout to vent length > 80 mm) consumed prey > 20 mm. Adult CRLF (snout to vent length > 100 mm) body weights reportedly range from 74 to 247 g (Scott and Rathbun, 2001), suggesting that it is unlikely that a 37 g CRLF would eat terrestrial vertebrate prey.

Page 97. As with the dose-based probit slope of 2.54, the dietary-based probit slope of 10.1 was not discussed as to its reliability or how it compared to values derived for other bird species.

Page 112. The case for effects to CRLFs as a result of effects to terrestrial habitat is very weak. One study is cited, Hanley and Whiting (2004) as the basis for assessing effects to terrestrial plants. In this study, an application of 0.02 lb ai/A caused a "decreased biomass" to two species of dicots. No indication is provided in the text as to whether there was a significant rate-response relationship or what magnitude of decreased biomass was experienced by the plants. The effects determination also ignores the obvious that dimethoate is routinely applied to a wide variety of crops at rates that are orders of magnitude higher than 0.02 lb ai/A. If adverse impacts to crops were occurring as a result of dimethoate application at the label application rates, farmers would not use the product. Two recent tier II terrestrial plant studies by Porch et al. (2011a,b) that were submitted to EPA back this point up. Porch et al. (2011a,b) evaluated the application of technical dimethoate at rates from 0.25 to 1.5 lb ai/acre to four monocot and six dicot crop species. No significant adverse effects were observed at the highest application rate for 21-day seedling emergence, survival, height, dry weight or condition of any the 10 terrestrial plant species tested. The application rate in the Porch et al (2011a,b) studies is 75-fold greater than the rate used by EPA to estimate impacts to CRLF terrestrial habitat. Thus, it seems highly unlikely that terrestrial plants are experiencing adverse impacts at anywhere close to those predicted by EPA in their effects determination.

Table 46. Downstream dilution factors to reduce RQs to levels equal to the LOC are provided in this table for agricultural lands (dilution factor = 27.3) and orchard, vineyard and forests (dilution factor = 37.3). However, no information was provided in the text detailing how the dilution factors were calculated. It seems obvious that one dilution factor for each of the use groups cannot possibly be applicable to all aquatic systems in California. Stream flow rates near agricultural fields will vary from seasonally dry (i.e., zero) to very high for large rivers during spring. Similarly, flow rates from fields and distances to streams will have a large impact on the dimethoate flow rates into aquatic systems. As the dilution factors are used to estimate the extent of the action area, this is a serious deficiency in the effects determination.

Table 47. As with the downstream dilution factors, the procedures used to calculate "downstream distance added" to include in the action area beyond the initial area of concern are not described. This is unacceptable scientific practice for such an important piece of information.

Table 48. The spray drift distances for not exceeding the LOC are presented here for agricultural lands (all non-woody crops) and orchards, vineyards and forests. Although the text notes that AgDISP was used to derive the distances, no other information is provided in the text. For example, which non-woody and woody crops were used to calculate the spray drift distances? Was aerial or ground application assumed? What size were the droplets? As the RQs are quite variable between crops, it would make much more sense to use crop-specific spray drift distances. This would have the effect of likely reducing the size of the action area. Further, the spray drift distances of over 10,500 feet for non-woody and woody crops are orders of magnitude beyond the distance for which AgDISP is considered reliable (300 m; see additional comments on the use of AgDISP above). Clearly, the calculated spray drift distances are highly unreliable. Yet these distances are principal in estimating the action area.

Page 124. The estimated exposures in aquatic habitat due to precipitation grossly exceed what likely occurs in the real world. First, the maximum concentration measured in precipitation was used in all calculations. Second, the calculations assume that, "the entire mass of dimethoate contained in the precipitation runs off from the [10 ha] field to the [1 ha] pond or is deposited directly into the pond." Third, "there is no degradation of dimethoate between the time it leaves the air and the time it reaches the pond." It is inconceivable that more than a small fraction of the rain contacting a 10 ha field would reach a one hectare pond because much of the water would absorb to plants and soil, degrade, evaporate to air, or leach to groundwater. In the end, these extreme assumptions are used to predict concentrations of dimethoate in aquatic habitat as a result of deposition in rain (Table 52 in the effects determination). However, no context is provided as to what these extreme exposure estimates could mean in terms of risk to CRLF. What was the point of this exercise?

4.0 CONCLUSIONS AND RECOMMENDATIONS

The CRLF effects determination for dimethoate makes the case that the pesticide potentially poses a risk to CRLFs either directly or indirectly via effects to their prey and habitat. This is not an uncommon outcome for screening-level assessments that rely on highly conservative methods and assumptions, as was the case with EPA's dimethoate effects determination. The normal practice in risk assessment is to then conduct more refined analyses to determine the likelihood, magnitude and ecological consequences of effects for those use scenarios that passed through the initial screen. In fact, the EPA Scientific Advisory Panel endorsed such a tiered approach for ecological risk assessments of pesticides conducted by EFED (SAP, 2000). Clearly, refined analyses are required for the CRLF effects determination to better understand potential risks of dimethoate and to then enact risk mitigation measures that are protective of CRLFs while also not unduly affecting agricultural stakeholders. Such refined analyses were not part of EPA's CRLF effects determination for dimethoate.

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APPENDIX A
DATA QUALITY EVALUATIONS OF AMPHIBIAN TOXICITY STUDIES

Acceptable Studies

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Schneider S., T.Z. Kendall, S.P. Gallagher, and H.O. Krueger. 2011. Dimethoate Technical: A 96 Hour Flow-through Acute Toxicity Test with Tadpoles of the African Clawed Frog (*Xenopus laevis*). Wildlife International, LTD. Project No. 232A-133. Final report dated Sept 26, 2011.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: African clawed frog (*Xenopus laevis*)

Endpoint(s): 96 h LC50 >98 mg/L (no effects seen at highest test concentration)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	**Y**	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	**Y**	OECD (203), ASTM
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	**n/a**	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	**Y**	Dimethoate technical (98.1 % w/w), received from Cheminova. Batch No. 60526-00, CAS No. 60-51-5.
5	**Were effects endpoints ecologically relevant?**	Y	Survival
6	**Were an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No mortality in controls
8	**Were the statistical procedures reported and appropriate?**	n/a	The NOEC was determined by visual interpretation because there were no mortalities at the highest concentrations.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Flow-through test and samples were measured throughout test duration
10	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, strain, sex, age, life stage, length, weight)?**	Y	Tadpoles (lifestage NF Stage 51), mean weight = 0.24 g, tadpoles were acclimated for 12 d under flow through prior to test
11	**Were appropriate test conditions (*e.g.*, pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y	12 h light:12 h dark, 1070-1958 lux, DO >86%, temperature 22-22.5°C, pH 8.2, specific conductance 346 µS/cm, hardness 142 mg/L as $CaCO_3$, alkalinity 177 mg/L as $CaCO_3$
12	**Was a dose/response relationship demonstrated?**	n/a	There were no mortalities in any of the treatment groups.
13	**Were the concentrations/doses provided?**	Y	Nominal:0, 6.3, 13, 35, 50, 100 mg/L Measured:0, 6, 11, 25, 51, 98 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Schneider, S.Z., T.Z. Kendall, and H.O. Krueger. 2012. Dimethoate: Amphibian Metamorphosis Assay. Wildlife International, Ltd., Easton, Maryland. Wildlife International Ltd. Project No. 232A-132A, Unpublished report. May 4, 2012.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: African clawed frog (*Xenopus laevis*)

Endpoint(s): 21 d NOEC (Development, growth, survival) ≥ 100 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD 231, OPPTS 890.1100
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate Technical, 98.1% purity, supplied by Cheminova, Batch No. 60526-00, CAS No. 60-51-5.
5	**Were effects endpoints ecologically relevant?**	Y	Survival, developmental stage, body weight, snout-to-vent length, hind limb length, and thryroid abnormalities.
6	**Was an appropriate exposure duration used and reported?**	Y	21 d
7	**Were appropriate controls included, reported and results adequate?**	Y	96.3% control survival
8	**Were the statistical procedures reported and appropriate?**	Y	OECD TG 231 and OPPTS 890-1100, Fishers Exact test for survival, Step-down Jonckheere-Terpstra trend test to examine trends, Dunnett's multiple comparison test to compare treatment groups, Shapiro-Wilk's test for normality, and Levene's test for homogeneity of variance.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Flow-through exposure, samples measured weekly. Mean measured concentrations 96-100% of nominal.
10	**Were the test species acclimated and characteristics of the test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Tadpoles from eggs spawned in same lab. Acclimated (16 d) then exposed at NF Stage 51 (16 d post-fertilization). 20 tadpoles per test chamber.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	12 h light: 12 h dark, 680 – 1660 lux lighting, 3 – 6 µg/L iodide concentration, 66 mL/min flow rate, 22 ± 1 °C, DO 6.4 mg/L (≥73% saturation), pH 8.0 – 8.3, 132 – 144 mg/L hardness as $CaCO_3$, 176-184 mg/L alkalinity as $CaCO_3$, 364-388 µS/cm specific conductance, 20 tadpoles per test chamber, fed 3 times daily and once of day 21.
12	**Was a dose/response relationship demonstrated?**	n/a	No significant effects on survival, weight, length, or developmental stage at highest concentration tested.
13	**Were the concentrations/doses provided?**	Y	< LOQ, 6.25, 25, and 100 mg/L (nominal) < LOQ, 6.0, 24, and 100 mg/L (measured)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Unacceptable studies

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Jayawardena, U.A., R.S. Rajakaruna, A.N. Navaratne, and P.H. Amerasinghe. 2010. Toxicity of agrochemicals to common hourglass tree frog (*Polypedates cruciger*) in acute and chronic exposure. Int J Agri Biol 12:641-648.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species tested: Hourglass tree frog (*Polypedates cruciger*)

Endpoint(s): 48 h LC50 (5-d post-hatch) 8.4 mg/L
120 d NOEC (survival) 0.75 mg/L (formulation, effect concentration in mg a.i./L could not be calculated because purity of formulation was not provided)
120 d LOEC (survival) 1 mg/L (formulation, effect concentration in mg a.i./L could not be calculated because purity of formulation was not provided)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	N	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y/N	Commercial formulation of Dimethoate (EC 40®), chemicals were received from the Pesticide Registrar's Office (Peradeniya, Sri Lanka)
5	**Were effects endpoints ecologically relevant?**	Y	LC50 and survival after chronic exposure
6	**Were an appropriate exposure duration used and reported?**	Y	48 h (acute), monitored until metamorphosis (chronic) – the exact number of days is not reported because it depended on how long it from the frog to reach metamorphosis (Control took ~120 days, estimation based on an TE50 (forelimb growth) of 57 days for controls.
7	**Were appropriate controls included, reported and results adequate?**	Y/N	Included controls in both tests, percent survival for acute test not reported. Chronic test had 95.5-97.5% survival.
8	**Were the statistical procedures reported and appropriate?**	Y	Probit analysis, chi-squared test and Anova

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y/N	Not reported for acute tests. For the chronic tests the medium was renewed weekly.
10	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, strain, sex, age, life stage, length, weight)?**	Y/N	Eggs collected from field and raised in lab. 5 days post hatch tadpoles (Gosner stage 25-26) were used in test.
11	**Were appropriate test conditions (*e.g.*, pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	N	Temperature 27-31°C, photoperiod of 12 h light:12 h dark. Other parameters not reported.
12	**Was a dose/response relationship demonstrated?**	Y	Dose-response relationship was demonstrated.
13	**Were the concentrations/doses provided?**	Y	Acute test: 25.0, 18.75, 15.00, 11.25, 9.5 mg/L Chronic test: 0.25, 0.5, 0.75, 1.0 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Khangarot, B.S., A. Sehgal, and M.K. Bhasin. 1985. Man and biosphere - Studies on the Sikkim Himalayas. Part 6: Toxicity of selected pesticides to frog tadpole *Rana hexadactyla* (Lesson). Acta Hydrochim Hydrobiol. 13(3):391-394. ECOTOX 11521.

Secondary reference:

Is the primary reference study a GLP study?: No

Species tested: Frog (*Rana hexadactyla*)

Endpoint(s): 24 h LC50 0.0078 mg/L (formulation), 0.0023 mg a.i./L
96 h LC50 0.0078 mg/L (formulation), 0.0023 mg a.i./L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	Y	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate (Rogor®) 30 EC, Rallis India Ltd..
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	12, 24, 48, 72, 96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No mortality in controls
8	**Were the statistical procedures reported and appropriate?**	N	LC50 calculated after Harris (method is unknown to us). Cumulative percentage mortality was plotted on a log-probit scale.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static renewal (24 h)
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Tadpoles, 20 mm long and 500 mg in wet weight, acclimation before testing (no length provided)
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	Temperature 16°C (air), 14°C (water), pH 6.2, alkalinity 25 ppm (as $CaCO_3$), acidity 20 ppm (as $CaCO_3$), total hardness 20 ppm (as $CaCO_3$), DO 6.5 ppm, parameters stayed constant over experiment (except DO ranged from 5.5-8 ppm)
12	**Was a dose/response relationship demonstrated?**	N	No raw data provided to verify dose response
13	**Were the concentrations/doses provided?**	N	Not reported, tested 7-10 concentrations

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Sayim, F. and U. Kaya. 2006. Effects of dimethoate on tree frog (*Hyla arborea*) larvae. Turk J Zool 30:261-266.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species tested: Tree Frog (*Hyla arborea*)

Endpoint(s): 96 h LC50 (21st stage) 20.3 mg/L
96 h LC50 (25th stage) 37.4 mg/L

GENERIC CRITERIA		Y/N	COMMENTS
1	**Single chemical exposure?**	N	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	N	Not specified
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	N	Few details provided.
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Source, purity not specified. Formulation grade (Korumagor 40 EC, Koruma Tarim A.S.)
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Were an appropriate exposure duration used and reported?**	Y	96 hours
7	**Were appropriate controls included, reported and results adequate?**	Y	There was no control mortality.
8	**Were the statistical procedures reported and appropriate?**	Y	Probit analysis

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Test concentrations were nominal only.
10	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, strain, sex, age, life stage, length, weight)?**	N	Test species were collected from a clean, permanent pond in Turkey. Information on acclimation not provided. Experiments were conducted on pre-feeding larvae in the 21st and 25th fully aquatic stage. Weight, length not reported.
11	**Were appropriate test conditions (*e.g.*, pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	N	Eggs were reared in the lab at 22°C ± 1°C with natural lighting. No other details provided. Raw data not provided.
12	**Was a dose/response relationship demonstrated?**	Y	Data not shown. LC10, LC50 and LC90 were reported with CI. Author state that mortality correlated with dimethoate concentration.
13	**Were the concentrations/doses provided?**	Y	21st Stage: 22, 26, 30, 34 and 38 mg/L 25th Stage: 16, 26, 36, 46, 56 mg/L Concentrations were calculated from the % a.i. of the formulation.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

APPENDIX B
DATA QUALITY EVALUATIONS OF FRESHWATER FISH TOXICITY STUDIES

Acceptable Studies

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Armstrong, K., C.Y. Caley, B.D. Cameron, B. Knight, and B.E. Hall. 1992. Prolonged Toxicity Test (LC50) of the EC Formulation of Dimethoate Containing 400 g/L to Rainbow Trout (21 d, Semi Static). Inverest Research International, Scotland. Report No. 6914. CHA Doc. No. 119 DMT.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species Tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 21 d LC50 22.7 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD 204
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dark blue liquid, 38.9%, EC formulation 400 g/L; Batch No. 5905657, Shell Agrar GmBh and Company KG, Germany
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	21 d
7	**Were appropriate controls included, reported and results adequate?**	Y	No control mortality
8	**Were the statistical procedures reported and appropriate?**	Y	Maximum likelihood estimation to the probit model.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static renewal, measured throughout test
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	4-6 cm in length; acclimation to laboratory conditions for at least 14 d prior to test.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	10 fish/23 L, 0.84 g fish/L, fed daily during testing, temperature 11.3-12.5°C, 16 h light: 8 h dark, light intensity 550 lux, pH 6.9-8.1, DO 78-92%; 0.17-0.21 mS.
12	**Was a dose/response relationship demonstrated?**	Y	Raw data provided. Dose-response relationship demonstrated.
13	**Were the concentrations/doses provided?**	Y	Six test concentrations (0.2, 0.6, 2, 6, 20 and 60 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE () SUPPLEMENTAL () UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Brougher, D.S., T.Z. Kendall, S.P. Gallagher, and H.O. Krueger. 2012a. Dimethoate: A 96-h Static-renewal Acute Toxicity Test with the Rainbow Trout (*Oncorhynchus mykiss*). Wildlife International Ltd., Easton MD. Wildlife International Ltd. Project No. 232A-136A.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 48 h LC50 24 mg/L
72 h LC50 24 mg/L
96 h LC50 24 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD Guideline 203, OPPTS 850.1075, and ASTM Standard E729-96
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate technical, batch number 60526-00, CAS No. 60-51-5, 98.1% active ingredient, supplied by Cheminova
5	**Were effects endpoints ecologically relevant?**	Y	Survival
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	Dilution water control mortality was 0%.
8	**Were the statistical procedures reported and appropriate?**	Y	48, 72 and 96 h LC50 values calculated by nonlinear interpolation and 95% confidence intervals determined by binomial probability.

CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static-renewal at 48 h. Test concentrations confirmed by HPLC in newly prepared solutions at beginning of test and at 48 h renewal, and in old solutions at 48 and 96 h. Measured concentrations ranged from 84 to 99.8% of nominal and endpoints were calculated based on mean measured concentrations.
10	**Were the test species acclimated and characteristics of the test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Juveniles received from Thomas Fish Company, Anderson CA. Held for a minimum of 14 d in same water as used for test. At the end of the test the average total length of fish in the control group was 4.2 cm and the average wet weight was 0.65 g.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	Instantaneous loading (total wet weight of fish per litre of test water) for controls was 0.22 g fish/L, 16 h light: 8 h dark, DO 7.9-10.7 m/gL, pH 8.4-9.0, light intensity 438 lux, temperature 11.1-12.5°C, hardness at test initiation 150 mg/L as $CaCO_3$
12	**Was a dose/response relationship demonstrated?**	Y	Dose-response relationship demonstrated.
13	**Were the concentrations/doses provided?**	Y	<LOQ (0.600), 1.2 mg/L, 2.3 mg/L, 4.7 mg/L, 9.5 mg/L, 19 mg/L, 38 mg/L (mean measured concentrations)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Brougher, D.S., T.Z. Kendall, S.P. Gallagher, and H.O. Krueger. 2012c. Dimethoate: A 96-hour Static-renewal Acute Toxicity Test with the Bluegill (*Lepomis macrochirus*). Wildlife International Ltd., Easton, MD. Wildlife International Ltd. Project No. 232A-135.

Secondary reference: *n/a*

Is the primary reference study a GLP study?: Yes

Species tested: Bluegill (*Lepomis macrochirus*)

Endpoint(s): 96 h LC50 31 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD Guideline 203, OPPTS 850.1075, ASTM Standard E729-96.
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate technical, Batch No. 60526-00, CAS No. 60-51-5, 98.1% active ingredient, supplied by Cheminova
5	**Were effects endpoints ecologically relevant?**	Y	Survival
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	Dilution water control included and mortality was 0%.
8	**Were the statistical procedures reported and appropriate?**	Y	96 h LC50 calculated by Probit analysis.

CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS

9	**Were the test concentrations or doses measured / maintained?**	Y	Static-renewal at 48 h, mean measured concentrations determined by HPLC at beginning of test, before and after renewal, and at the end of the test. Measured concentrations ranged from 94 to 113% of nominal, and endpoints calcuated based on mean measured test concentrations.
10	**Were the test species acclimated and characteristics of the test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Juvenile bluegills obtained from Osage Catfisheries, Osage Beach, MO, held for a minimum of 14 d prior to test in same water as that used in test. Average total length and wet weight of control fish measured at end of test was 2.7 cm and 0.27 g, respectively.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	Loading rate of control fish 0.18 g fish/L, 16 h light: 8 h dark, pH 8.3-8.7, light intensity 668 lux, temperature 21.3-21.9°C, DO 6.7-9.0, hardness 148 mg/L as $CaCO_3$
12	**Was a dose/response relationship demonstrated?**	Y	Dose-response relationship demonstrated
13	**Were the concentrations/doses provided?**	Y	<LOQ, 3.8, 7.5, 15, 29, 59 and 125 mg/L (mean measured test concentrations)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Caley, C.Y., B.D. Cameron, B. Knight, K. Armstrong, and B.E. Hall. 1992a. Determination of Acute Toxicity (LC50) of EC Formulation of Dimethoate Containing 400 g/L to Bluegill Sunfish (96 h, semi static). Inverest Research International, Scotland. Report No. 6944. CHA Doc. No. 121 DMT.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species Tested: Bluegill sunfish (*Lepomis macrochirus*)

Endpoint(s): 96 h LC50 44 mg/L (17.1 mg a.i./L)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD 203
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dark blue liquid, 38.9%, EC formulation 400 g/L; Batch No. 5905657, Shell Agrar GmBh and Company KG, Germany
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No control mortality
8	**Were the statistical procedures reported and appropriate?**	Y	Maximum likelihood estimation to the probit model.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static renewal, measured concentrations
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	3-6 cm in length; acclimation to laboratory conditions for at least 14 d prior to test
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	10 fish/20 L; 0.844 g fish/L, not fed 24 hours prior to testing and during testing, temperature 20.2-20.9°C, 16 h light:8 h dark, 550 lux, pH 7.5-7.6, DO 80-87%, 0.16-0.21 mS.
12	**Was a dose/response relationship demonstrated?**	Y	Raw data provided. Dose-response relationship demonstrated.
13	**Were the concentrations/doses provided?**	Y	Five test concentrations (6.25, 12.5, 25, 50, 100 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE () SUPPLEMENTAL () UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Caley, C.Y., B.D. Cameron, B. Knight, and B.E. Hall. 1992b. EC Formulation of Dimethoate Containing 400 g/L: Determination of Acute Toxicity (LC50) to Rainbow Trout (96 h, Semi Static). Inverest Research International, Scotland. Report No. 6912. CHA Doc. No. 120 DMT.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species Tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 96 h LC50 61.3 mg/L (23.8 mg a.i./L)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD 203
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dark blue liquid, 38.9%, EC formulation 400 g/L; Batch No. 5905657, Shell Agrar GmBh and Company KG, Germany
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No control mortality
8	**Were the statistical procedures reported and appropriate?**	Y	Maximum likelihood estimation to the probit model.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static renewal, measured concentrations
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	4-6 cm in length; acclimation to laboratory conditions for at least 14 d prior to test
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	10 fish/20L, 0.765g fish/L, not fed 24 h prior to testing and during testing, temperature 11-11.9°C, 16 h light: 8 h dark, 550 lux, pH 7.2-7.6, DO 80-90%, 0.15-0.16 mS.
12	**Was a dose/response relationship demonstrated?**	Y	Raw data provided. Dose-response relationship demonstrated.
13	**Were the concentrations/doses provided?**	Y	Five test concentrations (6.25, 12.5, 25, 50, 100 mg/L)

CRITERIA FOR A SUPPLEMENTARY STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE () SUPPLEMENTARY () UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Hamitou, M. 2009b. Dimethoate 400 g/L EC (CHA 3621-04): Acute Toxicity to Bluegill Sunfish (*Lepomis macrochirus*) Under Static Conditions. Springborn Smither Laboratories (Europe) Study No. 1005.028.100. CHA Doc. No. 764 DMT.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Bluegill sunfish (*Lepomis macrochirus*)

Endpoint(s): 96 h LC50 >100 mg/L (>37.7 mg a.i./L)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD #203 (1992)
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate EC (37.7 % w/w.) was received from Cheminova A/S, Denmark (Jan. 2009), batch 965-VN-83
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Were an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No control mortality
8	**Were the statistical procedures reported and appropriate?**	n/a	LC50 was empirically estimated, there was no effects seen at the highest concentration tested

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static test, concentrations were measured at 0 and 96 h.
10	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, strain, sex, age, life stage, length, weight)?**	Y	Fish were obtained from Osage Catfisheries, USA, they were 0.24 g and 27 mm, fish were acclimated for 14 d
11	**Were appropriate test conditions (*e.g.*, pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y	Temperature 22.9°C, 280-317 lux, 16 h light: 8 h dark, DO >60%, pH 6.72-7.55, conductivity 372 µS/cm, loading density 0.17 g/L test solution.
12	**Was a dose/response relationship demonstrated?**	n/a	No effect seen at highest concentration tested
13	**Were the concentrations/doses provided?**	Y	Hour 0: 6.27, 12.6, 25, 49, 98 mg test item/L (measured, not a.i.) Hour 96: 5.91, 12.2, 24, 48, 97 mg test item/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Strawn, T.L. and M. Muckerman. 1994. Early Life-stage Toxicity of Dimethoate to the Rainbow Trout (*Oncorhynchus mykiss*) Under Flow-through Conditions. ABC Laboratories, Inc. Columbia, Missouri, Report No. 40864. MRID 43106301, MRID 43106302 and MRID 43106303.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species Tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 96 d NOEC (60 d post hatch growth) 0.43 mg/L
96 d LOEC (60 d post hatch growth) 0.84 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	ABC Protocol No. FIFRA 72-4 RBT
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	White chunks, 99.1%, Batch 20522-00, Cheminova Agro A/S.
5	**Were effects endpoints ecologically relevant?**	Y	NOEC, LOEC (egg hatchability, survival and growth)
6	**Was an appropriate exposure duration used and reported?**	Y	96 d (60 d post hatch)
7	**Were appropriate controls included, reported and results adequate?**	Y	Control mortality 96.7%.
8	**Were the statistical procedures reported and appropriate?**	Y	One-tailed Fisher's test and chi-square (hatchability and survival); One-way analysis of variance ANOVA (growth).

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Flow-through, concentrations measured throughout study.
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Newly fertized eggs (< 4 h post fertilization), acclimated for 2.5 h.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	30 eggs/concentration, 4 replicates, DO 7.9 to 10 mg/L, temperature 8.6 to 10.8°C, pH 7.85 to 8.16, 158 to 382 µS, alkalinity140-176 mg/L, hardness 140-166 mg/L, 16 h light: 8 h dark.
12	**Was a dose/response relationship demonstrated?**	Y	Raw data available, dose-response demonstrated.
13	**Were the concentrations/doses provided?**	Y	Five test concentrations (0.38, 0.75, 1.5, 3, and 6 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE () SUPPLEMENTAL () UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Wüthrich, V. 1990a. Dimethoate: 21-Day Prolonged Toxicity Study in the Rainbow Trout Under Flow-Through Conditions (Amendment 1 included). RCC Umweltchemie AG Study No.: 264475. Unpublished report. CHA Doc. No.: 95 DMT.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species Tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 21 d NOEC (growth) 0.4 mg/L
21 d LC50 8.875 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	OECD 204
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	99% purity, batch 611A; white greyish-yellow solid; provided by the Dimethoate Task Force from the Federal Republic of Germany
5	**Were effects endpoints ecologically relevant?**	Y	LC50, NOEC
6	**Was an appropriate exposure duration used and reported?**	Y	21 d
7	**Were appropriate controls included, reported and results adequate?**	Y	No mortality in controls
8	**Were the statistical procedures reported and appropriate?**	Y	Logit model

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Flow-through, measured
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Acclimation for 19 d; 2.35 g on average; 62 mm on average;
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	10 trout/treatment, pH 8-8.4, DO 9.4 to 10.9 mg/L, temperature 14-16°C, food provided daily, 12 h light/12 h dark.
12	**Was a dose/response relationship demonstrated?**	Y	Dose-response relationship observed.
13	**Were the concentrations/doses provided?**	Y	Five concentrations (0.08, 0.4, 2, 10 and 50 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE () SUPPLEMENTAL () UNACCEPTABLE

Comments:

Supplemental Studies

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): EPA (United States Environmental Protection Agency). 1977. Biological Report of Analysis. Static Jar Test 1069. Test method TSD 1.206. Performed by the Agricultural Research Center, USDA, Beltsville, MD.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 96 h LC50 7.5 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y	[72-1] Freshwater Fish Acute-warm and coldwater species with TGAI or TEP (FIFRA 158.490); TSD 1.206
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	95%, Cygon Technical; Montedison S.P.E., Milan, Italy.
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	24, 48 and 96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	Controls included, 0% mortality.
8	**Were the statistical procedures reported and appropriate?**	Y	Chi-square

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Static, not measured.
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y/N	Acclimation period not provided; weight 0.66-0.77 g; length 4.15-4.4 cm
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	N	Number of fish/test concentration reported; other parameters not reported
12	**Was a dose/response relationship demonstrated?**	Y	Raw data available, dose-response demonstrated.
13	**Were the concentrations/doses provided?**	Y	Five to eight test concentrations (2.4, 3.7, 5.6, 8.7, 14, 21, 32 and 49 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE (X) SUPPLEMENTAL () UNACCEPTABLE

Comments:

Unacceptable Studies

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Aboul-Ela, I.A. and M.T. Khalil. 1987. The acute toxicity of three pesticides on organisms of different trophic levels as parameters of pollution in Lake Wadi El Rayan. Ei Fayoum. Egypt Proc Zool Soc AR Egypt 13:31-26.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Cladoceran (*Daphnia longispina*), copepod (*Cyclops strenuus*), amphipod (*gammarus pulex*), snails (*Biomphalaria alexandrina* and *Bulinus truncatus*) and fish (*Tilapia niloticam* and mullet fry).

Endpoint(s): 96 h LC50 0.0052 mg/L (*Tilapia niloticam*)
96 h LC50 0.0023 mg/L (mullet fry)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	N	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Not reported
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	N	Not reported
8	**Were the statistical procedures reported and appropriate?**	N	Semi-logarithmic graph

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Static
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Cladoceran (*Daphnia longispina*) (average length 1.3 mm), copepod (*Cyclops strenuus*) (average length 1.1 mm), amphipod (*Gammarus pulex*) (average length 0.90 cm), snails (*Biomphalaria alexandrina* (average MD was 11.6 ± 0.33 mm) and *Bulinus truncatus* (average shell length 10.8 ± 0.4 mm)) and fish (*Tilapia niloticam* (average length 15.3 ± 2.3 cm) and mullet fry (average length 5.2 ±1.2 cm)). Acclimated for 5 days.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y/N	Photoperiod 14 h light:10 h dark, temperature 27 ± 2°C, 10-20 animals/test concentrations, 2 replicates
12	**Was a dose/response relationship demonstrated?**	N	Not reported
13	**Were the concentrations/doses provided?**	N	Not reported

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Anees, M.A. 1975. Acute toxicity of four organophosphorus insecticides to a freshwater teleost *Channa punctatus* (Bloch). Pakistan J Zool 7(2):135-141.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species tested: *Channa punctatus*

Endpoint(s): 96 h LC50 20.5 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	N	Followed methods by Doudoroff et al 1951.
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y/N	Pesticides were obtained from Punjab Plant Protection Institute, Lahore. Purity not reported
5	**Were effects endpoints ecologically relevant?**	Y	LC50 (TLM)
6	**Were an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y/N	Used controls, but survival not reported
8	**Were the statistical procedures reported and appropriate?**	N	Results plotted on log dose paper, straight line graphical interpolation

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Not reported
10	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, strain, sex, age, life stage, length, weight)?**	Y	Fish were collected from fresh water bodies (Khori Fish sanctuary, Lalyani, Mehta Suja, Malam Kalan). Fish weight ~60 g, length~15 cm. Fish were acclimated to lab conditions for at least four days,
11	**Were appropriate test conditions (*e.g.*, pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y/N	Temperature 24.2°C (Malathion) and 25.3°C (Dimethoate), pH 7.2 ±0.1, total hardness 160 mg/L (as $CaCO_3$), DO 7 mg/L
12	**Was a dose/response relationship demonstrated?**	Y	Provide 24-96 hour TLM values, as well as visual graphs of data, dose-response demonstrated
13	**Were the concentrations/doses provided?**	Y	0.01, 0.1, 1.0, 10 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Begum, G., S. Vijayaraghavan, P.N. Sarma, and S. Husain. 1994. Study of dimethoate bioaccumulation in liver and muscle tissues of *Clarias batrachus* and its elimination following cessation of exposure. Pest. Sci. 40:201-205.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Walking catfish (*Clarias batrachus*)

Endpoint(s): *96 h LC50 50 mg/L*

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	N	Insufficient details provided.
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Technical (>94%); M/s Rallies India Ltd.
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y/N	Controls used. Control mortality not reported.
8	**Were the statistical procedures reported and appropriate?**	Y	Probit method and graphical plot.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Static
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Acclimated to laboratory conditions for 2 weeks, 38 ± 2 g and 20 ± 2 cm length.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	N	Six fish/test concentration, six replicates, not fed 24 hours prior to and during testing.
12	**Was a dose/response relationship demonstrated?**	N	Raw data not provided
13	**Were the concentrations/doses provided?**	N	Six concentrations, concentrations not provided.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Canton, J.H., R.C.C. Wegman, A. Van Oers, A.H.M. Tammer, E.A.M. Mathijssen-Spiekman, and H.H. Van den Broek. 1980. Milieutoxicologisch Onderzoek met Dimethoaat en Omethoaat. Intern Rapport 121/80 CBS VI/RA. RIJKS Instituut voor de Volkgezondheid, Bilthoven. [Dutch]. English title: Ecotoxicological Studies with Dimethoate and Omethoate.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Water flea (*Daphnia magna*); green algae (*Chlorella pyrenoidosa*), guppy (*Poecilia reticulata*), Japanese killifish (*Oryzias latipes*), rainbow trout (*Oncorhynchus mykiss*).

Endpoint(s): 24 h LC50 620 mg/L (*Poecilia reticulata*)
48 h LC50 560 mg/L (*Poecilia reticulata*)
72 h LC50 560 mg/L (*Poecilia reticulata*)
96 h LC50 560 mg/L (*Poecilia reticulata*)
24 h EC50 (immobility) 185 mg/L (*Oryzias latipes*)
48 h EC50 (immobility) 128 mg/L (*Oryzias latipes*)
72 h EC50 (immobility) 118 mg/L (*Oryzias latipes*)
96 h EC50 (immobility) 108 mg/L (*Oryzias latipes*)
24 h LC50 133 mg/L (*Oncorhynchus mykiss*)
48 h LC50 10 mg/L (*Oncorhynchus mykiss*)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y/N	Dutch Normalisation Institute
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	Y	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate (98%) obtained from Luxan
5	**Were effects endpoints ecologically relevant?**	Y	EC50, LC25, LC50, NOEC
6	**Was an appropriate exposure duration used and reported?**	Y	Species specific durations provided in a table.
7	**Were appropriate controls included, reported and results adequate?**	N	Control mortality not reported.
8	**Were the statistical procedures reported and appropriate?**	N	Statistics not reported.

CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS

9	**Were the test concentrations or doses measured / maintained?**	Y	Stability study performed separately. Analyses of high and low concentrations in *Daphnia* and *Poecilia* tests.
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y/N	10 fish per group (*P. reticulata, O. latipes)*, 5 fish per group (*O. mykiss*). 3-4 wk of age (*P. reticulata*), 4-5 wk of age (*O. latipes*), 6 mo of age (*O. mykiss*). No acclimation procedure reported.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y/N	Temperature 23 ±2°C (*P. reticulata, O. latipes*), 12 ±1°C (*O. mykiss*). 10 fish/L (*P. reticulata, O. latipes*), 5 fish/10L (*O. mykiss*). 14 h light: 10 h dark. Hardness and pH reported on media, but no water quality from tests. Author's state that pH and DO were measured during tests and no influence was observed during experiments.
12	**Was a dose/response relationship demonstrated?**	N	No raw data reported to verify dose-response relationship.
13	**Were the concentrations/doses provided?**	N	Test concentrations not reported.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Gupta, P.K., V.S. Mujumdar, and P.S. Rao. 1984. Studies on the toxicity of some insecticides to a freshwater teleost *Lebistes reticulatus* (PETERS). Acta Hydrochim. Et Hydrobiol. 12(6):629-636.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Guppy (*Lebistes reticulatus*)

Endpoint(s): 12 h LC50 27.61 mg/L (formulation)
24 h LC50 25.29 mg/L (formulation)
48 h LC50 22.59 mg/L (formulation)
72 h LC50 21.28 mg/L (formulation)
96 h LC50 18.97 mg/L (formulation)
Effect concentrations in mg a.i./L could not be calculated because purity of the formulation was not provided.

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	N	Insufficient details provided.
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Rogor (30 EC); source not provided.
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	12, 24, 48, 72, 96 h
7	**Were appropriate controls included, reported and results adequate?**	N	Information not provided
8	**Were the statistical procedures reported and appropriate?**	Y	Probit method

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static renewal (every 24 hours)
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Average length (3.75 cm) and average wet weight (2.68 g); acclimated to laboratory conditions for 15 days;
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y	10 fish/test concentration, 3 replicates, no feeding 48 hours prior to and during testing, temperature 25.5°C, alkalinity 198 mg/L, hardness 228 mg/L, pH 7.9 and DO 6.3 mg/L.
12	**Was a dose/response relationship demonstrated?**	N	Raw data not provided
13	**Were the concentrations/doses provided?**	N	No data provided.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Leber, R. Bathe, and Th. Frei. 1982a. Acute Toxicity to Carp of Dimethoate. R C C Research & Consulting Company Ltd, Switzerland. R C C Project 013702.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Carp (*Cyprinus carpio*)

Endpoint(s): 96 h LC50 694 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	Y	Requirements of the West German Biologische Bundesanstalt fuer Land- und Forst-wirtschaft (BBA Merkblatt Nr. 33, September 1975)
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Paraffin-like, solid; purity and source not provided.
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No control mortality
8	**Were the statistical procedures reported and appropriate?**	Y	Logit model

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	**Y**	Static, measured
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	**Y**	Average weight (4.1 g) and average length (68 mm); acclimated to laboratory conditions for 10 days
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	**Y/N**	Temperature 21 ± 1°C, 5 fish/15 L tanks, pH 7.3-7.5, DO 7-7.5 mg/L.
12	**Was a dose/response relationship demonstrated?**	**Y**	Dose-response relationship observed.
13	**Were the concentrations/doses provided?**	**Y**	Four test concentrations (500, 600, 750, 1000 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Leber, R. Bathe, and Th. Frei. 1982b. Acute Toxicity to Rainbow Trout of Dimethoate. R C C Research & Consulting Company Ltd, Switzerland. R C C Project 013691.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Rainbow trout (*Oncorhynchus mykiss*)

Endpoint(s): 96 h LC50 30.2 mg/L

GENERIC CRITERIA		Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	Y	Requirements of the West German Biologische Bundesanstalt fuer Land- und Forst-wirtschaft (BBA Merkblatt Nr. 33, September 1975)
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Paraffin-like, solid; purity and source not provided.
5	**Were effects endpoints ecologically relevant?**	Y	LC50
6	**Was an appropriate exposure duration used and reported?**	Y	96 h
7	**Were appropriate controls included, reported and results adequate?**	Y	No control mortality
8	**Were the statistical procedures reported and appropriate?**	Y	Logit model

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	Y	Static, measured
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y	Average weight (5.4 g) and average length (77 mm), acclimated to laboratory conditions for 10 days.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y/N	Temperature 16 ± 1.5°C, 3-4 fish/15L tanks, pH 7.3-7.5, DO 7-7.9 mg/L.
12	**Was a dose/response relationship demonstrated?**	Y	Dose-response relationship observed.
13	**Were the concentrations/doses provided?**	Y	Five test concentrations (8, 15, 35, 50, 100 mg/L)

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): unknown

Secondary reference: 1) Mayer, F.L., and M.R. Ellersieck. 1986. Manual of Acute Toxicity: Interpretation and Data Base for 41 Chemicals and 66 species of Freshwater Animals. United State Department of the Interior Fish and Wildlife Service, Resource Publication 160. MRID 40098001,
2) Johnson W.W., and M.T. Finley. 1980. Handbook of Acute Toxicity of Chemicals to Fish and aquatic Invertebrates. United States Fish and Wildlife Service; Resource Publication 137.

Is the primary reference study a GLP study?: No

Species Tested: Rainbow trout (*Oncorhynchus mykiss*), bluegill sunfish (*Lepomis macrochirus)*, water flea (*Daphnia magna), Gammarus lacustrus,* Stonefly *(Pteronarcella californica)*

Endpoint(s): 96 h LC50 6 mg/L (*Lepomis macrochirus)*
96 h LC50 6.2 mg/L, 8.6 mg/L (*Oncorhynchus mykiss)*

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	Y/N	Stated that test was conducted using good laboratory practices and was conducted in lab and field of Columbia National Fisheries Research laboratory, generally used ASTM methods for static and flow through tests (not specific though)
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	N	Provided only general materials an method description
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Dimethoate, (97%) technical material, no source
5	**Were effects endpoints ecologically relevant?**	Y	LC50, EC50
6	**Was an appropriate exposure duration used and reported?**	Y	48, 96 h
7	**Were appropriate controls included, reported and results adequate?**	N	Control mortality not reported.
8	**Were the statistical procedures reported and appropriate?**	N	Did not describe LC50/EC50 calculation, only comparisons between tests and factors affecting toxicity

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Static
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y/N	Did not provide acclimation information, size, weight and lifestage provided for each test.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y/N	Provided pH, temperature and hardness for every test
12	**Was a dose/response relationship demonstrated?**	N	Raw data not provided
13	**Were the concentrations/doses provided?**	N	Not reported

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluations

Compound: Dimethoate

Study reference (Primary): Slooff, W., and J.H. Canton. 1983. Comparison of the susceptibility of 11 freshwater species to 8 chemical compounds. II. (Semi) Chronic toxicity tests. Aquat Toxicol 4(3):271-282.

Secondary reference: n/a

Is the primary reference study a GLP study?: No

Species Tested: Guppy (*Poecilia reticulata*), Medaka (*Oryzias latipes*), African clawed frog (*Xenopus laevis*), water flea (*Daphnia magna*), mosquito (*Culex pipiens*), brown hydra (*Hydra oligactis*), great pond snail (*Lymnaea stagnalis*), blue-green algae (*Microcystis aeruginosa*), blue-green algae (*Scenedesmus pannonicus*), duckweed (*Lemna minor*), bacteria (*Pseudomonas fluorescens*)

Endpoint(s): 28 d NOEC (mortality) 32 mg/L (*Poecilia reticulata)*
28 d NOEC (growth) 10 mg/L (*Poecilia reticulata)*
28 d NOEC (behaviour) 0.1 mg/L (*Poecilia reticulata)*
40 d NOEC (hatching/growth) 100 mg/L (*Oryzias latipes)*
40 d NOEC (mortality) 0.32 mg/L (*Oryzias latipes)*

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, ETC.)?**	N	Not stated.
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used acceptable laboratory practices?**	Y	Multiple tests on different species; static or static renewal. Duration varies 0.3 to 100 days, Table of experimental methods provided.
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Source and purity not reported.
5	**Were effects endpoints ecologically relevant?**	Y	NOEC
6	**Was an appropriate exposure duration used and reported?**	Y	0.3 d, 4 d, 7 d, 21 d, 25 d, 28 d, 40 d, 100 d
7	**Were appropriate controls included, reported and results adequate?**	N	Not reported
8	**Were the statistical procedures reported and appropriate?**	N	Statistical procedure is not reported.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations or doses measured / maintained?**	N	Not measured, but some renewal of test solutions.
10	**Was the test species acclimated and characteristics of test species reported (e.g., strain, sex, age, life stage, length, weight)?**	Y/N	Age or life stage reported. No details on rearing, acclimation.
11	**Were appropriate test conditions (e.g., pH, conductivity, salinity, light intensity, temperature, DO, hardness of water, feeding, photoperiod, loading density, etc.) measured, reported and within acceptable ranges?**	Y/N	Temperature and loading density reported. Water quality parameters not reported.
12	**Was a dose/response relationship demonstrated?**	N	No data given to evaluate dose-response.
13	**Were the concentrations/doses provided?**	N	Stated that concentrations in all tests varied by √10 (i.e., 3.2). No specific concentrations given.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE () SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

APPENDIX C
DATA QUALITY EVALUATIONS OF MAMMALIAN TOXICITY STUDIES

Acceptable

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Brooker, A.J., B.A. Homan, C.A. Parker, J.M. Offer, A. Anderson, I.S. Dawe. 1992. The Effect of Dimethoate on Reproductive Function of Two Generations in the Rats, Volume I. Huntingdon Research Centre Ltd., 10 January 1992. Unpublished Report. DTF 11/91154.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Rat (Crl;CD (SD) BR VAF/plus strain)

Endpoint(s): 2 generation NOEL (reproductive effects (decreased fertility, live pups per litter, pup body weight)) 1.2 mg/kg bw/d

2 generation LOEL (reproductive effects (decreased fertility, live pups per litter, pup body weight)) 5.75 mg/kg bw/d

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	Y	Based on 1) OECD Method 416 and 3) EPA Pesticide Assessment Guideline Series 83-4.
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Source: Work performed by the Dimethoate Task Force. Purity: 96.44%; Batch No.: 611A.
5	**Were the effects endpoints ecologically relevant?**	Y	Numerous reproductive parameters.
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	Y	2 generations, no post observation period.
7	**Were appropriate controls included, reported and the results adequate?**	Y	Test diet without substance, treated with carrier as per test diet with substance. Four controls were sacrificed for poor health (out of a total of 56); no other parental mortality observed. Pup loss did not exceed 6.6% in the control group.
8	**Were statistical procedures reported and appropriate?**	Y	See list of tests on Page 34: Kruskal-Wallis test, Fisher's Exact , Shirley's test, Williams' test.

	CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	Y	Nominal Concentrations: 0, 1, 15 and 65 mg/kg diet. Concentrations in the diet stayed the same, and therefore daily doses (mg/kg/d) decreased over the course of the study.
10	**Were test diets concentrations or doses measured (acute and chronic) / maintained (chronic)?**	Y	Diets were analyzed during the study at the start of the pre-mating period, at the start of mating, and at the end of pregnancy/ start of lactation. Homogeneity and stability of test compound in the diet was studied.
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	Y	Animals were acclimated for 5 d, allocated to a test group, and acclimated again for 15 d. Source: Charles River France Ltd, St. Aubin les Elbeuf, France. Sex: 28 males and 28 females per test group. Age: 7 wk old at beginning of treatment. Weights were recorded (109-155 g for males; 100-139 g for females) at test initiation.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y	Temperature and humidity set at 21°C and 55%, respectively (ranges not given). Photoperiod: 12 h light: 12 h dark. Density: 4/cage pre-mating. After mating, females were housed individually and males returned to their former cagemates.
13	**Were individual body weights measured during testing and observation periods?**	Y	Individual body weights were recorded at the start of each generation and subsequently at weekly intervals.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	Y	Ad libitum; Food consumption of F0 and F1 parents was determined regularly during premating phases.
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	Y	Numerous reproductive parameters recorded.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
16	**Was a concentration- or dose-response relationship demonstrated?**	Y	Raw data included. Dose response demonstrated.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Kynoch, S.R. 1986. Acute Oral Toxicity to Rats of Chemathoate (Dimethoate) Technical. Huntingdon Research Centre Ltd. HRC Report No. 851338D/CHV 33/AC. 10 February, 1986. Unpublished report. CHA Doc. No. 146 DMT.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Rat (Sprague-Dawley)

Endpoint(s): 1 dose (14 d observation) LD50 (male and female survival) 387 mg/kg bw
1 dose (14 d observation) LD50 (male survival) 358 mg/kg bw
1 dose (14 d observation) LD50 (female survival) 414 mg/kg bw

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	Y	Based on recommendations of the US EPA Pesticide Assessment Guidelines Subdivision F. Hazard Evaluation Human and Domestic Animals 81-1 Acute Oral Toxicity Study.
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Chemathoate (Dimethoate) Technical O,O-Dimethyl-S-(N-methylcarbamoyl-methyl)phosphorodithionate; Source of Substance not provided. However, Chemathoate is a Cheminova product. Purity: 97.6%.
5	**Were the effects endpoints ecologically relevant?**	Y	LD50
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	Y	Single oral dose. Observations frequently on Day 1, and at least twice per day on subsequent days, for 14 d.
7	**Were appropriate controls included, reported and the results adequate?**	N*	No information provided on controls. Test substance was prepared in corn oil.

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were statistical procedures reported and appropriate?**	Y	LD50: Probit analysis (Finney, 1971), with Chi-squared test to check for non-parallelism.

*Control not required for EPA LD50 test.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	Y	Test substance was prepared in corn oil and administered using a syringe and plastic catheter. Nominal: 250, 320, 400, 500 and 640 mg/kg bw.
10	**Were test diet concentrations or doses measured (acute and chronic) / maintained (chronic)?**	n/a	Oral Gavage study.
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	Y	Animals were acclimated for a minimum of 5 d. Source: Charles River UK Limited, Margate, Kent, England. Sex: male and female. Age: approx 4-6 wk. Weight: 96-150 g.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y	Temperature: mean daily minimum and maximum = 20°C and 22°C. Mean daily relative humidity= 55%. Ranges not reported. Photoperiod: 12 h light; 12 h dark. Density: Five rats of same sex per cage.
13	**Were individual body weights measured during testing and observation periods?**	Y	Individual body weights were recorded on Days 1 (day of dosing), 8 and 15 and at death.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	n/a	
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	n/a	

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
16	**Was a concentration- or dose-response relationship demonstrated?**	Y	Raw data provided for mortality, clinical signs, body weight. Dose-response observed for females. Males went from 0% mortality at 320 mg/kg to 100% mortality at 400 mg/kg (the next highest dose).

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE () SUPPLEMENTAL ( ) UNACCEPTABLE

Comments: No control was used to ensure the vehicle (corn oil), or handling of the animals, did not result in mortality or other effects. However, this is not required under EPA testing guidelines.

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Mellert, W., J. Hellwig, C. Gembardt, K. Deckardt, B. Van Ravenzwaay. 2003. Dimethoate – Two-generation Reproduction Toxicity Study in Wistar Rats Administration in the Diet. BASF Aktiengesellschaft. Project ID 70R0466/99118. August 7, 2003. Unpublished report.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Rat (Wistar)

Endpoint(s): 2 generation NOEL (systematic toxicity (decreased body weight gain) for F0 and F1 parental rats) 1 mg/kg bw/d
2 generation NOEL (reproductive performance and fertility for F0 and F1 parental rats) 6.5 mg/kg bw/d
2 generation NOEL (developmental toxicity (growth and development of offspring) for F1A/F1B and F2A/F2B progeny) 6.5 mg/kg bw/d

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	Y	Based on 1) EC Commission Directive 87/302/EEC 2) OECD Method 416 and 3) EPA Test Guidelines OPPTS 870.3800.
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate (CAS 60-51-5) Source: Cheminova. Purity: 99.1%. Batch No.: 20522-00
5	**Were the effects endpoints ecologically relevant?**	Y	Numerous reproductive, including developmental parameters.
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	Y	2 generations, no post observation period (adjusted according to repro cycle, per period) .
7	**Were appropriate controls included, reported and the results adequate?**	Y	Test diet without substance. No un-natural effects occured in controls.
8	**Were statistical procedures reported and appropriate?**	Y	See Sections 3.7.3, 3.8.3, 3.9.4 for complete list of statistical tests.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	Y	Doses: 0, 0.2, 1.0 and 6.5 mg/kg bw/d.
10	**Were test diets concentrations or doses measured (acute and chronic) / maintained (chronic)?**	Y	Dietary adjustments were made weekly to maintain doses. Homogeneity and concentration control analyses were conducted regularly during the test.
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	Y	Animals were acclimated for about 7 days. Source: Charles River Deutschland GmbH, Sulzfeld, Germany. Sex: 25 male and 25 female per test group. Age: 35 ± 1 d old at beginning of treatment. Weights were recorded (mean weight = 95.1 g for males and 89.1 g for females) at test initiation.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y	Temperature: Range of 20-24°C. Relative humidity: Range of 30-70%. Photoperiod: 12 h light; 12 h dark. Density: Housed individually except females and their litters.
13	**Were individual body weights measured during testing and observation periods?**	Y	Individual body weights of F0 and F1 were recorded regularly.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	Y	Ad libitum; Food consumption of F0 and F1 parents was determined regularly during premating, gestation and lactation periods.
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	Y	Numerous reproductive parameters recorded.
16	**Was a concentration- or dose-response relationship demonstrated?**	Y	Raw data included.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Supplemental

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Myers. D.P. 2003. Amended Report. Consolidation of Amendments 1 and 2 Into the Final Report for MRID 45529703: The Dimethoate Developmental Neurotoxicity Study in the CD Rat by Oral Gavage Administration. Report 003881. Unpublished study. MRID MRID 45529703.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Rat (Crl:CD BR)

Endpoint(s): 10 d NOEL (increased litter/pup mortality, poor general condition among offspring and reduced early weight gain in pups) 0.5 mg/kg bw/d

10 d LOEL (increased litter/pup mortality, poor general condition among offspring and reduced early weight gain in pups)) 3 mg/kg bw/d

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	Y	OPPTS 870.6300
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate (batch number 20522-00) supplied by Cheminova Inc.; 99.1% purity.
5	**Were the effects endpoints ecologically relevant?**	Y	Assessing nervous system change was the primary goal of the study but mortality and growth also measured.
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	Y	Following protocol for OPPTS 870.6300 (Day 0 mating, Day 65 termination).
7	**Were appropriate controls included, reported and the results adequate?**	Y	N=24 and handled the same as treatment groups; some control mortality (less than 20%).

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were statistical procedures reported and appropriate?**	Y	Statistical evaluation was performed and was considered appropriate using Startox program with various method based on data: e.g., Fisher's Exact test, Bartlett's test).

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	Y	0.1, 0.5 and 3.0 mg/kg/d given to dam and both sexes of F1 pups once daily via gavage.
10	**Were test diets concentrations or doses measured (acute and chronic) / maintained (chronic)?**	n/a	Quality control of dosage solutions was conducted.
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	N	Actual acclimation times not presented. Likely 5 days: female animals arrived from Charles River at facility October 11 2000 and pairing with stock males commenced 16 October 2000. Body weight at delivery and during acclimation not noted.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y/N	Actual room temperature and humidity not presented, but it was noted that no excursions from these ranges were considered to have an effect on study outcome (Room temperature target range: 19-23^{o}C; Humidity target range: 40-70%). Photoperiod: 12 h light:12 h dark.
13	**Were individual body weights measured during testing and observation periods?**	Y	Dams: weighted on gestational day 0, 3, 6, 10, 14, 17, 20, then daily until parturition; during lactation: on post-natal day 1, 4, 7, 11, 14, 17, 21. Pups: weighed on post-natal day 1, 4, 7, 11, 14, 17, 21 and weekly from PND28 to study termination on PND 65±2.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	n/a	Food consumption in dams measured during gestation and post-natally.
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	Y	As well as sex ratio.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
16	**Was a concentration- or dose-response relationship demonstrated?**	Y	Pups (0.5 mg/kg/d): some pup mortality (24 compared to 15 in control). Pups (3 mg/kg/d): Some increased pup mortality (45 compared to 15 in controls). A NOEL (for pup mortality) of 0.5 mg/kg/d was established; though pup mortality was observed at 0.5 mg/kg/d, mortality was comparable to two years of background control data (data provided in study amendment). Dose-response relationship observed.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE (X) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments: This "supplemental" study is not being considered for uses in the ERA because the route of exposure (gavage) is not ecologically relevant, especially under a chronic exposure scenario. The study was originally conducted in 2001, however additional amendments were made and were added to the current document in 2003 therefore making the final full document citation listed as 2003.

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Myers, D.P. 2001. Dimethoate Effects on Cholinesterase in the CD Rat (Adult and Juvenile) by Oral Gavage Administration. Huntington Life Sciences Ltd., Cambridgeshire, England. CHV/070 Report 012226. Unpublished study.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Rat (Crl:CD)

Endpoint(s): ~5 wk NOEL (adult male and female body weight and survival) ≥3 mg/kg/d
~3 wk NOEL (pup body weight and survival) ≥3 mg/kg/d

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	Y	OPPTS 870.6300
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate (batch number 20522-00) supplied by Cheminova Inc.; 99.1% purity.
5	**Were the effects endpoints ecologically relevant?**	Y	Assessing effects on plasma, erythrocyte and brain acetyl cholinesterase activity was the primary goal of the study but mortality and body weight also measured.
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	Y	Following protocol for OPPTS 870.6300 (up to 60 d of observation).
7	**Were appropriate controls included, reported and the results adequate?**	Y	Controls included and received water for formulation using same treatment regime. No control mortality.

	GENERIC CRITERIA	Y/N	COMMENTS
8	**Were statistical procedures reported and appropriate?**	Y	Dependent on the heterogeneity of variance between treatment groups, parametric tests followed by Williams' test or non-parametric tests followed by Shirley's test were used to analyze these data, as appropriate. Where 75% of more of the values for a given variable are the same, Fisher's exact test was used.

	CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	Y	0.1, 0.5 and 3.0 mg/kg/d by oral gavage once daily to adult males and females, mated dams and selected offspring. The mean concentrations in test solutions analyzed during the study were within ± 2% of nominal.
10	**Were test diets concentrations or doses measured (acute and chronic) / maintained (chronic)?**	n/a	
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	Y	Crl:CD (SD) IGS BR strain obtained from Charles River UK Limited, England. 104 females (ordered at 9-10 wk of age and 200-220 g body weight) allowed a minimum of 5 d acclimatization. At test start the 84 animals allocated had a weight range 216-260 g and were approximately 10-11 wk in age. 70 male and 70 females (ordered at 5-6 wk of age and 120-175 g bodyweight for males and 100-150 g for females) allowed a minimum of 12 d acclimatization. At test start the 64 adults of each sex allocated were 7-8 wk of age and males ranged from 221-286 g and females 166-210 g.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	Y/N	Actual room temperature and humidity not presented, but it was noted that no excursions from these ranges were considered to have an effect on study outcome (Room temperature target range: 19-25^{O}C; Humidity target range: 40-70%). Photoperiod: 12 h light:12 h dark.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
13	**Were individual body weights measured during testing and observation periods?**	Y	Adult males and females were weighed the day before treatment and daily until test termination. Mated females weighed on gestational day 0, 3, 6, 10, 14, 17 and 20, then daily until parturition. During lactation females were weighed on post-natal day 1, 4, 7, 11, 14, 17 and 21. Pups weighed on post-natal day 1, 4, 7, 11, 14, 17, 21 and 28, then weekly until termination and on post-natal day 60.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	n/a	
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	Y	As well as sex ratio.
16	**Was a concentration- or dose-response relationship demonstrated?**	n/a	No statistically significant effects on body weight or survival at the highest concentration tested.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: () ACCEPTABLE (X) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments: This "supplemental" study is not being considered for uses in the ERA because the route of exposure (gavage) is not ecologically relevant, especially under a chronic exposure scenario. The study was originally conducted in 2001, and amendments were made in 2002.

Unacceptable

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Budreau, C.H., and R.P. Singh. 1973. Effect of fenthion and dimethoate on reproduction in the mouse. Toxicology and Appiled Pharmacology 26: 29-38

Secondary reference: N/A

Is the primary reference study a GLP study?: No

Species tested: CD-1 mice

Endpoint(s): 5 generations NOEL (reproduction) > 60 (9.5-10.5)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate given in drinking water.
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	N	
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	Y	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate was obtained in two batches from American Cyanamid Corp: Batch X.90108- and 1341-90 at 95.7% and 99.8% purity, respectively.
5	**Were the effects endpoints ecologically relevant?**	Y	Neonates were counted, weighed and examined for malformations at birth and every 4 days thereafter until weaning. Reproductive performance, mating success, reproduction time, and pup survival were assessed.
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	Y	5 generation study.
7	**Were appropriate controls included, reported and the results adequate?**	N	14 females and 10 males in control group; survival of pups in control group from Generation II, IV and V ranged from 73% to 100%, and appeared related to days after birth.

	GENERIC CRITERIA	Y/N	COMMENTS
8	**Were statistical procedures reported and appropriate?**	**N**	Comparisons between controls and dose group conducted against p values of 0.01 and 0.05. However, the actual statistical test used and a discussion of data distribution were not included.

	CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	**Y**	60 ppm dimethoate in drinking water (between 9.5-10.5 mg/kg based on previous study with rats given 60 ppm); dimethoate dissolved in 95% ethanol to give a 6% stock solution; working solutions (60 ppm) were prepared by adding 0.5 ml of stock solution per 500 ml tap water.
10	**Were test diets concentrations or doses measured (acute and chronic) / maintained (chronic)?**	**Y**	60 ppm in drinking water for all 5 generations.
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	**Y/N**	Acclimation time not noted for the initial group of animals, however, there was a 1-month period before mating.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	**N**	This information was not provided in the paper; however, preliminary experiments were undertaken to study the optimal housing condition.
13	**Were individual body weights measured during testing and observation periods?**	**Y**	For control animals and first and second litters from generation II, IV and V.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	**n/a**	
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	**Y**	Neonates were counted, weighed and examined for malformations at birth and every 4 d thereafter until weaning. Reproductive performance, mating success, reproduction time, and pup survival were assessed. Liver and kidney histopathy also assessed.
16	**Was a concentration- or dose-response relationship demonstrated?**	**N**	A dietary level of 60 ppm was suggested as the minimal dosage at which toxicity effects may be expected.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments: This appears to be a well conducted study yet lacks certain details that would allow for suitable replication.

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Levinskas, G.J., J. Bowenkamp, C. Clark, B. Javier, C. McCroskery, J. O'Grady, A. Stefanov, L. Vidone, G. Winter. 1959. Dimethoate: 90-day Repeated Feeding to Rats. CL 12, 880. American Cyanamid Company. Unpublished report number 59-13.

Secondary reference:

Is the primary reference study a GLP study?: No

Species tested: Albino rats (Wykoff strain)

Endpoint(s): 70 d NOEL (growth) >400 mg/kg diet
90 d NOEL (growth) >32 mg/kg diet

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *etc.*)?**	N	
3	**If NO to 2, was a complete description given of the physical test system and methods? Were the methods used considered acceptable laboratory practices?**	Y/N	See comments below
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Better than 95% purity, supplied by Research Department, Agricultural Division (Stamford); source number S-3439-64-2.
5	**Were the effects endpoints ecologically relevant?**	Y	Mortality, changes in body weight, food intake measured.
6	**Were an appropriate exposure duration and post-exposure observation period used and reported?**	N	
7	**Were appropriate controls included, reported and the results adequate?**	Y	No mortality occurred in control groups.
8	**Were statistical procedures reported and appropriate?**	N	Only p values are presented.

	CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS
9	**Were test diet concentrations or doses provided?**	Y	Male and female rats given 0, 2, 8 or 32 mg/kg dimethoate in diet for 90 d (given as ppm in report).
10	**Were test diets concentrations or doses measured (acute and chronic) / maintained (chronic)?**	N	No information provided.
11	**Were the test species acclimated and characteristics of the test species reported (*e.g.*, source, sex, age, weight)?**	Y/N	Male and female rats came from Lederle Laboratory Division Pearl River. Age, acclimation procedure and mass at arrival not reported.
12	**Were appropriate test conditions (*e.g.*, temperature, light intensity, humidity, photoperiod, loading density, *etc.*) measured, reported and within acceptable ranges?**	N	No information provided.
13	**Were individual body weights measured during testing and observation periods?**	Y/N	Data are body weights numerically shown at the end of the study compared to controls. Data are shown graphically for entire study duration but it was not explicitly stated that data were measured and that the graphs is not based on trend lines.
14	**For dietary studies, was feeding consumption measured, or at least estimated, during the study?**	Y/N	Feed consumption presented for the end of the study compared to controls. Data are shown graphically for entire study duration but it was not explicitly stated that data were measured and that the graphs is not based on trend lines.
15	**For reproduction tests, were the number of pups, development of the pups, viability of the pups, percent offspring survival and growth measured and evaluated?**	n/a	
16	**Was a concentration- or dose-response relationship demonstrated?**	N	32 mg/kg (ppm) appears to be the 90-day study NOEL for weight gain, food intake and survival (2.6 mg/kg/d for females; 2.2 mg/kg/d for males). 50 mg/kg (ppm) appears to be study NOEL for weight gain, food intake and survival from 33 d dietary study.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments: Results of three studies are presented in the report. Test 1 was based on giving Nelson strain 4 week old albino rats 100 mg dimethoate/kg diet (reported as ppm) for 2 weeks followed by 1 week of 200 mg dimethoate/kg diet followed by 400 mg dimethoate/kg diet for 10 weeks (total 90 days). No changes in food intake or mortality were observed during the course of the study compared to controls. At 400 mg dimethoate/kg diet, decreased weigh gain was observed after roughly 5 weeks of exposure compared to controls. In test 2, male and female Wykoff rats were given 2, 8, and 32 mg dimethoate/kg diet for 90 days. At the 2 mg dimethoate/kg diet dose, females showed significant weight gain reduction and decreased food intake compared to controls. Given these effects were not observed at the 8 and 32 mg/kg doses, effects were not considered treatment related. In test 3, 6 male and 6 female albino rats (CFN strain) were given 50 mg dimethoate/kg diet for 33 days. No change in food intake or body weight was seen compared to controls.

APPENDIX D
DATA QUALITY EVALUATIONS OF ALGAE TOXICITY STUDIES

Acceptable

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Caley, C.Y., B.D. Cameron, B. Knight, K. Armstrong, and B.E. Hall. 1992d. Alga, Growth Inhibition Test (72 h, EC50) With EC Formulation of Dimethoate Containing 400 g/L. Inveresk Research International Report Number 6924. Inveresk Reserach International, Trenant, Scotland.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Green algae *(Selenastrum capricornutum)*

Endpoint(s): 72 h EC10 (average specific growth rate) 179.23 mg/L (69.72 mg a.i./L) measured, 190.96 mg/L (74.28 mg a.i./L) nominal
72 h EC50 (average specific growth rate) 476.64 mg/L (185.41 mg a.i./L) measured, 562.77 mg/L (218.92 mg a.i./L) nominal
72 h NOEC (average specific growth rate) 56.5 mg/L (21.98 mg a.i./L) measured, 62.5 mg/L (24.31 mg a.i./L) nominal
72 h EC10 (area under growth curve) 94.47 mg/L (36.75 mg a.i./L) measured, 93.82 mg/L (36.50 mg a.i./L) nominal
72 h EC50 (area under growth curve) 233.12 mg/L (90.68 mg a.i./L) measured, 260.17 mg/L (101.21 mg a.i./L) nominal
72 h NOEC (area under growth curve) 56.6 mg/L (22.0 mg a.i./L) measured, 62.5 mg/L (24.3 mg a.i./L) nominal
72 h LOEC (average specific growth rate, area under growth curve) 126 mg/L (49.0 mg a.i./L) measured, 125 mg/L (48.6 mg a.i./L) nominal

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD Guidelines for Testing of Chemicals, Section 201 (1984).
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	EC formulations of dimethoate containing 400 g/L, received from Shell Agrar GmbH and Company, active ingredient content of 38.9%.
5	**Were effects endpoints ecologically relevant?**	Y	Growth

GENERIC CRITERIA		Y/N	COMMENTS
6	**Was an appropriate exposure duration used and reported?**	Y	72 h
7	**Were appropriate controls included, reported, and the results adequate?**	Y	Controls included, cell numbers in control increase >16-fold in 72 h in accordance with study method validity criteria.
8	**Were the statistical procedures reported and appropriate?**	Y	EC10 and EC50 calculated by probit analysis, NOEC calculated using one-way analysis of variance and pair-wise t-tests if assumption of homogeneity of variance met, calculated using one-way non-parametric analysis of variance and Dunn's procedure if assumption of homogeneity of variance not met.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	Y	Test concentrations analyzed using HPLC.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Starter cultures (strain 278/4) obtained from the Culture Collection of Algae and Protozoa, transfers of the alga made into fresh algal growth medium to provide suitable axenic subcultures, which were in exponential growth phase for test inoculations. Test inoculum contained 10^4 cells/mL.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Growth medium prepared according to OECD (1984), pH 8.0.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y	Continuous illumination 4800 lux, temperature range of environmental chamber 22-25°C, pH was outside protocol specifications at test end associated with algal growth and not thought to have affected study outcome.
13	**Was a concentration/response relationship demonstrated?**	Y	Concentration-response relationship demonstrated.
14	**Were the concentrations provided?**	Y	62.5, 125, 250, 500, 1000 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Caley, C.Y., B.D. Cameron, B. Knight, B. Hall, and K. Armstrong. 1992c. Alga, Growth Inhibition Test (72 h, EC50) With Technical Dimethoate. Inveresk Research International Project Number 381038. Inveresk Research International, Tranent, Scotland.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes.

Species tested: Green algae (*Selenastrum capricornutum*)

Endpoint(s): 72 h EC10 (average specific growth rate) 54.75 mg/L measured, 55.37 mg/L nominal
72 h EC50 (average specific growth rate) 282.29 mg/L measured, 282.07 mg/L nominal
72 h NOEC (average specific growth rate) 30.5 mg/L measured, 33.0 mg/L nominal
72 h EC10 (area under growth curve) 12.68 mg/L measured, 12.75 mg/L nominal
72 h EC50 (area under growth curve) 90.43 mg/L measured, 91.67 mg/L nominal
72 h NOEC (area under growth curve) 30.5 mg/L measured, 33.0 mg/L nominal
72 h LOEC (average specific growth rates, area under growth curves) 100 mg/L measured and nominal

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD Guidelines for Testing of Chemicals, Section 201 (1984).
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Technical dimethoate received from Industria Prodotti Chimici, active ingredient content 96.7%.
5	**Were effects endpoints ecologically relevant?**	Y	Growth
6	**Was an appropriate exposure duration used and reported?**	Y	72 h
7	**Were appropriate controls included, reported, and the results adequate?**	Y	Controls included, cell numbers in control increase >16-fold in 72 h.

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were the statistical procedures reported and appropriate?**	Y	EC10 and EC50 calculated by probit analysis, NOEC calculated using one-way analysis of variance and Dunnett's test if assumption of homogeneity of variance met, calculated using one-way non-parametric analysis of variance and Dunn's procedure if assumption of homogeneity of variance not met.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	Y	Test concentrations analyzed using HPLC.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Starter cultures (strain 278/4) obtained from the Culture Collection of Algae and Protozoa, transfers of the alga made into fresh algal growth medium to provide suitable axenic subcultures, which were in exponential growth phase for test inoculations. The inoculum volume was calculated to yield approximately 10^4 cells/mL.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Growth medium prepared according to OECD (1984), pH 8.0.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y	Temperature range of environmental chamber 22 to 24°C, continuous illumination 4800 lux, pH range 7.3 to 9.3.
13	**Was a concentration/response relationship demonstrated?**	Y	Concentration-response relationship demonstrated.
14	**Were the concentrations provided?**	Y	0.33, 1.0, 3.3, 10, 33, 100, 330, 500 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Porch, J.R., T.Z. Kendall, and H.O. Krueger. 2011c. Dimethoate TGAI: A 96-hour Toxicity Test with the Freshwater Alga (*Pseudokirchneriella subcapitata*). Wildlife International Ltd. Project Number 232A-129. Wildlife International Limited. Easton, MD.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Green algae (*Pseudokirchneriella subcapitata)*

Endpoint(s): 72 h EC50 (cell density) > 95 mg a.i./L
96 h EC50 (cell density) >95 mg a.i./L
72 h NOEC (cell density) 23 mg a.i./L
96 h NOEC (cell density) 23 mg a.i./L
72 h EC50 (growth rate) >95 mg a.i./L
96 h EC50 (growth rate) >95 mg a.i./L
72 h NOEC (growth rate) 47 mg a.i./L
96 h NOEC (growth rate) 23 mg a.i./L
72 h EC50 (yield) >95 mg a.i./L
96 h EC50 (yield) >95 mg a.i./L
72 h NOEC (yield) 23 mg a.i./L
96 h NOEC (yield) 23 mg a.i./L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD Guideline 201, Official Journal of the European Communities No. L383, Method C.3, and EPA OPPTS 850.5400.
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate TGAI, purity 99.1% w/w, provided by Cheminova. Purity was taken into account when authors calculated exposure concentrations.
5	**Were effects endpoints ecologically relevant?**	Y	Cell density, growth, yield
6	**Was an appropriate exposure duration used and reported?**	Y	72 and 96 h
7	**Were appropriate controls included, reported, and the results adequate?**	Y	Logarithmic growth obtained in negative controls during test period, mean cell density in controls increased by a factor of 259 in 72 h.

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were the statistical procedures reported and appropriate?**	Y	Non-linear regression to calculate EC50 values, treatment groups compared to controls using one-tailed Dunnett's test.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	Y	Measured at beginning and end of test, analytical method is HPLC. At day 4 recoveries were 83 to 90% of nominal.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	10 000 cells /mL initial concentration.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Cultures had been actively growing in culture medium for at least 2 wk prior to test initiation, transferred to fresh medium 3 d prior to test. Culture medium had pH 7.5.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y	Continuous lighting, light intensity range 5400 to 6580 lux, temperature range 23.8 to 25.3°C, pH range 7.4 to 8.6.
13	**Was a concentration/response relationship demonstrated?**	Y	Significant reduction in cell density and growth rate at two highest concentrations tested. Concentration-response demonstrated.
14	**Were the concentrations provided?**	Y	6.3, 12.5, 25, 50 and 100 mg a.i./L nominal concentrations

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Porch, J.R., T.Z. Kendall, and H.O. Krueger. 2011d. Dimethoate TGAI: A 96-Hour Toxicity Test With the Freshwater Alga (*Anabaena flos-aquae*). Wildlife International Ltd. Project Number 232A-125B. Wildlife International Ltd., Easton, MD.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Blue-green algae (*Anabaena flos-aquae*)

Endpoint(s): 72 h EC50 (cell density) 7.6 mg a.i./L
96 h EC50 (cell density) 37 mg a.i./L
72 h NOEC (cell density) 30 mg a.i./L
96 h NOEC (cell density) 30 mg a.i./L
72 h EC50 (growth rate) >98 mg a.i./L
96 h EC50 (growth rate) >98 mg a.i./L
72 h NOEC (growth rate) 30 mg a.i./L
96 h NOEC (growth rate) 9.0 mg a.i/L
72 h EC50 (yield) 6.6 mg a.i./L
96 h EC50 (yield) 36 mg a.i./L
72 h NOEC (yield) 30 mg a.i./L
96 h NOEC (yield) 30 mg a.i./L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD Guideline 201, Official Journal of the European Communities No. L383, Method C.3, OPPTS 850.5400, ASTM Standard E1218-04.
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate TGAI purity 99.1% w/w, provided by Cheminova. Purity was taken into account when authors calculated exposure concentrations.
5	**Were effects endpoints ecologically relevant?**	Y	Cell density, growth, yield
6	**Was an appropriate exposure duration used and reported?**	Y	72 and 96 h
7	**Were appropriate controls included, reported, and the results adequate?**	Y	Logarithmic growth obtained in negative controls during test period, mean cell density in control flasks increased by a factor of 43.7.

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were the statistical procedures reported and appropriate?**	Y	Non-linear regression to calculate EC50's, treatment groups compared to controls using one-tailed Dunnett's test.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	Y	Measured at beginning and end of test, analyzed using HPLC. Recoveries on day 4 ranged from 68.4 to 97.9% of nominal.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Initial cell concentration 10000 cells/mL.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Algal cells used in the test obtained from cultures that had been actively growing in culture medium for at least 2 wk prior to test. Algal cells cultured and tested in freshwater algal medium. pH 7.5.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y	Continuous lighting, light intensity ranged from 2020 to 2320 lux, temperature ranged from 24.0 to 25.0°C, pH range 7.7 to 7.7.
13	**Was a concentration/response relationship demonstrated?**	Y	Cell density significantly reduced in highest concentration tested, growth rate and yield significantly reduced in two highest concentrations tested. Concentration-response demonstrated.
14	**Were the concentrations provided?**	Y	Nominal concentrations 0.81, 2.7, 9.0, 30, and 100 mg a.i./L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Porch, J.R., T.Z. Kendall, and H.O. Krueger. 2011e. Dimethoate TGAI: A 96-Hour Toxicity Test With the Freshwater Diatom (*Navicula pelliculosa*). Wildlife International Ltd. Project Number 232A-128. Wildlife International Ltd. Easton, MD.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Diatom (*Navicula pelliculosa*)

Endpoint(s): 72 h EC50 (cell density) >98 mg a.i./L
96 h EC50 (cell density) >98 mg a.i./L
72 h NOEC (cell density) 98 mg a.i./L
96 h NOEC (cell density) 98 mg a.i./L
72 h EC50 (growth rate) >98 mg a.i./L
96 h EC50 (growth rate) >98 mg a.i./L
72 h NOEC (growth rate) 98 mg a.i./L
96 h NOEC (growth rate) 98 mg a.i./L
72 h EC50 (yield) >98 mg a.i./L
96 h EC50 (yield) >98 mg a.i./L
72 h NOEC (yield) 98 mg a.i./L
96 h NOEC (yield) 98 mg a.i./L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD Guideline 201, EU Directive 92/69/EEC Method C.3, OPPTS 850.5400.
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate TGAI purity 99.1% w/w, provided by Cheminova. Purity was taken into account when authors calculated exposure concentrations.
5	**Were effects endpoints ecologically relevant?**	Y	Cell density, growth rate, yield.
6	**Was an appropriate exposure duration used and reported?**	Y	72 and 96 h
7	**Were appropriate controls included, reported, and the results adequate?**	Y	Cell density in controls increased by a factor >16 in 72 h.

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were the statistical procedures reported and appropriate?**	Y	EC50's calculated using non-linear regression, treatment groups compared to controls using Dunnett's test.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	Y	Measured at beginning and end of test using HPLC, concentrations at end of test were 93 to 96% of nominal.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Initial cell concentration 10000 cells/mL.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Algal cells used in the test had been actively growing in culture medium for at least 2 wk prior to test. Algal cells cultured and tested in freshwater algal medium with silica constituents. pH 7.5
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y	Continuous lighting, light intensity range 4080 to 4560 lux, temperature range 23.2 to 25.4°C, pH range 7.2 to 7.8.
13	**Was a concentration/response relationship demonstrated?**	n/a	No significant difference for cell density, growth rate, and yield between highest tested concentration and controls.
14	**Were the concentrations provided?**	Y	Mean measured test concentrations: 6.1, 12.2, 24, 47, and 98 mg a.i./L.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Porch, J.R., T.Z. Kendall, and H.O. Krueger. 2011f. Dimethoate TGAI: A 96-Hour Toxicity Test With the Marine Diatom (*Skeletonema costatum*). Wildlife International Ltd. Project Number 232A-130. Wildlife International Ltd., Easton, MD.

Secondary reference: n/a

Is the primary reference study a GLP study?: Yes

Species tested: Marine diatom (*Skeletonema costatum*)

Endpoint(s): 72 h EC50 (cell density) >96 mg a.i./L
96 h EC50 (cell density) >96 mg a.i./L
72 h NOEC (cell density) 96 mg a.i./L
96 h NOEC (cell density) 96 mg a.i./L
72 h EC50 (growth rate) >96 mg a.i./L
96 h EC50 (growth rate) >96 mg a.i./L
72 h NOEC (growth rate) 96 mg a.i./L
96 h NOEC (growth rate) 96 mg a.i./L
72 h EC50 (yield) >96 mg a.i./L
96 h EC50 (yield) >96 mg a.i./L
72 h NOEC (yield) 96 mg a.i./L
96 h NOEC (yield) 96 mg a.i./L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	Y	OECD Guideline 201, EU Directive 92/69/EEC Method C.3, OPPTS 850.5400.
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	n/a	
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	Y	Dimethoate TGAI purity 99.1% w/w, provided by Cheminova. Purity was taken into account when authors calculated exposure concentrations.
5	**Were effects endpoints ecologically relevant?**	Y	Cell density, growth, yield.
6	**Was an appropriate exposure duration used and reported?**	Y	72 and 96 h
7	**Were appropriate controls included, reported, and the results adequate?**	Y	Negative control used, maintained exponential growth throughout test, mean cell density in controls increased by a factor of 75 in 72 h.

GENERIC CRITERIA		Y/N	COMMENTS
8	**Were the statistical procedures reported and appropriate?**	Y	EC50's calculated using non-linear regression, treatment groups compared to controls using one-tailed Dunnett's test.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	Y	Measured at beginning and end of test using HPLC, at test end measured concentrations were 89.3 to 92.5% of nominal.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Initial cell concentration 10 000 cells/mL, CCMP strain number 1332.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Algal cells used in the test had been actively growing in culture medium for at least 2 wk prior to test, cultured and tested in saltwater medium, salinity 30 ppt, pH 8.0.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y	16 h light: 8 h dark, light intensity range 4400 to 4730 lux, temperature range 20.0 to 21.1°C, pH range 8.0 to 8.4.
13	**Was a concentration/response relationship demonstrated?**	n/a	No significant difference between highest concentration tested and control for cell density, growth rate, or yield.
14	**Were the concentrations provided?**	Y	Measured concentrations: <LOQ, 6.1, 12, 24, 47 and 96 mg a.i./L.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: (X) ACCEPTABLE ( ) SUPPLEMENTAL ( ) UNACCEPTABLE

Comments:

Unacceptable

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Abdel-Hamid, M.I. 1996. Development and application of a simple procedure for toxicity testing using immobilized algae. Wat Sci Tech 33(6): 129-138.

Secondary reference: N/A

Is the primary reference study a GLP study?: No

Species tested: Green algae (*Selenastrum capricornutum)*

Endpoint(s): 4 d EC50 (growth) 36 mg/L (free cultures in microplate test)
4 d EC50 (growth) 37 mg/L (immobilized cultures in microplate test)
4 d EC50 (growth) 36 mg/L (Bottle test)

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	Y	Dimethoate
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	N	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	Y	Details on methods provided. Bottle assay references methods from Greene et al. (1989).
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	N	Tested as composite commercial products. Purity not reported.
5	**Were effects endpoints ecologically relevant?**	Y	Growth
6	**Was an appropriate exposure duration used and reported?**	Y	4 d
7	**Were appropriate controls included, reported, and the results adequate?**	Y/N	Control used, but results of control growth not reported.
8	**Were the statistical procedures reported and appropriate?**	N	Graphical plotting of data, EC50 calculated using straight-line graphical interpolation method. T-test used to examine for significant differences between means of treatment and control.

CRITERIA FOR AN ACCEPTABLE STUDY	Y/N	COMMENTS

9	**Were the test concentrations measured / maintained?**	N	Measurement of concentrations not reported.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Strain NIVA-CHL 1, obtained from the culture collection of the Norwegian Institute for Water Research, 5 d old culture used for testing. Initial algal density of 10^4 cells/mL.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Cultivated in standard AAM medium, culture flasks placed on a shaking table at 22±2°C under continuous illumination.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	N	Not reported.
13	**Was a concentration/response relationship demonstrated?**	N	Growth stimulated at <1.0 mg/L, then decreased with increasing concentration. Raw data not provided to show statistically significant differences between algal cell densities at different concentrations.
14	**Were the concentrations provided?**	Y	0.0032, 0.01, 0.032, 0.1, 0.32, 1.0, 3.2, 10, 32, 100, 320 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Canton, J.H., R.C.C. Wegman, A.V. Oers, A.H.M. Tammer, E.A.M. Mathijsen-Spiekman, and H.H. van den Broek. 1980. Ecotoxicological Study with Dimethoate and Omethoate. National Institute of Health, Bilthoven.

Secondary reference: N/A

Is the primary reference study a GLP study?: No

Species tested: Algae (*Chlorella pyrenoidosa*)

Endpoint(s): 48 h EC50 (growth inhibition) 300 mg/L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	**Y**	Dimethoate technical
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	**N**	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	**Y/N**	Referenced method from Canton (1976).
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	**Y**	Purity 98%, sample obtained from Luxan.
5	**Were effects endpoints ecologically relevant?**	**Y**	Growth inhibition.
6	**Was an appropriate exposure duration used and reported?**	**N**	48 h
7	**Were appropriate controls included, reported, and the results adequate?**	**N**	Not reported.
8	**Were the statistical procedures reported and appropriate?**	**N**	Not reported.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	N	Not reported.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Age- log phase of growth, cell concentration 10^4 cells/mL.
11	**Was the method and medium of cultivation reported and appropriate?**	Y/N	Wanka media used.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y/N	Temperature 23 ±2°C, continuous lighting at 3000 lux, pH not reported.
13	**Was a concentration/response relationship demonstrated?**	N	Not reported, raw data not provided.
14	**Were the concentrations provided?**	N	Not reported.

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

Study Quality and Acceptability Evaluation

Compound: Dimethoate

Study reference (Primary): Das, M.K., and S.P. Adhikary. 1996. Toxicity of three pesticides to several rice-field cyanobacteria. Trop. Agric. (Trinidad) 73(2):155-157.

Secondary reference: N/A

Is the primary reference study a GLP study?: No

Species tested: *Anabaena fertilissima, Anabaena variabilis, Nostoc sphaericum, Nostoc linckia, Nostoc muscorum, Calothrix parietina, Calothrix sp., Scytonema multiramosum, Scytonema sp., Westiellopsis sp.*

Endpoint(s): 15 d EC50 (growth) 0.35 mg/L (*Anabaena fertilissima*, UU 146), 0.11 mg a.i./L
15 d EC50 (growth) 0.28 mg/L (*Anabaena variabilis* UU 147), 0.084 mg a.i./L
15 d EC50 (growth) 0.52 mg/L (*Nostoc sphaericum* UU 1413) 0.16 mg a.i./L
15 d EC50 (growth) 0.51 mg/L (*Nostoc linckia* UU 1415) 0.15 mg a.i./L
15 d EC50 (growth) 0.54 mg/L (*Nostoc muscorum* UU 1416) 0.16 mg a.i./L
15 d EC50 (growth) 0.58 mg/L (*Calothrix parietina* UU 1423) 0.17 mg a.i./L
15 d EC50 (growth) 1.16 mg/L (*Calothrix sp.* UU 2427) 0.35 mg a.i./L
15 d EC50 (growth) 0.23 mg/L (*Scytonema multiramosum* UU 1431) 0.069 mg a.i./L
15 d EC50 (growth) 0.29 mg/L (*Scytonema sp.* UU 2433) 0.087 mg a.i./L
15 d EC50 (growth) 0.51 mg/L (*Westiellopsis sp.* UU 2443) 0.15 mg a.i./L

	GENERIC CRITERIA	Y/N	COMMENTS
1	**Single chemical exposure?**	**Y**	Dimethoate formulation
2	**Was the study conducted according to a recognized international standard (OPPTS, OECD, ASTM, ISO, *ETC.*)?**	**N**	
3	**If NO to 2, was a complete description given of the test system and methods? Were the methods used considered acceptable laboratory practices?**	**N**	A complete description not provided, missing some details on test system and methods.
4	**Were the identification, purity and source of test substance given and comparable to the current technical material and formulation?**	**Y/N**	Rogor 30% EC, source not provided.
5	**Were effects endpoints ecologically relevant?**	**Y**	Growth
6	**Was an appropriate exposure duration used and reported?**	**N**	15 d, generally algal studies are 72 h in duration.
7	**Were appropriate controls included, reported, and the results adequate?**	**N**	No controls reported.
8	**Were the statistical procedures reported and appropriate?**	**N**	Not reported.

CRITERIA FOR AN ACCEPTABLE STUDY		Y/N	COMMENTS
9	**Were the test concentrations measured / maintained?**	N	Stock solutions of the pesticides were prepared with distilled water and added aseptically to the culture medium to obtain the desired pesticide concentrations. No indication of concentrations being measured.
10	**Were characteristics of the test species reported and appropriate (*e.g.*, strain, age, initial cell concentration/frond number, weight)?**	Y	Experiments conducted with test organisms in exponential growth phase. Strain provided.
11	**Was the method and medium of cultivation reported and appropriate?**	Y	Cultures grown in nitrogen free BG-11 medium at 26 ±1°C under a light intensity of 7.5 W/m^2 provided from daylight fluorescent tubes, pH 7.8.
12	**Were appropriate test conditions (*e.g.*, pH, light intensity, photoperiod, temperature) measured, reported and within acceptable ranges?**	Y/N	pH 7.8, continuous light 7.5 W/m^2, temperature during test not specified.
13	**Was a concentration/response relationship demonstrated?**	N	Not reported, no raw data provided.
14	**Were the concentrations provided?**	Y	0.01, 0.02, 0.05, 0.1, 0.2, 0.5, 1, 2, 5, 10 and 20 mg/L

CRITERIA FOR A SUPPLEMENTAL STUDY

Studies that meet the generic criteria only.

UNACCEPTABLE STUDY

Studies that do not meet the generic criteria.

EVALUATION: ( ) ACCEPTABLE ( ) SUPPLEMENTAL (X) UNACCEPTABLE

Comments:

APPENDIX E
HOME RANGE OF PREY (CALIFORNIA MOUSE) OF TERRESTRIAL ADULT CALIFORNIA RED-LEGGED FROG

California red-legged frogs (CRLFs) consume a variety of insect and invertebrate species (Hayes and Tennant, 1985). They have also been reported to consume larger prey such as fish (e.g., *Gasterosteius aculeatus*), amphibians (e.g., Pacific tree frog -- *Hyla regilla*), and mammals (e.g., California mouse -- *Peromyscus californicus*) (Hayes and Tennant, 1985). Of these prey, species from the genus *Peromyscus* (e.g., California mouse, deer mouse) and *Hyla* may inhabit areas where dimethoate is applied. Although unlikely, there is a potential for CRLFs to consume *Peromyscus* or *Hyla* that were exposed at the site of dimethoate application and then traveled to CRLF habitat. Home range information for *H. regilla* indicates a home range is approximately 33 m for resident frogs, with movements of up to 400 m for migrating frogs (Morey, 2005). The home range of *P. californicus* varies greatly from 150 to 3,788 m^2, with average ranges of 1,161 to 1,500 m^2 (Ribble and Salvioni, 1990; USC, 2006). Home ranges for deer mice (*P. maniculatus*) also vary greatly, ranging from 242 to 3,000 m^2 (Bunker, 2001). Mean home ranges reported in the EPA *Wildlife Exposure Factors Handbook* for deer mice vary from 140 to 1,280 m^2 (EPA, 1993). Using a conservative approach to select from the available data, the maximum home range of 3,788 m^2 for *P. californicus* was used to estimate the distance from a treated field that a mouse could potentially travel. The maximum home range was converted to a radius using the following equations:

$$Area\ of\ a\ circle = \pi R^2$$

$$3{,}788\,m^2 = \pi R^2$$

$$R = \sqrt{\frac{3{,}788\,m^2}{\pi}}$$

$$R = 34.7 \approx 35\,m$$

where R = radius (m). Thus, the likely maximum distance that a California mouse would travel from the center of its home range is 35 m. It would thus be an unusual event for CRLFs, which forage in or near aquatic habitats, to encounter California mice or other small mammals that occur on fields treated with dimethoate.

APPENDIX F
RISK CATEGORIES FOR EFFECTS TO CALIFORNIA RED-LEGGED FROG

For both aquatic and terrestrial exposure scenarios screening through to the refined assessment, risk curves will be used to quantify risk.

Each exposure distribution will be integrated with an effects distribution (*e.g.*, species sensitivity distribution or exposure-response curve) to derive a risk curve that indicates the probability of exceeding effects of differing magnitude. The risk curve will then be used to categorize risk as *de minimis*, low, intermediate, or high for each use pattern.

The Ecological Committee on FIFRA Risk Assessment Methods (ECOFRAM, 1999) referred to risk curves as "joint probability curves" while others use the term used herein, i.e., "risk curves" (e.g., EPA, 2004b; Giddings et al., 2005). This approach has been used in ecological risk assessments performed for EPA at the Calcasieu Estuary, Louisiana, the Housatonic River, Massachusetts (EPA, 2002; EPA, 2004b) and by others in ecological risk assessments of pesticides (Giesy et al., 1999; Giddings et al., 2005; Moore et al., 2006a,b; Moore et al., 2010a,b).

The risk categories of *de minimis*, low, intermediate and high are intended to be qualitative descriptors of the risks to California red-legged frogs, their prey and their habitat exposed to dimethoate in standard-sized ponds adjacent to treated fields.

In this assessment, the probability of an exposure concentration exceeding a level of effect is quantified as the area under a risk curve (risk curve AUC). The AUC will be used to categorize risk.

For each exposure scenario, risk is categorized as follows:

- If the *area under the risk curve (AUC)* is less than the AUC associated with a risk product (risk product = exceedence probability x magnitude of effect) of 0.25%, then the risk is categorized as *de minimis*;
- If the *AUC* is equal to or greater than the AUC associated with a risk product of 0.25% but less than 2%, then the risk is categorized as low;
- If the *AUC* is equal to or greater than the AUC of 2% but less than 10%, then the risk is categorized as intermediate; and
- If the *AUC* is equal to or greater than the AUC associated with a risk product of 10%, then the risk is categorized as high.

CRLFs are opportunistic predators and thus effects limited to sensitive populations of prey species are unlikely to lead to adverse effects to CRLFs via reduction in food availability. The high reproductive potential of most aquatic invertebrate species allows them to recover in a relatively short time after experiencing low-to-moderate adverse effects (van den Brink et al., 1996; Sherratt et al., 1999; Suter et al., 2000; Barnthouse, 2004). Liess and Schulz (1999), however, showed that recovery can take a very long time (months to years) for aquatic invertebrates when local populations are extirpated. Thus, exposure scenarios in the high risk

category would be of concern because of the long periods of time potentially required for recovery.

Aquatic ecosystems exhibit "functional redundancy" in the temperate zone (Baskin, 1994; Moore, 1998). This means that multiple species are generally present to perform each critical function. Agricultural ecosystems are, to some degree, already affected because of changes brought by the presence of humans, crop fields, livestock, infrastructure, and so on. It is a generally accepted notion among ecologists that systems in relatively unstable environments (the case for most agro-ecosystems) are more likely to recover from new disturbances (*e.g.*, a pesticide application), especially those that mimic historical disturbance events (*e.g.*, previous pesticide applications; Denslow, 1985; Rapport et al., 1985; Moore, 1998).

The risk category boundaries, as described above are shown in Table F-1, Figure F-1 and Figure F-2. The risk categories are based on several considerations including:

- An effect level of 10% is unlikely to be ecologically significant to a local population. Such an effect generally cannot be reliably confirmed by field studies (Moore, 1998; Suter et al., 2000). Thus, when concentrations of a pesticide are less than the 10^{th} percentile on the low-effects SSD or 10^{th} percentile on a single species dose-response curve, it is likely that the community or species are being protected;
- Controlled exposure–response experiments with microcosms and mesocosms have demonstrated that, at some level of exposure, temporary changes occur in the abundance of a few, sensitive species. At a higher level of exposure, more severe and longer lasting effects occur that may have pronounced ramifications for community structure and function. The transition from minor to major effects usually occurs at concentrations greater than the 10th percentile of single-species low-toxic-effect values (Giddings et al., 1996, 1997; Solomon et al., 1996; Versteeg et al., 1999);
- Suter et al. (2000) concluded, based on an analysis of EPA regulatory practice, that decreases in an ecological assessment endpoint of <20% are generally acceptable. For example, the approximate detection limit of field measurement techniques used in regulating contaminants based on bioassessment of aquatic ecosystems is 20%. The community metrics for an exposed benthic invertebrate community must be reduced by >20% compared with pristine reference sites to be considered even slightly impaired in the EPA rapid bioassessment procedure (Plafkin et al., 1989);

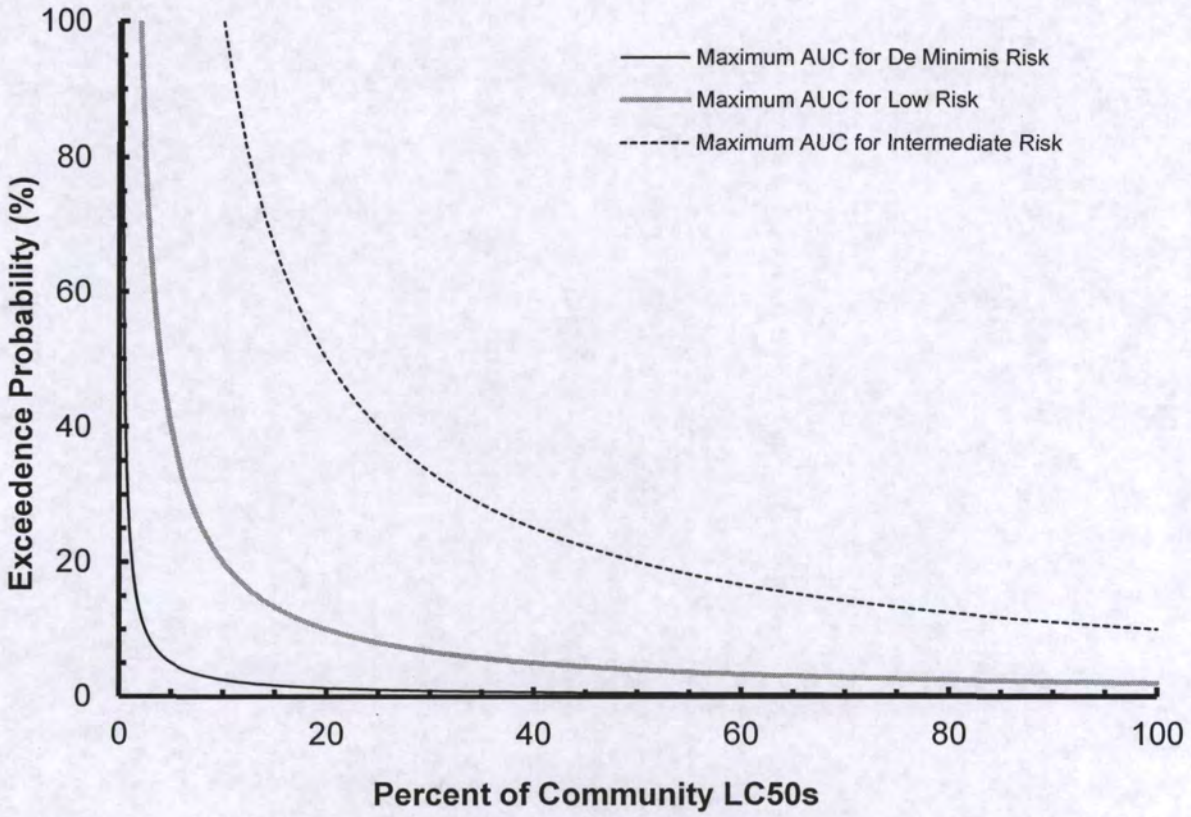

Figure F-1 Risk curves defining the AUC boundaries for risk categorization.

Table F-1 Summary of AUC boundaries for refined risk assessment	
Risk Boundary	***Area Under the Curve (AUC)[a]***
De minimis – Low	1.75
Low – Intermediate	9.82
Intermediate – High	33.0

[a] Calculated by integrating the risk curves associated with 0.25, 2 and 10% maximum risk product (see Figure D-1).

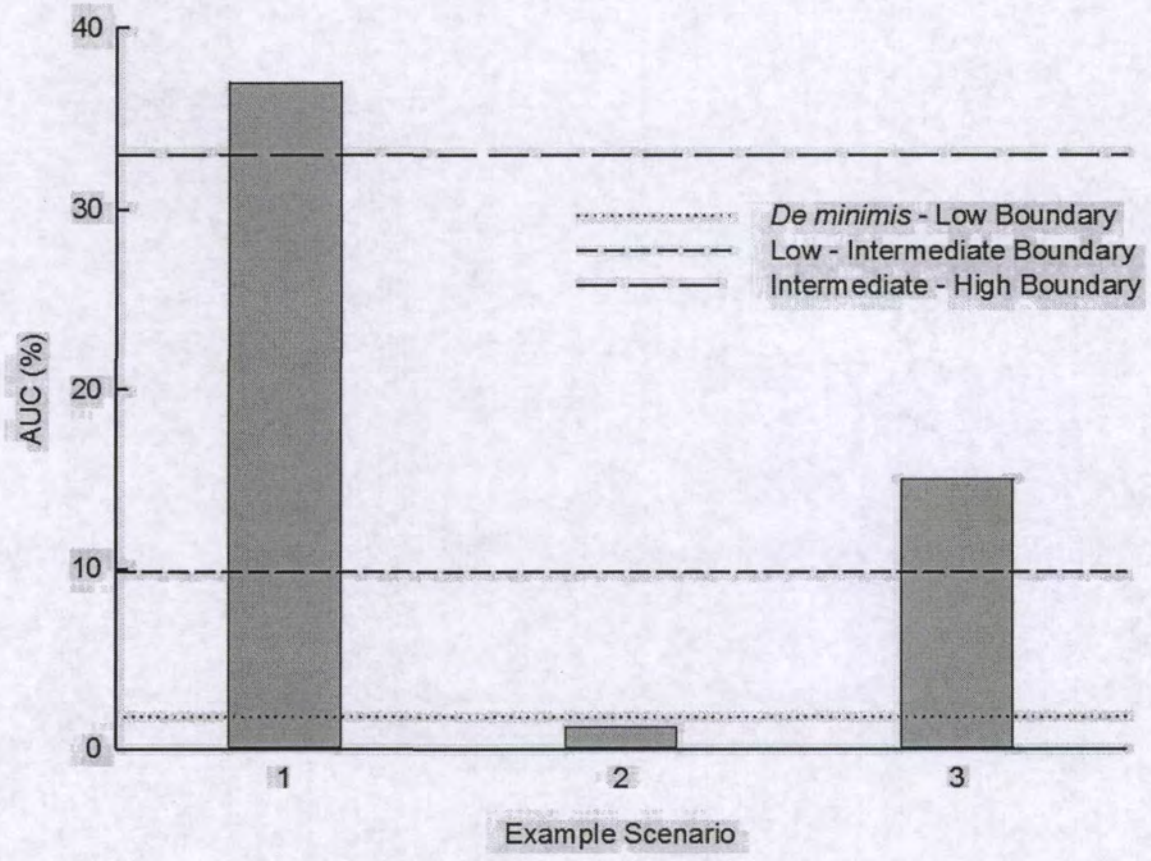

Figure F-2 AUC boundaries for risk categorization.