Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Re-evaluation Decision Document RRD2006-24

Naled

The purpose of this Re-evaluation Decision Document (RRD) is to notify registrants, pesticide regulatory officials and the Canadian public that Health Canada's Pest Management Regulatory Agency (PMRA) has re-evaluated the active ingredient naled and its associated uses as an insecticide for use on greenhouse food and non-food, livestock, food and feed crops, structural sites, commercial outdoor ornamental crops and woodlots.

On 6 August 2004, Proposed Acceptability for Continuing Registration (PACR) document PACR2004-33, *Re-evaluation of Naled*, was published for consultation. The PMRA has reviewed the comments received and provides a response in Appendix I of this RRD. These comments did not result in any substantial changes to the regulatory decision as described in the PACR; however, they did not result in some revision to the required label statements.

The PMRA has determined that naled is acceptable for continued registration. Mitigation measures to further protect workers and the environment are described in Appendix II of this RRD. The registrants have been informed by letter of the specific requirements, including the confirmatory data requirements specified in Section 9.0 of PACR2004-33, affecting their product registrations and the regulatory options available to comply with this decision.

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Appendix I Comments and Responses

1.0 Comment on the Labelling of Toxicological Information

It was suggested to separate "Toxicological Information" into two sections: (1) Poisoning Symptom, and (2) Information for doctors.

Response
The wording of this section remains unchanged as it is consistent for all Commercial Class organophosphate pesticide labels.

2.0 Comments Pertaining to Human Health

2.1 Comment on the Actual Test Dose

The low-concentration animal group was exposed for a significant time to higher concentrations of naled; the actual dose the animals received during this period of the study cannot be discounted.

Response
Animals were exposed intermittently by inhalation to naled for 6 hours/day, 5 days/week for 13 weeks. The target concentration for the first 12 exposures in the low-concentration group was 0.5 µg/L (0.15 mg/kg bw/day). On exposure day 13, the protocol was amended, and the target concentration was reduced to 0.2 µg/L (0.06 mg/kg bw/day) due to the results of cholinesterase assays. During the entire exposure period, the average chamber concentration was 0.23 µg/L (0.07 mg/kg bw/day), based on the mean of daily average measurements.

During the first 12 exposures, concentrations that were slightly greater than average were noted only on 5 treatment days. During exposure days 1 to 3, daily average concentrations ranged from 0.25 to 0.74 µg/L (0.08 to 0.23 mg/kg bw/day) and, on exposure days 14 and 15, daily average concentrations were 0.24 and 0.28 µg/L (0.07 mg/kg bw/day and 0.09 mg/kg bw/day), respectively. As exposures were intermittent, and concentrations were slightly elevated for only a very short duration at the start of the study, it is unlikely that these exposures confound the interpretation of results at the low dose.

Furthermore, the mean concentration of the first 12 exposures, while highly variable (0.28 ± 0.21 µg/L), was not substantially different from the mean concentration of the remaining exposures (0.22 ± 0.09 µg/L, excluding the outlier on day 51 of exposure). As it is impossible to determine with certainty that observed responses were attributable to the differential concentration, it is reasonable for the PMRA to average the daily exposures of the entire study duration for the purposes of risk assessment.

2.2 Comment on Bromodichloroacetaldehyde

At the lowest exposure level, there was a significant amount (50:50 ratio) of the breakdown product bromodichloroacetaldehyde (BDCA) present, due to high humidity levels inside the chamber (humidity levels ranged from 40% to 80% during the treatment period). BDCA is an aldehyde; aldehydes are known upper airway irritants and are known to be selectively irritating to the nasal tissues of rodents. BDCA needs to be considered as a cause of the nasal tissue pathology in rats exposed to naled.

Toxicity data on BDCA were not presented. However, the 1991 Integrated Risk Information System (IRIS) toxicity report for acetaldehyde was provided for review by the PMRA.

Response

Mean humidity levels for control and treated animals were within normal range (i.e., 51–56%) during the treatment period. Toxicity data on BDCA were not available for comparison with the parent compound. Therefore, relevant toxicological studies for naled and acetaldehyde were reviewed for comparison of toxicity and relative potency of each compound in the upper respiratory tract.

In short-term inhalation studies conducted with acetaldehyde in rats (the most sensitive species), the upper respiratory tract is consistently affected at lowest concentrations, with similar effects noted in critical studies. At ≥ 720 µg/L acetaldehyde [considered to be the lowest observed adverse effect level (LOAEL)], degenerative changes were observed in the nasal epithelium of rats exposed for 4 weeks (Appelman et al. 1982[1]). The no observed adverse effect level (NOAEL) for acetaldehyde in short-term inhalation studies was 270 µg/L, based on the absence of adverse effects in rats exposed (intermittently or continuously) for 4 weeks (Appelman et al. 1986[2]).

In the single identified short-term inhalation study conducted with naled, the LOAEL for effects in the upper respiratory tract of rats was 3.4 µg/L based on nasal epithelial lesions in animals treated intermittently for 3 weeks to the lowest concentration; an NOAEL was not established in this study. As naled induced degenerative lesions in the nasal epithelium of rats at concentrations that are several orders of magnitude less than those observed for the putative breakdown product acetaldehyde, the data suggest that toxicity in the upper respiratory tract is due primarily to exposure to naled.

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1 Appelman, L.M., R.A. Woutersen and V.J. Feron. 1982. Inhalation toxicity of acetaldehyde in rats. I. Acute and subacute studies. *Toxicology*. 23: 293–307.

2 Appelman, L.M., R.A. Woutersen, V.J. Feron, R.N. Hoofman and W.R.F. Notten. 1986. Effect of variable versus fixed exposure levels on the toxicity of acetaldehyde in rats. *Journal of Applied Toxicology*. 6: 331–336.

However, it is unknown whether BDCA may be more potent than acetaldehyde; hence, there is a possibility that BDCA may enhance the response elicited by naled. Given that naled can be used during meteorological conditions that may favour formation of BDCA (i.e., high humidity), there is no reason to discount this response as irrelevant to the human health risk assessment.

2.3 Comment on Salivation

The PACR incorrectly attributes the few reports of salivation in animals in the lowest exposure group to 0.23 µg/L naled. However, this negligible effect occurred during the early part of the study when the concentration of naled was substantially higher.

Response

Salivation, a common response to a cholinesterase inhibitor, was variable (noted between day 1 and day 54 of exposure) but dose-related in both sexes throughout the treatment period. In the control, low-, mid- and high-concentration groups, salivation was observed in 1, 5, 5 and 22 males and in 0, 1, 4 and 19 females, respectively. Observations of salivation in the low concentration group were not limited to treatment days where exposures were higher than average; higher exposure concentrations in conjunction with salivation were noted only on two treatment days. In fact, of the six low-dose animals showing signs of salivation, only one was clearly related to a higher than average concentration received by the animals in the early part of the study. The remaining animals all experienced salivation following receipt of a daily exposure less than the average concentration of 0.23 µg/L. Thus, salivation is considered to be a treatment-related clinical observation.

2.4 Comment on Nasal Pathology

The PACR attributes the sporadic reports of nasal rhinitis and dysplasia in animals in the lowest exposure group to 0.23 µg/L naled. However, these effects were noted in one or two animals only, and BDCA needs to be considered as the cause of these findings.

Response

Nasal pathology was restricted to treated animals and exhibited dose-response in females. The incidence of nasal epithelial dysplasia in control, low-, mid- and high-exposure animals was 0/12, 0/12, 3/12, 2/12 in males and 0/12, 1/12, 1/12, 3/12 in females, respectively. The incidence of chronic nasal rhinitis in control, low-, mid- and high-exposure animals was 0/12, 2/12, 1/12, 1/12 in males and 0/12, 2/12, 3/12, 4/12 in females, respectively. The results of this study are supported by those of a three-week inhalation study in which salivation and nasal epithelial lesions were also observed in the same strain of rats exposed by inhalation to low concentrations of naled (LOAEL = 3.4 µg/L; lowest tested concentration). Site-of-contact effects are consistent with the toxicity database for naled, with degenerative lesions at the site of entry also noted following dermal exposure. In view of the weight of evidence, the nasal pathology noted in the low-exposure group is considered to be treatment-related and adverse.

However, the PMRA re-examined the incidence data for salivation, cholinesterase inhibition and nasal pathology in the 13-week study and concluded that the lowest tested concentration is at the threshold between the NOAEL and LOAEL. Therefore, it requires the use of a LOAEL for inhalation risk assessment and a revision of the margin of exposure from 300 to 100 (i.e., removal of the 3× safety factor for lack of a NOAEL).

There is no reason to discount the potential response induced by BCDA as irrelevant to the human health risk assessment.

2.5 Comment on Portable Foggers

Application by portable foggers needs to be retained as not all greenhouse operators have access to automatic foggers.

Response
The application of naled by portable handheld foggers in greenhouses is not a registered method.

The fogging instructions on the current labels are as follows:

> For fogging treatment, apply with stationary (automated) fogging equipment only. All workers must vacate the premises during the fogging operation and must not re-enter until the greenhouse has been ventilated.

For further clarification, the PMRA will remove “stationary” and emphasize “automated”.

2.6 Comment on Vapour Treatment

Vapour treatment (cold pipe application) of naled needs to be retained because not all greenhouse operators have access to automatic foggers.

Response
Potential exposure from cold pipe application (vapour treatment) of naled and re-entry into greenhouses following application was assessed. Vapour treatment can remain on the label provided that the mitigation in Appendix II is followed.

2.7 Comment on the Maximum Number of Applications per Year

The number of applications permitted per season in greenhouse crops is not clear.

Response
The number of applications has been confirmed as three per crop per cycle. This includes one application after harvest. A minimum seven-day spray interval is also required for greenhouse uses.

2.8 Comment on Volume Limit When Using Handheld Equipment

The specification of 1000 L volume limit for handheld equipment is not clear. Does it refer to volume of spray mix or of product?

Response
The limit is 1000 L of diluted product as per the label instructions.

3.0 Comments Pertaining to the Environment

3.1 Comment on the Reduction of Bird and Mammal Populations

It is not clear what information was relied upon to establish that access to contaminated food would reduce bird and mammal populations by half within 0.4–7 and 1.3–22 days of exposure, respectively. To judge the scientific merit of this statement, it would be useful to see the details of the model used, the empirical data on which the model was based and the assumptions that were made.

Response
The following provides some of the details in response to this comment.

Birds and Mammals
Birds and mammals can be exposed to naled from spray drift as well as by consuming sprayed vegetation or contaminated prey. Immediately after application, food sources such as seeds and small insects in a treated field can have concentrations of the active ingredient (a.i.) of 3.7–64.3 and 21.7–375.6 mg a.i./kg (dry weight), respectively (Table 1). The residue concentrations on food items (Table 1) immediately after application at the various recommended rates were determined using modified (Fletcher et al. 1994 [3]) nomogram developed by the United States Environmental Protection

[3] Fletcher, J.S., J.E. Nellessen and T.G. Pfleeger. 1994. Literature review and evaluation of the EPA food-chain (Kenaga) nomogram, an instrument for estimating pesticide residues on plants. *Environmental Toxicology and Chemistry*. 13:1383–1391.

Agency (USEPA) from the data of Hoerger and Kenaga (1972)[4] and Kenaga (1973)[5], for use in ecological risk assessment (Urban and Cook 1986[6]).

Table 1 Residue Concentration on Vegetation Immediately after Application

Environmental Compartment	Concentration Dry Weight (mg a.i./kg) at Different Application Rates (kg a.i./ha)			
	0.11	**0.275**	**0.95**	**1.9**
Short-range grass	77.7	194.2	670.9	1342.4
Leaves and leafy crops	135.5	338.8	1170.4	2341
Long grass	47.4	118.6	409.6	819.3
Forage crops	71.3	178.2	615.6	1231.2
Small insects	21.7	54.3	187.7	375.6
Pods with seeds	4.6	11.5	39.6	79.3
Large insects	3.7	9.3	32.1	64.3
Grain and seeds	3.7	9.3	32.1	64.3
Fruit	11.2	28	96.7	193.5

Data on the acute oral toxicity for mallard duck (52.2 mg a.i./kg) were used to obtain acute oral toxicity data for a more relevant species such as field sparrow by extrapolation, using the procedure of Mineau et al. (1996)[7]. The theoretical acute oral toxicity for a sparrow-sized bird was estimated to be 26.75 mg a.i./kg.

To determine the potential risk to wild birds (e.g., sparrow) based on acute oral toxicity data, different parameters such as food consumption, body weights have to be taken into consideration. These are as follows:

4 Hoerger, F., and E.E. Kenaga. 1972. Pesticide residues on plants: correlation of representative data as basis for estimation of their magnitude in the environment. In: F. Coulston and F. Korte, editors, *Environmental Quality and Safety—Global aspects of chemistry, toxicology and technology as applied to the environment*, Vol. I. Thieme, Stutgart, and Academic Press, New York. pp. 9–28.

5 Kenaga, E.E. 1973. Factors to be considered in the evaluation of the toxicity of pesticides to birds in their environment. In: F. Coulston and F. Korte, editors, *Environmental Quality and Safety—Global aspects of chemistry, toxicology and technology as applied to the environment*, Volume II. Thieme, Stuttgart, and Academic Press, New York. pp. 166–181.

6 Urban D.J., and N.J. Cook. 1986. *Hazard Evaluation Division, Standard Evaluation Procedure: Ecological Risk Assessment*. United States Environmental Protection Agency EPA 540/9-85-001, Washington, DC. 96 p.

7 Mineau, P., B.T. Collins, and A. Baril. 1996. On the Use of Factors to Improve Interspecies Extrapolation of Acute Toxicity Birds. *Regulatory Toxicology and Pharmacology*, 24:24–29).

- mean food consumption (kilogram of dry weight of food/individual/day) of the control group
- mean body weight per individual in the control group
- expected environmental concentration (EEC) value (from EEC in diet proportional to food sources eaten, as mg a.i./kg dw)
- lethal dose to 50% of the population (LD_{50}) and no observed effect level (NOEL) (mg a.i./kg bw) (if not available, 1/10 of the LD_{50} is used)

The above values are entered into a spreadsheet and the output provided is as follows:

a) The daily intake (DI) of active ingredient by a wild species equivalent to the LD_{50} ($LD_{50(ind)}$/DI).
b) The daily intake of active ingredient by a wild species equivalent to the NOEL ($NOEL_{(ind)}$/DI).

Food consumption (FC) and body weight per individual (BWI) data are required because a direct comparison of EECs and toxicity endpoints cannot be made owing to differing units (mg a.i./kg dw and mg a.i./kg bw, respectively). These new data are used to convert the toxicity endpoints "mg a.i./kg bw" to "mg a.i./ind" (e.g., NOEL × BWI = $NOEL_{(ind)}$).

After entering FC, BWI and EEC into the spreadsheet, it calculates DI = (FC × EEC), $LD_{50(ind)}$ = (LD_{50} × BWI) and $NOEL_{(ind)}$ = (NOEL × BWI). When the $NOEL_{(ind)}$ (or $LD_{50(ind)}$) is divided by the daily intake, the units cancel, leaving only the time term. The value indicates the amount of time (in days) that the bird would have to feed to consume enough of the pesticide to reach the toxicity endpoint. As this interpretation is for acute exposures, times longer than one day are not considered hazardous, whereas those less than one day are considered hazardous. A value greater than one day indicates that dietary (chronic) exposure may be a more important route of exposure. Thus, the results for naled indicated that birds would have to consume contaminated food sources for only 0.04 to 0.7 days only to reach a dose equivalent to the NOEL. As the value is less than one day, an acute risk to birds has been identified. Similarly, birds would have to consume contaminated food sources for 0.4 to 7 days to reach a dose equivalent to the LD_{50}. An alternate interpretation is that birds (or mammals) need only consume part of their daily intake to reach exposure levels that will cause effects.

The same procedure is followed for mammals. The results indicated that small mammals would have to consume contaminated food sources for 0.1 to 2.2 days to reach a dose equivalent to one that had no observed effect on individuals in the laboratory population. Small mammals would have to consume contaminated food sources for 1.3 to 22 days to reach a dose equivalent to the LD_{50}.

3.2 Comment on the Toxicity Level to Birds and Overall Conclusion

It was claimed that observed effects on bird populations around the field can be estimated to take place within 58 minutes of exposure (0.04 of a day); how does this classify as a low level of acute risk to birds? That birds will begin dying within an hour after application suggests that the safety of this product is in question.

Response
The PMRA agrees that the statement from the naled PACR document "for terrestrial organisms, there are low levels of acute risk to birds" was an error. As was described in detail above, there is risk to birds of acute effects. Mortality of birds would be expected if 100% of their diet was contaminated with naled.

3.3 Comment on the Chronic Toxicity to Birds

There is no mention of chronic or reproduction tests in birds. This test has been part of the basic, first tier registration requirements for the last 30+ years, especially when there is widespread potential field exposure. A strong rationale should be outlined if the PMRA does not believe that this information is needed.

Response
The PMRA did carry out an evaluation of the chronic toxicity of naled to birds. Chronic toxicity (reproduction) studies conducted on mallard duck and bobwhite quail showed that the mallard is the more sensitive of the two species, with a no observed effect concentration (NOEC) of 260 mg a.i./kg. The endpoint was a reduction in the number of eggs. The NOEC of 260 mg a.i./kg from the avian reproduction study on the mallard indicated that the chronic risk to birds (risk quotient of 0.01–0.25) is low.

3.4 Comment on LD_{50} Data from the Literature

A search of the published literature provides LD_{50} data for seven species of birds rather than the three taken by the PMRA from the 1999 USEPA document. All seven species should be used in the assessment.

Response
The PMRA review considered toxicity data provided in the USEPA document on the mallard duck, the Canada goose and the sharp-tailed grouse. The PMRA also estimated effects endpoints for smaller species of birds (e.g., American robin sized and field sparrow sized) to make the assessment more relevant to smaller-sized birds. These data were extrapolated from the mallard acute toxicity data, using an equation from Mineau et al. (1996)[8].

3.5 Comment on Modelling

Some of the highest application rates of naled are for pests and crops predicted to lead to the highest degree of wildlife exposure (e.g., up to 864 g a.i./ha in pastures, 1900 g a.i./ha in alfalfa). An empirical field-based model (Mineau 2002)[9], which has now been validated, could provide better prediction of avian mortality.

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[8] Mineau, P., B.T. Collins and A. Baril. 1996. On the use of scaling factors to improve interspecies extrapolation of acute toxicity in birds. *Regulatory Toxicology and Pharmacology*. 24:24–29.

[9] Mineau, P. 2002. Estimating the probability of bird mortality from pesticide sprays on the basis of the field study record. *Environmental Toxicology and Chemistry*. 24(7):1497–1506.

Response
Environmental risk assessment methods are currently in transition, and the initial risk assessments for organophosphates were conducted prior to the publication of the paper. Thus, the model referred to was not available at the time that the environmental risk assessment of naled was conducted. The PMRA is aware of the model and will take the model together with its validation data into consideration for incorporation and improving the Agency's avian risk assessment methods.

3.6 Comment on the Effect of Conversion on Food Sources

Because of naled's rapid conversion to dichlorvos, an assessment should consider likely impacts resulting from dichlorvos as well.

Response
Information on percent transformation of naled to dichlorvos on contaminated food sources was not available; hence, the risk from dichlorvos to birds and mammals was not determined. However, given the similar modes of action and the similar dietary toxicity for birds, exposure to naled via potential food sources would not be expected to add significantly to the risk to birds and mammals. Dichlorvos is also currently under re-evaluation.

3.7 Comment on Aquatic Assessment

Conclusions of the aquatic assessment are as follows:

> The assessment concluded that for all aquatic invertebrates and plants acute risks from use of naled was high to extremely high at all application rates.

It is not clear how these assessment results are taken into account given that the PMRA proposes to reregister most uses of naled.

Response
The decision for continuing registration of naled is a risk management decision that considers many factors, including risk to the environment. The environmental assessment used a conservative approach in characterizing risks to the environment. For acutely toxic pesticides such as naled, one of the major concerns and sources of input to aquatic systems is through spray drift. The observance of buffer zones, however, can effectively mitigate the risk to aquatic non-target organisms resulting from spray drift.

3.8 Comment on Toxicity Endpoints and Calculation of Risk Quotient

To evaluate naled's risk to the aquatic environment, a risk quotient is calculated from toxicological data and estimated environmental concentrations. PACR2004-33 states that naled is very highly toxic to aquatic organisms. However, it is difficult to evaluate the toxicity data, as they are not referenced.

Response
The standard practice in re-evaluation is to rely on the USEPA's Reregistration Eligibility Decision (RED) and other credible foreign reviews. References are made to the foreign reviews, which are based on evaluation of original studies. We do not normally reference individual study authors, except when we review new studies not covered in the foreign reviews. These foreign reviews do not usually provide the raw data on the toxicity studies to determine if the NOEC was empirically derived or not. In those cases where NOEC values are not reported but LD_{50} values are presented, an NOEC value is derived as $0.1 \times LD_{50}$.

3.9 Comment on the Calculation of EECs

The method and data for calculating EEC are not provided in the PACR2004-33.

Response
The PACR document is a summary document; therefore, it does not include details on the method and data used in the calculation of EECs in soil, water and food sources for birds and mammals. The EECs are based on label application rates and environmental media and have no relevance to species. For example, the EEC_{water} of naled for rates of 0.11–1.9 kg a.i./ha would range from 0.037 to 0.63 mg a.i./L in 30 cm depth of water. This represents a scenario of 100% deposit into the body of water and is a conservative assessment.

3.10 Comment on the Toxicity Data of Dichlorvos

After naled enters the aquatic environment, it has a half life of < 5 days. A significant and toxic breakdown product is dichlorvos, which is another registered organophosphate pesticide. Toxicity data for dichlorvos are not presented in the report although it clearly should be a consideration in determining acceptable levels of risk, and there is much data reported in the scientific literature.

Response
The transformation of naled to dichlorvos was taken into consideration. The maximum amount of dichlorvos formed from naled is approximately 20% of the applied active ingredient. Using the molecular weight ratio of dichlorvos to naled (0.58), the amount of dichlorvos (220 g/ha) in water was determined based on the naled maximum application of 1900 g/ha and the transformation of 20%. As mitigation of risk to the aquatic environment is through specification of buffer zones, the buffer zones were calculated to address the additional input of the transformation product. The results showed that buffer zones for naled as the parent compound are larger than for dichlorvos. Thus, buffer zones calculated for naled were chosen as a proper mitigation measure to minimize effects of naled and dichlorvos to the aquatic environment.

3.11 Comment on Additional Information Affecting the Buffer Zone

The technical registrant suggests that the PMRA revise the proposed buffer zone based on additional data submitted.

Response

The PMRA agrees that given the available data for toxicity of naled to aquatic invertebrates, the endpoint used in determination of buffer zones could be reconsidered. The USEPA RED (1977 and following revisions up to 2002) lists LC_{50} values of 0.4 and 0.3 ppb for *Daphnia magna* from studies conducted with the technical grade active ingredient, 90 and 91.6% a.i., respectively (MRID 40098001 and BA0NAL02/00097572). The results of the study attached to the comments from the registrant were also listed in 1977 RED (MRID 00263578). However, the PMRA notes this study was conducted with an end-use product (58% a.i.) and only the LC_{50} of 1.5 ppb was reported in the RED. The PMRA evaluated the submitted study for consideration in the assessing risk to aquatic systems.

Since the initial determination of the buffer zones, the PMRA has modified how it determines buffer zones. As well, when sufficient scientifically sound data is available, the PMRA now considers modifying endpoints for determination of buffer zones to include consideration of mesocosm results or, in some cases, to use species sensitivity distributions (SSDs) to determine the concentration that will protect 95% of species (HC_5) based on LD_{50} values. The PMRA believes this approach will be protective of aquatic invertebrate communities.

In the case of naled, reconsideration of the effects endpoint and consultations with the registrant on specifications for aerial applications (i.e., restricting aerial applications to meet certain spray quality parameters) have resulted in buffer zones for some aerial applications.

In reconsidering the effects endpoint for buffer zone determination, the PMRA took an approach to mitigate risk for aquatic invertebrate communities as a whole. In order to determine an endpoint that would be protective of the invertebrate community, an SSD was used to determine the hazardous concentration affecting 5% of species (HC_5) was calculated using a software program, ETX 2.0 (van Vlaardigen et al. 2004)[10]. At this concentration, 95% of species would not be affected at the LC_{50} level, which, for invertebrates, is thought to be protective at the community level. The HC_5 value of 0.3 µg a.i./L was derived from available invertebrate toxicity data (see Table 2) for naled, including information received from Environment Canada. The concept of using a

[10] Van Vlaardingen, P.LA., T.P. Traas, A.M. Wintersen and T. Aldenberg. 2004. ETX 2.0. *a Program to Calculate Hazardous Concentrations and Fraction Affected, Based on Normally Distributed Toxicity Data*. RIVM Report 601501028.

species sensitivity distribution for the protection of communities or populations is established in the ecotoxicology literature (Posthuma et al. 2002)[11].

Table 2 Species Sensitivity Distribution of Invertebrate Acute Toxicity Data for the Insecticide Naled, With Hazardous Concentration to 5% of Species (HC_5)

Species Name	Common Name	Endpoint	Study Duration (d)	Geometric Mean LC_{50} (µg/L)
Daphnia pulex	Water flea	EC_{50}	96	0.35
Pteronarcys californicus	Stonefly	LC_{50}	96	11.31
Gammarus lacustris	Amphipod	LC_{50}	48	13.5
Gammarus fasciatus	Amphipod	LC_{50}	96	15.9
Palaemonetes kadiakensis	Grass shrimp, freshwater prawn	LC_{50}	96	91
Asellus brevicaudus	Aquatic sowbug	LC_{50}	96	97.1
Palaemon macrodactylus	Korean or Oriental shrimp	LC_{50}	96	8.13
Palaemonetes vulgaris	Marsh grass shrimp	LC_{50}	96	9.3
Simocephalus serrulatus	Daphnid	EC_{50}	48	1.1
Daphnia magna	Water flea	EC_{50}	48	0.513
Mysidopsys bahia	Shrimp	LC_{50}	96	8.8
Toxorhynchites splendens	Mosquito	LC_{50}	48	551.4
Crassostrea virginica	Eastern oyster	EC_{50}	96	190

HC_5 = 0.3 µg/L (lower limit: 0.85%, upper limit:17.3%)

In consultation with the registrant on their reponse to PACR2004-33, clarification was sought on the spray characteristics for aerial applications. The registrant specified a medium drop size distribution (American Society of Agricultural Engineers [ASAE] medium, volume mean diameter [VMD] = 294 µm) for aerial applications for control of specified pests in sugarbeet, beans, peas, cole crops, alfalfa, clover, vetch, celery, lettuce, spinach, potato, tomato, strawberry, ornamentals, rangeland, field areas and pastures. For

[11] Posthuma, L., G.W. Suter II and T.P. Traas. 2002. *Species Sensitivity Distributions in Ecotoxicology*. Lewis Publishers.

aerial applications to corrals, feedlots, holding pens and woodlands for control of specified pests a very fine spray was specified (ASAE very fine, VMD = 82 µm).

Based on the above considerations, both ground and aerial buffer zones were recalculated. Based on the revised buffer zones, it was determined that ground applications can be supported for all uses, provided that buffer zones for protection of aquatic ecosystems are observed. For aerial applications, uses other than aerial applications to woodlands, can be supported provided that buffer zones for protection of aquatic ecosystems are observed (Appendix II) and applications are conducted with the spray quality parameters as specified on the label.

4.0 Comment on the Use of Naled for Mosquito Control

It is not clear from the PACR whether naled can still be used for mosquito control in Canada.

Response
The use of naled to control mosquitoes will remain as presently registered. Naled may still be applied (by ground mist blowers and/or aerial application) for adult mosquito control in Canada in the following areas:

- livestock pastures;
- feedlots
- corrals;
- holding pens;
- woodland areas; as well as in and around
- dairy barns;
- livestock barns;
- pig pens;
- poultry houses;
- cider mills; and
- wineries.

It must not be used in residential areas to control adult mosquitoes.

The proposed acceptable uses of naled are listed in Appendix II.

Appendix II Revised Use Standard for Commercial Class Products Containing Naled

NOTE: The information in this appendix summarizes the acceptable uses, limitations and minimum personal protective equipment (PPE) for the commercial class products containing naled resulting from this re-evaluation. This use standard does not identify all label requirements for individual end use products such as first aid statements, disposal statements, precautionary statements, and supplementary PPE that may be required. Additional information on labels for currently registered products should not be removed unless it contradicts information in this use standard.

COMMON NAME: **Naled**

CHEMICAL NAME: 1,2-dibromo-2,2-dichloroethyl dimethyl Phosphate

FORMULATION TYPES: Emulsifiable concentrate

SITE CATEGORIES:
4—Forests and Woodlots
5—Greenhouse Food Crops
6—Greenhouse Non-Food Crops
13—Terrestrial Feed Crops
14—Terrestrial Food Crops
20—Structural
27—Outdoor Ornamentals

GENERAL LIMITATIONS:

Do not use in conjunction with products containing trichlorfon or dichlorvos.

TOXICOLOGICAL INFORMATION:

Naled is a cholinesterase inhibitor. Typical symptoms of overexposure to cholinesterase inhibitors include headache, nausea, dizziness, sweating, salivation, runny nose and eyes. This may progress to muscle twitching, weakness, tremor, incoordination, vomiting, abdominal cramps and diarrhea in more serious poisonings. A life-threatening poisoning is signified by loss of consciousness, incontinence, convulsions and respiratory depression with a secondary cardiovascular component. Treat symptomatically. If exposed, plasma and red blood cell cholinesterase tests may indicate degree of exposure (baseline data are useful). Atropine, only by injection, is the preferable antidote. Oximes, such as pralidoxime chloride, may be therapeutic if used early; however, use only in conjunction with atropine. In cases of severe acute poisoning, use antidotes immediately after establishing an open airway and respiration. With oral exposure, the decision of whether to induce vomiting or not should be made by an attending physician.

For those products that contain greater than 10% petroleum distillates, the following text should also be added to the Toxicological Information section (placed at the end of the paragraph presented above), as an additional aid to the attending physician:

"NOTE: Product contains a petroleum distillate solvent."

PRECAUTIONARY STATEMENTS:

PROTECTIVE CLOTHING AND EQUIPMENT:

Groundboom:
- Mixers, loaders and applicators must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, a respirator, chemical-resistant gloves and eye protection when applying to areas larger than 30 ha in one day.
- Mixers, loaders and applicators must wear cotton coveralls over a long-sleeved shirt and long pants, a respirator, chemical-resistant gloves and eye protection when applying to areas smaller than 30 ha in one day.

Airblast:
- Mixers, loaders and applicators must wear cotton coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves and eye protection.

Aerial application:
- All applications must use closed mixing/loading systems.

Low-pressure handwand:
- Mixers, loaders and applicators must wear cotton coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves and eye protection.

Backpack:
- Mixers, loaders and applicators must wear cotton coveralls over a long-sleeved shirt and long pants, chemical-resistant gloves and eye protection.

High-pressure handwand:
- Mixers, loaders and applicators must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, respirator, chemical-resistant gloves and eye protection.
- Workers must not handle more than 1000 L of diluted product per day.

Greenhouse Vapour Treatment:
- Mixers, loaders and applicators must wear chemical-resistant coveralls over a long-sleeved shirt and long pants, respirator, chemical-resistant gloves and eye protection.

RESTRICTED ENTRY INTERVAL (REI):

- Do not allow worker entry into treated areas (outdoor or indoor) for 48 hours following application.

- If animals must be handled within 48 hours of application, wear chemical-resistant gloves.
- Greenhouses must be fully ventilated before re-entry. If the greenhouse cannot be ventilated after vapour treatment or fogging, the application should not be made.

ENVIRONMENTAL HAZARDS:

- TOXIC to aquatic organisms. Observe buffer zones specified under DIRECTIONS FOR USE.

DIRECTIONS FOR USE:

Greenhouse Vapour Treatment:
- Apply using a squeeze bottle only. Do not apply using a paintbrush or any other method.
- Apply to cold pipes only. Do not apply to hot pipes
- Maximum of 3 applications (including one postharvest) per crop per cycle.
- Minimum 7-day spray interval.

Greenhouse Fogging Treatment:
- Apply with automated fogging equipment only. All workers must vacate the premises during the fogging operation.
- Maximum of 3 applications (including one postharvest) per crop per cycle.
- Minimum 7-day spray interval.

Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification.

Airblast application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** direct spray above plants to be treated. Turn off outward pointing nozzles at row ends and outer rows. **DO NOT** apply when wind speed is greater than 16 km/h at the application site as measured outside of the treatment area on the upwind side.

Aerial application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply when wind speed is greater than 16 km/h at flying height at the site of application. For application to field crops including pastures, **DO NOT** apply with spray droplets smaller than the American Society of Agricultural Engineers (ASAE) medium classification. For application to corrals, feedlots and holding pens, **DO NOT** apply with spray droplets smaller than the ASAE very fine classification. **DO NOT** allow nozzle spacing to exceed 65% of boom length. **DO NOT** apply by air in woodlots. Workers using the maximum rate of 1.9 kg ai/ha must limit area treated to 200 ha per day.

Buffer zones:

The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive aquatic habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats).

Crop	Method of Application		Buffer Zones (metres) Required for the Protection of: Aquatic Habitat of Depths:		
			< 1 m	1–3 m	> 3 m
Sugarbeet, beans, peas, cole crops, alfalfa, clover, vetch	Field sprayer*		65	25	10
Celery, lettuce, spinach			50	20	10
Potato, tomato, strawberry			35	15	5
Ornamentals			40	15	5
Rangeland, field areas, pastures			30	10	4
Woodlands	Ground application (early growth stage)		55	35	25
Woodlands	Ground application (late growth stage)		45	25	15
Feed lots, pastures	Ground application		50	35	25
Beans, peas	Aerial	Fixed-wing	800	550	350
		Rotary-wing	650	375	200
Clover, vetch, alfalfa	Aerial	Fixed-wing	725	475	300
		Rotary-wing	525	300	175
Potatoes, tomato (field)	Aerial	Fixed-wing	800	550	300
		Rotary-wing	675	325	150
Pastures	Aerial	Fixed-wing	800	125	30
		Rotary-wing	425	95	25
Corrals, feedlots, holding pens	Aerial	Fixed-wing	800	400	150
		Fotary-wing	800	275	95

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy or ground, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy or ground, the labelled buffer zone can be reduced by 30%.

ACCEPTABLE COMMERCIAL USES FOR NALED:

General			EMULSIFIABLE CONCENTRATE UNLESS OTHERWISE STATED USE THE FOLLOWING INSTRUCTIONS AND LIMITATIONS **Use Directions:** Begin application at first sign of insects. On all sites apply as a contact spray or thorough cover spray. **Ground application:** Dilute with water to 100–300 L/ha unless otherwise stated. **Aerial application:** Use only where aerial application is indicated. Unless otherwise stated, dilute with water to 10–30 L/ha when aerial application is specified. **Limitations:** Maximum 2 applications per season, unless otherwise specified. Do not apply to food or forage crops within 4 days of harvest or grazing, unless otherwise specified. Do not apply when temperature is over 32°C. Do not re-enter treated sites for 48 hours. High-pressure handwand application: Workers must not handle more than 1000 L of diluted product per day.
Site	**Pest**	**Rate (g a.i.)**	**Application Instructions and Limitations**
Broccoli, Brussels sprouts, cabbage, cauliflower	Imported cabbageworm, diamondback moth caterpillars, aphids	950/ha	Ground spray application only.
	Cabbage looper	950–1900/ha	
Beans (dry or field), lima beans, peas (processing)	Alfalfa looper, aphids, red spider mites	950–1900/ha	Ground and aerial application. Workers using the maximum rate of 1900 g a.i./ha must limit the area treated to 200 ha per day.
Alfalfa, clover, vetch	Aphids, leafhoppers, loopers, lygus bugs	950–1900/ha	
Celery, lettuce, spinach	Looper caterpillars, aphids	950–1425/ha	Ground spray application only.
Onion (bulb or seed only)	Thrips, onion maggot	475/ha	
Potato	Colorado potato beetle, leafhoppers, flea beetles	950/ha	Ground and aerial application.
Strawberries	Red spider mites, aphids, spittlebugs	950/ha	Ground spray application only.
Sugarbeets	Red spider mites, leafhoppers	1900/ha	Ground spray application only. Do not apply to food or forage crops within 5 days of harvest or grazing.

General			EMULSIFIABLE CONCENTRATE **UNLESS OTHERWISE STATED USE THE FOLLOWING INSTRUCTIONS AND LIMITATIONS** **Use Directions:** Begin application at first sign of insects. On all sites apply as a contact spray or thorough cover spray. **Ground application:** Dilute with water to 100–300 L/ha unless otherwise stated. **Aerial application:** Use only where aerial application is indicated. Unless otherwise stated, dilute with water to 10–30 L/ha when aerial application is specified. **Limitations:** Maximum 2 applications per season, unless otherwise specified. Do not apply to food or forage crops within 4 days of harvest or grazing, unless otherwise specified. Do not apply when temperature is over 32°C. Do not re-enter treated sites for 48 hours. High-pressure handwand application: Workers must not handle more than 1000 L of diluted product per day.
Site	**Pest**	**Rate (g a.i.)**	**Application Instructions and Limitations**
Tomato (field)	Fruit flies (*Drosophila* spp.)	950/ha	Ground and aerial application. **Ground:** Use 400 L of water/ ha minimum. Make first application at 5–7days before first picking and if necessary, reapply once 5–7days later. **Aerial:** Use 70–100 L water/ha.
	Tomato fruit worm, hornworms, leafminers	864/1000 L of water	Ground application. Spray plants thoroughly. Use up to 2000 L diluted spray/ha.
Rangeland, field areas and pastures	Young grasshoppers	475–734/ha	Ground and aerial application. Animals may be present during treatment. If animals must be handled within 48 hours of application wear chemical-resistant gloves.
	Adult grasshoppers	605–864/ha	
Livestock pastures, feedlots, pastures (dairy cattle present)	Adult mosquitoes, gnats, house fly	110–275/ha	**Mist blower application:** 6048–10368 g a.i./1000 L of water. Calibrate equipment (rate of travel and output) to apply 110–275 g a.i./ha. Make applications during peak of infestation. **Aerial application:** Apply diluted with water or No. 2 fuel oil. Apply 6–22 L of diluted spray/ha. Time application for peak infestation. It is not necessary to avoid farm buildings or dairy barns. If animals must be handled within 48 hours of application wear chemical-resistant gloves.
Corrals, adjacent pastures, holding pens (dairy or beef cattle, sheep, horses, hogs present)	Mosquitoes, adult house fly	110–275/ha	**Aerial application:** Use 128 to 318 mL of dibrom per hectare (110–275 g a.i./ha). Dilute 1.44 L to 3.67 L in 100 L. Apply 9 L diluted spray/hectare. Apply over areas with animals present.To supplement control, treat buildings and protected areas with a space spray. If animals must be handled within 48 hours of application wear chemical-resistant gloves.

General			EMULSIFIABLE CONCENTRATE **UNLESS OTHERWISE STATED USE THE FOLLOWING INSTRUCTIONS AND LIMITATIONS** **Use Directions:** Begin application at first sign of insects. On all sites apply as a contact spray or thorough cover spray. **Ground application:** Dilute with water to 100–300 L/ha unless otherwise stated. **Aerial application:** Use only where aerial application is indicated. Unless otherwise stated, dilute with water to 10–30 L/ha when aerial application is specified. **Limitations:** Maximum 2 applications per season, unless otherwise specified. Do not apply to food or forage crops within 4 days of harvest or grazing, unless otherwise specified. Do not apply when temperature is over 32°C. Do not re-enter treated sites for 48 hours. High-pressure handwand application: Workers must not handle more than 1000 L of diluted product per day.
Site	**Pest**	**Rate (g a.i.)**	**Application Instructions and Limitations**
Roses and cut flower crops (greenhouse)	Whiteflies, spider mites, aphids, leafrollers, mealybugs	**Fog:** 6–12/100m^2	**Fog:** Maximum of 3 applications per crop, per cycle. Minimum 7-day spray interval. Make no application closer than 2 days to harvest. Apply with automated fogging equipment ONLY. All workers must vacate the premises during fogging operation and must not re-enter until the greenhouse has been ventilated. Do not re-enter treated areas for 48 hours after application. Thoroughly ventilate premises before re-entering. If the greenhouse cannot be ventilated after vapour treatment or fogging, the application should not be made. NOTE: Dibrom has not been assessed for phytotoxicity to all varieties of roses and cut flowers. If in doubt about crop safety, treat a small area of the crop to assess phytotoxicity before treating the entire greenhouse. WARNING: Avoid over treatment and direct application to plants as injury may result. White butterfly roses, Golden rapture, Green wandering jew and Dutchman's pipe may be injured by dibrom.

General			EMULSIFIABLE CONCENTRATE **UNLESS OTHERWISE STATED USE THE FOLLOWING INSTRUCTIONS AND LIMITATIONS** **Use Directions:** Begin application at first sign of insects. On all sites apply as a contact spray or thorough cover spray. **Ground application:** Dilute with water to 100–300 L/ha unless otherwise stated. **Aerial application:** Use only where aerial application is indicated. Unless otherwise stated, dilute with water to 10–30 L/ha when aerial application is specified. **Limitations:** Maximum 2 applications per season, unless otherwise specified. Do not apply to food or forage crops within 4 days of harvest or grazing, unless otherwise specified. Do not apply when temperature is over 32°C. Do not re-enter treated sites for 48 hours. High-pressure handwand application: Workers must not handle more than 1000 L of diluted product per day.
Site	**Pest**	**Rate (g a.i.)**	**Application Instructions and Limitations**
Tomato, cucumber, roses and cut flower crops (greenhouse)	Whiteflies, spider mites, aphids, leafrollers, mealybugs	**Vapour treatment:** 8.6/100m^3	**Vapour treatment:** Maximum of 3 applications per crop, per cycle. Minimum 7-day spray interval. Make no application closer than 2 days to harvest. Apply to cold pipes only. **Do not** apply to hot pipes. Apply undiluted to cold pipes by means of a plastic squeeze bottle. Do not apply using a paint brush or any other method. Make application when plants are dry. Apply continuously or to intermittent sections of pipe on each side and on one or more pipes through the centre of each range depending on the width of the range. Application to cold pipes should be followed by immediate heating of pipes to 41°C in steam houses, close vents for at least 1 hour after pipes are hot. With hot water systems, close house for at least 3 hours. Houses may remain closed overnight following treatment. Do not re-enter treated areas for 48 hours after application. Thoroughly ventilate premises before re-entering. If the greenhouse cannot be ventilated after vapour treatment or fogging, the application should not be made. Protect beehives in cucumber houses by covering with plastic or rubber sheet during treatment and until house is ventilated. NOTE: Dibrom has not been assessed for phytotoxicity to all varieties of roses and cut flowers. If in doubt about crop safety, treat a small area of the crop to assess phytotoxicity before treating the entire greenhouse. WARNING: Avoid over treatment and direct application to plants as injury may result. White butterfly roses, golden rapture, green wandering Jew and Dutchman's pipe may be injured by dibrom vapour treatment.

General			EMULSIFIABLE CONCENTRATE **UNLESS OTHERWISE STATED USE THE FOLLOWING INSTRUCTIONS AND LIMITATIONS** **Use Directions:** Begin application at first sign of insects. On all sites apply as a contact spray or thorough cover spray. **Ground application:** Dilute with water to 100–300 L/ha unless otherwise stated. **Aerial application:** Use only where aerial application is indicated. Unless otherwise stated, dilute with water to 10–30 L/ha when aerial application is specified. **Limitations:** Maximum 2 applications per season, unless otherwise specified. Do not apply to food or forage crops within 4 days of harvest or grazing, unless otherwise specified. Do not apply when temperature is over 32°C. Do not re-enter treated sites for 48 hours. High-pressure handwand application: Workers must not handle more than 1000 L of diluted product per day.
Site	**Pest**	**Rate (g a.i.)**	**Application Instructions and Limitations**
In and around dairy barns, livestock barns, pig pens, poultry houses, cider mills, wineries	House fly, lesser house fly, mosquitoes, gnats, fruit flies (*Drosophila* sp.)	2.6/L of water	**Space spray:** Direct spray throughout fly infested area. In dairy barns, livestock barns and pig pens spray around and above animals but not directly at animals. If animals must be handled within 48 hours of application wear chemical-resistant gloves. Do not use in milk processing rooms. Do not use inside dwellings. Do not use in poultry houses when birds are present. Do not apply to birds or contaminate eggs with spray.
Cider mills, wineries	Fruit flies (*Drosophila* sp.)	5.2/L of water	**Coarse spray:** Apply as a coarse spray to walls, floors, doorways, windows, refuse and cull piles where insects congregate. Do not apply to cull fruit or refuse piles to be fed to livestock. Avoid contamination of feeds, foodstuffs and food processing machinery. Do not apply when plants are in operation or when foods are present or exposed. Do not spray surfaces that will come into contact with foods. Cover food containers during spraying periods.
Outdoor ornamentals: roses, dahlias, chrysanthemums, Canterbury bells, arborvitae, pittosporum, snowball, Chinese magnolia, aucuba, zinnia, stocks, azalea, willow, privet	Aphids, leafhoppers, red spider mites, tent caterpillars, birch and holly leafminers, willow leaf beetle	1080–1000 L of water	Ground spray application only. Thorough spray coverage and contact of insects are necessary.
Woodland	Mosquitoes, gnats, house fly	110–275/ha	**Mist blower application:** For areas less than 500 ha only. Dilute 6048–10368 g a.i./1000 L of water. Calibrate equipment (rate of travel and output) to apply 110–275 g ai/ha. Make applications during peak of infestation. Equipment used for spraying should not be washed in the vicinity of lakes or streams.