Pesticide Risk Mitigation Engine

Small Mammal Risk Index

White Paper

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Summary

This index estimates the toxicity of pesticides to mammals by using species-sensitivity principles. Toxicity, application rates and pesticide first-order loss rate from vegetation are combined into a single predictor which is then used in a logistic model to predict the outcome of several field studies carried out on small mammals under both enclosed and non-enclosed conditions. The index score is expressed as the probability that residues will persist long enough at a toxic level to cause changes in the population trajectory of small mammals directly exposed to the spray.

Data Sources

Typically, mammal acute toxicity information is in the form of a rat Median Lethal Dose (LD_{50}); occasionally, other species' data (e.g. mouse, guinea pig, rabbit, dog, etc.) can be obtained. Limited comparison of rat data with field impacts of pesticides on small rodent populations (voles, field mice) suggested that: 1) acute toxicity data may be preferable to chronic toxicity information to predict population effects in the field, and 2) it would be preferable to use a species sensitivity distribution (SSD) approach and incorporate data for all mammalian species when those data are available than to rely on a single rat LD_{50} (Mineau *et al.* 2006, Mineau 2008).

The chosen SSD approach was the ETX 2.0 program (Van Vlaardingen *et al.* 2004) developed by the Dutch Government to calculate the hazardous concentrations and fraction of species affected by predicted exposure levels. It assumes log-normally distributed toxicity data. Distribution-fitting was carried out for all datasets with more than 5 data points. Visual inspection of the data was critical to ascertain normality. If the sample was considered normal based on a cumulative probability plot and the Anderson – Darling test, an SSD (species sensitivity distribution) was generated. If on the other hand normality was not met, the small sample method was used (Aldenberg and Luttik 2002). This consists in estimating the HD_5 on the basis of a mean LD_{50} and a pooled variance estimate of 0.36 (for the log10 LD_{50} values) calculated for a large group of pesticides at large. The median estimate of the HD_5 was calculated in order not to bias for data availability.

Note: Alternative toxicity descriptors that were tested against the field impact information (Mineau 2008) included: 1) the geometric mean of all reported rat LD_{50} values, the geometric mean of all reported mouse LD_{50} values, the lowest LD_{50} of any tested rodent, the LD_{50} for the most phylogenetically-appropriate surrogate species, and the chronic mammalian MATC (geometric midpoint between NOAEC and LOAEC) as determined by European regulatory authorities or corresponding 'chronic population adjusted dose' (cPAD) as given by the USEPA. The 'most appropriate surrogate species' strategy was possible because a number of key field studies also carried out an LD_{50} determination on the wild rodent species that were studied. This *approach did provide the best fit to the model but is impractical for the purpose of a general model.*

For modeling/validation purposes, a total of 23 studies on 8 active ingredients were found in the literature (see Mineau *et al.* 2006 and Mineau 2008 for references and data summary). The data are heavily biased towards a few active ingredients (especially azinphos-methyl, eight studies) due to EPA-sponsored research attempting to validate their risk assessment paradigm with that active ingredient. The field studies used in the model represent worst-case situations, because they are cases where pastures or old fields are sprayed directly. In many row crops, small mammal activity is probably concentrated around field edges, and their home ranges also include non-crop habitat. A population response was variously defined as reductions in some age or sex cohorts which could indicate mortality, or as changes in reproductive rates (e.g. pregnancy rates etc.) indicative of a more targeted effect on the reproductive process. With the selection of compounds represented in the dataset, the majority of effects were of the first type with only a few pesticides (e.g. carbaryl) showing reproductive effects over and beyond maternal toxicity. (This undoubtedly explains why chronic toxicity descriptors did not yield suitable models.) Because of the paucity of data, both types of effects were pooled without consideration of their causal nature or the ease with which they could be reversed post-spray. Although small mammal populations are able to bounce back very quickly from catastrophic mortality events, the impact may have ripple effects on consumers.

Index Structure

Logistic modeling of these field data showed that both toxicity/application rate and foliar half lives (DT_{50} for median Dissipation Time) provided the most parsimonious model to explain the field results. The biological plausibility of this finding increases our 'comfort' with an index structure that explains impacts at the population level by incorporating both acute toxicity and foliar persistence of the pesticide. In order to reduce the model to a single independent variable (given the small sample size), logical combinations of the toxicity and DT_{50} variables were explored. The best variable proved to be one entirely analogous to the chronic index in birds, namely the number of days after application where the lethal Risk Quotient (RQ) remains above one (Mineau 2008). (*Note: The area under the RQ over time curve was also calculated, but this variable did not prove as good as the simple number of days.*) This RQ is calculated based on a standard small herbivorous mammal feeding scenario. The model returns an index which is the probability that a population-level impact will be seen.

Details and Algorithms

We used the small herbivorous mammal (vole) scenario outlined in the EU guidance document (European Commission 2002). This scenario assumes a 25 g animal with a daily energy requirement of 68 kj/day. Given a diet of cereal shoots with an energy content of 18 kj/g dry weight, moisture content of 76.4% and assimilation efficiency of 46%, this scenario results in a net consumption of ~ 35 g fresh weight per day or 139% of body weight per day (European Commission op. cit.). The exact scenario used will not result in relative rankings being changed.

In keeping with this scenario, we used an average residue per unit dose value of 54.2 ppm, the value proposed for grasses and cereals in the latest EU guidance (EFSA 2008). In combination with a UPAF where applicable, this is used to estimate C_0, the initial residue concentration on foliage and other foods.

- C_0 (ppm or µg a.i./g of grass) = Application rate (kg a.i./ha) * 54.2 * UPAF

The critical residue level (C_{crit} - in ppm or µg/g) beyond which lethal effects are expected following a full day of feeding is calculated as follows:

- C_{crit} = HD_5 (in mg/kg body weight) * 0.025 kg bw * 1000 / 35 g of grass

The final calculation entails estimating the critical amount of time (T_c) needed for residues to drop from C_o to C_t, assuming first order loss rate and using the foliar DT_{50} as the best estimate of residue persistence in grasses and other foods.

- If $C_o < C_{crit}$, risk = 0, which is 0 days

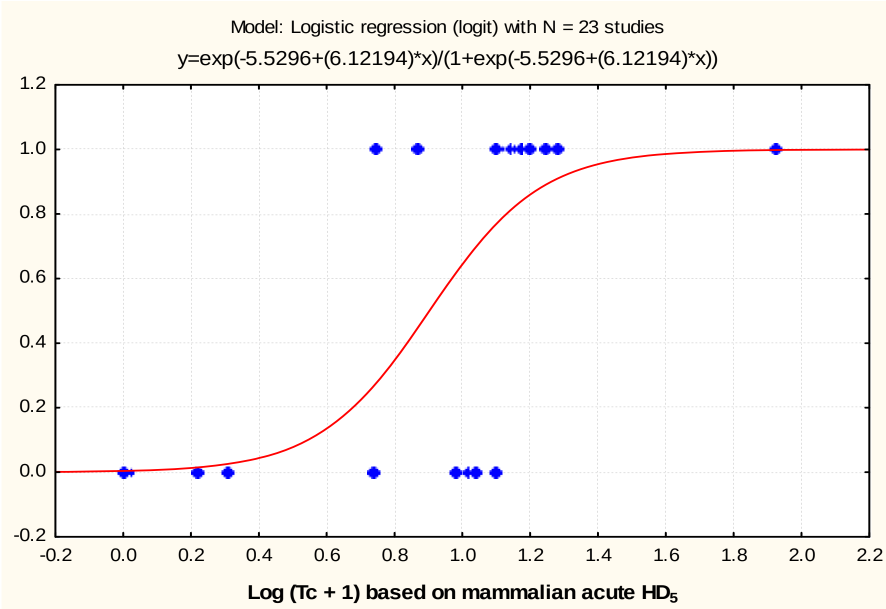
- If $C_o > C_{crit}$, measure the number of days required to drop to C_{crit} given the foliar half life.

Measure the removal rate K from foliar half life (DT_{50} or $t^{1/2}$)

- $K = \ln(0.5) / t^{1/2}$

…. and the critical time $T_{crit} = (\ln(Co / Ct)) / -k$ … measured in days.

The following logistic plot summarizes the available field evidence (23 field studies). We added the value of 1 to all T_{crit} values to avoid log 0 values and plotted them against the logistic score of 0 (no population effect seen in study) or 1 (significant population effect recorded).



Logistic model showing the probability of small mammal population response on the Y axis (0=no response; 1=significant effect) using, as predictor, a log transform of the critical time (in days) that residues in the environment are predicted to be at a level exceeding the 5% acute toxicity threshold determined from a species sensitivity distribution.

The resulting model has the following formula:

$$p = \left(\frac{e^{a+bx)}}{1+e^{a+bx)}} \right)$$

Where p is the probability of a population effect, x is the value of log (T_c + 1), and …

- a = -5.5296
- b = 6.12194

The index score will simply be p, the probability that a population impact will be seen given the length of time residues are calculated to persist at hazardous levels in the environment.

UPAFs

Use Pattern Adjustment Factors (UPAFs) are different from those developed for birds, reflecting a few key differences in exposure potential. It is considered unlikely that small mammals would be interested in sand-based granules although shrew species are likely to encounter all granule types adhering to earthworms and other soil invertebrates. It is also likely that small mammals rely less on movement of their prey than birds for foraging and are therefore more interested in dead or moribund insects knocked down from the vegetation by a spray application. In the absence of relevant field data, scenarios are difficult to verify, and it is even more difficult to rate different formulations on the same scale. Nevertheless, the following UPAFs are proposed. As with the avian reproductive index, the UPAF is to be applied to the calculated exposure.

It is recommended that we use the same UPAFs as those for the acute bird index for liquid formulations.

APPENDIX B: Table 1: Proposed avian "Use Pattern Adjustment Factors"

Pre-Plant or Pre-Emergence				Post-Emergence		Either
Soil Applied: Liquid	Soil Applied: Granular	Soil Applied: Unspecified	Seed Treatment	Ground Foliar Applied	Soil Applied: Liquid	Aerial Application
0.5 (surface) 0.1 (sub-surface) 0 (application followed by tarping)	See below	0.5	See below	1	0.5 (surface) 0.1 (sub-surface)	1

For granulars, we assume a low attractiveness for all but corn cob granules. We also assume tarping is unlikely to be effective at keeping out small mammals.

Silica granules	Corn cob (organic) granules	Heat treated montmorillonite and other non friable clays, cellulose	Friable granule bases: bentonite and gypsum	Tarping follows granular application
0.1	2	0.1	0.1	1

Literature cited (Note : Author's articles and reports available upon request)

EFSA. 2008. Scientific Opinion of the Panel on Plant protection products and their residues on a request from the EFSA PRAPeR Unit on risk assessment for birds and mammals. The EFSA Journal (2008) 734, 1-181.

Mineau, P. C. Morrison, M. Whiteside, and K. Harding. 2006. Developing risk-based rankings for pesticides in support of standard development at Environment Canada: Preliminary terrestrial rankings. National Agri-Environmental Standards Initiative Technical Series Report No. 2-43, Environment Canada, 92 pp.

Mineau, P. 2008. Attempts to validate/calibrate mammal risk assessments. Appendix 19; Scientific Opinion of the Panel on Plant Protection Products and their Residues on Risk Assessment for Birds and Mammals, EFSA Journal (2008) 734, 13pp.

Van Vlaardingen, P.L.A., T.P. Traas, A.M. Wintersen, and T. Aldenberg. 2004. ETX2.0. A program to calculate hazardous concentrations and fraction affected, based on normally-distributed toxicity data. RIVM report (and software) 601501028/2004. National Institute for Public Health and the Environment, The Netherlands.

Appendix 1. Comparison of proposed small mammal population scores calculated with a sample of in use pesticides in apples and the NASS-determined national average application rate. Scores are given in decreasing order of risk. This is for illustration purposes only since actual scores will depend on actual application rates entered into PRiME. Also, these are raw scores without any mitigating UPAF.

AI Accepted Name	Application Rate (g ai/ha)	Acute Population Risk for Small Mammals
Copper hydroxide	2933.66	1.00
Formetanate HCL	858.69	1.00
Paraquat	1338.47	1.00
Endosulfan	1634.42	0.89
Oxamyl	236.53	0.88
Phosmet	1803.69	0.58
Azinphos-methyl	932.67	0.53
Diazinon	1685.98	0.35
Chlorpyrifos	1683.74	0.19
Methomyl	589.65	0.03
Dimethoate	1268.97	0.00
Benzyladenine	38.11	0.00
Carbaryl	1249.92	0.00
Captan	2228.55	0.00
Clofentezine	232.05	0.00
Lambda-cyhalothrin	34.75	0.00
Cyprodinil	205.14	0.00
Dodine	896.80	0.00
Diuron	1663.56	0.00
2,4-D	508.93	0.00
Ethephon	543.69	0.00
Fosetyl-al	2738.60	0.00
Glufosinate-ammonium	832.90	0.00
Glyphosate iso salt	1337.35	0.00
Imidacloprid	96.41	0.00
Kresoxim-methyl	124.43	0.00
Malathion	3021.10	0.00
Mancozeb	2999.80	0.00
Metiram	2898.91	0.00
Myclobutanil	143.49	0.00
NAA	22.42	0.00
NAA, Sodium	13.45	0.00
NAD	65.02	0.00
Acetamiprid	164.79	0.00
Oxyfluorfen	1256.64	0.00
Pendimethalin	1617.60	0.00
Permethrin	190.57	0.00

Pyraclostrobin	1.12	0.00
Pyridaben	278.01	0.00
Pyrethrins	143.49	0.00
Simazine	1592.94	0.00
Spinosad	116.58	0.00
Sulfur	7051.09	0.00
Terbacil	925.95	0.00
Chlorothalonil	1460.66	0.00
Trifloxystrobin	73.99	0.00

Appendix 2: Peer Review Comments

This white paper was reviewed by the following independent experts. Below are their comments, listed anonymously, along with the author's responses.

- **Anne Fairbrother**, senior managing scientist, Exponent
- **Rich Marovich**, staff environmental scientist, California DPR

General comments:

- I can envision great utility for this approach as a comparative tool for assessing risks among pesticides or between different organism classes. I'm not sure that this tool will necessarily replace any others, but I do think it will be very useful when conducting comparative risk analyses, either among chemicals or between classes of organisms for individual chemicals. It also is a very good communication tool for these types of assessments.

Detailed comments and responses:

Comment 1: I applaud the author's mention in the supporting materials for the Mammalian model that this is not a useful tool for making risk-based management decisions about one particular pesticide.

Comment 2: I agree with the use of the LD50 (acute toxicity) data in a species sensitivity distribution approach.

Comment 3: The summary states that "because of the paucity of data, both types of effects were pooled without consideration of their causal nature or the ease with which they could be reversed post-spray." I agree with pooling all the data, but I do NOT agree with calling this index an "acute population risk" index. First of all, I think "acute population effects" is a misnomer and secondly I do not believe that a single mortality event (or even several within in one summer spaced 3 or more weeks apart) would have a population effect on a small mammal. These animals breed very quickly and their populations would rebound quickly from that type of insult (see next sentence in the text). They may suffer more from a reproductive impact if it were sufficiently long in duration but even then may not have a population effect. Rather than arguing about the terminology, why not just call this an index of "Small mammal acute risk" since it really is analogous to the Avian Acute Risk index.

> **Response:** *We agree. This index is not based on a few single mortality events but on a measured deviation from a population trajectory. Perhaps the solution is to merely call it the "Small Mammal Index" without specifying.*

Comment 4: I think this sentence can be deleted as it has no consequence on the method development: "Although small mammal populations are able to bounce back very quickly from catastrophic mortality events, the impact may have ripple effects on consumers."

> **Response:** *I disagree. This adds ecological justification for the index.*

Comment 5: This sentence can be deleted: "The biological plausibility of this finding increases our 'comfort' with an index structure that explains impacts at the population level by incorporating both acute toxicity and foliar persistence of the pesticide." Intuitively, coupling acute toxicity (single or very short exposure) to persistence (which implies opportunity for multiple exposures) does not make a lot of sense. I suspect this has more to do with Toxic Units per hectare and increased opportunity for exposure of multiple generations than it does to anything else. Again, we are not really assessing "population level" risk.

> **Response:** *Actually, this is indeed the reason the index is improved by a consideration of exposure time.*

Comment 6: As with the avian reproductive risk index, I like the concept of risk being indexed to the length of time that exposure remains above a toxic threshold.

Comment 7: Determination of dietary intake is appropriate (and the model is not particularly sensitive to its exact value), as is calculation of initial concentration.

Comment 8: Calculation of critical time (t) is appropriate.

Comment 9: I have concerns about this index for application in California. Grain bait vertebrate pesticides are not discussed even though they are widely used here and pose the most extreme risk to non-target mammals, dwarfing all other pesticide risks.

> **Response:** *This version of PRiME will not differentiate between different bait materials. All will trigger a warning. A new model would be needed to consider secondary potential. This may be for further development of PRiME.*

Comment 10: The use of voles as a reference mammal is understandable, but they are an agricultural pest and damage crops when populations explode periodically--typically once every seven years. These explosions occurred even in crops like citrus when they were treated with parathion, raising questions about the relationship of OP exposures to populations.

> **Response:** *Anecdotal evidence is difficult to use. Several studies with OPs were included in the model.*

Comment 11: In this small mammal model, ingestion rates were calculated based on a vole eating vegetation. Ingestion rates will differ (and not linearly) for invertiverous animals or ganivores. Therefore, simply applying a linear UPAF may not be correct. Perhaps the Nagy dietary equations could be used in some manner instead…? Just a thought…

Comment 12: At the very end, the statement is made that:

> Rodenticides are extremely toxic to vertebrates. The key to safe use of rodenticides is to exclude all but the target species from the bait through the use of efficient bait boxes. Dead rodents should also be disposed of in a way that will make it impossible for scavengers to find.

It is not clear to me why it is here. After all, similar warnings could be made about granular pesticides ingested by birds or mammals. It is true, but is it really necessary?

> **Response:** *Yes, because these products do not fit the model structure.*

Comment 13: We have federally listed mammals in California, notably San Joaquin kit foxes that occasionally traverse agricultural fields. The small mammal index might be used to justify banning certain pesticides from agricultural fields, leading in turn to a backlash against conservation, even though there is no field evidence that these pesticides are impacting kit foxes. The lack of known impact on farm dogs that enter fields following treatment also raises questions about the significance of field exposures. Many crops such as alfalfa and tomatoes provide excellent foraging sites for raptors and are key components of conservation for the state listed Swainson's Hawk. Rodents are abundant in these fields in spite of pesticide applications. California ground squirrels are ubiquitous in agriculture and gophers are also major pests, especially in orchards. The abundance of small rodents in agriculture begs the question of whether and how pesticides could be adversely affecting their populations.

> **Response:** *Point taken. Effects documented in the model are likely short term. This is an issue for risk management rather than risk assessment.*