

US EPA ARCHIVE DOCUMENT

SAP Report No. 99-01A, January 22, 1999

REPORT:

**FIFRA Scientific Advisory Panel Meeting, December 8, 1998,
held at the Sheraton Crystal Hotel, Arlington, VA**

*I - A Set of Scientific Issues Being Considered by the
Environmental Protection Agency Regarding:*

**Methodology for Conducting Comparative Ecological
Risk Assessments**

Larry C. Dorsey
Designated Federal Official
FIFRA/Scientific Advisory Panel
Date: _____

Dr. Ernest E. McConnell
Chair
FIFRA/Scientific Advisory Panel
Date: _____

FEDERAL INSECTICIDE, FUNGICIDE, AND RODENTICIDE ACT SCIENTIFIC ADVISORY PANEL MEETING

I - A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding Methodology for Conducting Comparative Ecological Risk Assessments

The Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) has completed its review of the set of scientific issues being considered by the Agency regarding methodology for conducting comparative ecological risk assessments. Advance public notice of the meeting was published in the Federal Register on November 13, 1998. The review was conducted in an open Panel meeting held in Arlington, VA, on December 8, 1998. The meeting was chaired by **Dr. Ernest E. McConnell** of Toxpath, Inc. **Mr. Larry Dorsey**, SAP Executive Secretary, served as the Designated Federal Official.

Participants

FIFRA Scientific Advisory Panel Members:

Dr. Ernest E. McConnell, Toxpath, Inc., Raleigh, NC

Dr. Fumio Matsumura, Professor, Institute of Toxicology and Environmental Health, University of California at Davis, Davis, CA

Herb Needleman, M.D., Professor of Psychiatry and Pediatrics, School of Medicine, University of Pittsburgh, Pittsburgh, PA

Dr. Mary Anna Thrall, Professor, College of Veterinary Medicine & Biomedical Sciences, Colorado State University, Fort Collins, CO

FQPA Science Review Board Members:

Dr. Bill Adams, Kennecott Copper Company, Magna, UT

Dr. Arthur Buikema, Jr., Professor, Department of Biology, Virginia Polytechnic Institute and State University, Blacksburg, VA

Dr. Richard DiGiulio, Professor, Nicholas School of the Environment, Duke University, Durham, NC

Dr. Christian Grue, Leader, Washington Cooperative Fish & Wildlife Research Unit, Seattle, WA

Dr. Alan Maki, Environmental Advisor, Exxon Corporation, Houston, TX

Dr. Tom Mueller, Professor, University of Tennessee, Knoxville, TN

Dr. Raymond J. O'Connor, Professor, Department of Wildlife Ecology, University of Maine, Orono, ME

Dr. Jim Oris, Department of Zoology, Miami University, Oxford, OH

Dr. Reynaldo Patino, Texas Cooperative Fish and Wildlife Research, Lubbock, TX

Dr. Don Wauchope, Agricultural Research Service, United States Department of Agriculture, Tifton, GA

Oral statements were received from the following individuals:

Dr. James A. Gagne, American Crop Protection Association

Written statements were received from:

American Cyanamid, Inc.

Summary of Agency Presentations

Mr. Douglas Urban (EPA, Office of Pesticide Programs) presented a proposed methodology for comparative analysis of the ecological risks from pesticides and their uses. Comparative analyses are generally included as a component of all major ecological risk assessments and characterizations for pesticides, and therefore standard methods are needed. In addition, comparative analyses are needed to aid in final decision-making to ensure consistency in risk management decisions and to focus these decisions on those pesticides that pose the greatest risk to fish and wildlife.

Methods were presented for comparing the potential ecological risk of pesticides used on similar crops sites. Risk indices were calculated and the results were compared to established levels of concern (LOC). In addition, since numerous calculations were made using a range of use rates and toxicity values, pesticides, and their use sites were compared based on frequency distributions of LOC exceedances. The comparisons included acute and chronic endpoints for terrestrial and aquatic organisms, as well as incident reports and information on extent of use. Pesticide specific ecotoxicology data and environmental fate and transport data were used in the analysis. Models such as GENIC and FATE were used to estimate pesticide exposure.

Panel Response to Agency Presentation and Questions

General Comments

The Panel commends Mr. Urban, his co-workers, and the Agency on an excellent presentation and a well organized document. Panel members believe the Agency has done a commendable job in attempting to get the most out of the available methods and data. The Panel appreciates the limitations of the data the Agency has to work with and the reality that decisions related to comparative risk and risk management have to be made within those limitations. However, Panel members believe there are too many scientific uncertainties in the approach to allow one to assume that the results do more than provide a rough estimate of relative, not absolute, risk within a narrow class of pesticide uses. The validity and use of the proposed approach (or a portion thereof) depends on the intended use of the results. It was not clear to the Panel how the proposed approach would be used within the existing regulatory framework. Therefore, it was difficult for the Panel to answer the specific questions below without knowing exactly how the calculations will be used and without having a clear statement of the limitations and assumptions that went into the risk calculations.

Panel members agreed that, as a first level screening tool or as a method of setting risk management priorities, the general approach of using risk quotients (RQs) (more accurately termed hazard quotients, [HQs]) is useful. In addition, Panel members agreed that the conventional use of the term "risk" in "Risk Quotient" may not be the best use. The Panel encourages the Agency to change the term risk to "hazard". The calculation of the RQ does not include elements of risk, but it is a useful indicator of potential hazard in the field. The term "risk" implies a probabilistic value scaled between 0 and 1 or presented in a ratio (e.g., 1 per 100,000). Since the Agency's calculations of RQ can range from 0 to infinity, RQ is not a risk quotient, but a HQ. As presented, it would be very easy to misconstrue RQ values as a measure of true risk such that the values can be used for quantitative comparison purposes when, in fact, they cannot.

Several members of the Panel believe that comparisons of relative risk by simple combinations of RQs may not be meaningful. The validity of the proposed calculations beyond the individual RQs depends on the assumption that the RQs used in the computations are linear for a particular pesticide and additive across pesticides. Panel members note that it is invalid to sum ranks (i.e., ordinal data) since the ordinal nature of the scale is not necessarily additive, rank data does not indicate whether the differences between rank neighbors are large or small. Concerns over the RQ as a risk scale are critical to the evaluation of the validity of the proposed approach to estimating total and relative risk. Unless the Agency is willing to argue that the RQ values actually quantify risk on what is technically a ratio scale, the proposed method of computing relative risk is problematic. In addition, it is not clear to Panel members what different conclusions beyond the RQs would be derived as a result of the analyses. Like the Agency, Panel members look forward to the adoption of probabilistic measures of risk (e.g., ECOFRAM) but note that the data needed to implement the latter (e.g., actual exposure data) are currently lacking and would have also improved calculations of the RQs as presented.

If used to set priorities for a higher tier assessment of prioritized chemicals, the approach described (or at least a portion thereof) appears to be useful. On the other hand, use of the analysis as a definitive assessment of ecological risk with which to review registrations and labels or require mitigation of exposure and/or effects associated with the worst-ranked chemical would be inappropriate. As detailed below, the Panel believes there are too many scientific uncertainties in the approach to allow one to assume that the results in fact quantify the true ecological risk. In addition, the assumption that all products are interchangeable is not always true.

With respect to the document, the reader is led through the effects and exposure calculations on which the resultant risk quotients and subsequent comparative risk analysis are based. Relevant data are presented in both graphical and tabular formats and secondary information is provided in appendices. The use of the case study data takes the reader through the steps of the process and elevates the document from a basic theoretical discussion to a "real-world" application of results.

Agency Questions

The Agency presented the following questions to the FIFRA SAP regarding methodology for conducting comparative ecological risk assessment. The questions are keyed to the Agency background document entitled *A Comparative Analysis of Ecological Risks from Pesticides and Their Uses: Background, Methodology & Case Study, November, 1998*.

1. Based on the typical sets of studies, data, and information provided for pesticide risk assessment purposes in the regulatory context and the use of the current risk assessment methods, is this approach useful/meaningful for evaluating the relative potential risk of pesticides and pesticide uses, especially for ascertaining large distinctions between the risks posed by pesticides?

Panel members agreed that, as a first level screening tool or as a method of setting risk management priorities, the general approach of using RQs (more accurately termed HQs as described above) is useful. However, several members of the Panel believe that comparisons of relative risk beyond comparison of individual RQs may not be meaningful or appropriate. Insufficient information was provided to fully evaluate the use and statistical characteristics of these additional calculations.

Because the procedure (calculation of RQs) provides only relative measures of risk, it should only be used as a tool to set priorities to identify pesticide uses which should be examined in more detail. No attempt has been made to relate the calculated indices to real impacts other than incidents of wildlife mortality, which themselves may be severely biased (the Panel provides greater analysis in response to Question 8 below).

The validity of the proposed calculations beyond the individual RQs depend on the unstated assumption that the RQs used in the computations are linear for a particular pesticide and additive across pesticides (e.g., calculation of RQ sum). The Panel notes that the Agency's proposal states "The risk quotients are intended to be used as rough indicators of comparative risk and cannot be used to predict how many birds will actually die or experience impaired reproduction." (p. 21 of the Agency's background document). This statement has two implications: 1) a pesticide with a higher risk quotient may be regarded as a higher risk than one with a lower RQ depending on the accuracy of the RQ, other species, and site specific factors and; 2) since the scale is relative rather than absolute, the most risky member of a group may in reality be quite safe, or, conversely, the least risky member may be quite damaging. Such a scale is commonly referred to as a rank or ordinal scale.

Page 26 of the Agency's background document further states: "It is assumed that all the potential risk for a particular endpoint on a particular crop site could be represented by the sum of the RQ values that exceeded the LOC for all the pesticides used on that crop site." This introduces two important assumptions. The first assumption is that it is valid to sum the RQs. Panel members note that it is invalid to sum ranks (i.e., ordinal data) since the ordinal nature of the scale does not ensure additivity. (One does see ranks summed in non-parametric tests, but those sums are evaluated as outcomes of permutations under the null hypothesis and not as possessing the

property of additivity). This restriction is important because one can arrive at the same sum by adding different combinations of rank values and yet have the true underlying values (if known) sum to a total corresponding to a different rank value. For example, if one cannot claim that an RQ of 5 corresponds to five times the risk of an RQ of 1 and that an RQ of 4 corresponds to twice the risk associated with an RQ of 2, then the summed RQ of 6 derived from the 5+1 can equate to a very different risk compared to that for the RQ of 6 derived from the 4+2: the first sum could be larger or smaller or equal to the second and one has no way of knowing which of these is the case.

The second assumption is that risk is associated only with pesticides whose RQ values exceed the LOC (p. 26; i.e., the EEC is greater than the LOC and therefore the $RQ > 1.0$). Panel members questioned ignoring RQs < 1.0 when computing total risk.

Concerns over the RQ as a risk scale are critical to the evaluation of the validity of the proposed approach to estimating total and relative risk. Unless the Agency is willing to argue that the RQ values actually quantify risk on what is technically a ratio scale (which the Panel would not support), the proposed method of computing relative risk is problematic. Panel members noted that even though the results of the proposed calculations match qualitative and other data (e.g., reports of mortality of fish or wildlife in the field), one can come to a correct conclusion for the wrong reasons, and have no assurance of success in subsequent analyses if the RQ scale is not linear. In view of this, it was difficult to answer the remaining questions as the validity of the assumptions underlying the calculations was questioned by the Panel.

2. Is the Agency's approach in the graphical presentation useful/meaningful for comparing the relative potential risk of pesticides and pesticide uses?

Assuming that the results of the analyses (input data) are an accurate reflection of risk within a valid conceptual framework, visual display of the data would be preferable to data tables. This approach allows better dissemination of this material to non-technical groups that care deeply about this issue. The Panel commends the Agency for considering their needs and using a graphical presentation. The Panel found the stacked, colored bar presentation easy to grasp; however, given the flexibility in today's software, it would have been nice to see other formats to more effectively answer the question. For example, it is possible to print out pie chart and numerous other 3-D formats that may also prove useful and effective in showing the relative contribution of each compound to the RQ sum. The bar graph summarizing the various endpoints was also informative, but difficult to understand. Perhaps labels and legends can be improved. One also needs to recognize that the graphical representation used is potentially subject to a number of visual biases. For example, choice of color used to represent safe and risky categories can subtly influence the viewer toward particular conclusions. The Agency's background document admirably acknowledges the role of subtle biases in reaching a final conclusion in the absence of sensitivity analysis of decision criteria and the Agency needs to consider explicitly the sources of visual bias within a graphical presentation of evidence.

Most Panel members agreed that the presentation of the final analysis (the percent of

potential risk) was not particularly useful. There are questions here concerning the actual readability of the graphs (too much information conveyed in a single plot) as well as the appropriateness of the input data (i.e., the constructed index of potential risk, as discussed below). These detailed graphs provide little additional information compared to the stacked bar chart of the percent contribution to the RQ sum (Figs. 1 and 2 of the Agency's background document). In addition, the Panel did not find any differences in the conclusions drawn from examination of the two types of plots. Therefore, the Panel questions the utility of the complex presentation versus individual graphs.

3. There are a number of new calculations for expressing potential risk, such as the percent contribution to the RQ sum, the frequency of RQ exceedance, the percent contribution to the time to RQ =1 sum, and the percent risk. Are these useful parameters for comparing the potential risk of pesticides?

In light of comments presented in question 1, Panel members questioned the validity of risk calculations beyond the individual RQs. In addition, it is not clear to Panel members what different conclusions would be derived as a result of the additional analyses. More specifically, the percent risk calculation is the most problematic as it assumes that a proportional increase in relative risk is equivalent in effect to an increase in the relative frequency of exceedances. No data are presented to justify this assumption.

The Panel is also concerned with the notion that the frequency of LOC exceedances is a useful measure. For this to be valid, the LOC would need to be a valid measure of risk. In the Agency's background document, the only quantitative statement the Panel found on this is in the footnote on p. 21, which states that the choice was based on field study data indicating that pesticide applications resulting in environmental concentrations of at least 1 LD₅₀/ft² have resulted in avian mortality. The problem with using exceedances above the LOC as derived is that the metric assumes that the LOC is known with certainty, whereas it is essentially an arbitrarily selected threshold. A rigorous analysis would model the occurrence of mortality in relation to the environmental concentration, most likely as a logistic equation predicting avian mortality in relation to a threshold determined from the data. The resulting threshold would then constitute a level of concern parameter whose statistic had a known uncertainty of estimation. This distribution could then be folded into the distribution of exceedances to provide an uncertainty to the distribution of exceedances. This might then, for example, be used in weighting the exceedances statistic when evaluating the evidence for the particular pesticide. Presumably, the uncertainty associated with the LOC would be common to all pesticides (or perhaps a class thereof) since it would be estimated for data pooled across pesticides. Therefore, the final weight to be attached to frequency of exceedances would depend on the relative uncertainty of exceedance distribution and the LOC. Clearly, such an approach would rapidly merge into a full-blown probabilistic risk assessment, but the fact that a realistic consideration of the present proposal for treating LOC exceedances so quickly points in that direction suggests that the concept is of limited value outside a probabilistic assessment process.

In the absence of such an analysis, a useful stop-gap would be to compute the exceedance values for a variety of LOC values (e.g., values of 0.4 and 0.6 versus only 0.5) and to examine how the frequency of exceedances varies within this sensitivity analysis. If the relative ranking of chemicals is unaltered, the analysis is robust, but if the ranking changes with the LOC inputs close to the standard threshold, conclusions reached with the standard value would be suspect in their lack of robustness.

With respect to the time to $RQ=1$, Panel members expressed concern that the time measure ignores the distribution of amplitude over time. The Panel would prefer to see an integral of risk over the time to $RQ=1$ used as the metric. For example, attaching the same weight to a pesticide that remains level at 30% above LOC for six days and one that declines linearly from 60% to 0% over the same time period.

As previously noted, Panel members questioned the validity of summing RQs. In addition, they suggest that if the metric is used, the calculation should not be limited to only those values exceeding the LOCs. The use of LOCs as a cutoff for inclusion in the sum is artificial and arbitrary, and should be kept separate from this calculation.

Panel members expressed concern over the use of market share (extent of use) in the risk (hazard) calculations. In many cases, these are transitory data. Each year, depending on weather, crop acreage, insect infestations, changes in crop varieties, company marketing programs, commodity prices, company consolidations, introduction of new active ingredients, and changes in registrations, the percent market share may shift substantially. These data have substantial uncertainty and will change dramatically over time.

4. The graphs presented by the Agency are in order of decreasing percent of acres treated. Otherwise, the extent of use would not be factored into the risk calculations. Is this appropriate?

Panel members agreed that it is useful to have data on extent of use acreage available when examining the risk calculations; however, these data should not be used in a quantitative sense (i.e., should not be part of the calculations). Plotting the pesticides in order of usage is acceptable, but then there is no need to include the actual value as a bar in the histogram. Several Panel members suggested providing the information as a separate graph.

The Panel noted that the plotting of incidents in combination with the acreage data introduces a bias against large acreage crops. For two crops with exactly the same true (but unknown) risk but with extensive and limited cultivation, respectively, the crop with the larger acreage is more likely by chance alone to have a mortality incident detected and attributed to it. The Agency proposes to attach no weight to the frequency of incidents nor to the probability of detecting those that do happen. However, one verified incident puts the chemical into the "risky" category. Therefore, the assessment of relative risk is biased by the proposed procedure.

5. Does the Panel agree that avian chronic risk should be included for sprayable formulations despite the Agency's inability to include this risk element for granular formulations? Should the Agency explore ways to use the avian chronic risk quotient for sprayable formulation as a surrogate to address this risk factor when comparing granular formulations?

The Panel was unified in its recommendation that chronic risk for sprayable formulations should be included irrespective of the Agency's current inability to include chronic risk for granulars and that data for sprayable formulations not be used as surrogates for granulars. It was not clear to Panel members why the Agency or the registrants have not already addressed this issue. The Panel believes that relatively simple laboratory and field experiments can be designed to overcome these problems and provide a basis for accurate exposure calculations for granulars.

6. Is the Agency's tabular presentation for decision analysis useful/meaningful for comparing the relative potential risk of pesticides and pesticide uses?

Members of the Panel were concerned about the validity of the assessment of relative risk as discussed above. In addition, the Panel noted that a potential weakness in the approach is a violation of independence among the input variables. Many of the values indexing toxicity are intercorrelated. It was also not clear to the Panel how distinctions are made between decision values if no levels of error or uncertainty are incorporated in the method (e.g., is 7.0 different from 9.0?)

7. Decision analysis software allows the user to deal with some uncertainty by running multi-scenarios. Does the Panel agree that the use of this approach is useful and can increase the confidence of conclusions derived from the results?

The Panel found the scenario analysis very useful. However, Panel members suggested a systematic investigation of the effects of varying all variables, not merely the subjectively chosen combinations presented. Instead of changing weights of the different ecological components, it would be useful to test the rankings by changing the values of the input variables (e.g., HQs, EECs, toxicity values). These manipulations can lend insight to the robustness of the rankings, increase the confidence in the predictions, and move toward a better understanding of the effect that varying levels of uncertainty can have on the predictions. In effect, Panel members favor running these scenarios as part of a sensitivity analysis rather than as a scenario analysis.

8. The Agency treated pesticide incidents as important when they existed. However, when there were no incident reports, this element was given a zero weight in the analysis. Is this an appropriate use of incident data for this comparative analysis?

Panel members were unanimous in their recommendation that incident data should be excluded from the risk analysis. Incident data should be pulled out of the calculations and presented separately from the index values. The problem with the scheme used here is that an

incident is treated as a direct measure of risk and weighted against the compound, without any regard for the likelihood of encountering such incident by chance. On the other hand, failure to have an incident on file should not be viewed as a favorable representation of the pesticide. The Panel realizes that no incident reporting is not the same as no risk, but is concerned about the bias (weighting) included with the formal incorporation of these data.

A possible solution would be to take the existing incident database and use a logistic regression (or other) model to try to predict the occurrence of an incident on the basis of selected predictor variables (e.g., acreage and timing of use with respect to animal behavior). If a successful model were obtained, it could be used to predict whether or not a particular compound should or should not have an incident recorded. For example, if the true chance of observing a fish kill is 1/1,000 acres, then one would expect to observe 0 incidences over 500 acres, 1 over 1,000, and 10 over 10,000 acres.

Finally, Panel members agreed that the Agency should increase its efforts to improve incidence reporting and to use these data in the overall risk assessment. The Panel agreed that currently these reports generally have too much bias and uncertainty to be formally included into the quantitative comparisons at the heart of the proposed approach. However, they do provide, at least in some instances, useful ancillary information. Perhaps the use of incident reports should focus upon states where these activities are stressed (e.g., California and New York).

Appendix 1 below presents comments on the Agency's background document by several Panel members. Even though several of these comments were not presented during the SAP meeting, they are provided to the Agency as suggested revisions to their document.

Appendix 1. Comments by SAP Members Concerning the Agency's Background Document

Page 14. Lines two and three of the table appear to be for the same freshwater fish chronic data and yet the equations for the lines are quite different. It is not readily obvious why these are different. Also, some further discussion is needed of the r values. Several do not appear to be significant and thus a straight line does not properly describe the data.

Page 17. Several questionable assumptions have been made to generate the EEC values, specifically use of ASM to predict foliar dissipation. While the Panel understands the logic of using ASM's as a means to measure foliar dissipation, it would be better to use the more direct measurement in the cited text. The Panel's concern is based on the fact that ASM and foliar dissipation are via totally different processes. ASM is dominated by degradation via microorganisms and chemical means while the pesticide is adsorbed or associated with soil particles. Foliar losses are dominated by volatilization, photodegradation and chemical degradation. Foliar losses will vary tremendously based on rainfall and incident solar radiation levels, and may be much more rapid than ASM rates, leading to possible orders of magnitude lower exposures depending on pesticide chemistry.

Page 20. One Panel member commented that in the Agency's discussion of the quotient method is actually a misnomer and often results in more confusion than necessary. A comparison of ecological exposure and effects is the core of all ecological risk assessment approaches. Although the present example generates a direct quotient, it is important to understand that all ecological risk assessments revolve around the same comparison, some are just more sophisticated than others. However, another Panel members disagreed commenting that probabilistic assessment do not result in risk or hazard quotients.

Page 38. The data seem to indicate that the chronic risk to freshwater invertebrates is indeed significantly greater than risks to marine fish. To answer the question directly, one needs to look at the variables that control the exposure and the relative toxicity to marine and freshwater species. It may be that the freshwater exposure is significantly higher due to a greater runoff potential and/or the freshwater species are more susceptible. The scale differences are the result of the method and remain important to the relative risk comparison.

Page 57. Since the method has clearly identified "G" as the standout compound of greatest risk, a review of the input variables would be appropriate to the same conclusion would occur with more simplistic toxicological or fate data. Is it possible to get the same relative risk ranking by simply comparing acute or chronic toxicological numbers? Or some aspect of the fate data?

Page 90. The heading of Ecological Risk Characterization seems to be a misnomer. The text does not really go through a risk characterization as much as a sensitivity analysis using updated and different input variables. If new or additional information becomes available, it would seem better to revise the original toxicity and fate data that went into the calculation of the Risk Quotient rather than try to tweak the system at this late stage. The text simply is not a risk characterization, it is instead a re-work of the original input variables.

NOTES