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OFFICE OF PREVENTION, PESTICIDES AND TOXIC SUBSTANCES

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SUBJECT: Evaluation of "Avian Probabilistic Ecological Analysis for Chlorfenapyr (AC 303630) in Cotton" (MRID 448098-01)

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INTRODUCTION

American Cyanamid and the Weinberg Group should be commended for their efforts in attempting to quantify variability associated with a number of important variables critical to exposure characterization.

The Environmental Fate and Effects Division (EFED) has performed a preliminary review of the probabilistic risk assessment entitled "Avian Probabilistic Ecological Analysis for Chlorfenapyr (AC 303630) in Cotton" produced by The Weinberg Group, Incorporated for American Cyanamid Company. Currently EFED is actively engaged in developing approaches and tools for probabilistic risk assessment through the ECOFRAM process. However, because this proces is not complete, this review centered on consistency with generic Agency-wide policy (USEPA/ORD/NCEA Policy for use of Probabilistic Analysis in Risk Assessment, May 15, 1997; available through www.epa.gov/nceaw1/mcpolicy) for the acceptance of probabilistic risk assessments and a number of assumptions and variables that had a high degree of influence on the output distributions of the analysis.

Despite American Cyanamid's assertion that the Risk Quotient method should not be considered appropriate for regulatory decisions, the submitted probabilistic risk assessment is fundamentally a calculation of risk quotients. The assessment is quasi-probabilistic because it attempts probabilistic analysis only for the exposure estimates. The characterization of toxicological effects relies on the single point estimate for a threshold of reproductive effects. A distribution of risk quotients is established by dividing an exposure probability distribution by the toxicological threshold. Although, the assessment does not address the likelihood and magnitude of effects, its general approach is an improvement over point estimates of exposure. As currently presented, EFED believes that a number of fundamental assumptions and mathematical approaches for establishing probability density functions for important input variables are inappropriate. Consequently, EFED does not believe that the probabilistic risk assessment submitted by American Cyanamid is technically complete or correct for regulatory purposes. EFED's reasons for this conclusion are highlighted in the ensuing documentation by the following major points:

1. American Cyanamid's definition of bird population boundaries is not consistent with Agency concerns for birds in treated cotton fields. American Cyanamid's definition extends into cotton agroenvironments not treated with chlorfenapyr, and essentially includes birds not foraging in cotton agroenvironments. This results in a large dilution effect with respect to exposure. Although consideration of large scale assessments may be appropriate for some widely ranging and randomly distributed bird species, assessments of effects at the field and local geographical scales should also be presented to for a more complete assessment with respect to different scales to facilitate management decisions. Considering solely the risks to populations defined in large scales may result in erroneous conclusions for some species in localized areas.

2. Numerous incorrect probabilities and/or probabilistic distribution functions severely limit other aspects of the exposure analysis.

IMPLICATIONS OF THE DEFINITION OF BIRD POPULATIONS FOR THE PROBABILISTIC ASSESSMENT OF EXPOSURE

The probabilistic risk assessment states that the analysis is for bird populations, and defines a population as a group of the same species inhabiting the portions of southern and western United States where cotton agroenvironments exist. The geographic scale for populations is therefore very large and has allowed for exposure dilution through the incorporation of treatment probabilities and population segments that do not forage in cotton agroenvironments. In order to understand the effect of this scale of population one must be familiar with the general exposure model incorporated into the assessment, which is as follows:

$$C_{diet} = (C_{diet\text{-}field} + C_{diet\text{-}buffer}) * P_{CAforage} * P_{treatment}$$

where: C_{diet} = total avian dietary exposure to chlorfenapyr

$C_{diet\text{-}field}$ and $C_{diet\text{-}buffer}$ = the dietary concentration of chlorfenapyr from cotton field and surrounding buffer, respectively

$P_{CAforage}$ = probability that a bird will select a cotton agroenvironment to forage

$P_{treatment}$ = probability that a field will receive chlorfenapyr treatment

As can be seen from the equation, the concentration of chlorfenapyr residues in treated fields and in buffers exposed to drift are effectively reduced by the fractional probability of a cotton acre being treated with chlorfenapyr across the cotton-growing portions of the United States ($P_{treatment}$, mean value 0.02, minimum 0.00065, maximum 0.26075) and a random bird's probability of selecting a cotton agroenvironment as a place to forage ($P_{CAforage}$, mean value 0.28, minimum 0.11, maximum 0.83). Unfortunately, this approach prevents a determination of the distribution of avian dietary exposures to chlorfenapyr at an individual treated field level or any geographic scale between field and national scales. Reliance on this broad definition of population presents an assessment only at the national level. EFED believes that the probabilistic risk assessment process should begin at the treated field level and provide for expansions of the consideration of impacts to populations defined over larger geographical scales. EFED believes that risk predictions for larger scales of population should be expressed in terms of the fraction of the total population affected at levels consistent with individual treated areas and that dilution of overall population exposure levels by the fraction of population exposed is not appropriate.

Furthermore, the use of national probabilities of field treatment requires an assumption that all bird species associated with cotton are evenly distributed throughout the cotton belt. A review of any avian field guide and the avian census data developed by American Cyanamid will show this assumption to be incorrect. If populations are to be defined as extending over the 750,000,000 acres of the cotton states, then the probabilistic assessment is only applicable to those species with true random distribution across the cotton states and is of questionable utility to any bird species with more restrictive geographical distribution. The probabilistic risk assessment presents no data to support an assumption of random and broad distribution for most of the 136 species observed in American Cyanamid studies of cotton agroenvironments. Most species distributions are habitat dependent, raising further questions regarding the basic assumption of this probabilistic risk assessment.

SELECTED DISTRIBUTION FOR $P_{infests}$ VARIABLE AND ITS EFFECT ON THE VARIABLE $P_{treatment}$

As stated in the above discussion of population definition, EFED questions the incorporation of the variable $P_{treatment}$, the likelihood that any given cotton field will be treated with chlorfenapyr for control of budworm, bollworm, and beet and fall armyworms, into the exposure assessment. EFED believes that the use of this variable shifts the risk assessment from exposures on treated fields to exposures on all cotton fields (including those never treated with chlorfenapyr), potentially leading to erroneous conclusions or at least overlooking significant effects. However, in-so-far as the variable is presented in the probabilistic risk assessment and exerts a great influence in the resulting output distributions of exposure, EFED has reviewed the derivation of this variable and believes that there are errors in the establishment of distributions of values for the variables that contribute to the computation of $P_{treatment}$.

The variable $P_{treatment}$ is a function of the probability that any given cotton field will be infested with the listed pests above an economic threshold triggering the need for treatment (P_{infest}) and the probability that the pesticide used will be chlorfenapyr (P_{market}) such that $P_{treatment} = P_{infest} * P_{market}$. It is important to note that, for all the bird species modeled in the probabilistic risk assessment, the sensitivity analysis of each variable's impacts on the output distribution of bird exposure is dominated by the variable P_{infest}. This variable alone accounts for 46% to 66% of the variance of the output distribution, depending upon bird species modeled.

P_{infest} is established by dividing a distribution of infestation acres for cotton for the years 1988 to 1996 by the average (point estimate) number of acres in cotton for the period 1965 through 1995. The assessment contends that the limits of the distribution for area infested is 170,000 to 9,260,000 acres. However, these limits represent a critical mathematical error that is founded on an unrealistic assumption regarding the available pest infestation data. The assessment considered each pest (budworm, bollworm, and beet and fall armyworms) *separately,* and used only the available 1989 fall armyworm data as the lower limit of the distribution and only the 1995 budworm/bollworm data as the upper limit of the data. This approach has effectively shifted the entire distribution to underestimate the acres requiring pesticide treatment in any given year. A more appropriate method for assigning the upper and lower limits of the acres infested would be to sum the acres infested with each of the pest infestations for each given year. This would be consistent with the problem formulation statement that the probabilistic risk assessment addresses all the pests, not just one. This appropriate approach could be made even more realistic with a possible correction to account for areas infested with more than one pest, though the probabilistic risk assessment includes insufficient data to allow for this. Using the available data cited in the probabilistic assessment, but without a correction for multiple pest overlap, the actual lower limit of acres infested with the pests of concern occurs in 1989 with 5,383,482 acres requiring treatment, and the upper limit occurs in1995 with 12,454,548. The implications for this error also extend to the calculation of the mean value of the distribution. *The net effect of this error is an underestimation of the probability of treatment (possibly ranging from 25% to 80%).*

Another error in the development of a distribution for P_{infest} is the use of the mean number of acres of cotton cultivated between 1965 and 1995 as the denominator for the variable P_{infest}. This incorrect approach ignores the potential for the variability in annual cotton production to affect variability in infestation. A more appropriate denominator for this variable may be the annual cotton acres that correspond to the year of infestation data (e.g., 1989 cotton acres infested/1989 total cotton acres), or use the distribution of cotton cultivated between 1965 and 1996, or the bounds.

The assumed shape of the probability distribution for P_{infest} may also be impacted by the approach of evaluating each pest species infestation separately. The approach used yields 28 data points (combinations of pest species acreage and year). However the correct number of data points is only 9 (total pest acres for the years 1989 to 1996). Incomplete infestation data for 1988 should eliminate this year from such an assessment. The number of data points and the corresponding values have resulted in a probabilistic assessment conclusion of a log-normal distribution of the data. However, the correct approach (9 data points for infestation, with each divided by area specific to each year's total cotton production) may not support such a conclusion.

ASSUMPTION OF INFESTATION PATTERNS AND EFFECT ON THE VARIABLE P_{infest}

A tacit assumption in the use of P_{infest} is that the probability of infestation is the same for all cotton acres. This assumption unrealistically ignores the potential confounding effects of field size, proximity of fields to presently infested fields, the variability in spacial relationship between fields, and the impacts of the Boll Weevil Eradication Program on the probability of infestation for certain pests (e.g. the beet armyworm). Ignoring these effects on the probability of infestation may result in underestimated probabilities for infestation in specific geographic areas, especially those subject to organized control programs for pests not included in the probabilistic risk assessment.

SUFFICIENCY OF DATA TO SUPPORT THE DISTRIBUTION FOR THE VARIABLE P_{market} USED TO ESTABLISH THE $P_{treatment}$ DISTRIBUTION

The variable P_{market} represents the probability that a field requiring treatment for control of the listed pests will receive chlorfenapyr. The values and distribution for this variable are based on estimates regarding American Cyanamid's market share. Without appropriate documentation this assumption cannot be validated. Furthermore, the assumptions of market share are subject to the influence of available alternatives to chlorfenapyr and therefore may be wholly inaccurate for predictive risk assessment purposes.

DISTRIBUTION FOR VARIABLE $P_{CAforage}$, THE AMOUNT OF TIME BIRDS SPEND IN THE COTTON AGROENVIRONMENT

The variable $P_{CAforage}$ is defined in the probabilistic risk assessment as the probability that a bird will select a cotton agroenvironment as a foraging area. The sensitivity analysis of variable effects on the output distribution of bird exposure reveals that this variable alone accounts for 10% to 14% of the variance in the exposure distribution.

To understand how the probabilistic assessment establishes values for $P_{CAforage}$, an understanding of the probabilistic assessment's definition of cotton agroenvironment is needed. The probabilistic risk assessment defines the cotton agroenvironment as a cotton field and its adjacent buffer. In their probabilistic assessment American Cyanamid has elected, on the basis of input data for residue variables, to define the buffer areas extending 150 feet off the cotton field. The probabilistic assessment uses the data presented in MRID444642-02 (as summarized in MRID444526-14) as the basis for the probability distribution for $P_{CAforage}$. The probabilistic assessment assumes, based on these data, that birds spend between 11 to 83% of their total time in an agroenvironment.

EFED believes that there are two important questions with the use of the cited data to represent the time birds spend in the cotton agroenvironment. First, the data cited in the probabilistic assessment from MRID444642-02 (as summarized in MRID444526-14) represents only the proportion of total bird sightings from study plots that encompass the cotton field and a buffer of approximately 150 feet that were actually within the cotton fields. Therefore, the probabilistic risk assessment actually underestimates the sightings of birds in the cotton agroenvironment (field and buffer) by assuming the cotton field observations (as a proportion of total observations) data cited from MRID44642-02 represents the total cotton agroenvironment (field and buffer). The probability of a bird being in a cotton agroenvironment from the MRID444642-02 study is 100% since all birds observed in this study were within the confines of the cotton agroenvironment as defined in the probabilistic risk assessment.

Second, even if the data were accepted as representing avian use of cotton agroenvironments, the probabilistic risk assessment uses the mean values of proportional census data from each study area in MRID444642-02. The use of mean data does not capture the true temporal, geographic, and species variability of field use versus agroenvironment use of birds from each cotton region where census data were collected. For example, the mean proportion of census sightings in Arizona fields adjacent to desert scrub habitats was 83% for birds actually in the cotton fields. However, a look at the top five species from these areas shows the proportions of sightings actually in cotton fields ranged from 40.6% for Gambrel's quail to 99.9% for red-winged blackbirds. The probabilistic risk assessment does not account for such variability about each mean value used in the exposure assessment. The probabilistic risk assessment uses four bird species for development of exposure probability functions and ultimate output distributions for risk quotients. However, the distribution of values assigned to the use of cotton field agroenvironments by these species were not employed in the exposure assessment. Instead the risk assessment relies on regional averages and assumes that the birds species assessed are generic representatives of feeding guilds.

SEED RESIDUE DISTRIBUTIONS $C_{seed-field}$ AND $C_{seed-buffer}$

The probabilistic risk assessment text indicates that the data for $C_{seed-field}$, the concentration of chlorfenapyr residues in weed seeds from fields, are derived from MRID444526-16. The text should be modified to also indicate that additional data were taken from MRID444526-08.

The data from MRID444526-16 were for weed seed heads taken from within fields treated with a single application of 0.35 lb a.i./acre. The methodology presented in MRID444526-16 suggests that samples were collected two days after application of the pesticide. These samples may represent an underestimate of time-zero residues in seeds because data from another weed seed study (MRID444526-08) show more than a 50% decline in weed seed head residues over the first 3 days after application of chlorfenapyr.

The additional data selected for use in the probabilistic risk assessment that originate from MRID444526-08 represent an important departure from the selection process for data selected from MRID444526-16. Unlike MRID444526-16, MRID444526-08 involved three consecutive applications of chlorfenapyr. The probabilistic risk assessment selects residue data corresponding to the third of the 3 applications of chlorfenapyr to treated fields. These data are then divided by the total application rate (all three applications added) to derive an application rate normalized residue concentration, which is then adjusted to reflect the application rates selected for the probabilistic risk assessment. American Cyanamid contends in the June 31, 1999 response to EFED technical questions regarding this probabilistic risk assessment, these values were selected "because they are the most conservative representing the maximum concentrations reached during the course of the study." Although the actual residues in weed seeds from the third application are slightly higher than residues from seeds collected after the first two applications, the normalization to the total mass of chlorfenapyr applied yields lower estimates of residue/pound ai/acre applied than estimates based on the first application or second application residues. For example, weed seed head residues of chlorfenapyr from MRID444526-08 were 27.2 mg/kg , 32.7 mg/kg, and 42.4 mg/kg for the first, second, and third treatments of 0.35 lb a.i./acre. The third application residues are higher than the first or second and their selection would, at first consideration, seem appropriately conservative. However, dividing each residue measurement by the total chlorfenapyr applied to normalize for application rate yields the following results for total application rate normalized seed residues:

first application	27.2 mg/kg ÷ 0.35 lb ai/acre = 77.7 mg/kg/lb a.i./acre
second application	32.7 mg/kg ÷ 0.70 lb ai/acre = 46.7 mg/kg/lb a.i./acre
third application	42.4 mg/kg ÷ 1.05 lb ai/acre = 40.4 mg/kg/lb ai/acre

The probabilistic assessments reliance on the residues associated with the third application results in appreciable (in the case above almost 50%) underestimates of time zero residues in seeds from the data in MRID444526-08. The use of these data serves to underestimate the distribution of values for inclusion in the variable $C_{seed\text{-}field}$.

The variable $C_{seed\text{-}buffer}$ is used in the probabilistic risk assessment to represent the distribution of chlorfenapyr residues in seeds from buffer areas outside the treated field but subject to contamination by drift. The data cited for this variable originated from MRID444526-05, a study of seed residues in off-field buffer areas (0 to 150 feet) associated with treated fields in Mississippi. As was the case for the data from MRID444526-08, the probabilistic risk assessment selected the residue data for the third of three applications; normalized these data by dividing by the total chlorfenapyr rate for all applications, and then adjusted to the rate used in the probabilistic risk assessment. Again, this approach yields results that underestimate the residues in seeds. Furthermore, the three applications for study fields in MRID444526-05 is wholly unsuitable for estimating residues under label conditions because the minimum application interval is 5 days for the label but the intervals for the applications in the residue study are as high as 30 days.

EFED is also concerned with extrapolation of weed seed residues from two sites to all cotton agronenvironments across the United States. EFED believes that the probabilistic risk assessment assumption of homogeneity of weed seed distributions across the Cotton Belt (American Cyanamid's June 31, 1999 response to EFED technical questions) should be supported by statistical analysis of the available weed seed data.

INSECT RESIDUE DISTRIBUTIONS $C_{insect-field}$ AND $C_{insect-buffer}$

The raw data for establishing a distribution of values for the variable $C_{insect-field}$ originate from one field study in Pulaski County, Georgia (the reader should note that residue data for larval lepidopterans shortly after pesticide application were actually from laboratory feeding studies). These residue data are then extrapolated to all cotton agroenvironments across the United States. American Cyanamid's June 31, 1999 responses to EFED's technical questions indicate that the probabilistic risk assessment assumes that insect residue distributions are homogeneous across all cotton agroenvironments in the Cotton Belt. EFED is unaware of any chlorfenapyr insect residue data to support this assumption of homogeneity. There are likely to be a variety of meteorological and technological sources of residue variability across the different cotton-growing regions of the United States and EFED believes that some accounting for extrapolation uncertainty would be warranted in applying site-specific residue data to large geographical areas.

FRUIT RESIDUE DISTRIBUTIONS $C_{fruit-field}$ AND $C_{fruit-buffer}$

The input data for establishing a distribution of values for chlorfenapyr residues in fruit on a treated field ($C_{fruit-field}$) is based on data used to establish residues on fruits and vegetables for human consumption. American Cyanamid's June 31, 1999 response to EFED technical questions states that data for tomatoes, strawberries, and grapes were used as the surrogates for wildlife fruits. EFED believes that these data may underestimate exposure. Many of these items are much larger than those encountered by wildlife in natural environments, and therefore differ in the surface to mass ratios critical to extrapolating residues from cultivated fruits to wild types. As an illustration, many wildlife fruits are typically less than 1 inch in diameter (fruit diameter examples include black cherry 0.375 inch, mulberry 0.75 inch, pin cherry 0.25 inch, and hackberry 0.375 inch, and pokeweed 0.25 inch). Even assuming a large wild fruit (0.5 inch diameter) and a grape, strawberry, or tomato of only 1 inch diameter, the surface areas of the two would be 0.785 and 3.14 square inches, respectively. Volumes of the wild fruit and the test fruit would be 0.06544 and 0.5236 cubic inches, respectively. Assuming equivalent density (1) for the two fruits, the surface to mass ratios of the wild fruit would be 11.99 and the test fruit would be 5.99. The higher surface to mass ratio for the wild fruit suggests that residues on such a food item would be approximately twice that of a test fruit with a 1 inch diameter. Given that many wild fruits are considerably smaller than the 0.5 inch assumed for the example, and that a 1 inch tomato would be unusually small, it is reasonable to expect that the use of the tomato, grape and strawberry data are underestimates of residues on fruits that wildlife consume. This problem extends to the variable $C_{fruit-buffer}$ as this variable is based on $C_{fruit-field}$.

PROBABILITIES OF FORAGING IN EITHER FIELD OR BUFFER AREAS ($P_{field\text{-}forage}$ and $P_{buffer\text{-}forage}$)

The probabilistic risk assessment uses the probability that a bird will feed in the cotton field ($P_{field\text{-}forage}$) and in the buffer area adjacent to a cotton field ($P_{buffer\text{-}forage}$) as factors to modify the contribution of in-field and in-buffer chlorfenapyr residues to total dietary exposure. EFED has concerns that the data for this variable closely coincide with the data used to approximate $P_{CAforage}$, to the extent that incorporation of both variables amounts to a "double counting" of proportions of bird time in fields.

The probabilistic risk assessment uses the summary conclusions for avian census data from MRID444526-16 as the input data for these variables. At first consideration, these data appear reasonable. However, the reliance on the summary values of 13% of observations in-field and 50% in edge habitat from this study ignores the richer data set for each individual study area which show in-field percentages as high as 25%. Furthermore, the data from this study may be unreliable because birds observed in flight were excluded from habitat use statistics, even though they may have been observed landing in specific habitats during the observation periods.

EFED also believes that this data set may not likely be representative of cotton agroenvironments outside of the limited area studied. This is because the study areas were from only one state, Louisiana, which, according to MRID444642-02, is most likely representative of areas with low avian visitation of cotton fields. The probabilistic risk assessment does not account for observed regional differences in the proportion of birds using fields versus buffers. Instead, according to American Cyanamid's June 31, 1999 responses to EFED technical questions, the probabilistic risk assessment views all cotton agroenvironments as homogeneous in nature with respect to conditions of bird populations. EFED believes that such large scale probabilistic risk assessments should account for extrapolation uncertainty, when applying data from one locale to overall growing regions.

Although the use of avian census data from MRID444642-02 was used to predict the distributions for $P_{CA\text{-}forage}$ (see discussion item above), it should have been included in the establishment of values for the variable discussed here. Not including these data in this variable represents a significant isue in the probabilistic risk assessment. The data from MRID444642-02 shows that the frequency of observations in the cotton fields (interpreted by the probabilistic risk assessment as an indicator of the probability of foraging in cotton) is generally much higher (as much as 600 % higher) than suggested by the summary census conclusions used from MRID444526-16.

Finally, the reliance on avian census data as an indicator of dietary origin contains considerable uncertainty. Because individual birds are not followed throughout an active feeding period (which would facilitate some measure of feeding time spent in a field), it is not possible to determine if the proportion of birds observed in a field actually represents the time spent foraging in a field, or more critically the proportion of the bird's diet originating from the field. The probabilistic risk assessment does not account for such a potentially significant source of uncertainty.

CONCLUSION

American cyanamid and their consultant should be commended for their efforts to refine the risk assessment associated with the use of chlorfenapyr on cotton. However, EFED believes, as discussed above, that a number of the fundamental assumptions and approaches for developing probability density functions for important input variables, as well as the overall model, need further attention or revision to adequately refine estimates of risk from chlorfenapyr treatment of cotton fields to non-target species. As currently presented, American Cyanamid's analysis is not technically complete nor correct, and should not be used in and of itself for regulatory purposes.