UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
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Office of Prevention, Pesticides
and
Toxic Substances

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SUBJECT: Methyl Parathion: HED Response To Cheminova Comments On Risk Assessment, DP Barcode: D285403, PC Code: 053501

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This memo addresses the comments provided by Cheminova on the latest version of the methyl parathion risk assessment in an August 9, 2002 letter to the Agency. A "triage" analysis has been completed by the Agency for each point raised by Cheminova in their letter. For each issue raised by Cheminova, the Agency has provided a background summary, presented the issue, and proposed a course of action to address the comment. The numbering system in this document tracks with the numbering system used by Cheminova. In some cases, comment numbers skipped ahead. Also, it should be noted if the comments addressed the same technical issue, they were combined and responded to accordingly.

I. Generic Issues - A. External Exposure vs. Absorbed Dose

Background:

The Agency has back calculated from urinary levels of paranitorphenol (PNP) to skin exposure estimates then applied an endpoint from a dermal tox study.

The dermal and inhalation endpoints are essentially equivalent when the dermal endpoint has been adjusted for the use of an additional 3x because it is a NOAEL. They are presented below:

I. 28 day rat dermal tox, LOAEL = 0.3 mkd
II. 1 yr rat neurotox, NOAEL = 0.11 mkd

Exposures for handlers and post-application workers are thought to be predominantly from the dermal route which is seen in PHED data (e.g., airblast open cab, 360 dermal vs. 4.5 inhalation µg/lb ai) and in the walnut post-application study completed for parathion where no positive samples were found from the stationary air monitors.

Cheminova advocates the use of the oral toxicity endpoint (1 yr neurotoxicity study with NOAEL of 0.11 mkd) for risk assessment which would require adjusting for the metabolism of the absorbed dose of parathion to PNP (i.e., 91.8% conversion).

The Agency used the 28 day dermal tox endpoint which required back calculation to the dermal exposure estimate. This required adjusting for the metabolism of the absorbed does of parathion to PNP (i.e., 91.8% conversion as with above) and also for the amount of parathion that is absorbed through the skin (i.e., ~80%). When coupled together, the total adjustment factor is ~72% which equates to a ~20% difference in calculated dose. The Agency's calculations result in higher dose estimates and hence, risks.

Issue:

Use of a route-specific dermal toxicity endpoint when dermal exposure is known to be predominant contributor to exposure instead of using an oral toxicity endpoint to calculate risks using absorbed dose. The use of a dermal endpoint results in slightly higher dose estimates as opposed to the oral endpoint where risks would be calculated based on absorbed dose.

Proposal:

Maintain the current approach given recent HIARC policies concerning route-specificity and what is known about the key contributors to exposure.

I. Generic Issues - B. Central Tendency vs. 90th Percentile

Background:

Unit exposures from the chemical-specific biomonitoring studies were presented as both a central tendency estimate and as 90th %tile values. Cheminova compared this calculation with PHED and indicated that no rationale was provided for such calculations.

The Agency indicated there were fewer replicates in the biomonitoring data than PHED and there were also uncertainties with some PPE and activities in the biomonitoring data. Cheminova objected and raised several issues including:

- PHED has no microencapsulant data (study 423 does have small # reps)
- AHETF/PHED is outdated (only really applies to closed)
- PHED doesn't have Micromatic DV liquid transfer system (specific closed loading equipment)
- PHED doesn't have all PPE on label from MOA
- Biomonitoring studies have sufficient replicates
- PHED doesn't give absorbed dose

"Because that there are indeed fewer uncertainties with the biomonitoring data, EPA should not deviate from the normal practice of using central tendency unit exposure estimates, as is done with PHED data, to estimate unit exposures for methyl parathion handlers."

Issue:

Cheminova states there are fewer uncertainties with the biomonitoring data so only a central tendency should be used to calculate risks as with PHED.

Proposal:

The Agency has always advocated the use of distributions. PHED can even calculate exposure distributions but this has generally not been done because of the compositing approach used in PHED (combining data from different studies of different designs). The PHED estimates are central tendency values that are commonly used for risk assessment. The 90th percentile values from the methyl parathion data are merely included for illustrative purposes to inform risk managers. Where it is appropriate to use the biomonitoring data, the use of a central tendency value is recommended for regulatory purposes. It is reasonable to use the central tendency because it is combined with upper end application rates and acres treated to calculate exposures that are protective.

I. Generic Issues - C. Geometric Mean/Log Normal Dislodgeable Foliar Residues

Background:

The Agricultural Reentry Task Force (ARTF) has proposed several statistical methods for the calculation of DFRs, transfer coefficients, and resulting risk estimates. One of these approaches is to do all calculations using geometric means since it appears to be based on an ARTF analysis that all data are lognormally distributed.

The Agency has not concurred with this approach at this point and is in the process of reviewing this approach in the context of the complete ARTF database.

Issue:

Selection of an appropriate statistic to calculate exposures, transfer coefficients (TCs), and dislodgeable foliar residues (DFRs).

Proposal:

The Agency is currently using arithmetic means to complete these types of calculations.

The ARTF has proposed the use of geometric means but the Agency has not yet concurred on this approach as it will take much more analysis of the database. The Agency believes that this would only be an interim measure as the ultimate goal is a move to probabilistic risk assessment methods.

The impact of using geometric means compared to the current practice is unclear at this point.

I. Generic Issues - D. EPA Policy 3.1

Background:

Cheminova indicated that the Agency should update the TC policy 3.1 and make use of more data. An example of "Field corn" was used where the hand harvest/detasselling and irrigation/scouting TCs were 17,000 and 1,000 cm^2/hour, respectively. Cheminova indicates the activities associated with "field corn" are scouting (immature and mature crops) and handweeding where the TCs range from ~56 to 960. Other issues raised focused on more complete use of ARTF data.

Issue:

The interpretation of field corn activities and overall implementation of policy 3.1.

Proposal:

There appears to be a confusion from Cheminova's perspective on the interpretation of policy 3.1. The transfer coefficient group that includes both field and sweetcorn is the overarching crop group that is appropriate for both crops. The policy also specifies the "crop" and continuous corn and 1st year corn (what is likely being interpreted as "field corn" by Cheminova) are separated from sweet corn which has its own listings within the overarching transfer coefficient group.

It should be noted that policy 3.1 only lists hand harvest for sweet corn and that detasseling is included in both field and sweet corn. The Agency, however, is keenly aware that this activity is generally only done for seed production in both field and sweet corn and therefore represents a small percentage of the corn market compared to if it was done for all "field corn" production. The other TC values used by the Agency are similar to those described by Cheminova (given rounding and uncertainty).

It is not clear what other updates that Cheminova is concerned with considering the crops where parathion is used. The Agency has recently started to include the greenhouse data completed by ARTF and also revised the tree fruit thinning TC because of a math error included in that study. It is possible that Cheminova is indicating recent proposals by ARTF for irrigation and grouping low field crops based on leaf type. These issues are still under scrutiny by the Agency.

I. Generic Issues - E. Activity based REIs

Background:

ARTF has developed a series of transfer coefficients for an array of crop/activity combinations. There are 18 crop groups and degrees of exposure within each group. There are different TC values for each type of exposure within each crop group.

Cheminova, along with ARTF and others in the industry, have been advocating for labels that would stipulate Restricted Entry Intervals (REIs) in a matrix-like form that would be reflective of different crop/activity combinations. There are efforts in California, the Agency (Office of Pesticide Programs, enforcement, and regions), and USDA to address this issue, particularly for low/no contact activities.

Issue:

The key issue is development of workable labels that reflect in as much detail as possible the crop/activity transfer coefficients generated by ARTF. Enforceability, ease of use, and posting issues are at the heart of controversy.

Proposal:

The Office of Pesticide Programs' SRRD has developed labels based on our current assessments. We have routinely provided risks for the array of crop/activity combinations. As an example, the risk benefit team for AZM and phosmet went through crops one by one and developed label recommendations. Risk assessments should continue to provide risks based on our multiple crop/activity policy and then work with SRRD on their interpretation and label development.

I. Generic Issues - F. Consideration of PHI in setting REIs

Background:

In many/most cases, harvesting has the highest exposure associated with it because it involves the most contact with the treated plants. When chemicals are applied near harvest they can have extended REIs associated with them because of the high exposures. This can be problematic for labeling, especially when considering other low exposure activities that are necessary for production (e.g., irrigation or scouting).

Cheminova's example is the PHI for sweet corn is 12 days and the predicted REI for hand harvest is 5 days and 3 days for irrigation and scouting. Cheminova asks why not set the REI at 3 days, let the PHI address harvesting, and add an REI exception for hand harvest?

Issue:

The issue is whether or not to let the harvest and other late season activity REIs be driven by the PHI so REIs can be set on lower exposure activities that generally require less duration in the REI. This would be coupled with a specific exception that harvesting would have to occur at a later time (this is needed for enforcement purposes).

Proposal:

This approach has been considered by the Agency on a case by case basis. As an example, for phosmet, this approach was used on nut crops. In phosmet, the final decision was also aided by the extensive benefits information that was collected, input from commodity groups, and consideration of enforcement issues.

If this approach is employed for labeling purposes, a mechanism must also be in place to ensure if that any future changes were made to the PHI, for whatever reason, also included a review of the harvesting REI for affected crops. This would ensure that the harvesting REI was appropriate.

I. Generic Issues - G. ARTF Transfer Coefficients (Table of values)

Background:

Cheminova created a table that compared the transfer coefficients used by the Agency with the ones that they proposed. In most cases they are different than those used by the Agency. The Agency revised the transfer coefficient policy on 8/7/00. The TC values are considered interim until the ARTF has been completed. The only exceptions would be the obvious "low hanging fruit" which should be altered (e.g., the Agency recently revised the apple thinning TC because of a math error in the study). The complete ARTF database will be considered in the Agency's final decisions on transfer coefficient values.

One discrepancy raised by Cheminova, for example, was for irrigating and scouting corn and several field crops (alfalfa, rice, rye, oats, barley, wheat, and canola) with full foliage where the TCs were 1000 and 1500 cm^2/hour, respectively. Cheminova proposed values of 960 for scouting both crops and 1000 for irrigation. The TC for corn scouting used by the Agency was a central tendency value from a corn scouting study (range ~ 400 to 2000). The TC for the field crops used by the Agency was also a central tendency value from a dry pea scouting study (range ~ 500 to 2800).

Issue:

Consider proposed TCs from Cheminova or retain interim policy 3.1 TC estimates.

Proposal:

Retain interim policy 3.1 TC estimates until the ARTF effort is complete and all results can be considered concurrently. Cheminova completed a series of studies using the microencapsulant formulation of methyl parathion. The results of these studies were different enough that they should probably be considered for those particular scenarios as was done in the risk assessment (sweet corn harvest, cotton scouting, and nut harvest).

II. Issues related to microencapsulant formulation - 1. Use of DFR and reentry data from same site

Background: For sweet corn, Cheminova conducted a series of dislodgeable foliar residue (DFR) studies in Florida, New York, and California. Additionally, a biological monitoring study was conducted in Florida that monitored sweet corn harvesting. A transfer coefficient (TC) was derived using the Florida sweet corn harvester and DFR data. This TC was used by the Agency to calculate risks along with DFR data from California. DFR data from New York and Florida were not used quantitatively to calculate risks (except indirectly the FL data to calculate the TC value). Dissipation kinetics ($t_{1/2}$ or half life) differed for each region where the DFR data were collected: Florida (0.4 days), New York (1.1 & 3.5 days), and California (4.8 days). The Agency used the "highest half life value... since no trend in climate and half life could be determined." When using the TC and predicted DFR values based on California data to calculate risks, MOEs were ~1 or less on the day of application for all activities. For hand harvesting or detasseling, MOEs reached 100 at 52 days after application. For irrigating and scouting, MOEs reached 100 at 31 days after application. Body burden estimates were also taken directly from the corn harvesting study (workers were monitored 4 days after application). The MOE for the average exposure was 27 based on the average study interval of 5.6 hours. If this estimate was extrapolated to an 8 hour workday, the MOE is 19. Cheminova also provided some background information on the microencapsulant formulation.

Issue: Use of DFR data from different regions to calculate risks rather than just the California DFR data which had the longest half life.

Proposal: Calculate risks using the regional data which is consistent with Agency guidelines. Results for the body burden estimates in the Florida corn harvester study should also be considered along with the regional DFR/TC risk estimates.

II. Issues related to microencapsulant formulation - 2.Use of DFR and reentry data from same site

Background: A series of biomonitoring studies using the microencapsulant form of methyl parathion were completed. The studies which quantified exposure to applicators monitored open cab groundboom applications to potatoes in Florida, Washington, and Wisconsin (MRIDs 454490-01 & 455024-01). Each applicator treated approximately 200 acres of potatoes at 1.5 lb ai/acre. These applicators wore a coverall over normal work clothing, gloves, respirators, eyewear, and headgear. The biomonitoring-based geometric mean unit exposure (which represents total exposure) is 0.000468 mg/lb ai.

Cheminova proposed using their biomonitoring data to scale to other types of common agricultural uses such as closed cab airblast and closed cockpit aerial applications. This proposal was based on their development of scaling factors which were calculated by comparing the exposures from PHED for these scenarios. For comparative purposes, the PHED unit exposures with similar clothing/equipment during groundboom application are 0.011 mg/lb ai for dermal and 0.00015 mg/lb ai for inhalation exposures. Likewise for airblast closed cab and aerial closed cockpit applications, the unit exposures were as follows: airblast (dermal = 0.019 mg/lb ai and inhalation = 0.00045 mg/lb ai) and aerial (dermal = 0.005 mg/lb ai and inhalation = 0.000068 mg/lb ai). Cheminova proposed scaling by the dermal unit exposures so for airblast the biomonitoring data would be increased by a factor of 72 percent. The aerial value would be decreased to 45 percent of its initial value. Cheminova then calculated MOEs using their approach of 25 for aerial applicators (1 lb ai & 1200 acres) and 125 for airblast applicators.

Issue: Use of the biological monitoring data for open cab groundboom applications for extrapolation to closed cab airblast applicators and closed cockpit aerial applicators. The scaling factors for the extrapolation are based on differences in PHED unit exposures for the proposed scenarios.

Proposal: The approach presented by Cheminova appears to be logical given the unique attributes of microencapsulant formulations. However, the underlying quality of the data should be considered as well as the end results based on this method. For aerial applicators, the PHED data are considered medium confidence and the calculated MOE is 25 which is still of concern to the Agency. For the airblast applicators, the PHED dermal data are considered to be high confidence and the newly calculated MOE is 125 which exceeds the Agency's level of concern (MOE = 100). It should also be noted that the groundboom applicator study used open cabs, but the scenarios to which it has been extrapolated include the use of closed cabs/cockpits. It is recommended that confirmatory data should be collected for the airblast applicators and for pilots given the uncertainties associated with this approach.

II. Issues related to microencapsulant formulation - 3. Biological monitoring represents 8 hr day

Background: In the postapplication worker risk assessment, the Agency calculated risks using two techniques including: (1) the development of a transfer coefficient from the biomonitoring studies then using the standard approach of coupling DFRs and transfer coefficients to calculate risks and (2) using the biomonitoring-based body burden estimates directly from the studies to calculate MOEs only for the specific day of reentry monitored in the study. For the second approach, the Agency completed the calculations based on the actual measurements and also adjusted the body burden estimates for the time spent in the field during the study up to an 8 hour work day. Corn harvesting was monitored for an average of 5.6 hours in the field on the 4th day after application. Cotton scouting was monitored on the 4th and 5th days after application for an average duration of 4.5 hours. Walnut harvesting activities were monitored on the 14th and 15th days after application for an average duration of 6 hours in the field. Using the unadjusted average exposure values, MOEs were 27 for corn harvesting, 140 for cotton scouting, and 500 for walnut harvesting. If the monitored values were adjusted for an 8 hour day, MOEs were 19 for corn harvesting, 78 for cotton scouting, and 380 for walnut harvesting (i.e., the cotton scouting MOE became a concern). For the unadjusted 90th percentile exposure values, there was no impact on the overall risk picture.

Issue: The issue raised by Cheminova is the adjustment of the actual study monitoring durations up to an 8 hour workday.

Proposal: The first issue that should be considered is that there is no impact on the overall risk picture when the body burdens are adjusted except for cotton scouts using average exposure values (i.e., for cotton scouts, MOEs go from 140 to 78). It appears from the reviews of the studies that corn harvesters worked over the entire study period which might be expected for that crop. Cotton scouts were monitored during scouting cycles which involved in-the-field time followed by reporting time which would be consistent with what would be expected. For this study, the authors also indicated that the dosimeters were worn over an 8 hour period even though the amount of in-the-field time did not approach that with an average of 4.5 hours. Walnut harvesters wore their dosimeters for approximately 8 hours but had 6 hours in-the-field. In all cases, the investigators indicated that the activities were representative of what would be expected. For scouts, the Agency would agree. For the walnut and corn harvesters, it is likely that many people involved in this activity would have similar workdays to those monitored in the study. However, given the production oriented nature of these activities, that the Agency's extrapolation of the study intervals to an 8 hour day is also appropriate. The risk picture did change for scouts due to the extrapolation that was completed. It is possible that on some days that scouts would spend 8 hours continuously in the field. However, it is probable that most days would contain the reporting element as included in the study. As such, the Agency believes that the unadjusted value would be representative of most scouts.

II. Issues related to microencapsulant formulation - 4. Mechanical harvesting & the PHI

Background: Cheminova compared scouting exposure to mechanical harvesting exposure. They indicated that the level of exposure would be 1/60th of a scout.

Issue: How to address mechanical harvesting in the risk assessment.

Proposal: The Agency does not on a routine basis quantitatively address mechanical harvesting in its risk assessments. Mechanized practices can be divided into fully mechanized activities that meet the definition of "No contact" in the Agency's Worker Protection Standard (WPS) and mechanically assisted practices with potential for exposure. In the case of fully mechanized activities, the Agency does not complete a quantitative exposure assessment but addresses these types of potential exposures qualitatively by allowing early entry as described in the WPS.

> "A worker may enter a treated area during a restricted-entry interval if the agricultural employer assures that both of the following are met: (1) The worker will have no contact with anything that has been treated with the pesticide to which the restricted-entry interval applies including, but not limited to, soil, water, air, or surfaces of plants; and (2) no such entry is allowed until any inhalation exposure level listed in the labeling has been reached or any ventilation criteria established by § 170.110 (c)(3) or in the labeling have been met."

In cases of partially mechanized activities where the potential for exposure exists, the Agency assesses the resulting exposures similarly to those resulting from hand labor activities for "high exposure potential" activities (i.e., transfer coefficients are used to represent exposures associated with the activity). Partially mechanized activities with "low exposure potential"are assessed qualitatively. Available use and usage information have been used to characterize the predominance of these activities that meet the fully mechanized ("No contact") and the mechanically assisted definitions in the risk assessment to allow risk managers flexibility in their decisions with regard to various segments of the exposed population. The Agency also acknowledges that there is some potential for exposure because individuals engaged in fully mechanized activities have short-term excursions from the protected area for various reasons (e.g., unclogging machinery or equipment inspection for breakage). In these cases, the WPS § 170.112(c) *Exception for short-term activities* applies.

II. Issues related to microencapsulant formulation - 5. Use of biomonitoring vs. TCs for decisions

Background: The Agency calculated risks using biomonitoring results taken directly from the monitoring studies and also used the data from these studies coupled with appropriate DFR data to calculate transfer coefficients and risks based on DFR dissipation. The MOEs for average exposures taken directly from the biomonitoring studies were 27 for corn harvesting, 140 for cotton scouting, and 500 for walnut harvesting. Cheminova indicated these values are more appropriate for use in risk management decisions than risk estimates calculated with transfer coefficients. They also indicated that the REI would be less than 14 days for walnut harvesters because the MOE was 500 at 14 days after application.

Issue: Use of the direct biomonitoring results versus transfer coefficient calculated risk estimates.

Proposal: The Agency believes that both approaches should be considered in the interpretation of the risks for methyl parathion. The use of the direct monitoring data provides insight into the field conditions on the particular day that was monitored but the use of the transfer coefficient approach has positives in that it can be used for calculating risks on different days and locations. Cheminova indicated that the REI would be less than 14 days for walnut harvesters but did not describe a method for defining the risk number. As such, the Agency believes that the use of the transfer coefficient is a valid approach.

II. Issues related to microencapsulant formulation - 6. Mixing/loading with mini-bulk tanks

Background: For Penncap M, two biomonitoring studies were completed that quantified exposures to individuals who mixed and loaded spray solutions for aerial applications. In each of these studies, 2.5 gallon containers were used. Cheminova's contention is that closed systems employing mini-bulk and bulk containers (about 95% of the market for large acreage applications by their estimation for field corn in the midwest) "eliminates activities that would normally result in chemical exposure to workers."

Issue: Whether or not to call the mini-bulk and/or bulk packaging a zero exposure scenario.

Proposal: The Agency is not prepared to define these systems as a zero exposure scenario. This is supported by the data generated in MRID 455276-01 in which methyl parathion 4 EC was mixed/loaded using a closed loading system (i.e., Micromatic DV). The following statement which indicates that measurable exposures occurred, even with the use of a closed loading system, was excerpted from the Agency review of that study: *"For all sites combined, the arithmetic mean net urinary 4-NP values rose from a baseline of 0.12 µg/kg to 0.19 µg/kg after one day of exposure."* The Agency proposes that the Micromatic DV exposure data be used to assess the risks associated with the use of bulk and/or mini-bulk packaging if indeed these systems are closed in a manner analogous to the Micromatic system. For the remaining uses where 2.5 gallon containers would be used the data from the original monitoring studies that employed those containers should be used to assess risks (MRIDs 455130-01 and 453271-01) recognizing it is a small percentage of the overall market. The toxicity of methyl parathion should also be considered to add perspective to this discussion because it does not take a significant amount to get on the skin for the Agency to have risk concerns (i.e., less than 1 drop of the 4EC formulation on the skin would result in MOEs <100). The Agency also wants to promote the use of engineering controls as it recognizes that the Micromatic DV system does effectively reduce exposures as can be seen in a comparison of the unit exposure estimates from open loading (2.5 gallon jugs) and the Micromatic DV are 0.000201 and 0.000030 mg/lb ai, respectively (i.e., a ~ 93% reduction in exposure).

III.A. Issues related to EC formulation - 1.& 2. Labeling issues (closed cabs & packaging) for EC

Background: In page2/2nd paragraph of the executive summary, Cheminova objects to the following "A few emulsifiable concentrate labels restrict the application of methyl parathion to enclosed cabs/cockpits only and most products are packaged [with] Micromatic DV liquid transfer enclosed mixing/loading systems." Cheminova also objected to "most products are packaged [with] Micromatic DV liquid transfer enclosed mixing/loading systems." Cheminova suggests that in the 1999 Memorandum of Agreement (MOA) that there was a requirement for closed cabs/cockpits and closed system packaging like the Micromatic DV.

Issue: Compliance with the 1999 MOA and the possibility that other manufacturer's labels need updating. Cheminova believes this requirement should apply to all methyl parathion products.

Proposal: SRRD should follow up on this issue and appropriate changes will be made to the risk assessment.

III.A. Issues related to EC formulation - 3. Labeling issues (flagger exposures) for EC

Background: In page 3/3rd paragraph of the executive summary, Cheminova objects to the inclusion of flaggers as an exposure scenario in the risk assessment as flaggers were apparently excluded in the 1999 MOA.

Issue: Compliance with the 1999 MOA and the possibility that other manufacturer's labels need updating. Cheminova believes this requirement should apply to all methyl parathion products.

Proposal: SRRD should follow up on this issue and appropriate changes will be made to the risk assessment.

III.A. Issues related to EC formulation - 4. Labeling issues (handheld equipment) for EC

Background: In the last paragraph of the executive summary, Cheminova objects to the characterization that the use of backpack and other handheld equipment is prohibited on some labels.

Issue: Compliance with the 1999 MOA and the possibility that other manufacturer's labels need updating. Cheminova believes this requirement should apply to all methyl parathion products.

Proposal: SRRD should follow up on this issue and appropriate changes will be made to the risk assessment.

III.A. Issues related to EC formulation - 5. Labeling issues (handheld equipment) for EC

Background: On page 9, Cheminova objects to the inclusion of chemigation in the risk assessment as an exposure scenario/use practice.

Issue: Cheminova believes this statement is in error and that all methyl parathion product labels prohibit chemigation on the label.

Proposal: SRRD should follow up on this issue and appropriate changes will be made to the risk assessment.

III.A. Issues related to EC formulation - 6. Use of PHED data in risk assessment

Background: PHED data should not be used to assess risks from exposure to the methyl parathion EC formulation during mixing/loading because PHED does not have any data which monitored the use of the Micromatic DV system. The Micromatic DV system is the only apparent system in which methyl parathion EC products are marketed.

Issue: Cheminova has indicated that the Micromatic DV system is the only one that is used to market methyl parathion. A chemical- and system-specific exposure study was conducted. Cheminova's comment is that these data should be used as opposed to PHED.

Proposal: If the Micromatic DV system is the only one to be used for the marketing of methyl parathion products, then the use of the data contained in MRID 455276-01 should be the basis for risk management decisions by the Agency as it appears to be of sufficient quality for this purpose. However, the Agency is always interested in a comparative analysis of PHED with specific studies as this process allows for a more informed risk management decision. For this purpose, it is appropriate to include the PHED-based results.

III.A. Issues related to EC formulation - 7. & 8. Creatinine excretion

Background: The Agency corrected 4NP values for individual workers using average creatinine levels measured in those individuals. This was done to account for variability in outputs for each individual over the course of the study and to account for potentially lost urine voids. Cheminova disagreed with the Agency's approach, particularly the justification for adjusting to account for lost urine voids. Cheminova's position is that creatinine excretion is not constant but that there is normal variability in the amount of creatinine excreted on a daily basis (i.e., there is an expected range in creatinine outputs). This was supported by several citations. Cheminova indicated that the Agency's method for correcting urine levels is "scientifically unfounded."

Issue: Determination of the appropriate method for calculating exposures based on urinary metabolites (i.e., whether or not to correct for creatinine).

Proposal: The Agency acknowledges that Cheminova's points have scientific credibility. However, Cheminova did not suggest an alternative method for analyzing the methyl parathion urine data. It is implied in their response that the values should have remained uncorrected. The impact of this approach versus the approach used by the Agency was not examined by Cheminova so it is not clear if there would be significant differences in the final risk estimates. The Agency used a creatinine correction approach because it is a standard approach used by many investigators. This approach also can account for uncollected urine. The Agency used average creatinine values specific to each individual in the study because it believed that the data from the specific individuals provides a more appropriate correction factor than published estimates for the general population. Also, it should be noted that the Agency's approach reduced residues in a number of samples (probably around ½ of the total number) because the creatinine levels were higher than the averages for the individuals. In effect, it is possible that uncorrected residues could result in higher exposure estimates because of this downward correction. For example, this could be particularly true immediately after the exposure interval where high levels of 4-NP were excreted (as would be expected) and the corresponding creatinine levels were also higher than average meaning that a downward residue adjustment would occur.

III.A. Issues related to EC formulation - 9. "Normal" use of double layer clothing & eng. controls

Background: On page 24, Cheminova objects to the Agency's statement that the use of double layer clothing and a respirator are not "normally worn by worker operating closed systems" because the Agency failed "to inform the reader that the PPE worn in the study reflects what is required on the labels for the methyl parathion EC formulations per the 1996 MOA. Therefore, EPA's reference to 'normal' is irrelevant."

Issue: Compliance with the 1999 MOA and the possibility that other manufacturer's labels need updating. Cheminova believes this requirement should apply to all methyl parathion products.

Proposal: SRRD should follow up on this issue and appropriate changes will be made to the risk assessment for better characterization.

III.A. Issues related to EC formulation - 10. & 12. PHED vs. Biomonitoring Unit Exposures

Background: Cheminova commented on the characterization by the Agency pertaining to the differences in the unit exposures from PHED and those monitored in the EC formulation studies that used the Micromatic DC device (both studies used engineering controls: 0.0086 mg/lb ai - PHED & 0.000030 mg/lb ai - MP studies, >99% exposure reduction). The Agency indicated the differences could be from the additional PPE worn in the study. The Agency value represents single layer clothing with gloves while the Cheminova value represents double layer clothing, gloves, respirators, eyewear, face shields, rainhats, and aprons. Cheminova also indicated that PHED data are not based on the Micromatic DV system and that PHED is based on exposure, not absorbed dose.

Issue: Understanding the cause of the differences in the PHED unit exposures and the unit exposures measured in the methyl parathion mixing/loading studies using the EC formulation and the Micromatic DV device.

Proposal: The Agency will add additional characterization as appropriate to the risk assessment. For example, the Agency believes that the use of additional PPE likely lowered the exposures in comparison to PHED. It is also likely that the Micromatic DV system could produce lower exposures than those contained in PHED for several reasons including the effectiveness of the actual systems used in PHED compared to the Micromatic DV and how sensitive the monitoring techniques were in the PHED studies compared to the methyl parathion data. Also, the impact of the use of a 100 percent dermal absorption factor should be considered.

III.A. Issues related to EC formulation - 11. Agency did not include 0.75 lb ai/acre application rate

Background: On various pages, Cheminova commented that the Agency did not include the application rate of 0.75 lb ai/acre for the EC formulation on barley, cotton, grasses, oats, rice, rye, soybeans, and wheat.

Issue: Risk estimates for the crops mentioned above at the 0.75 lb ai/acre rate.

Proposal: The Agency did not quantitatively calculate risks for every possible scenario that could occur for methyl parathion. However, this does not mean that the Agency will ignore these crops in the risk management process. The Agency presented risks for values which would bracket the risks anticipated for these crops at 0.75 lb ai/acre. The Agency will interpolate based on the currently calculated values to address the risks anticipated for these crops.

III.A. Issues related to EC formulation - 20. Number of PHED vs Biomonitoring replicates

Background: On page 32, the Agency indicated that there are more PHED replicates than in the biomonitoring study (16 to 32 vs. 16). Cheminova questioned the statement because it "insinuates that there is uncertainty when in fact there is none, it is not clear what point EPA is trying to make with this statement." Cheminova then added more discussion about why the biomonitoring data are more appropriate.

Issue: To raise uncertainty in the mixer/loader assessment due to the number of replicates.

Proposal: See the response entitled ***Differences in PHED vs. Biomonitoring Unit Exposures*** above. Additionally, it should be noted that the Agency's guidelines have for years indicated that the minimum number of replicates in a study should be 15 per activity. The number of people monitored in the biological monitoring study was 16 using the actual system used to market methyl parathion (Micromatic DV). It is clear that the biological monitoring data are the most appropriate dataset for risk management in this case.

III.B Issues related to EC formulation - 1. Use of ARTF Transfer Coefficients

Background: On page 4, the Agency indicated that transfer coefficients determined from the ARTF will be used for all scenarios. Cheminova indicates that the Agency has used Policy 3.1 which does not yet contain the entire TC database developed by ARTF.

Issue: Complete use of ARTF data.

Proposal: The Agency has attempted to use the most germane data possible in its assessment of postapplication worker risks. It should be noted that the ARTF is still an ongoing project and that many of the final decisions about clustering of jobs, calculation of transfer coefficients, and risk assessment methods cannot be completed until the ARTF is completed and all of the data have undergone a thorough analysis by the Agency which includes final decisions and agreements on the transfer coefficients to be used. At this point in time, these analyses have not yet been completed. This comment is also very difficult to respond to since there were no specifics included.

III.B. Issues related to EC formulation - 2. Use of 1 lb ai/A in postapplication risk assessment

Background: On pages 50 & 51, the Agency assessed postapplication risks for rice, rye, oats, barley, wheat, and canola at an application rate of 1 lb ai/acre. Cheminova indicated that the "supported use rate for rice, rye, barley, and wheat is 0.75 lb ai/acre. The supported use rate for canola is 0.5 lb ai/acre."

Issue: Use of correct application rates in the postapplication risk assessment.

Proposal: The Agency will verify the application rates suggested by Cheminova and will recalculate the risks if needed. Based on 1 lb ai/acre, the MOE on day 0 for irrigating and scouting is <1 and would still be <1 even with either corrected rate. The MOE exceeds 100 on day 4 (i.e., is 240). It is likely that even with the adjustment that the MOEs still would not exceed 100 until a few days after application.

III.B. Issues related to EC formulation - 3. DFR Data Evaluation

Background: On pages 50 & 51, Cheminova raised several questions concerning calculation of the DFR curves based on their monitoring data. These issues include development of a generic policy, use of the limit of quantification in calculations, correction for field recovery results, use of Day 0 DFR estimates, addition of parent and oxon residues, and use of the geometric mean.

Issue: Several issues were raised by Cheminova concerning how the DFR values were calculated. The Agency has responded on an individual basis below.

Proposal: Cheminova made several comments on many issues pertaining to DFR calculations.

Workshop: If Cheminova went back and reviewed the meeting minutes from the joint regulatory meetings with ARTF they would find that the Agency has indeed proposed that this topic be addressed in a workshop several times. The Agency has always been under the impression that this would be a joint effort under the auspices of the joint regulatory committee followed by some sort of peer review. Cheminova, as a member of the task force should make an effort to work with the Agency on the development of such a project.

½ LOQ: Cheminova argues that use of ½ LOQ adds conservatism to the assessment and that LOQs should not be corrected for field recovery. The Agency does not agree that ½ LOQ always adds conservatism because any value >½ LOQ but <LOQ would be reported as ½ LOQ which would actually reduce risk estimates rather than adding conservatism. Also, the Agency has never advocated correcting ½ LOQ values for field recovery. If this has been done with methyl parathion then it should be changed although it is very unlikely it would have an impact on the overall risk picture. When parent methyl parathion and the oxon are added together, if both levels are <LOQ then a single LOQ (not 2*1/2LOQ) should be used for the risk assessment. Also, the Agency concurs with Cheminova that when the [oxon] was <LOQ that ½ LOQ for the oxon should be added to the parent residues to calculate total DFRs.

Day 0 DFRs: Cheminova argues against including Day 0 DFRs in the kinetics analysis. The Agency agrees that there can be an argument made for excluding Day 0 DFRs from a kinetics analysis based on the physical-chemical parameters mentioned by Cheminova. However, the Agency also would not agree that this would be the case particularly if the Day 0 residues essentially tracked with other DFR values in a study. This can be quantitatively considered by reviewing the correlation coefficients determined in regressions of the data. For the EC formulation, all correlation coefficients were 0.85 or greater (all but 1 were >0.9) which indicates good agreement of the calculated line that was based on all data including Day 0 residues with the actual monitoring data.

Geometric Mean DFRs: The use of geometric mean DFRs is still under review by the Agency. If the Agency would concur on this issue, the Agency would also have to adjust all of its transfer coefficients accordingly upward to account for changes in the DFR (i.e., the denominator in the calculation of transfer coefficients is DFR so if DFR goes down, the TC will go up).

III.B. Issues related to EC formulation - 4. DFRs & Climatic Data

Background: The Agency developed risk assessments based on a series of dislodgeable foliar residue data that were collected on various crops (corn, cotton, walnuts) in different regions throughout the country (CA, GA, TX, FL, LA). For the postapplication risk assessment in each crop "to be protective, the site with the longest half life was chosen." Cheminova objected to the approach taken by the Agency and indicated instead that the Agency should have considered a regional approach in its assessment. Cheminova also indicated that the Agency also should consider climatological factors in addition to rainfall in its interpretation of the results for different studies such as humidity, light intensity, and temperature. Cheminova commented that the DFR show a clear difference in dissipation rates. For corn, DFR data were available from Louisiana, California, and Florida. Louisiana data with a 0.5 day half life and residues that were measurable out to 2 days after application were selected for risk assessment. For the other sites, residues were <LOQ on the day of application. For cabbage, DFR data were available from Georgia, Louisiana (2 sites), and California. Louisiana data from site 1 (cooler season study) with a 1.1 day half life and residues that were measurable out to 10 days after application were selected for risk assessment. For the other sites, half lives were <1 day and residues were <LOQ at 5 days or less. For cotton, DFR data were available from California, Louisiana, and Texas. Texas data with a bi-phasic decay pattern (0.3 day ½ life based on 0-3 day samples, residues <LOQ at 21 days after application) were selected for risk assessment. Results were similar for Louisiana and California except that residues reached the LOQ at 7 and 10 days after application, respectively.

Issue: To consider regional differences in the risk assessment based on DFR data.

Proposal: It does appear that the use of regional data could impact the overall results because the endpoint for methyl parathion is such that lower exposure estimates are needed to achieve Agency risk targets and these exposure levels relate to DFR levels that occur several days after application. It should also be noted that the Agency's guidelines for conducting postapplication risk assessments are consistent with a regional approach. Using cabbage as an example, it took 13 days for MOEs to exceed 100 for hand harvesting based on the Louisiana site 1 data which monitored dissipation during December through February which is apparently consistent with cabbage cultivation. However, if the California cabbage data are used, residues are <LOQ 3 days after application which would likely shorten the duration of an associated REI. Cheminova also indicated that the Agency did not consider a series climatological parameters in determining how DFR data were to be used in this assessment (e.g., light intensity). The Agency used whatever data were available when deciding how to use the data. It should be noted that Cheminova did not propose an approach nor reference any such data. Additionally, Cheminova indicated that "DFR data show a clear difference in dissipation rates between sites." Cheminova offered no statistical analysis of the data which would support a quantitative approach for this claim.

III.B. Issues related to EC formulation - 5. DFRs & Climatic Data

Background: The Agency developed risk assessments for cabbage based on a series of dislodgeable foliar residue data that were collected in Georgia, Louisiana (2 sites), and California. Louisiana data from site 1 (cooler season study) with a 1.1 day half life and residues that were measurable out to 10 days after application were selected for risk assessment. For the other sites, half lives were <1 day and residues were <LOQ at 5 days or less. Cheminova disagrees with the Agency's approach of using the cooler season cabbage data for risk assessment purposes. Cheminova indicated is that although cabbage is grown during the timeframe that the study was conducted (December through February) that the season was unusually cool during this study and not representative of a typical growing season. Additionally, they indicated that methyl parathion would not even normally be used under such conditions because the pest complexes of interest would be naturally controlled by the weather. Cheminova conducted a second DFR study in Louisiana during August and September under climatological conditions which they indicated were much more representative of those that would be expected under normal growing conditions in this region. Cheminova advocated the use of both sets of data for risk assessment purposes (e.g., a mean of the two) and that the Agency should consider efficacy issues when deciding which set of data to use.

Issue: Determine which set of Louisiana cabbage DFR data to use in the risk assessment (cooler season/Site 1 or summer data/Site 2 which were deemed more representative by Cheminova).

Proposal: It is clear that there are differences in the results for the 2 DFR studies conducted in Louisiana and that the differences are likely due to climatological conditions. It could also be possible that the results of the August/September trial could be more representative of cabbage cultivation in that region of the country because of the climatological issues. During Trial 1, minimum air temperatures ranged from 24°F to 68°F while maximum air temperatures ranged from 36°F to 76°F. During Trial 2 , minimum air temperatures ranged from 64°F to 76°F while maximum air temperatures ranged from 76°F to 112°F. It is also possible that lower temperatures would reduce the pest pressure and that methyl parathion would not be used under conditions similar to those seen in the cooler season study. However, the Agency is not prepared to use the August/September over the cooler season data for several reasons:

- there are no temperature restrictions on labels for when applications could be made;
- it is not clear how different from typical conditions the cooler season data are - some evaluation of any quantitative (statistical) differences would be useful;
- cabbage is a cool season crop which would also not normally be planted in Louisiana at the height of summer - use of the warmer season data (Site 2) could underestimate risks because it could underestimate exposures; and
- there was no agronomic rationale supporting Cheminova's claim that pest pressures would be reduced and methyl parathion would not be used in conditions similar to those at Site 1.

Cheminova needs to provide further information on this subject. In lieu of additional information, the Agency should retain the current assessment for cabbage in Louisiana.