UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

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Re: Chlorpyrifos petition dated September 12, 2007; January 2013 Response

Dear Mr. Colangelo and Dr. Reeves:

I am writing to further update you on the U.S. Environmental Protection Agency's (EPA) efforts to respond to the Natural Resources Defense Council (NRDC) and Pesticide Action Network North America (PANNA) jointly submitted September 12, 2007[1], petition and our related efforts to complete the registration review of chlorpyrifos. In my letter to you of December 18, 2012[2], I provided you with an update on our efforts to implement label changes to put in place additional limitations to reduce primary spray drift from chlorpyrifos. I can report that EPA has now approved those changes for all 41 chlorpyrifos agricultural products subject to these use limitations.

As we also noted in December, while we have made significant progress in completing work on the four petition issues that EPA did not address in its July 16, 2012[3], partial response to your petition, we were not able to provide you with a complete response in December, as we previously believed we could. However, we committed to providing you with a response this month that further addresses the petition and outlined the approach we are taking for completing our response. Accordingly, this response will address what EPA has done and will do to address each of the following four outstanding claims that: (1) EPA failed to incorporate inhalation routes of exposure from pesticide volatilization; (2) EPA failed to incorporate into its risk

[1] Available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2007-1005-0005
[2] Available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2007-1005-0096
[3] Available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2007-1005-0095.

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assessment, in a quantitative manner, data indicating that long-lasting effects result from early life exposure to chlorpyrifos in children; (3) EPA disregarded data demonstrating that there is no evidence of a safe level of exposure during pre-birth and early life stages; and (4) EPA failed to cite or quantitatively incorporate studies and clinical reports suggesting potential adverse effects below 10% cholinesterase inhibition.

As I indicated in the December response, EPA has been working to complete an assessment that will evaluate the potential risks of volatilization from chlorpyrifos applications. In early February 2013, we will publish a notice in the Federal Register announcing the availability of this preliminary assessment for public comment. This assessment represents a significant advancement in the evaluation of pesticide risks, as it will be the first probabilistic assessment of the risks posed by the post-application volatilization of a semi-volatile pesticide. Our approach builds upon the methodology we previously employed for volatile pesticides in the recent fumigant pesticide risk assessments[4] to assess bystander inhalation exposure from volatilization. In addition, it is consistent with the recommendations from the December 2009 Federal Insecticide, Fungicide, and Rodenticide Act Scientific Advisory Panel (SAP)[5] meeting on the scientific issues associated with field volatilization of conventional (semi-volatile) pesticides. The content of the preliminary volatilization assessment is further informed by Dow AgroSciences' recently submitted chlorpyrifos field volatility study[6] coupled with existing volatility data found in the open literature, and EPA modeling tools.

This assessment will supplement the July 2011 Preliminary Human Health Risk Assessment[7] (HHRA) and evaluates bystander exposure from chlorpyrifos and chlorpyrifos-oxon emitted from treated fields. Although the volatilization of chlorpyrifos was addressed in the preliminary HHRA, that analysis involved only a deterministic assessment based on limited monitoring data that did not attempt to evaluate a range of field conditions and, therefore, had correspondingly limited utility in a regulatory setting. Given the groundbreaking nature of the new assessment and its potential for use in guiding additional risk mitigation, EPA believes it is critical to involve the public in the development of this assessment before it is finalized. Further, EPA is examining other semi-volatile pesticides to determine if bystander volatilization assessments are needed. Any comments received on this assessment will serve to inform those assessments as well. Accordingly, EPA will begin taking public comment on the draft version of the assessment in February 2013, after publication of the Federal Register notice announcing its availability in docket number EPA-HQ-OPP-2008-0850.

Following completion of the public comment period and EPA's subsequent evaluation of the comments, EPA will determine whether additional regulatory action is necessary to address

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[4] The assessments can be found in the dockets for each fumigant. Four of which are provided here chloropicrin - EPA-HQ-OPP-2007-0350; dazomet - EPA-HQ-OPP-2005-0128; metam sodium/potassium - EPA-HQ-OPP-2005-0125; and methyl bromide - EPA-HQ-OPP-2005-0123

[5] U.S. EPA 2009. FIFRA Science Advisory Panel Meeting Minutes - Scientific Issues Associated with Field Volatilization of Conventional Pesticides. Available at http://www.epa.gov/scipoly/sap/meetings/2009/december/120309meetingminutes.pdf

[6] Rotondaro, A. and Havens, P. (2012). Direct Flux Measurement of Chlorpyrifos and Chlorpyrifos-Oxon Emissions Following Applications of Lorsban Advanced Insecticide to Alfalfa; Sponsor: Dow AgroSciences LLC, 9330 Zionsville Road Indianapolis, IN 46268-1054. EPA MRID 48883201.

[7] Available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2008-0850-0025.

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these risks and, if so, whether the nature of that risk supports the need to take action in advance of our completion of the final broader HHRA, currently scheduled for December 2013.

Regarding the remaining three petition issues addressing chlorpyrifos toxicity identified above, as we have indicated previously, the analysis is complicated and multifaceted because it involves many lines of scientific evidence, including many recently conducted studies and peer review evaluations and recommendations. That work includes consideration of: *in vivo* and *in vitro* experimental toxicology studies that evaluate neurodevelopmental effects in laboratory animals, adverse outcome pathway framework analyses, exposure, the results of multiple human epidemiology studies, and biomonitoring data. Notwithstanding the complexity of this analysis, it was our hope to provide you with a written response last December that included our scientific conclusions on these issues. As you know, we convened a FIFRA SAP meeting in April 2012[8] to inform our work in generating a weight-of-evidence evaluation integrating the epidemiologic data with the experimental toxicology studies for the neurodevelopmental outcomes and acetylcholinesterase (AChE) inhibition. At the time EPA provided its partial petition response to you in July 2012, EPA had just received the written SAP report from the April meeting. EPA therefore had not had time to begin pursuing the SAP's recommendation when EPA provided its response to you and to the 9th Circuit in our ongoing litigation over this matter.

Thus far, EPA has not encountered epidemiological data of sufficient quality to support quantitative risk assessment of conventional pesticide chemicals. Before EPA decides how to use the epidemiological data on chlorpyrifos, we believe it is critical to attempt to resolve questions about these studies regarding the extent of the cohort members' exposures to chlorpyrifos, as well as the impact of exposure to other compounds capable of causing or contributing to the observed neurological outcomes. We acknowledge the lengthy conduct of our assessment, including multiple SAP reviews, but we believe the deliberate and considered approach we are taking is the most scientifically defensible method for re-evaluating our current approach to assessing risks from chlorpyrifos and other organophosphorous pesticides generally, and, specifically, for evaluating the strengths and weaknesses of the epidemiological data.

The July 2012 SAP report is in accord with EPA's assessment that the Agency should attempt to resolve certain key questions about the epidemiological data. Specifically, the SAP recommended that EPA pursue a number of possible approaches for attempting to resolve whether the neurological outcomes observed in the studies occurred in the absence of AChE inhibition – the effect EPA's current regulatory approach is designed to preclude. Further, given that the women and children studied in the Columbia University-sponsored epidemiology study[9] were exposed to multiple chemicals (including other pesticides, polycyclic aromatic hydrocarbons and lead), the SAP cautioned the agency about attributing the outcomes to a single chemical based on the current analysis conducted by Columbia University researchers. These statements by the SAP lead the agency to believe that we need to further explore the extent to

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[8] Available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPP-2012-0040-0029

[9] Rauh, V., Arunajadai, S., Horton, M., Perera, F., Hoepner, L., Barr, D. B., & Whyatt, R. (2011). Seven-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. Environ Health Perspect, 119(8), 1196-1201. doi: 10.1289/ehp.1003160; Rauh, V. A., Garfinkel, R., Perera, F. P., Andrews, H. F., Hoepner, L., Barr, D. B., Whyatt, R. W. (2006). Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. Pediatrics, 118(6), e1845-1859. doi: 10.1542/peds.2006-0338.

which the observed neurological outcomes were influenced by exposure to these other chemicals.

Following receipt of the report EPA began conducting a number of analyses to address these recommendations. As I indicated in our December response, we are making progress in conducting a dose-reconstruction analysis of potential exposures to the women and children studied in the Columbia University-sponsored epidemiology study[10] in order to assess the degree to which the individuals in the cohort may or may not have been exposed to chlorpyrifos levels high enough to cause AChE inhibition. In addition to this assessment, to address the SAP recommendations EPA also intends in the coming months to complete an evaluation of cohort exposures to other chemicals. In order to complete both the dose reconstruction and analyses on other chemical exposures, however, we will need to analyze the original data ("raw data") from the Columbia University study to better understand the exposure to chlorpyrifos and other chemicals. To date, the study authors have declined our request to provide that information to us, but we are continuing to discuss our need for evaluating these data with the study authors and we are hopeful that a resolution can be reached.

In addition to further analysis of the exposures in the Columbia study, EPA has also followed up on a recommendation that was brought up in the SAP's oral deliberations regarding the administration and interpretation of diagnostic and analytic tools used to assess neuro and motor development in children like those used in the Columbia study. The SAP noted that it lacked expertise in evaluating these aspects of the data. Because this expertise is relevant in assessing the potential for effects from exposures to other chemicals, between August and October 2012, we obtained additional peer review from scientists within the federal government who have expertise in this field. EPA will include consideration of the results of this peer review when it completes its assessment, as further discussed below.

Finally, as our previous response indicated, last fall, the Columbia University researchers published a new epidemiology study[11] describing the results of magnetic resonance imaging on a subset of children in the cohort. We solicited comments between August 2012 and October 2012, from scientists within the federal government who have expertise in this scientific area and are currently evaluating this input to determine the extent to which this information informs the earlier Columbia University study results.

In light of our ongoing work described above, we are not in a position to provide you with our conclusions on the three remaining toxicology issues in the petition at this time, and it is difficult to provide a precise time frame for the completion of that assessment. It is our hope that we can maintain our current schedule to complete the full chlorpyrifos HHRA by the end of 2013

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[10] Rauh, V., Arunajadai, S., Horton, M., Perera, F., Hoepner, L., Barr, D. B., & Whyatt, R. (2011). Seven-year neurodevelopmental scores and prenatal exposure to chlorpyrifos, a common agricultural pesticide. Environ Health Perspect, 119(8), 1196-1201. doi: 10.1289/ehp.1003160; Rauh, V. A., Garfinkel, R., Perera, F. P., Andrews, H. F., Hoepner, L., Barr, D. B., Whyatt, R. W. (2006). Impact of prenatal chlorpyrifos exposure on neurodevelopment in the first 3 years of life among inner-city children. Pediatrics, 118(6), e1845-1859. doi: 10.1542/peds.2006-0338.

[11] Rauh VA, Perera FP, Horton MK, Whyatt RM, Bansal R, Hao X, Liu J, Barr DB, Slotkin TA, Peterson BS. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. Proc Natl Acad Sci U S A. 2012 May 15;109(20):7871-6. doi: 10.1073/pnas.1203396109. Epub 2012 Apr 30. PubMed PMID: 22547821; PubMed Central PMCID: PMC3356641.

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and respond to the remaining claims in your petition on the same time frame. As we previously explained to you, that schedule would result in our initiating any necessary regulatory action in early 2014. Given the complexity of the assessment, and in particular, the complications we are having in obtaining potentially important research data from the Columbia University study authors, I do have some concern about our ability to meet that time frame, but we will continue to work to meet that goal and will update you if our plans must change.

With that said, we have made significant progress in addressing the volatilization portion of your inhalation claim as will be evident with the release of the preliminary chlorpyrifos volatilization assessment in February. As noted, if, following review of the public comments, EPA determines that the risk posed from chlorpyrifos volatilization merits regulatory action in advance of the completion of the HHRA, we will initiate that action without first completing the entire HHRA.

Finally, I wish to reiterate that for efficiency purposes EPA does not intend to proceed with issuing a denial order of the six petition issues (the spray drift portion of your inhalation claim was granted) that we rejected in July 2012 until after we complete our review of all remaining issues. It has been our understanding that this approach is preferable to you as well. However, as previously indicated, if you wish to begin the objections process for the six denied claims and notify EPA in writing, we will publish a formal denial order for those claims, triggering your right to file objections under FFDCA section 408(g)(2).

Sincerely

Steven P. Bradbury, Ph.D.
Director, Office of Pesticide Programs

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