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Docket ID: **EPA-HQ-OPP-2012-0919**

Environmental Protection Agency
Office of Pesticide Programs (OPP) Docket
EPA Docket Center (28221T)
1200 Pennsylvania Avenue, NW
Washington, DC 20460-0001

Subject: **EPA-HQ-OPP-2012-0919-0013**, "Proposed Registration Decision for the New Active Ingredient Halauxifen-methyl"

The Weed Science Society of America (WSSA) and its affiliates, the Aquatic Plant Management Society, the Northeastern Weed Science Society, the North Central Weed Science Society, the Southern Weed Science Society, and the Western Society of Weed Science represent over 3000 members from around the world. Members include academic, governmental, and private industry research scientists, university extension professionals, educators, graduate students, and federal, state, county, and private land managers. Our scientific societies welcome the opportunity to comment on certain aspects of the proposed registration of halauxifen-methyl. The societies are not taking a position on whether the proposed registration should be approved. We trust an objective science-based decision will be reached following the Agency's consideration of the benefits and risks of this registration for halauxifen-methyl.

However, the National and Regional Weed Science Societies do wish to comment on a feature of the proposed registration that has broad implications for weed management that go far beyond halauxifen-methyl specific issues.

In this letter, the National and Regional Weed Science Societies wish to communicate our concerns and objections to the proposed tank mix prohibition for halauxifen-methyl uses.

Because of an uncertainty raised by synergism claims from uncited academic research and patent application filings, the Agency is proposing to prohibit the tank mixing of other herbicides with halauxifen-methyl. It is unfortunate the Agency does not list the specific sources for this uncertainty; it would be more possible to evaluate and respond to them if they were cited. We encourage the Agency to do this in the future. The approach the Agency is proposing is a divergence from the guidelines proposed in the National Research Council (NRC) report on "*Assessing Risks to Endangered and Threatened Species from Pesticides"* (McDowell et al.

2013). In the opening comments of the section of this report dealing with pesticides mixtures, the authors wrote: "*The toxicity of a chemical mixture probably will not be known, and it is not feasible to measure the toxicity of all pesticide formulations, tank mixtures, and environmental mixtures. Therefore, combined effects must be predicted on the basis of models that reflect known principles of the combined toxic action of chemicals*" (El-Masri et al. 1997). The following points regarding pesticide mixtures are made in the Conclusions and Recommendation section (pages 133-135) in Chapter 4 "Effects" of the NRC report:

1. *The toxicity of the pesticide active ingredient is central to the assessment. Other chemicals are relevant only if they modify the toxicity of the pesticide active ingredient or the susceptibility of the species of concern to the active ingredient.*
2. *The toxicity end point most relevant to the species of concern must be determined before initiation of the effects analysis.*
3. *Mixture components that do not elicit the relevant response in the species of concern do not need to be considered in the effects analysis. Mixture components that do elicit the relevant response need to be considered in the effects analysis.*
4. ***In the absence of any data that would support the hypothesis of a synergistic interaction between the pesticide active ingredient and other mixture components, the effects analysis should proceed on the assumption that the components have additive effects.***
5. *For chemicals that have common mechanisms of action and parallel slopes in the concentration-response curves, concentration addition is a reasonable approach for modeling additive effects. However, caution should be exercised in using concentration-addition modeling as a default approach when no mechanistic data or concentration-response data are available.*
6. *For chemicals that have different mechanisms of action, response addition (a zero correlation of individual tolerances) is a reasonable approach for modeling additive effects. For this case, mixture components will contribute to the response only when present in the environment in concentrations that elicit the response. That is, such components do not need to be considered at concentrations below their toxic thresholds.*
7. *Potential synergistic interactions need be considered only when a synergist is present in the environment above its interaction threshold concentration. In the case of synergism, it is probably prudent to generate information on toxic interactions to ensure accurate evaluation of potential responses of the species of concern.*
8. *In the case of antagonism, uncertainties associated with both exposures and toxic interactions will seldom justify a quantitative modification of the effects analysis.*
9. ***The use of uncertainty factors to compensate for the absence of information on potential interactions of mixture components is not recommended.*** *When data are available, quantitative methods can be used to evaluate the interactions.*

At a minimum, we interpret the NRC report recommendations to imply that halauxifen-methyl, a synthetic auxin, could be mixed with other herbicides, or other pesticides, that are not synthetic auxins (Point #6). Or, it could be mixed with other synthetic auxins if additive action was assumed (Point #5). Finally, many potential halauxifen-methyl tank-mix partners would not elicit the "relevant response in the species of concern" (Point #3) and need not be considered in the effects analysis. This would indicate that insecticides and fungicides need not be considered

as they do not cause plant injury (the "relevant response"). In addition, as halauxifen-methyl is a broadleaf plant herbicide, other herbicides, like ACCase inhibitors, that are grass specific herbicides should also not be included in any tank-mix prohibition. Finally, if uncertainty concerning potential injury to endangered plant species is driving the tank-mix prohibition proposal, then this should only apply to those counties containing endangered plant species of concern.

Perhaps the most telling statement concerning mixtures in the report was: "**The committee (National Research Council) emphasizes that the complexity of assessing the risk posed by chemical mixture should not paralyze the process**".

Beyond the divergence from the NRC recommendations, the proposed tank-mix flies in the face of a major justification the Agency uses for proposing to approve the registration: "*The EPA expects halauxifen-methyl would provide an additional tool for growers to include in resistance-management programs, in order to control biotypes of weeds that have shown resistance to other common herbicides, such as glyphosate and ALS inhibitors*" (EPA-HQ-OPP-2012-0919-0013, page 7).

However, it is now well established that tank-mixes, including two or more effective herbicide mechanisms of action (MOAs), in a simultaneous application is one of the most effective herbicide strategies for delaying the evolution of herbicide resistance (Beckie 2006, Diggle et al. 2003, Dill et al. 2008, Gustafson 2008, Green and Owen 2011, Norsworthy et al. 2012). There are numerous publications showing this but Beckie and Reboud (2009) serves as an often-cited example. When they used a herbicide by itself just one time over a 4 year period, they observed a nearly 8-fold increase in resistant weed seed production. However, if they applied the same herbicide every year, but mixed it with another effective herbicide, resistant weed prevalence remained statistically the same as if they had never used the herbicide at all.

While herbicide (MOA) use rotation, rather than tank mixtures, is often recommended as a useful strategy for delaying herbicide resistance evolution, it is not considered as effective as tank mixing for this objective. A part of the best management practices for delaying resistance outlined in Norsworthy et al. (2012), rotations were seen as "useful but not sufficient because they subject a weed population to a single [herbicide mode of action] at a time". However, recent work (Evans et al. 2016) suggests that rotation actually increases the likelihood of finding herbicide resistant weeds.

Evans et al. (2016) surveyed glyphosate-resistance waterhemp incidence, as well as landscape, soil, weed, and farm-management data that included almost 500 site-years of herbicide application records collected between 2004 and 2011 from 105 central Illinois grain farm. They found that weed management decisions were the most important factor in predicting the presence of glyphosate resistance. Rotating herbicide MOAs actually increased the frequency of glyphosate resistance. On the other hand, farmers who used multiple herbicides per application were the least likely to have resistance on their farms. **When tank mixing an average of 2.5 MOAs per application, farmers were 83 times less likely to have glyphosate resistance** compared to those who used only 1.5 MOAs per application.

This outcome is not surprising and parallels findings in other areas of pest and disease management where mixtures of multiple pesticides or drugs administered simultaneously can slow or halt the evolution of resistant traits (Palumbi 2001). These measures are the most effective because the probability of evolving target-site resistance to multiple pesticide or drug MOAs is the product of the individual resistance probabilities.

Not allowing tank mixing as part of a proposed herbicide registration that is intended to help manage known herbicide resistant weeds and to delay the evolution of additional herbicide-resistant weeds is at best contradictory, but more likely counterproductive to these objectives. It is entirely predictable that this prohibition will promote the evolution of halauxifen-methyl resistant weeds. As indicated in the proposed registration, halauxifen-methyl will be available alone and as a component in the herbicide Quelex™. Quelex will contain the active ingredient florasulam, an acetolactate synthase (ALS) inhibitor, in addition to halauxifen-methyl which is a synthetic auxin. While Quelex would seem to bring two effective MOAs to bear against many broadleaf weeds, one of the targets for Quelex use is actually ALS resistant weeds (EPA-HQ-OPP-2012-0919-0013, page 6). Thus, without the opportunity to add addition effective MOAs as a tank mix when ALS resistant weeds are present, Quelex applications will actually be selecting for halauxifen-methyl resistance. Auxin herbicide resistant weeds are already known to exist and the halauxifen-methyl use without effective tank-mix partners will likely lead to their expansion and further evolution. The unintended outcome of a ban on tank mixing could be a further increase in resistant weeds, rather than the opposite.

Apparently, beyond the impact the tank-mix prohibition would have on resistance management, the Agency understands some of the other implications such a decision would have on the practical aspects of weed management. Included in the material associated with the Proposed Registration Decision for the New Active Ingredient Halauxifen-methyl (EPA-HQ-OPP-2012-0919-0013, page 9) is the statement:

> *"The practice of tank mixing can result in **significant economic benefits** to the grower by allowing control of a wider variety of pests in a single application without incurring the expense of sequential applications. Additionally, by reducing the number of visits to the agricultural field, the grower is also **reducing fossil fuel use** and emissions from large agricultural equipment, **as well as the potential exposure to pesticides** that can result from multiple visits to the same area being treated. It is also widely accepted that the **practice of mixing products with different modes of action is essential to the management of weed resistance**. Because weed resistance is known to have a very costly impact to overall crop yields, which in turn negatively impacts growers' harvests and the price of commodities to the consumer, tools that aid in the prevention of resistance are considered to be a very important benefit to agriculture".*

Yet, despite these certainties, the Agency has proposed the tank-mix prohibition for halauxifen-methyl. Unfortunately, it is our opinion that the value growers experience from tank mixing compared with the "uncertainty" they will have concerning the proposed prohibition will lead them to ignore it. For example, costs of herbicide ground application are estimated at $6.00 to $9.00 per acre (Halich 2016, Ibendahl 2016). Individually, a grower could be faced with an additional cost of thousands to tens of thousand of dollars for an operation for which they do not

see a value. Of course, collectively, the tank mix prohibition could cost farmers millions of dollars. The agency could be creating a situation that will encourage growers and others to disregard the label. And, without the opportunity to actually review the literature that lead to the uncertainty in the Agency, we cannot comment of the specific merits of the basis for that uncertainty.

We urge the Agency to reconsider this prohibition. It is counter-productive for herbicide resistance management, will result in significant economic costs to growers, will increase the carbon-footprint associated with weed management, and could be, frankly, ignored by many practitioners.

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Sincerely,

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cc: House Committee on Agriculture
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