May 26, 2023

SUBMITTED VIA EMAIL

Mr. Tulio Macedo, Chief
Pesticide Registration Branch
Department of Pesticide Regulation
California Environmental Protection Agency
1001 I Street
Sacramento CA 95814

Re: Comments Regarding Draft Guidance on Field Trial Requirements for Efficacy and Phytotoxicity Data

Dear Mr. Macedo:

The Biological Products Industry Alliance (BPIA) appreciates the opportunity to provide comments to the Department of Pesticide Regulation (DPR) regarding the proposed guidance on field trial requirements for efficacy and phytotoxicity data.

BPIA is a not-for-profit organization that promotes the responsible development of safe and effective biological products including biopesticides, biofertilizers, and biostimulants. These beneficial tools are used for commercial agriculture, forestry, golf courses, home gardens, horticulture, ornamentals, and more. BPIA also supports public health through education, outreach, and advocacy activities at the state, federal, and international levels. BPIA's membership includes both large and small producers of biological pest control products or biopesticides used extensively by farmers in California.

Following a detailed review of the proposed Notice, we would like to provide feedback for the following specific sections of the draft guidance:

1. Field Trial Design, and Data Analysis and Reporting – Field Trial Design bullet:

For biologicals, unlike synthetic chemicals, there is not always a linear rate-response effect observed in field trials and when there is a positive rate-response it typically has a "flatter curve" or less steep slope value. When using biologicals, more is not always better. Therefore, it should not be an expectation that optimal rate-responses will occur as with synthetic active ingredients. Biological products are often not intended to be used as stand-alone treatments, but rather as supplemental or preventative measures. "Untreated control" implies that the product will be compared to a treatment to which no other product with efficacy on the same target pest is applied, which is not representative of the way biological products can be used. We recommend replacing the term "untreated control" with "negative control" and clarifying that the negative control can include application of products with efficacy on the target pest, so long as this is a representative use for the product to be registered.

We respectfully request that DPR consider adding flexibility to the proposed new guidance to address the unique activity of biologicals as compared to conventional chemistries. Adding flexibility will assist in ensuring that growers are not denied access to biological products because of procedural impacts rather than true efficacy concerns.

2. Field Trial Design, and Data Analysis and Reporting – Considerations for Efficacy Trials bullet:

While we appreciate DPR's efforts to reduce the challenges to registrants to develop efficacy data on all target organisms, we are seeking clarity on how it intends to define "representative and difficult to control" insects/plant diseases. Additionally, some target organisms may only have one related disease process, although across multiple crop types. In these cases an exception to selection of two or more diseases will be necessary.Would DPR be open to providing listings of insects or diseases they consider to be "representative" for each order/genus? Alternatively, is this something the Department would be open to negotiating and defining with registrants in pre-submission meetings or other similar forums?

Please provide a definition for "host-specific." Most insect pests infest a limited number of crops. Does this mean that they are host-specific and that therefore data from multiple crops is required? We would argue that in cases where the crop life cycle/plant architecture is similar (e.g. tree fruits and tree nuts or cereals and legumes), a total of three field trials conducted in one or more representative crops across three geographical regions, should be sufficient to support product registration.

3. Field Trial Design, and Data Analysis and Reporting – Product Performance Standards bullet:

We respectfully request flexibility in the general 70% reduction benchmark outlined by DPR. Many products, including biopesticides, are more appropriately assessed on a qualitative basis rather than a strict quantitative control standard. Biopesticides work differently and are not generally contact or systemic in nature. The effects on target pests may take some time to be visible or may present themselves in ways other than traditional "kill" events. Efficacy of nematicides, in particular, is not always tied to a reduction in the number of nematodes. Nematode population numbers are extremely varied, so researchers rely on several parameters to assess efficacy. These parameters do not always rely on counts of the target nematode. Instead, in many instances, yield quality and quantity are parameters considered for nematicide performance. Currently, product performance in terms of percent pest reduction can range from 30% to 70% control for synthetic or biological nematicides.

Moreover, biopesticides are often used in rotation or tank-mixed with other pesticides such that the overall level of control is high but the stand-alone product control may be less than the 70% bright-line standard. Additionally, biopesticides are often used in organic agriculture where the number of allowable products is severely limited. Setting a rigid, quantitative standard for such products may deprive organic growers of organic-compliant control solutions.

This request for flexibility is consistent with the 1982 *U.S. EPA Pesticide Assessment Guidelines, Subdivision G: Product Performance* cited by DPR in which US EPA discusses unique considerations for specific types of pesticide products, specifically noting that "*the performance standards are useful for guidance purposes and would be applied flexibly. EPA recognizes that the level of control derived from a single pesticide dosage varies with each pest and site combination and a number of other factors, including the user group; the geographic region; crop grading and quarantine standards; users of the treated commodity; the anticipated level of pest population to be encountered by users; climatic conditions; soil textures; crop cultivars; and, in some instances, comparisons with existing control measures*."

We also request flexibility in the definition of "moderate to severe pest pressures" when measuring product efficacy. This threshold is difficult to determine quantitatively and subject to individual interpretation. Would the burden of defining "moderate to severe" fall with the researcher conducting a given efficacy study, the sponsor of that study, or a third-party regulatory authority? In addition, requiring a moderate to high level of infestation may work against the mode-of-action of a biopesticide that performs well when applied more as a preventative treatment than as a curative treatment. Economic thresholds that were established decades ago for neurotoxins may not be suitable to today's synthetic materials or for biopesticides.

Without flexibility in these definitions, the proposed guidance would fail to assess adequate efficacy for a number of product types. Further, this change has the potential to significantly increase workloads for both DPR and US EPA, as registrants may be required to submit amended labeling to both authorities to revise currently-labeled product claims. Because these changes would apply across product types, the resulting workload could be significant, and add to already lengthy backlogs at both agencies. Additionally, the net result of these changes likely will eliminate or severely limit a significant number of useful, innovative, and environmentally-sustainable control products available to growers in California and for organic growers who may have very few registered solutions to their pest challenges and are dependent upon certain biopesticides.

4. Field Trial Design, and Data Analysis and Reporting – Considerations for laboratory or controlled-environment efficacy testing bullet:

BPIA strongly recommends against limiting greenhouse-developed data to support only greenhouse applications. Opportunities for infection in the field vary greatly due to the weather, the pathogen, and the host. A greenhouse trial can provide an opportunity to get sufficient pressure to generate meaningful data compared to trials run in the field. Each greenhouse study should be evaluated on its own merit. For example, if you are looking at increasing yield or plant health parameters, it is likely highly dependent on typical soil, weather, and production practices. Crops grown in the greenhouse may have a different size and may grow differently than the same crops in the field. In that case, it makes sense to require more evidence of efficacy due to the nature of the claims (plant health, yield, biomass). An interaction can occur where the difference in efficacy between the greenhouse and field is greater when looking at products that change growth parameters or depend on the soil type to work. Although we recognize that in such cases, it would not be appropriate to accept greenhouse data in lieu of field data, in many instances, greenhouse data can provide an equivalent or even superior evaluation of product efficacy.

For claims of pest pressure, for example, the greenhouse typically provides more disease, and predictive pressure than the field. This allows for a better understanding and evaluation of each subsequent product, and in less time. It is difficult to imagine a scenario where actual field use of a product would differ significantly from the product efficacy demonstrated in the greenhouse assuming all rates, volumes, and application factors are the same. For any case involving efficacy of pest control products, it is reasonable to assume the greenhouse would provide a more commercially-relevant evaluation of a product's performance because the disease pressure would be higher than in the field. If the pressure is not moderate to severe in the greenhouse, then more trials in which disease pressure is higher should be provided, just like trials run in the field. Restricting data from the greenhouse can make it difficult or impossible to obtain data under

moderate to severe pressure conditions. Presumably, many universities and researchers utilize the greenhouse for these very reasons.

5. Field Trial Design, and Data Analysis and Reporting – Data Analysis and Reporting bullet:

BPIA suggests that DPR be open to using broader confidence levels when evaluating biopesticide efficacy data for the reasons previously discussed. For nematicides, BPIA recommends utilizing a confidence level of $\alpha = 0.10$. Due to the inherent variability of nematode data, it is not uncommon to use a higher alpha when working with nematicides. Similar alpha values may also be appropriate for other uses, such as insecticides and fungicides.

For data required for crops/pests/diseases not currently in California, it seems that the guidance proposes an impossible standard to meet. If the data is impossible to generate in California or California-like-conditions and data must be generated in California or in California-like-conditions, how can these data be obtained?

6. Site Selection, Including Requirements for Justifying California-like Conditions for Field Trials Conducted Outside of California – Site Selection bullet:

BPIA requests clarity from the Department on the following points:

- Clarify that a total of at least three field trials spread across different geographical locations would be required and not three field trials at each geographical location.
- Clarify that aside from the exception indicated for certain PGR products where consecutive two-year field trials at the same location will be required, for other products, single year trials may be conducted all in the same year or over multiple years.
- Clarify whether in cases where trials are required on multiple crops, a minimum of three trials across all crops would be acceptable, rather than requiring three trials per crop, which may not be necessary and would significantly increase the cost of registration, creating a barrier to entry and further limiting the availability of biopesticides in California.
- Will these new conditions affect existing, granted registrations, or be required only for new registration actions?
- Will this affect registered products for which efficacy is less than 70 percent, (now revised to make claims only for suppression)?

7. Site Selection, Including Requirements for Justifying California-like Conditions for Field Trials Conducted Outside of California – Requirements for justifying California-like conditions for field trials conducted bullet:

Light intensity is not a useful environmental factor for determining California-like conditions. It is too variable depending on cloud cover or the presence of hills or trees or other objects that might shade a particular field. Light intensity data is not required by international efficacy testing guidelines and therefore is not generally collected or available. A more useful and readily-available measurement may be day length. We encourage DPR to remove or replace light intensity with a more appropriate measurement.

For crop-specific factors, the guideline notes that tested crops (cultivar, variety, and ecotype), pests, and diseases must be present in both California and the test location. Cultivars/varieties/ecotypes tested outside of California and especially internationally, may not be

identical to those present in California, but may be similar enough for DPR to accept the trials. The same may be true in some cases for pests and diseases. The registrant should be given the opportunity to make a case for DPR to accept data even when crop-specific and environmental factors are similar, but not identical to those in California and this should be clarified in the guidance.

8. Closing Remarks:

It is BPIA's understanding that the State of California is actively working to develop new sustainability guidelines that have the potential to dramatically transform the landscape for growers and applicators throughout the state. California's sustainability initiative and IPM approach has been embraced by many of our member companies. However, the above-outlined guidance, if introduced without flexibility, has the potential to severely restrict entry to market for biologicals and other innovative products throughout California. Growers in California would ultimately bear the impact, losing access to new biological innovations that could sustainably manage pests in California. As such, we caution that the proposed new requirements, without modification or flexibility, may inadvertently work against the sustainability goals that California is trying to achieve.

Where the above-proposed guidance appears more structured toward products with conventional chemistries, we recommend a revision of the guidance to better account for the unique properties of biological products. Finally, noting the significance of the proposed guidance and considerable impact on registration procedures for all products, we request additional information from the Department as to how the new policies will be implemented, and transparency on associated timelines.

Thank you for the opportunity to provide comments on the proposed guidance. We welcome the opportunity to further discuss with DPR. Should you have questions about or wish to have further discussion regarding these comments, please contact me.

Sincerely,

BIOLOGICAL PRODUCTS INDUSTRY ALLIANCE

Keith J. Jones
Executive Director