Response to Public Comments Regarding Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis

On September 17, 2019 USEPA posted to its web site a document entitled "Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis" and requested comment on it. The public comment period closed on November 1, 2019. The Agency received six comments during that comment period and one additional comment after closure of the comment period. This document describes the comments and the Agency's response.

EPA received comments from two private citizens, the United States Department of Agriculture, CropLife America, the Humane Society of the United States, People for the Ethical Treatment of Animals, and the Physicians Committee for Responsible Medicine. In general, five commenters supported the guidance/waiver with one suggesting revisions. This commenter suggested EPA take a weight of evidence approach to considering chemical properties in waiver evaluations noting that a reliance on octanol water partitioning as a criterion for waiver evaluation may lead to an erroneous conclusion regarding pesticide potency and risk. One commenter and some that supported the guidance/waiver provided suggestions that are outside the scope of the waiver. One commenter was generally critical of all Agency efforts to reduce the scope and number of toxicity tests and provided no information specific to the draft guidance. Each of the comments in their totality are attached to document.

In light of the comments, the Agency produced a final version of the guidance/waiver. In response to the suggestion regarding the octanol-water partitioning, this final version includes a statement that no single criteria should be viewed as grounds for denial of a waiver request but rather should be evaluated in a weight of evidence assessment. EPA is not addressing the remaining comments that are outside the scope of the draft guidance/waiver.

United States Department of Agriculture

October 28, 2019

Richard P. Keigwin, Director
Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Ave., N.W.
Washington, DC 20460-0001

Re: USDA Comments on EPA's Draft Policy to Reduce Pesticide Testing on Birds, September 2019 (submitted via email to OPPeco@epa.gov).

Dear Mr. Keigwin:

Thank you for the opportunity to comment on EPA's Draft Guidance[1] for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis, released on September 17, 2019. USDA appreciates EPA's transparency and willingness to take public comments on potential methods for reducing animal testing burdens at EPA.

USDA supports EPA's proposal for granting waivers of the avian sub-acute dietary, based upon a transparent, retrospective analysis of numerous and varied risk assessment outcomes from 1998-2017. We agree with EPA's stated rationale for choosing relatively recent assessments, tied with active ingredients (AIs) representing some of the most recent, novel, and varied modes of action across multiple pesticide classes. In particular, we note the summary of AIs selected for analysis, across the numerous IRAC, HRAC, and FRAC mode of action groupings presented in Appendix A. In light of the results that showed a greater than 99% instance of data waivers not changing the risk assessment outcome, such breadth provides strength to EPA's position that the sub-acute avian study is very rarely likely to be needed for establishment of an adequately protective acute avian toxicity endpoint.

We also generally support EPA's criteria for potential exceptions where sub-acute dietary study results may still inform risk assessments, particularly for active ingredients where an accumulative effect is likely. We note that while high octanol-water partitioning coefficient is listed as a potential justification in denying a waiver, a number of active ingredients evaluated in the retrospective analysis meet this criterion yet still showed no risk assessment impact from the avian dietary study. We suggest to EPA that the criteria listed (on page 8) should be considered holistically and that waiver decisions consider overall weight of evidence, rather than having any single criterion disqualify an applicant's waiver request (i.e., "unless one of the conditions described below," page 8).

[1] https://www.epa.gov/pesticides/epa-releases-draft-policy-reduce-pesticide-testing-birds

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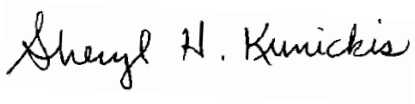
1400 Independence Avenue, S.W.
Washington, D.C. 20250-0314

USDA notes that many varied stakeholders—from registrants, to animal welfare advocates, to toxicologists, to EPA's Administrator[2]—share the goal of reducing unnecessary animal testing. EPA's proposal reflects sensitivity to animal welfare interests while also maintaining adequately protective methodology for assessing acute risks to birds for the practical purposes of pesticide registration. Streamlining the burdens, costs, and complexities for pesticide registration applicants is also ultimately of indirect benefit to growers seeking access to new and varied crop protection tools. We strongly support EPA's proposal as a positive step forward and stand ready to assist with any additional information needed by EPA risk assessors and risk managers.

Please let me know if you wish to discuss further.



Sheryl H. Kunickis, Ph.D.
Director

[2] https://www.epa.gov/newsreleases/administrator-wheeler-signs-memo-reduce-animal-testing-awards-425-million-advance

November 1, 2019

Environmental Protection Agency
Office of Pesticide Programs
1200 Pennsylvania Ave., NW
Washington, D.C. 20460

Submitted via email to: OPPeco@epa.gov

Re: CLA public comment on EPA's Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis

CropLife America (CLA), established in 1933, represents the developers, manufacturers, formulators and distributors of plant science solutions for agriculture and pest management in the United States. CLA's member companies produce, sell and distribute virtually all the crop protection and biotechnology products used by American farmers. CLA appreciates the opportunity to comment on Environmental Protection Agency (EPA)'s Draft Guidance[1] for Waiving the Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis referenced in a news release[2] published on EPA's website on September 17, 2019.

CLA supports EPA's decision to waive the sub-acute avian dietary study for some pesticides. Allowing this waiver will increase the efficiency of the pesticide registration process by reducing time and number of animals required for conducting and reviewing pesticide toxicity studies.

The sub-acute dietary study simulates a realistic exposure scenario than the acute oral gavage study (dietary vs. a one-time bolus dose), however, the acute oral gavage study alone provides sufficient information on which risk management decisions can be made, because the sub-acute dietary study rarely changes the outcome of the acute risk assessment. This is supported by the retrospective analysis of avian acute risk assessments for pesticides published by EPA and People for the Ethical Treatment of Animals (PETA).[3] The analysis showed that the acute risk assessment conclusions for birds were driven by the results of the acute oral gavage study for 99% of the 119 pesticides analyzed.

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[1] "Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registrations," *United States Environmental Protection Agency*, September 17, 2019. https://www.epa.gov/sites/production/files/2019-09/documents/draft-waiver-guidance-avian-sub-acute-dietary.pdf.

[2] "EPA Releases Draft Policy to Reduce Pesticide Testing on Birds," *United States Environmental Protection Agency*, September 2019. https://www.epa.gov/pesticides/epa-releases-draft-policy-reduce-pesticide-testing-birds.

[3] Hilton, G.M. E. Odenkirchen, M. Panger, G. Waleko. A. Lowit, A.J. Clippinger. 2019. Evaluation of the avian acute oral and sub-acute dietary toxicity test for pesticide registration. Regulatory Toxicology and Pharmacology, 105:30- 35

CLA concurs with the conditions described by EPA under which a waiver for the avian sub-acute dietary study would not be granted. When these conditions are met, there is clearly additional scientific information required that the sub-acute dietary can provide. We are currently preparing recommendations for how a sub-acute dietary study could capture the most scientifically robust information possible, when such a study is warranted.

Thank you for reviewing these comments. Please contact CLA if you have any questions or require additional information.

Respectfully submitted,

Manojit Basu, PhD
Managing Director, Science Policy
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PEOPLE FOR
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October 29, 2019

U.S. Environmental Protection Agency
Office of Pesticide Programs

Re: *Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration*

On behalf of People for the Ethical Treatment of Animals (PETA) and our more than 6.5 million members and supporters, we thank the U.S. Environmental Protection Agency (EPA) for the opportunity to submit the following comments on the EPA Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration.[1]

We applaud the EPA Office of Pesticide Programs for their initiative in identifying tests that may not provide value to the risk assessment process and collaborating on retrospective analyses that assess the usefulness of these tests. The results of the analysis of the avian sub-acute dietary test prove that it is not used for risk management, and can thus be waived without compromising health to terrestrial animals.[2] This policy is in the spirit of achieving EPA's goal of reducing animal testing and enhancing the quality of its risk management decisions to better ensure protection of humans and the environment.[3]

In an effort to maximize the impact of its guidance document, we recommend that the EPA undertake the following actions:

1. **Collaboration:** Continue to collaborate with non-government organizations that are able to expedite study reviews to identify gaps in study usage for risk management decision making.

2. **Transparency:** Make publicly available CBI-cleared EPA-generated documents (risk assessments, DERs, etc.). Data from these documents can be analyzed to evaluate which information is used for risk management. These data can also be used in the development of machine learning computational models, which will be valuable for environmental risk assessment.

3. **Harmonization:** Continue international communication to ensure harmonized acceptance of newly emerging policies to reduce or replace animal tests.

4. **Training:** Continue to receive regular training on *in silico* and *in vitro* methods from outside experts.

Affiliates:
- PETA Asia
- PETA India
- PETA France
- PETA Australia
- PETA Germany
- PETA Netherlands
- PETA Foundation (U.K.)

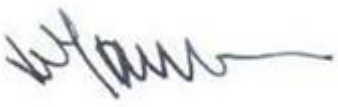
[1] https://www.epa.gov/pesticides/epa-releases-draft-policy-reduce-pesticide-testing-birds
[2] https://www.sciencedirect.com/science/article/pii/S0273230019300856
[3] https://www.regulations.gov/document?D=EPA-HQ-OPP-2016-0093-0003

5. **Outreach:** Ensure that regulated companies are aware of opportunities and processes to waive animal tests or to use non-animal methods.

PETA supports the EPA guidance for waiving the avian sub-acute dietary test, which will allow scientifically supported waivers for a test that is not needed to make sound risk management decisions and will free up resources that can be better spent implementing more relevant animal-free toxicity testing approaches.

We thank you for your time and consideration of these comments.

Sincerely,



Jeffrey Brown
Research Associate
Regulatory Testing Department

November 1, 2019

Rick P. Keigwin, Jr.
Director, Office of Pesticide Programs
Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

RE: Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis

Sent via e-mail: OPPeco@epa.gov

Dear Director Keigwin:

On behalf of the Humane Society of the United States (HSUS), Humane Society Legislative Fund (HSLF), and our members and supporters, we appreciate the opportunity to provide comments on the *Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis*. We applaud this proactive effort by the Environmental Protection Agency (EPA) Office of Pesticide Programs (OPP) to grant waiver requests for sub-acute avian dietary tests when registering conventional pesticides to be used outdoors.

OPP typically requires two types of tests using avian species for an ecological risk assessment of new conventional pesticide active ingredients used outdoors: acute oral toxicity studies and sub-acute dietary studies (one with an upland game bird and one with a waterfowl species).[1] In the sub-acute test, the pesticide is fed to 10 birds per five dosage levels plus a control group for five days to determine a median lethal concentration (LC50) response.[2] However, there are several limitations for the sub-acute dietary toxicity studies including inconsistent and arbitrary dosing and failure to factor in normal degradation of materials.[3]

OPP, with the help of PETA International Science Consortium Ltd, conducted a retrospective analysis of studies submitted in pesticide ecological risk assessments that contained both acute

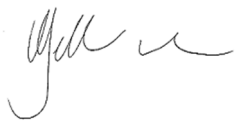
[1] 40 C.F.R. §158.630.
[2] Environmental Protection Agency. (2012). OCSPP 850.2200: Avian Dietary Toxicity Test. https://www.regulations.gov/document?D=EPA-HQ-OPPT-2009-0154-0011
[3] Ecological Committee on FIFRA Risk Assessment Methods. (1999). ECOFRAM Terrestrial Draft Report. https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/ecofram-terrestrial-draft-report

oral and sub-acute dietary avian studies and found that "in 99% of cases (118 of 119 chemicals evaluated quantitatively) the RQ [risk quotient] values for the sub-acute dietary risk assessment approach were lower than the RQs calculated using the single oral dose acute effects endpoint."[4] This retrospective analysis showed that decisions regarding acute risk to birds were based on the results of the avian acute oral toxicity test, not the sub-acute dietary test. Therefore, the sub-acute avian test could be waived for all but a few pesticides (such as those with delayed toxicity or high bioaccumulation)[5] without compromising protection of bird species.

By granting waivers for the sub-acute dietary toxicity test, OPP can reduce the number of birds used by a total of 60 birds per test. Given that usually two different species are tested, 120 birds could potentially be spared for each new pesticide chemical registered with EPA. HSUS and HSLF urge EPA to quickly finalize this guidance document and communicate its adoption to all pesticide manufacturers to ensure that no additional birds are subjected to this unnecessary test. We also hope that EPA will take every opportunity to communicate these results to the pesticide regulatory agencies of other countries as part of ongoing efforts to harmonize testing requirements globally. Otherwise, savings in birds' lives will likely be limited to only those new pesticides registered exclusively for use in the United States.

As part of the agency's effort to end reliance on all mammalian testing by 2035 as announced by Administrator Wheeler on September 10, 2019, OPP should continue to identify tests that are rarely used or are not helpful in risk assessments as it looks for additional opportunities to eliminate unnecessary animal studies. Thank you for the opportunity to comment.

Sincerely,



Vicki Katrinak
Manager, Research & Testing
Animal Research Issues
The Humane Society of the United States

Gillian Lyons
Senior Regulatory Specialist
Humane Society Legislative Fund

[4] U.S. EPA. OPP. (September 2019). Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis. https://www.epa.gov/sites/production/files/2019-09/documents/draft-waiver-guidance-avian-sub-acute-dietary.pdf

[5] Hilton, G. et.al. (2019). Evaluation of the avian acute oral and sub-acute dietary toxicity test for pesticide registration. Regulatory Toxicology and Pharmacology 105 (2019) 30–35. https://doi.org/10.1016/j.yrtph.2019.03.013

PhysiciansCommittee
for Responsible Medicine
PCRM.ORG
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November 1, 2019

Environmental Protection Agency
Office of Pesticide Programs, Mail Code 7506C
1200 Pennsylvania Ave., NW Washington DC 20460

To Whom It May Concern:

The Physicians Committee for Responsible Medicine (PCRM) thanks the Environmental Protection Agency (EPA) for the opportunity to comment on its *Draft Guidance for Waiving Sub-Acute Avian Dietary Tests for Pesticide Registration and Supporting Retrospective Analysis*. PCRM is a nationwide nonprofit organization comprised of over 175,000 supporters advocating for efficient, effective and ethical medical practice, nutrition, and research.

PCRM enthusiastically supports EPA's guidance for waiving avian sub-acute dietary tests, which provide little additional scientific information or environmental protection. Through its collaboration with People for the Ethical Treatment of animals, EPA has shown, by retrospective analysis, that avian acute oral studies normally give higher risk quotients than avian sub-acute dietary studies and therefore represent a protective approach. Waiving these unnecessary tests will spare approximately 720 birds per year while allowing EPA to focus on the information that is most relevant to its risk assessments.

Furthermore, the draft guidance is the product of a successful collaboration between EPA and one of its stakeholders. PCRM looks forward to working with EPA to reduce animal use in the testing of the substances it regulates.

Thank you for your attention to these comments. I can be reached at JManuppello@PCRM.org or at (202) 717-8677.

Sincerely,

Joseph Manuppello
Senior Research Analyst
Phone: 202.717.8677
Email: JManuppello@pcrm.org

From: H. Tomasz Grzybowski <leocatv@gmail.com>
Sent: Thursday, January 02, 2020 8:33 AM
To: oppeco
Subject: No more LD50, use NOAEL

Stop LD50 testing, use No Observed Adverse Effects Level.

H. Tomasz Grzybowski
tel. +48-780-129-544
email: leocatv@gmail.com
email: htg@interia.pl

From: augula@aol.com
Sent: Friday, September 20, 2019 9:46 AM
To: oppeco
Subject: Recent directives waiving tests on animals

Dear Mr. Andrew Wheeler:
So the EPA is now proposing to reduce or waive testing on birds in regards to the effects of pesticides. Previously you have directed massive reductions in all animal testing in regards to pesticides. I would normally ask why, but recent decisions to force out more than half of the researchers employed by the EPA is fairly self-explanatory, considering the motivations of the man who hired you, the man who denies global warming and other inconvenient facts.
These directives are in direct conflict with scientific findings: The bird population in the US has been in decline for the past 50 years. We have lost 3 billion birds during this period; 29% of all birds. Much of this tragedy is due to pesticides, although there are other factors responsible due to human action or inaction. This environmental slaughter is even more egregiously demonstrated in the deaths of untold billions of honeybees which have been killed by the class of neonicotinoid pesticides manufactured by petrochemical
giants like Bayer and Monsanto. These toxic products were thankfully banned in Europe years ago when their effects became known. But you know all that. So far the EPA does not even seem to care about the use
of the "weed-killer" sold as Round-Up, as its continued appearance in TV commercials illustrates. Will you and the EPA be okay with the inevitable number of deaths suffered by housewives using this product?
Cutting through the mumbo-jumbo of the new "Draft guidance for waiving sub-avian dietary tests, etc.", to deny that there is a cause-and-effect correlation to all these deaths is equivalent an ostrich burying its head in the sand - except that the ostrich is not receiving taxpayer money to do so.
I fervently hope you come to the realization that the man who hired you will no longer be handing out EPA paychecks in the near future and trust you have not based your "legacy" on the contrary.
Sincerely,
Augie Wiedemann, taxpayer and voter
921 Flatbush Rd
Kingston,NY 12401