
## *How to make pesticides safer for bees*

Honey bees are experiencing unsustainable colony loss rates, and many species of wild pollinators are experiencing range contractions and population declines. Pesticides are not the only reason for these problems, but hundreds of scientific studies show very clearly they're contributing.

For this and other reasons, some people think we should get rid of pesticides. But that's not currently practical. Our largely monocultural agricultural system is susceptible to pests, and non-pesticide control measures are currently inadequate. So, the truth is we need pesticides to ensure the reliability of our food.

Because of this, there are many pesticide companies that produce many pesticides, they all have a financial incentive to sell as much product as possible, and they have many tactics to ensure those sales occur. But those are topics for another day.

The topic for today is the fact that all pesticides must pass through a risk assessment process before they're registered and sold. In the USA, this process is overseen by the United States Environmental Protection Agency (EPA). This means all pesticides that are currently sold in the USA have passed the EPA's risk assessment process.

But we know that pesticides are currently causing problems for pollinators. This means the current risk assessment process is inadequate. Perhaps this shouldn't be surprising since the process isn't very old. For example, the EPA is only 53 years old, and the tool the EPA uses to assess risk to bees — BeeREX — is only 8 years old. Indeed, when you download BeeREX from the internet, the file is called "BeeREX Version 1.0." As with the first version of everything, there are kinks to work out.

So, what should go into "BeeREX Version 2.0"? What are the current shortcomings of the pesticide risk assessment process for bees, and how should those shortcomings be solved? These are the topics for the seventy-first *Notes from the Lab*, where I summarize ***"Breaking the cycle: Reforming pesticide regulation to protect pollinators,"*** written by Adrian Fisher and colleagues and published in the journal ***BioScience*** **[2023].**

The paper by Fisher and colleagues is an "ideas paper," which means it doesn't contain data. Instead, it contains references to lots of peer-reviewed literature highlighting problems within the current risk assessment process, and lots of ideas from the authors on how to improve the process. The Entomological Society of America provided support for the authors to initially meet and discuss common themes, then they wrote the paper.

**So, what are the major problems with the current risk assessment process?** The authors identify five major inadequacies of the current regulatory approach.

***Overreliance on short-exposure laboratory lethality assays (i.e., $LD_{50}$).*** Short-term $LD_{50}$s are problematic because pollinators generally experience exposure to pesticides for much longer than a few days, and toxicity is well-known to increase with duration of exposure.

***Failure to assess sublethal injurious effects on pollinators.*** Sublethal impacts on bee reproduction are particularly important due to the central role of reproduction in fitness and population change. Other sublethal effects, such as impacts on physiology and behavior, can also impact bee fitness.

***Inadequate assessment of exposure.*** As a prime example, exposure to wind-blown dust from seeds coated with neonicotinoids was not estimated to be a major route of exposure when these pesticides were approved. In addition, after a pesticide is approved there is currently no requirement for real-world exposure data to be obtained (see Photos 1 & 2). Thus, there is no mechanism to assess whether predictions concerning exposure are actually borne out in the real world.

***Overreliance on the western honey bee (Apis mellifera) as the model pollinator species.*** *Apis mellifera* lives in the largest colonies and is the most social of all ~20,000 bee species that exist in the world. Its colonies possess multiple social detoxification strategies that buffer impacts of pesticides. Because of this, it should not be surprising that numerous studies have found that other bee species, including stingless bees, bumble bees, and solitary bees, often experience more severe adverse impacts from pesticide exposure. This means a colony-level risk assessment approach using

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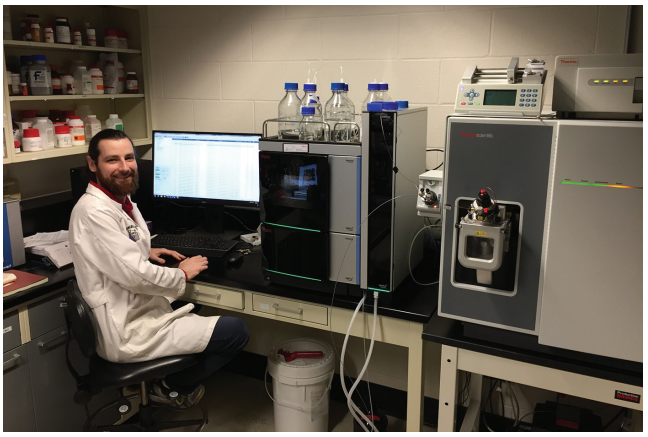

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**Photos 1 & 2** *A researcher collects pollen from a honey bee hive during commercial apple pollination, then pesticide residues are assessed in the lab. Such post-approval monitoring is not currently included in the pesticide risk assessment process overseen by the United States Environmental Protection Agency (EPA), European Food Safety Authority (EFSA), or other regulatory agencies.*

*A. mellifera* is not conservatively protective of pollinators.

***Narrow focus on isolated active ingredients.*** Many pesticide formulations contain "inert ingredients" that are, in fact, toxic to bees. Moreover, pollinators are often exposed simultaneously to a diverse suite of pesticides that can have additive or interactive effects. The current risk assessment approach does not assess risk from "inert ingredients," multiple-ingredient formulations, or co-exposures that commonly occur in the real world.

**OK, these definitely seem like problems. Do other people agree these are problems?** Yes. The most notable example is the European Food Safety Authority (EFSA), which is the European equivalent of the EPA. The EFSA recently updated their guidance on risk assessment for bees to address many of these problems (EFSA, 2023). Unfortunately, there are no current plans for an equivalent update at the EPA or other regulatory agencies.

**If the EPA or other regulatory agencies decide to update their processes, what should they do?** For each problem, the authors lay out proposed solutions. A visual representation of the proposed solutions is shown in Figure 1, where the current regulatory framework is shown on the left and the proposed framework is shown on the right. Note the current regulatory framework sometimes results in registered pesticides being banned, while the proposed framework avoids this shortfall of the current regulatory approach.

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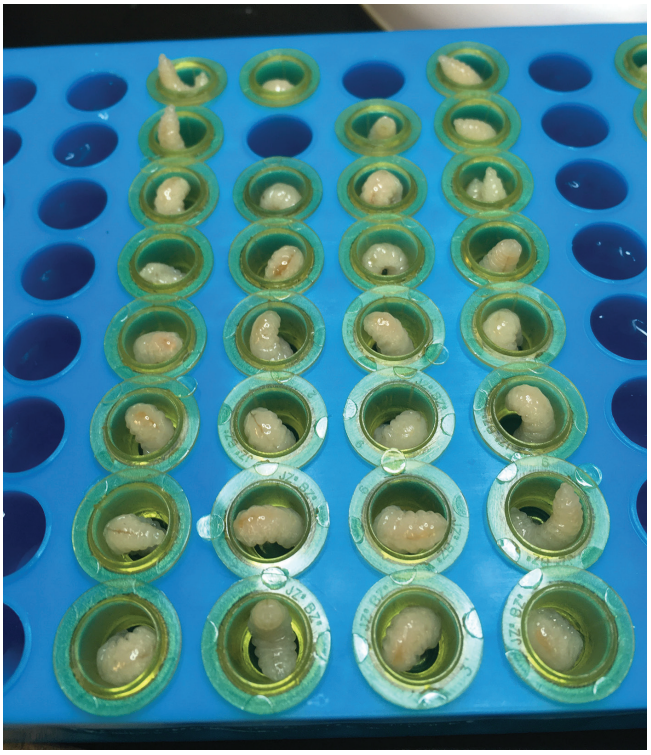

**Photo 3** *In a laboratory assay, honey bee larvae are co-exposed to field-realistic concentrations of a fungicide and insecticide that were both frequently present in pollen collected by bees during apple bloom (see Photo 1) and assessed for sublethal effects on development. Sublethal laboratory assays are not currently included in the pesticide risk assessment process overseen by the EPA, EFSA, or other regulatory agencies.*

**First, there should be greater realism in laboratory toxicity assays.** For many non-pollinator model organisms, the short 48-hr $LD_{50}$ approach is supplemented with additional endpoints and methods. These updated methods should be used for pollinators. For example, the new EFSA guidance recommends using the entire dose-response curve to extrapolate a no-observed-effect concentration, assessing time-reinforced toxicity, and assessing mixture toxicity (EFSA, 2023).

Technological advances have enabled scalable, cost-effective assays that assess synergistic impacts of pesticides on bees. One of these approaches, developed by Bayer scientists (Haas & Nauen, 2021), was highlighted in a previous *Notes from the Lab* column [see March 2021 column: 161(3):315-317]. Inexpensive lab-based approaches such as these, especially when developed and carried out by the pesticide companies themselves, can clearly be incorporated into the risk assessment process quite easily.

Perhaps most important, laboratory assessments of mortality should discard rigid timeframes, instead allowing the lifespan and natural history of test organisms, and the persistence of pesticide residues in relevant exposure matrices, to dictate test duration.

**Second, there should be sublethal testing.** Remember, the current problem with pollinators isn't just dying bees. It's range contractions and population declines. Because of this, impacts on reproduction and other

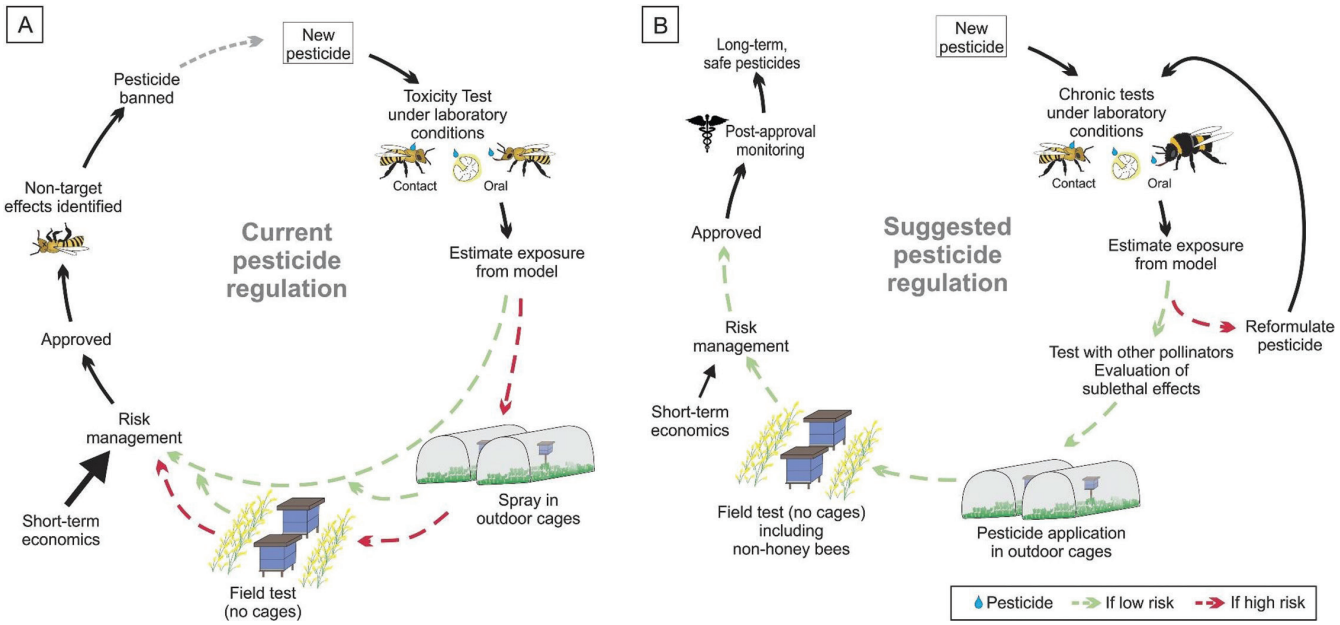


**Figure 1** *Comparison of current pesticide regulatory practices and a suggested model for improvement. (a) The current pesticide assessment process includes approval of a pesticide on the basis of low mortality of larvae and caged honey bee adults in contact and oral exposure tests. The current practices allow bypassing of spraying in outdoor cages and field tests (no cages) on the basis of short-term $LD_{50}$ evaluations. In addition, current practices in most countries do not include post-approval monitoring that could result in the banning of a pesticide due to nontarget effects. (b) The suggested improved pesticide approval and monitoring process includes requirements for multiple levels of testing with field- and taxon-relevant exposure conditions and risk assessment before a pesticide is approved. This process would also require assessing pesticide toxicity for diverse pollinator species, testing of sublethal effects, and synergistic interactions between pesticides. In addition, our proposed model includes post-approval monitoring, allowing for enhanced efficiency in detecting unanticipated negative effects.*

sublethal responses that shape bee fitness and population change are important to assess. Inexpensive methods for measuring sublethal effects are available and well-established for many pollinator taxa (for example, see Photo 3). These methods should be used.

**Third, in addition to *Apis mellifera*, other pollinator species should be assessed.** In the revised guidance for pollinator risk assessment from the EFSA, one bumble bee species (the buff-tailed bumble bee, *Bombus terrestris*) and one solitary bee species (the mason bee, *Osmia bicornis*) are recommended to be included in the risk assessment process (EFSA, 2023). These species are readily available because they're reared commercially in Europe. In the USA, similar species are readily available. The common eastern bumble bee (*Bombus impatiens*) and blue orchard bee (*Osmia lignaria*) are both reared commercially. Methods for conducting laboratory assays and field trials for these non-*Apis* species are available and well-established. These methods should be used.

**Fourth, there should be mandatory field-realistic testing.** The current tiered approach to risk assessment used by the EPA, EFSA, and other regulatory agencies means that experiments to quantify exposure are only conducted for a small number of highly toxic pesticides, with toxicity defined by short-term laboratory lethality assays (i.e., $LD_{50}$). Numerous recent pollinator-pesticide field experiments have demonstrated above-predicted exposures and/or negative outcomes for multiple pollinator taxa in the field. This means current regulatory approaches to predict exposure and/or the impacts of exposure are insufficient. A simple fix to this problem is mandatory field testing for all pesticides, instead of only the subset of pesticides identified as highly toxic in short-term laboratory lethality assays.

In addition, testing should not occur with isolated active ingredients, because that is not how pollinators are exposed to pesticide products in the field. Instead, field testing should occur with pesticide products as they're formulated and sold for use in the real world, to account for potential effects of "inert" ingredients and interactions among formulation components.

**Fifth, there should be post-approval monitoring and reassessment.** After a new drug for humans passes the risk assessment process overseen by the United States Food and Drug Administration (FDA) and is released for sale, it undergoes a post-approval monitoring process called pharmacovigilance. This process has saved the pharmaceutical industry millions, perhaps billions, of dollars in lawsuits for a simple reason: No risk assessment process is perfect. In other words, no matter how safe something seems, you can never be 100% sure until it's used in the real world under all the different conditions that exist outside of the laboratory and controlled field trials.

Unfortunately, while the FDA has a well-established post-approval monitoring process for drugs, such a process does not currently exist for pesticides overseen by the EPA or other regulatory agencies. Frankly, this is reckless, both for pollinators and the pesticide companies who must continually battle lawsuits armed with limited information about the nontarget impacts of their products in the real world.

Having given public testimony on this topic in the past, I can tell you that policymakers and the public are confused. Part of the reason is disinformation from the pesticide industry (if you don't believe me, check out the November 14 post on my lab's Twitter

account). But more importantly, the current risk assessment process is inadequate. If we improve the pesticide risk assessment process and make it adequate, just think of all the lawsuits and bans that will be avoided, money saved, *not*-confused policymakers, and pollinators that will be protected.

Until next time, bee well and do good work.

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