Precaution: Science and Policy

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In July 2014, the U.S. Fish and Wildlife Service (FWS), in announcing its decision to phase out the use of neonicotinoid pesticides on federal wildlife refuges, noted that the chemicals' prophylactic use (before identifying pest problems) and broad spectrum effect on non-target species runs contrary to its integrated and precautionary approach to pest management. The chief of the National Wildlife Refuge System, James Kurth, said, "We make this decision based on a precautionary approach to our wildlife management practices. . ." This statement introduces the concept of precaution into pesticide policy, an approach found in the *Organic Foods Production Act* (OFPA). However, the federal pesticide registration system managed by the U.S. Environmental Protection Agency under the *Federal Insecticide, Fungicide and Rodenticide Act* (FIFRA), operates with a bias against precaution, high allowable risk, and perpetual crisis management.

The Precautionary Principle

In 1998, a gathering of scientists, philosophers, lawyers, and environmental activists produced this statement of the Precautionary Principle (known as the Wingspread Statement):

> When an activity raises threats of harm to human health or the environment, precautionary measures should be taken even if some cause and effect relationships are not fully established scientifically. In this context the proponent of an activity, rather than the public, should bear the burden of proof. The process of applying the precautionary principle must be open, informed and democratic and must include potentially affected parties. It must also involve an examination of the full range of alternatives, including no action.[1]

Organic Foods Production Act (OFPA)

Perhaps the clearest embodiment of the precautionary principle in United States law is in OFPA. The law establishes criteria for determining which synthetic materials may be used in organic production that are clearly precautionary:

> [7 U.S.C. 6504] **National Standards for Organic Production.** To be sold or labeled as an organically produced agricultural product under this chapter, an agricultural product shall—
>
> (1) have been produced and handled without the use of synthetic chemicals, except as otherwise provided in this chapter;
>
> [7 U.S.C. 6517] **National List.**
>
> **(c) Guidelines for Prohibitions or Exemptions.**— (1) Exemption for prohibited substances in organic production and handling operations.—
>
> The National List may provide for the use of substances in an organic farming or handling operation that are otherwise prohibited under this chapter only if—
>
> (A) the Secretary determines, in consultation with the Secretary of Health and Human Services and the Administrator of the Environmental Protection Agency, that the use of such substances—
>
> (i) would not be harmful to human health or the environment;
>
> (ii) is necessary to the production or handling of the agricultural product because of the unavailability of wholly natural substitute products; and
>
> (iii) is consistent with organic farming and handling;

These three criteria are further elaborated in OFPA and its implementing regulations. They are utilized by the National Organic Standards Board (NOSB), which consists of representatives of all aspects of the organic community (including producers, handlers/processors, retailers, consumers, environmentalists, scientists, and certifiers), in determining acceptable materials in organic production.

The presumption against the use of synthetic materials in organic production establishes the burden of proof that is the key element of precaution.[2] OFPA is also precautionary because the burden of proof to show that the synthetic materials meet the three criteria rests with those who want to have it used in organic production. To be allowed for use under certified organic standards, the NOSB must approve the material by a two-thirds "decisive" vote, adding a further element of precaution.

Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA)

The burden of proof in many other regulatory schemes in the U.S. is anti-precaution and favors the allowance of risk. This is not always obvious in the statutory language. FIFRA, for example, is not explicitly anti-precaution. Rather, at least some of that bias has been added by EPA in its implementation.

FIFRA's safety standard allows a pesticide to be used if it does not result in "unreasonable adverse effects on the environment,"[3] defined as "(1) any unreasonable risk to man or the

environment, taking into account the economic, social, and environmental costs and benefits of the use of any pesticide, or (2) a human dietary risk from residues that result from a use of a pesticide in or on any food inconsistent with the standard under section 408 of the *Federal Food, Drug, and Cosmetic Act* (21 U.S.C. 346a)."[4] FIFRA's underlying standard is not as precautionary as OFPA's standard because OFPA requires that **both** need and lack of adverse effects be established. In addition to FIFRA allowing "benefits" to trump hazards (with its risk-benefit calculation), the greatest anti-precautionary aspect of U.S. pesticide regulation actually stems from the way EPA applies science to its unreasonable adverse effect determination.

A scientific test for toxicity or some other impact of a chemical is said to be "positive" when the a statistically significant number of test subjects (based on laboratory animal testing) exhibit a toxic effect that is greater in the dosed group than the control group. Those positive tests, which under FIFRA are performed by the manufacturer, other potential registrants, or a contractor hired by one of them, provide the potential support for denying a pesticide registration.

FIFRA requires EPA to register a pesticide if it does not cause unreasonable adverse effects on the environment, but the practice of EPA is to allow pesticide registration unless unreasonable adverse effects are demonstrated. Unlike OFPA, the burden of proof, as FIFRA is implemented by EPA, is on the agency to show harm.

Furthermore, because the tests that provide potential support for a decision to deny a registration require demonstration of statistically significant impacts without requiring a minimum power of the statistical test, the bias in favor of allowing the use of the pesticide is greater.

In the case of toxicological tests of pesticides, the experiment is attempting to disprove the hypothesis (known as the null hypothesis) that there is no difference between those test animals receiving doses of the pesticide and the controls (no exposure) –that is, that the pesticide has no effect. The experiment is arranged so that a positive result disproves the null hypothesis.

The **power** of a statistical test is the probability that it correctly rejects the null hypothesis when it is false. In the case of a test to determine whether a chemical is carcinogenic, for example, the null hypothesis is that the chemical does not cause cancer. Thus the power of the test is the probability that the test will determine that a carcinogen causes cancer. Scientists typically focus on **significance** or the **confidence level**, the probability that a test will not reject a true null hypothesis. In the example of carcinogenicity testing, the confidence level is the probability that the test will determine that a non-carcinogen does not cause cancer.

An investigation into statistical power and precaution

When a toxicological test is performed, the question as to whether or not there is an effect is determined by statistical tests performed on the data resulting from the test. Typically, the frequency of the effect (e.g., percentage of animals with tumors) in dosed animals is compared to the frequency in controls. One test that is often used is Fisher's Exact Test, and it is the one used in these calculations.

In statistical inference from the data, there are two types of errors that can be made:

- Type I errors are false positives –saying that a chemical causes tumors when it doesn't;
- Type II errors are false negatives –saying that a chemical does not cause tumors when it does.

Either kind of error can arise from random factors. When a result is judged to be "statistically significant," it means that the observed proportion of effects (tumors) is unlikely to have occurred by chance if the chemical has no effect. Usually, "unlikely" means it would happen less than 5% of the time. That means that the rate of type I errors that is allowed is less than 5%. The rate of type I errors is also called α , or the significance level. 1- α is called the confidence level.

The rate of type II errors is called β, and 1 - β is called the power of the test. It is the likelihood that the experiment would find an effect if there is one.

While α is generally reported, β almost never is. While there is a standard for statistical significance based on α, there is not a requirement for a minimum value of β. In a regulatory setting, type I errors hurt chemical manufacturers because they mean that a harmless chemical may be subject to regulation or restriction based on an effect that is not present. In the same setting, type II errors hurt consumers and the public because they mean that there may be exposure to a chemical that causes health impacts that were not recognized by testing.

If a regulatory program is precautionary, it should not be based on tests in which the allowed rate of false negatives is greater than the allowed rate of false positives.

According to the EPA test guidelines, each test group starts with 50 animals, but is permitted to be reduced to 13 animals by the end of the test. This number of animals is sufficient to detect an increase in the incidence of the effect from 10% to 100% that occurs 95% of the time. It is not sufficient to detect a fivefold increase from a back-

ground incidence of 10% that occurs even 80% of the time, or any increase up to 10X from a background rate of 5% or less that occurs 80% of the time. That means that unless the background rate is very low and the effect is very great, there will be many false negatives.

Furthermore, it is easy to manipulate the statistical power –if it is not controlled by oversight– to make it appear that a given experiment does not demonstrate a statistically significant effect. One need only reduce the effective total number of subjects (sample size, N), since EPA guidelines allow reductions of up to 75%. In reading reports of experiments submitted to EPA, one frequently sees evidence of the reduction of N over the course of the experiment. An animal may be found dead of causes unrelated to the experimental question. This may result from poor feed, unclean conditions, over-crowding, or other practices. It need not affect the control group more than the dosed animals. Any reduction in N will reduce the statistical power and make it less likely that the effect will be found to be statistically significant.

It is difficult, but possible, to find raw data on the underlying study and the possible reduction in N resulting in a lack of significance in the testing of pesticides. In Registration Eligibility Documents, the Integrated Risk Information System, and other documents, EPA reports study conclusions, but not details like the number of animals lost during the experiment. To find those details, it is necessary to file a *Freedom of Information Act* (FOIA) request for the EPA reviews of original study documents submitted by the registrant (chemical manufacturer). For example, in one study relied upon for the continued registration of atrazine, 50.5% of all the animals died over the course of the experiment, including 41% of the male controls and 57% of the female controls. Of the total, 41% were "found dead" in their cages. In addition to these, two mice were deleted for misidentification, two because they were mis-sexed, and one because the animal escaped from his cage. With these large reductions in the number of animals from the original 60/sex/dose, it is not surprising that the experiment failed to find a significant increase in the incidence of tumors.[5]

Thus, by requiring (1) that harm be demonstrated rather than the absence of harm, and (2) statistical significance while not explicitly controlling statistical power, EPA introduces a bias in favor of registration that goes beyond the statutory standard, and is thus anti-precautionary.

Conclusion

In addition to the complexities associated with establishing the "safety" or allowable hazards, given numerous gaps in information related to multiple exposures, mixtures, synergistic effects, pre-existing disease conditions, and individual vulnerabilities and genetic makeup, the scientific method behind policy implementation needs constant oversight and critiquing. It is not as simple as telling a regulatory agency to protect the health of the public, workers, and the environment based on risk assessment calculations that are subject to manipulation and false assumptions. The examination of statistical issues creates yet another urgent reason to embrace a national policy of precaution and prevention when it comes to the introduction of toxic chemicals, especially those being found to be unnecessary to achieving goals related to productivity, profitability, and quality of life.

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Endnotes

1. Wingspread statement. http://www.sehn.org/precaution.html.
2. The embedding of the precautionary approach in OFPA is evidence that the NOP justification for recent changes in the sunset procedures –that the standard for removing a material should be the same for adding it—is contrary to the spirit of OFPA.
3. FIFRA, Section 3(c)(5) APPROVAL OF REGISTRATION.—The Administrator shall register a pesticide if the Administrator determines that, when considered with any restrictions imposed under subsection (d)—
   (A) its composition is such as to warrant the proposed claims for it;
   (B) its labeling and other material required to be submitted comply with the requirements of this Act;
   (C) it will perform its intended function without unreasonable adverse effects on the environment; and
   (D) when used in accordance with widespread and commonly recognized practice it will not generally cause unreasonable adverse effects on the environment.
4. FIFRA Section 2(bb).
5. EPA, 1987. Data Evaluation Report of mouse oncogenicity study on atrazine, MRID #404313-02. Study sponsored by Ciba-Geigy Corp and performed at the Ciba-Geiby testing facility in Summit, NJ.