ECRONICON OPEN ACCESS

EC PHARMACOLOGY AND TOXICOLOGY
Perspective

On Reviewing Animal Toxicity Studies Submitted in Support of Pesticide Registrations: A Proposal for a More Efficient System that Produces a Better Product for Third Parties

John D Doherty*

PhD, Independent Toxicologist, Oakton, Virginia, USA

***Corresponding Author:** John D Doherty, PhD, Independent Toxicologist, Oakton, Virginia, USA.
E-mail ID: lakinplace@gmail.com.

Received: June 03, 2026; **Published:** June 18, 2026

Abstract

In order to register pesticides their safety to humans must be supported by a battery of animal toxicity studies. As submitted, the study reports can contain the biases of the study authors and sponsors. Thus, they are critically reviewed by toxicologists within governmental regulatory agencies. Often the reviews by one country's regulatory agency are used by third parties. Within the United States, the review of these toxicology studies is the responsibility of the Environmental Protection Agency (EPA) Office of Pesticide Programs (OPP). The procedure that OPP currently uses consists of preparing Data Evaluation Records (DERs) that have multi levels of reviewers. The DER formats for each study type are firmly set so that nearly all of their content has to be transcribed from the study report into the DER. In preparing the DER, the reviewers make their own tables for responses to treatment and in doing so they can be biased in selecting data based on their interpretations. This means that third parties see a secondhand account of the study containing the biases of the reviewers. In order to address this problem, it is proposed that standardized formats for each study type be designed by the regulatory agencies that will contain the critical study information so that it does not have to be transcribed. The reviewers will complete a table of concurrence/nonconcurrence for all of the critical aspects of each study type. They would make data tables only when they do not concur with the study report. The resulting review product will allow third parties to see the interpretation of the study as determined by the study authors as well as by the reviewers and can determine the significance of biases.

Keywords: *Animal Toxicity; Pesticide; Environmental Protection Agency (EPA); Office of Pesticide Programs (OPP); Data Evaluation Records (DERs)*

Introduction

In order to register a pesticide, a series of guideline animal toxicity studies are required by regulatory agencies. In the United States, the reviews of these studies are the responsibility of the Office of Pesticide Programs (OPP), within the Environmental Protection Agency (EPA). Currently, the review primarily consists of transcribing the study report into Data Evaluation Records (DERs) that become the official EPA documentation of its review [1] to ensure compliance with scientific guidelines for quality assurance (QA) and Good Laboratory Practices (GLP). The DER system was established in response to concerns for data fabrication and interpretation bias that occurred in the 1950s to 1970s. Since that time, there have been advances in GLP, QA guidelines, as well as standards for ethical treatment of animals, reporting and record retention. The DER products are used both internally and can also be used by third parties, including other countries and international regulatory advisories.

Problems with the DER system

Basically, because of advances in GLP, QA and standards for reporting the DER system is outdated. There is a rigid DER format for each study type and the reviewers can fill in the blanks. This process is wasteful, because information that cannot be changed is transcribed into the DER. Transcribing the study does not ensure that anything was checked against the supporting records. The Federal Insecticide, Fungicide Rodenticide ACT (FIFRA) [2] stipulates that the burden of proof for the safety of a pesticide is on the registrant. Therefore, the registrant should submit a document that does not need to be transcribed at government (taxpayer) expense. Also, important is that the DER product, although it may have primary and secondary reviewers, it may or may not always be an accurate transcription and may contain the reviewers' biases. Thus, the DER system produces a second-hand account of the study.

Currently, most submitted guideline studies already identify the obvious responses to treatment. If the reviewers determine there is a response to treatment not already identified by the study authors, they need to spend quality time making the case that the response is meaningful to the toxicity profile of the chemical. The time the reviewers spend trying to produce an accurate transcription is not quality time and would be better spent reviewing the supporting study methods and data. The quality of the review depends upon the expertise of the individual reviewers understanding of the chemical's nature and their ability to identify study deficiencies and meaningful subtle responses to treatment. Not in transcribing.

Proposal for a more efficient system

The OPP in conjunction with other agencies responsible for regulation of pesticides and possibly other types of chemicals should design formats that include the critical information for each study type. These formats, together with the complete study report, including all supporting methods and materials and tabulated data for all endpoints would be submitted.

The regulatory agencies would still have the option to require additional supporting data and conduct onsite auditing. Upon receipt of the completed submission, the reviewers would verify the accuracy of the completed formats against the supporting data and would complete a table of concurrence/non-concurrence.

Table of concurrence/nonconcurrence

This three-column table would be initially completed by the study submitter and be included in the submission and finalized by the Agency reviewers. The first column would be for naming the parameter, the second for the study authors input and for the third column for the reviewers' comments. The table would consist of rows for each of the many critical aspects depending on the study type. Some selected examples include that for all study types there would be rows for identity and purity of the test substance, description of the test animal, methods and materials, number of dose levels and animals per dose, body weight, food consumption and general comments on animal conditions including behavior observations. Rows for the NOAEL (no observable adverse effect level) and LOAEL (lowest observable adverse effect level) with statement on effects at the LOAEL and another row for effects at higher doses. For sub-chronic, chronic and carcinogenicity studies there would be separate rows for hematology, blood chemistry, necropsy and histopathology including preneoplastic and where appliable neoplastic responses and a row for a statement on if the study demonstrates carcinogenicity. For a developmental (or teratology) study there would be rows for maternal toxicity, fetal responses including body weight, skeletal and soft tissue parameters. For a neurotoxicity study, there would be separate rows for each type of neurotoxicity assessment made. The actual design of these tables including the specific rows would eventually be determined by the committees of study type experts. The study authors would include their conclusion for each row. The reviewers would enter "Concur", if they agreed with the study authors' entries. If the reviewers do not concur, they would state the basis for their differences and append a table or figure as needed that justifies their decision. This table of concurrence/nonconcurrence provides assurance that the reviewers reviewed the supporting data and are taking responsibility for the study's quality, the identification of deficiencies and responses to treatment.

Executive summary and study classification

In addition to completion of the table of concurrence/non-concurrence, the reviewers would complete an Executive Summary, together with their identification of the NOAEL/LOAEL and effects at the LOAEL, as well as significant effects at higher doses. A statement on the study classification and identification of study deficiencies would also be included.

Benefits of the proposal

A main benefit of the proposal is that the reviewers' time is moved from transcribing to having more quality time to identify deficiencies, as well as make a meaningful case for any subtle responses to treatment. The time spent trying to accurately transcribe what cannot be changed is not quality review time.

An equally important benefit is that the purpose of preparing reviews is for third parties. Third parties include internal agency peer review groups, as well as state, other countries and international regulatory agencies. With the DER system, third parties see a transcription of the study report that may or may not be accurate and may contain the reviewers' biases. With the proposed system, third parties see the report prepared by the study authors and reviewers' commentary, which may identify study deficiencies and subtle responses to treatment allowing third party comparisons.

The proposed system is a system of challenges

1. It challenges the study authors/registrants to provide a study without significant study deficiencies and identifies all responses to treatment.
2. It challenges reviewers to identify study deficiencies and subtle treatment responses not already identified in the study report.
3. It challenges third parties to interpret the differences between the study authors and reviewers and identify additional study deficiencies and assess the significance of the responses to treatment.

Conclusion

The reviewers will have more quality time to review the study. The review product will be more useful to third parties, because they can see the study as interpreted by both the study authors and reviewers and form their own interpretation. Although this system is devised for pesticide studies, it can be adapted for other types of chemicals.

Bibliography

1. These records, including over 4500 recently released documents covering toxicology, chemistry, and environmental fate are publicly available in Chem View.
2. FIFRA: United States Code of Federal Regulations 40 CFR Part 158. Data Requirements for Pesticides.

Volume 14 Issue 6 June 2026