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Nelson B. Kverno

*U.S. Bureau of Sport Fisheries and Wildlife, Denver, Colorado*

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## STANDARDIZATION OF PROCEDURES FOR DEVELOPING VERTEBRATE CONTROL AGENTS

NELSON B. KVERNO, Coordinator - Denver/AID Programs, United States Bureau of Sport Fisheries and Wildlife, Denver, Colorado

ABSTRACT: In research to develop methods for controlling damage by vertebrates, chemical evaluation procedures vary with every investigator, so that data cannot be meaningfully compared. Toxicology is one common area where standardization is both applicable and desirable. It is recommended that standard guidelines be developed through an international body recognized by the members of the discipline.

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### INTRODUCTION

In research to develop methods for controlling damage by vertebrates, chemical evaluation procedures seem to vary with every investigator. Frequently, the procedures employed by an individual or a research team are arbitrarily altered with each study. The results of such studies may satisfy the specific objectives, but the data have limited use when considered as a contribution to the general information pool. To achieve the maximum return from these data, testing procedures must be standardized.

Toxicology is one area of study common to all control methods investigators, and the area where standardization is the most appropriate and applicable. With standardization, data from many sources can be assembled with some assurance of comparability, thus easing the task of registration and facilitating the extension of a chemical's usefulness. At the Denver Wildlife Research Center, we have recognized the advantages of standardization and are in the process of establishing guidelines for developing bird and mammal control chemicals. To detail these methods would burden the reader and exceed the page limitations set by the editorial committee, so I will present only a summary of the testing procedures we use for developing acute lethal agents for mammals. In reviewing these procedures, please understand that our interest at this stage is not clinical but is oriented toward the solution of problems for a variety of pest situations under field conditions.

### EVALUATION PROCEDURES

#### LD50 Determination

The LD50 is perhaps the most useful information concerning the acute toxicity of a compound, but there are numerous ways of determining an LD50 and each procedure can produce significantly different results. It is, therefore, imperative that the test conditions be clearly defined to reduce variables and ensure a greater degree of reproducibility. Our test standards describe in detail: (1) selection of animals, based on condition, history, size, and sex; (2) fasting procedures; (3) carrier and volume permitted based on animal weights; (4) dosage progression; and (5) observation period.

LD50 figures are used as indicators and are important in understanding the properties of a compound. When working with wild animals, however, it is generally both impractical and unnecessary to get precise figures with close confidence limits. This would require large numbers of animals, but more important, the populations are often too heterogeneous to make the figures meaningful beyond that portion of the population sampled. Therefore, we have adopted the LD50 method described by Thompson (1947) and Thompson and Weil (1952). Using this procedure, we can determine an LD50 with as few as eight animals and establish confidence limits at the 95 percent level.

#### Acceptance Test

Differences in the order of toxicity make direct comparison of the acceptance of compounds difficult without at first establishing a common denominator. We have done this by adjusting the concentration of each compound on a selected bait carrier so that, for the mean animal size of any species, there is the equivalent of one LD50 on 1/10 of the daily amount of carrier usually consumed by one animal. The bait, carrier is determined, and then standardized for each species. Feeding tests are conducted to determine daily consumption. Each test animal is offered an amount equal to 10 LD50's, and acceptance is expressed in number of LD50's consumed in the first 24 hours (Kverno and Hood, 1965). Effect, or percent mortality, is also of primary importance in the evaluation.

Results of a single acceptance test have little value, but after a series of compounds have been evaluated, comparisons can be made between compounds or between species. These data should provide leads as to the general effectiveness of a compound or the most promising compounds for a given species.

#### Concentration Effect

The next step in the development of a mammalian lethal agent is to determine the most effective concentration for the target species. This is accomplished by evaluating a series of baits, with the only variable being the concentration of the chemical. Assuming that selection of the compound was based on good acceptance resulting in high mortality, there should be several concentrations where 100 percent mortality is achieved. A decision can then be made, depending upon the pest situation, to use the concentration where maximum consumption occurred, or the minimum concentration required to produce high mortality.

#### Secondary Hazard

The extent of secondary hazard will, of course, depend largely upon intended use. Nevertheless, some knowledge of whether a compound is secondarily toxic is needed before field evaluation. In our initial tests, white rats are used as the primary and secondary animal. The primary animals are administered, by gavage, an amount of chemical equal to 10 LD50's. After death the head, skin, tail, and feet are removed and the remaining portion is ground and fed back at a ratio of one primary rat to one secondary rat (each secondary animal receives the equivalent of 10 LD50's).

#### Initial Field Trial

The information gained from the preceding bioassays is generally adequate to determine the feasibility of an initial field trial from the standpoint of effectiveness. However, before field testing some knowledge is also required on: (1) dermal toxicity, (2) phytotoxicity, (3) stability of the formulation, and (4) pharmacological action. A dialogue is maintained with the chemical supplier throughout the testing program, and often much of this information is provided by them. Here again, guidelines are desirable to eliminate some of the variables in these tests.

#### DISCUSSION

It is not our intent to imply that these tests are the ultimate. They merely represent one way of evaluating lethal agents for field use. Perhaps what is more important is that they offer a set of procedures that can be improved and expanded and, hopefully, eventually developed into a set of internationally accepted procedures. Developing such standards is of particular importance now, when there is considerable interest throughout the world in establishing new control methods research programs.

I realize that there is an inherent reluctance on the part of free-thinking scientific investigators to promote "standardization" because it connotes a restriction of individual freedom. However, the term also implies organization and maturity. Vertebrate damage control has, in my opinion, reached maturity, and it is time we established our identity as an organized scientific discipline. The development of guidelines for the evaluation of chemicals will not alone satisfy this need, but this step can act as a catalyst for further uniting us.

Standard guidelines can only be developed through an international body that is recognized by the majority of the members within the discipline. Later this month a meeting is scheduled to discuss ways of coordinating international vertebrate damage control programs. There will be representatives from several countries as well as international organizations. At this meeting an effort will be made to create the necessary forum to undertake this task.

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