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TESTING AND REGISTRATION OF NEW CONTROL MATERIALS

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The Federal Insecticide, Fungicide, and Rodenticide Act broadly encompasses, " ... any substance or mixture of substances intended for pre venting, destroying, repelling, or mitigating...." a pest.

The act includes devices as well as chemicals used in the control of pests.

It is the responsibility of the manufacturer to provide authoritative evidence of the efficacy and safety of his pesticide product.

Within the scope of these four brief excerpts from the act there is much about which personnel engaged in research and development of vertebrate pest control products should be informed. As stated, the coverage of the act is very complete, omitting no form of mammal, bird, amphibian, reptile, or fish whether they be wild or domestic. The chemical or device used need not be lethal or injurious to the target species and thus includes toxic agents, irritants, repellents based on odor or taste, repellents based on mechanical action such as tacky or resistant films, anesthetizing chemicals, chemosteri-lants, fumigants, and energy wave lengths including sound, light, and super-sonic.

COVER EACH MAJOR SPECIES INVOLVED:

To begin with, the label submitted for registration must precisely iden-tify the species against which the product is directed. Broad terms such as "rodents," "nuisance birds," or "trash fish" will not be acceptable unless the supporting research data actually includes representatives from all the principal groups. Even such terms as "house rats and mice" will not be acceptable unless all three species, the brown rat (Rattus norvegicus), the roof rat (Rattus rattus), and the house mouse (Mus musculus) have been included in carefully controlled experimental studies. The Department recognizes that the albino laboratory rat and mouse are invaluable in the screening and study of new rodenticides, nevertheless acceptable evidence of efficacy must, in the final stages of the study, include the exact animal form against which the product is to be marketed.

There are several examples where members of closely related groups exhibit markedly different susceptibility to the same toxic agent. ANTU (alpha napthyl thiourea), for example, has an LD_{50} of 8 mg/kg for the brown rat and an LD_{50} of 220 mg/kg for the roof rat. Perhaps the most unusual example is found in the case of a new experimental chemical which has an LD_{99} of 5-15 mg/kg for the brown rat and an LD_{99} of approximately 2500 mg/kg for the house mouse. The difference in susceptibility need not be of this magnitude, however, to result in changed wording and modified claims in the remainder of the label. The well-known anticoagulants, for example, require some seven days feeding to bring a brown rat population under control, but the same formulated bait requires 21 days or better to achieve comparable results with house mice.

While figures on lethal dosage are very important, behaviorism may play an even more important role in species differences, - food preferences and feeding habits, for example. Many rodenticide products are sold as ready-prepared baits. If statements are to be made regarding the acceptance and palatability of this bait, then data from laboratory albino animals alone are not acceptable. Please recall that in any control method relying on voluntary feeding, the bait must compete favorably with alternate food sources - regardless of the poison used. It hardly seems necessary to point out the importance of species behaviorism when it comes to bird toxicants. Feeding is largely governed by sight in birds and very little change from customary size, shape, or color of food is enough to cause aversion. Foods that are effective baits for bird control may have to be limited (by label statement) to use in a particular season due to markedly changing food habits.

In some instances, plants and seeds are involved as carriers of the pesticide and claims of "non-phytoxic", or "no loss in seed viability", are made. Here again, generalizations based on one or two species are not acceptable. For example, an application for registration of a seed treatment with 10-20 per cent thiram by weight of the seed for bird repellency is not acceptable unless it is limited to certain southern pine species whose tolerance has been adequately established. The same would apply to a dog repellent spray on shrubs and foundation plantings about a home; to rabbit and deer repellent sprays on orchard, forest, and nursery stock; to plant-systemic chemicals, etc.

In most cases, acceptable data on the species level will not be complete unless both sexes have been covered in the test program. Since natural populations consist of both young and old animals, the influence of age on toxic susceptibility should be determined.

THE TEST DESIGN:

There should be personnel associated with the study that are thoroughly familiar with the life habits and behaviorism of the test species. This is particularly important when the goal is a repellent and the criterion for evaluation is a change in some established habit. For example, if reports are submitted on an attempt to rid an airport of gulls with a chemical repellent just prior to the time they would habitually leave for northern nesting grounds, the results are understandably open to question.

The anticipated method of field application should always be kept in mind when designing tests under cage or captive status conditions. For example, if the label states that spraying a perimeter belt about a lawn or garden will prevent dogs from entering the area, then the mere demonstration that the product is obnoxious to a dog when it is applied to a familiar object is not applicable proof of area repellence by perimeter treatment. Similarly, a product that appears to have value in stopping dogs from using scent posts because the applied over-riding odor interferes with urine odors that stimulate repeated acts, may have little value in stopping a habit not oriented by a sense of smell, like crossing a yard, resting on a favored rug, or any sight stimulus.

If a claim is made for a period of effectiveness, then the test design must reflect studies covering such a period of time. For example, several bird repellents that rely on continued tackiness and string of the bead of gel applied to a roost make the claim that it is "effective for one year". The Department is holding them responsible for tests that show that the gel does not scum or crust-over under different conditions of weathering and deposition of dust for a full year, or lacking such proof, the registrant has the privilege of removing the claim from the label. Quite similar claims that an indoor pet repellent does not stain upholstery, that a fish toxicant formulation will not cause off-taste or odor in water used subsequently for domestic purposes, that a rodent population can be satisfactorily controlled in seven days, etc., all need documented experimental evidence.

Tests in which the chemical is administered forcibly as by intubation or ad libitum feeding, where no alternative untreated foods *are* available, are informative for pharmacological data and as guides in formulation of finished baits and sprays. But since vertebrate populations "in the wild" nearly always have a free choice, the above tests should be supplemented by free choice experiments using treated and untreated portions of the same base food.

Research and development of vertebrate pesticides should always include tests conducted under actual field conditions. The factors of inter and intra species behaviorism, and the impact of environmental factors is so complex that cage tests simply cannot suffice.

FORM OF REPORTS:

In the field of vertebrate pesticides, the Department prefers to review "raw data", although there is no objection to its being accompanied by interpretations in the form of graphs and charts. In other words, the members of our staff, and experts from interested government agencies that are asked to review the data and comment thereon, should have available details of the test methods and copies of the actual work sheets. Personnel engaged in the study should be identified, and in the case where specific phases of a problem are awarded to a private contractor, then a full copy (or photostat) of his certified report should be submitted.

ENVIRONMENTAL HAZARDS:

Up to this point we have discussed only the supporting evidence that the product is effective as claimed against named vertebrates. It is with some dismay that applicants for registration under the Federal Insecticide, Fungicide, and Rodenticide Act learn that there are yet several major hurdles to be negotiated. Of importance is the question, "What are the effects on the associated beneficial plant and animal life, and on the environment?" How extensive this data must be depends upon the toxicity of the compound or the harmful nature of the device; whether the product tends to be stable or transitory on exposure, whether applications *are* made to plants or soils that will result in residues in food crops, whether the methods of application sharply focus the effect of the pesticide on the target species or blankets an environment, and what *are* the secondary and residual hazards. These questions can be more difficult to answer than all of those on efficacy.

A few examples of some of the problems in this category may be helpful. If a pesticide chemical has been found useful on Long Island Sound in the protection of oyster beds from the oyster drill, and shown to be non-toxic to fish and to cause no residue at harvest in the oyster, data will yet be required on the hazard to lobster, shrimp, and crabs if the pesticide is marketed in other coastal waters where the latter forms may also be present.

!f a toxic or repellent chemical is developed for systemic pick-up by seedling trees and found effective in preventing damage by browsing of rabbits, mice, and deer without mortality occuring in the latter species, it will still be necessary to petition for a tolerance from the Food and Drug Administration should the pesticide to be used in areas open to livestock grazing (as in the National Forests), which show any residue even in trace amounts in domestic livestock.

If a toxic agent is incorporated in a gel which is exposed as a bead on ledges, cornices, and roof ridges of buildings to control nuisance birds using these sites as a roost, it will be necessary to provide data not only on the effectiveness against each named species of bird, but to show 1) The amounts of poison that are transferred on the feet of birds to other sites, such as stored food materials; 2) The distribution pattern of dead birds and the secondary poisoning hazard they pose if consumed by domestic hogs, dogs, and cats; and 3) That residue on the building, itself, will not pose a continuing hazard to maintenance personnel.

HUMAN SAFETY:

Not the least troublesome is gathering the pharmacological data necessary to provide the Department an adequate basis for judging the adequacy of caution statements on the label, ..."necessary for the protection of the public." In the field of vertebrate pesticides, lethal dosage studies on mammals are commonly available, especially on the active ingredient. Unfortunately, the hazard to the public from the marketed product is often significantly changed by the solvents, wetting and dispersing agents, and other so-called inert components. Therefore, oral, skin absorption, and inhalation toxicity data for both the active ingredient and for the marketed formulation may be required. There is no inflexible requirement for long-term chronic toxicity studies (as in the case in human medicine), but depending on the nature of the chemical and its proposed use (or like a device producing super-sonic sound in human work areas), chronic toxicity and several generation reproductive studies may be required. In some cases human tissue tests may be requested when a high degree of species-specificity precludes any rationalization of human hazard.

THE INGREDIENT STATEMENT:

At this point it would be appropriate to consider the ingredient statement. On the application for registration the full formulation must be listed, giving each component therein by per cent. In the declaration of a pesticide chemical in the ingredient statement, proprietary names are not acceptable. If the chemical in question has a well-known common name, then this alone may be used.

An over-simplified rule is: Is it listed in Webster's dictionary? Coined common names may have been established for more recent pesticide chemicals, in which case the coined name should be explained by the exact chemical name following in parentheses or in a footnote. Lacking a common name of either type, the most accurate chemical name should be used. One authority for acceptable nomenclature is Chemical Abstracts. If the chemical has not been indexed in Chemical Abstracts, the matter should be referred to Dr. Leonard T. Capell, Nomenclature Director and Executive Consultant, Chemical Abstracts Service, Ohio State University.

Occasionally the common name of a compound is too indefinite for purposes of pesticide registration. Oil of mustard, for example, must be declared either as the synthetic, allyl-isothiocyanate, or, the natural expressed oil of mustard. If the active ingredient is a complex mixture from an organic source, such as hardwood oil or coal tars, then these should be accompanied by a specification sheet from the basic manufacturer in which identifying physical properties *are* listed.

EXCEPTIONS TO REGISTERED-USE PATTERN:

It is the custom that once an active ingredient has been accepted for registration on the basis of authoritative evidence in files of the Department, other applicants using precisely the same chemical will be held responsible only for any changes made in formulations and claims. This is not true, however, of a number of common products which are variable complex mixtures. Hardwood oil and bone oil are good examples of this in the vertebrate pesticide field. The infra-red and gas chromatograph studies of hardwood oil leave no doubt but that they differ significantly from manufacturing source to manufacturing source. Therefore, each applicant for registration of hardwood oil as a seed protectant to repel birds will have to conduct independent studies on the efficacy of his particular product.

USEFUL PRECAUTIONS:

In applying for registration of a pesticide in the vertebrate control field, the initial marketing claims should be limited to those that can be readily supported. Avoid comparisons with other products, and the use of the terms, "better" and "best", as data from comparative tests must then be required before registration will be granted. If, subsequently, information permitting new claims is acquired, the registration may easily be amended through the submission of additional authoritative data.

Try to anticipate questions that will arise from national marketing. If there are local or state laws that will affect the use of the product, then refer this to the customer's attention on the label. For example, most states have laws concerning the addition of any chemical to public waters. Thus the label in the case of a fish toxicant should state, "Consult State Fish and Game Authorities for permit to use this product in control of trash fish". Similarly, in the case of a bird control chemical, the label should carry the warning to check local laws governing the use of chemicals in bird control.

WHO MUST REGISTER:

Federal and State authorities are exempted from the penalties of the Federal Insecticide, Fungicide, and Rodenticide Act when engaged in their official duties. Interpretation No. I, exempts the professional Pest Control operator who deals in a service rather than the sale of a pesticide product from the need for registering the pesticide he transports across State lines for his own use. If, on the other hand, the pesticide is shipped by common carrier and thus leaves the direct control of the above mentioned organizations, then the product must carry labels in full compliance with the act. All other manufacturers, formulators, or distributors of pesticide products must register products entered in interstate commerce.

EXPERIMENTAL PERMITS:

Occasionally, the research data on efficacy (not safety) needs information that only controlled field tests in different ecological situations around the country can provide. As long as this can be accomplished under the direct supervision of a governmental agency authorized by law to conduct research, no permit to cover interstate shipment is necessary. On the other hand, if the experimental product is to be supplied to independent private agencies and individuals, then a permit for shipment for experimental purposes should be sought. A permit will not be issued for the purpose of a test market. The exact amount and the form of the pesticide to be supplied must be stated. The responsible investigators must be identified. If the permit is granted, it is effective for one year. At the end of this period the applicant is responsible for a documented report on the year's findings.

The Department has published in the Federal Register, January 16, 1964, a proposed revision of the Regulations for the enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act. When these new rules are formalized they will affect details in registration action, but principally apply to the format of the label and the permissible claims - not to basic testing.