obtained from industry and my own gleaning of the literature. The latter is of necessity limited so that in the future it is hoped industry will forward more material and thus assist in making the revision more complete.

The data for the new materials was largely supplied, or at least abstracted, from information received in answer to a request from industry. Some came *via* the Pesticide Technical Information Office of our department in Ottawa, having originally been obtained from industry. The format and details varied greatly. Some was of the type aimed at the agricultural extension specialist. This therefore required a great deal of concentration and necessitated either looking elsewhere for the remainder of the pertinent material for the Guide format or, if not available, unfortunately resulted in incomplete outlines. Since industry has most of the pertinent material or references for its own compounds, the preparation of a special outline of its new products under the headings of the Guide format, with appropriate literature references and summaries of analytical methods, would greatly facilitate the speed of material required in this sort of publication.

Compounds are listed alphabetically according to their common names. Where none is yet available, the chemical name is listed. A cross-reference index including trade, common, and chemical names assists in locating the listings. It is unfortunate that even chemical nomenclature is not always consistent. However, the greatest confusion is over the adoption of common names and the multitude of common names for formulations. It is to be hoped that the time interval for a selection of a common name will be greatly reduced and that it will truly be a common name for both sides of the Atlantic.

Complications occasionally arose when, for example, the Canadian branch of an American company was licensed to handle a European product, while another American company handled it in the United States. Somewhat similar confusion also arose when the same chemical was produced by more than one company under different trade names. Then there were instances when the data sheets from the parent company and the subsidiary in another country differed slightly in some details. Which should one choose without offending the other?

Bis-(methyl-Hg)-sulfate

$(CH_3Hg_O)_2SO_2$

$C_2H_6O_4HgS$

mol wt 326.6

Other names:	Cerewet, Aretan-nieuw (Farbenfabriken Bayer AG) Ceresan Universal-Feuchtbeize (1.2%).
History:	Introduced as experimental fungicide against seed-borne diseases in 1958 by Farbenfabriken Bayer AG. Protected by W. German Pat. 1,003,733, U.S. Pat. 2,917,526.
Manufacture:	Reaction of Grignard compounds or metal organic compounds with mercuric salts.
Physical properties:	White crystalline powder; soluble in water; insoluble in organic solvents; recrystalline from methanol; v.p. $< 10^{-5}$ Torr; mp 260°C; when heating slowly decomposition starts earlier.
Biological properties:	Effective against seed-borne diseases of cereals, beets, potatoes and flower bulbs. Acute toxicity to rats: oral LD_{50} 50 mg/kg; i.p. LD_{50} 13.75 mg/kg.
Formulations:	0.8 and 1.2% Hg as Bis-(methyl-Hg)-sulfate.
Analysis:	The substance is digested by wet combusion with sulfuric and nitric acid. When completely digested, the solution is diluted with water, mixed with urea to decompose the nitrous acid and precipitated with hydrogen sulfide for the gravimetrical determination of mercury, or potentiometrically titrated with potassium iodide solution for the volumetrical determination of mercury. (Leverkusen method).

Fig. 1.—Sample page of Guide.

Toxicity reporting tends to vary somewhat, *i.e.*, between animal species and mode of dosage. In order to reduce errors of comparison, the species and mode were always included when available. It is remarkable how the values can vary depending on these two factors.

The manner of collecting the pertinent data on revisions and new compounds needs streamlining to assist in keeping information more up-to-date and more complete. Some suggestions have been made which largely involve industry. Any additional ways of improving the preparation and usefulness of the Guide will be welcomed.

Some Pesticide Information Problems in the Pesticides Regulation Division and Their Possible Solution*

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Received May 19, 1964

The Pesticides Regulation Division is responsible for the enforcement of the Federal Insecticide, Fungicide, and Rodenticide Act which among other things requires that all economic poisons (pesticides) be registered with the U. S. Department of Agriculture prior to shipment in interstate commerce. Exports and imports of pesticides are also subject to certain requirements of the Act. Copies of the regulations for the enforcement of the Act and published interpretations of these regulations are available upon request. Pesticides (defined in the Act itself as economic poisons) include insecticides, fungicides, herbi-

* Presented before the Divisons of Chemical Literature and Agricultural and Food Chemistry, Pesticides Subdivision, Joint Symposium on "Problems of the Pesticide Literature and Some Solutions," 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 9, 1964.

cides, nematocides, germicides, rodenticides, plant growth regulators, algaecides, desiccants, defoliants and animal repellants, and animal poisons.

The Division also has certain assigned responsibilities under Public Law 518, 83rd Congress (Pesticides Chemical Amendment of the Federal Food, Drug and Cosmetic Act).

Any application for registration of a pesticide must be accompanied by a proposed label bearing information specified in the Act and supporting information to show that the product will be effective, can be used safely, and when applied as directed will not result in food or feeds deemed to be illegal under the Federal Food, Drug and Cosmetic Act. The information submitted by the registrant must be adequate to provide the Division with a basis for a favorable decision, and this information must then be stored in a retrievable manner. While most prospective registrants or applicants are reasonably familiar with the information which is required to appear on the labels for products, they do not fully appreciate the information problems associated with showing that pesticides can be used safely and effectively, and will not result in illegal food or feed residues.

The difficult information problems are for the most part associated with new chemicals although new information on old established pesticide chemicals occasionally provide unusually complex operational problems. The accumulation of sufficient information to support registration of a pesticide is a costly undertaking, particularly so if the pesticide is intended for use on growing crops or livestock. The Division encourages the prospective registrant to discuss with the scientific staff the proposed use and the specific information requirements prior to undertaking an experimental program. A hypothetical example will illustrate how an experimental study can be initiated so that all the information needed can be developed and issuance of the registration expedited. The Head of the Agricultural and Industrial Chemical Division of a company telephones the Pesticides Regulation Division Director and makes an appointment to discuss registration information requirements for a new herbicide for use on alfalfa.

A conference in the Director's office is arranged and attended by representatives from the chemistry, pharmacology, and agronomy staffs of the Division, and technical representatives from the company. The company representatives describe the pesticide chemical, the formulations, the proposed use, and the toxicity information. The Division chemist, after study of the molecular structure of the chemical, will raise questions concerning the assay and residue methodology and explain the method requirements for demonstrating whether or not a residue is likely to result in the harvested alfalfa. He will present the company representative with a "Guide" for evaluating "No-Residue" uses. The Guide was originally intended for the Division's use in reviewing applications for registration on a "No-Residue" basis, although it has proven very helpful to registrants in planning and carrying out residue studies. The company representative will be informed that if the proposed use results in a detectable residue in the harvested alfalfa, it will be necessary for him to petition the Food and Drug Administration for a tolerance or an exemption from the requirements of a tolerance. Information is available from the Food and Drug Administration on the submission of petitions.

The Division pharmacologist will then explain the type and quantity of toxicological information which must be provided to determine the caution or warning statement that will be required on the label. The Division agronomist will outline the type of performance or efficacy data that will be needed to support registration of the product and provide the visitor with detailed information on such matters as the preferred type of data, phytotoxicity, geographical areas within the United States most desirable for field studies, and procedures for the evaluation of various soil types on performance. A lengthy discussion will usually ensue on methods of application, dosage, timing of applications, and the type of weeds that are to be controlled.

At the conclusion of the conference, the company representative will have a detailed understanding of the requirements of the Act as they may affect his product and the type and quantity of information needed for registration. The Division becomes involved in many conferences of this type, and, with the basic information furnished by company representatives, it is usually possible to develop most effective and economical research programs for the companies which do provide data with the degree of reliability needed by the Division.

Specific information problems arise in connection with the registration of each type of pesticide. The large number of germicidal chemicals employed in formulas sold to sterilize, disinfect, sanitize, or provide practical antimicrobial benefits in environmental sanitation programs, and the great variety of situations in which such chemicals are employed, provide some very complex information problems insofar as the Department's registration and enforcement programs with these materials are concerned. In general, environmental sanitation programs are controlled by local public health, medical, and veterinary officials. There are great variations in local ordinances and recommendations by medical officials with respect to the use of chemicals within the different application areas. Acceptances and requirements under local ordinances and codes are considered as background information to both efficacy and safety. There are many areas where no ordinances and codes have been developed, and in these situations the Division must depend entirely on information furnished by the applicant and such evidence as may be available in the technical literature. There are some 2500 local milk ordinances and sanitary codes, approximately 3500 local restaurant and tavern codes, and over 2000 barber and beauty parlor ordinances and codes that must be considered. This illustrates the complexity of the problem of reviewing chemicals in this particular category for acceptability in each of these particular areas.

In the case of chemicals sold for the treating of drinking water and swimming pool water, the problem of obtaining adequate information on efficacy and safety is possibly more critical than in any other area since more people may be affected by a single application than in any other area.

Products sold for use in sterilizing surgical instruments, disinfecting in hospitals, and sanitizing laundry, and to provide similar benefits in the home, on the farm, and in institutions, all require some peculiar type of consideration.

The Division within this area employs standard labora-

tory bioassay methods which have been shown to provide accurate indexes to efficacy in various types of application as working guides. Information developed through *in situ* evaluations are seldom extensive enough to provide an accurate index to efficacy in any given application. Sampling errors and lack of adequate control in such procedures usually result in the accumulation of great volumes of misinformation contributing to the general confusion. It is preferable, therefore, to develop laboratory or bench tests which can be precisely controlled and accurately interpreted in terms of practical application benefits for use in the registration of these materials. These methods are also most useful in developing reliable information to support registration actions.

Rodenticides have always been subject to the provisions of the Act, but in 1962,[2] a regulation was published declaring additional forms of plant and animal life and viruses to be pests under certain conditions, and thus the coverage of the law was broadened to include other animal poisons.

The labels for such products submitted for registration must precisely identify the species against which the product is directed. Broad terms such as "rodents," "nuisance birds," or "trash fish" will not be acceptable unless the support-research data actually include 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 norvegious*), the roof rat (*Rattus rattus*), and the house mouse (*Mus musculus*) have been included in carefully controlled experimental studies. While the Division recognizes that the albino laboratory rat and mouse are invaluable in the screening and study of new rodenticides, acceptable evidence of efficacy must, in the final stages of the study, include data on 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 (α-napthylthiourea), 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_{50} of 5–15 mg./kg. for the brown rat and an LD_{50} of approximately 2500 mg./kg. for the house mouse.

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 also be determined.

In providing information supporting the efficacy and safety of a given product of this type, the Division prefers to review "raw data," although there is no objection to its being accompanied by interpretations in the form of graphs and charts. The tests that constitute this "information" should closely simulate anticipated customer use. For example, if the label states that spraying the perimeter belt around a lawn or garden successfully keeps dogs from entering the area, then the mere demonstration that the active ingredient is obnoxious to a dog when applied to some familiar object that he has to pick up, is not proof of area repellency. Likewise, if a claim is made for a period of effectiveness, then the test design must reflect studies covering such a period of time.

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

Our concern with pesticide information problems does not end with the registration of a product. The Division has field laboratories that are responsible for the analyses and testing of official samples of pesticides to determine whether or not they comply fully with the requirements of the Act. From time to time it is necessary for us to obtain residue data on samples where the crops have been treated strictly in accordance with directions on the registered labels and arrangements are made with Federal, State, or University scientists to supply us with such samples which are then analyzed in our pesticide residue laboratory at Beltsville, Maryland.

We have also installed an analytical program for the purpose of chemically screening pesticides for accidental adulteration or contamination with other pesticide chemicals. These measures are proving very useful in the solution of specific information problems.

The Information Retrieval System (IR) in the Pesticides Regulation Division.—As data of the type illustrated above are collected on individual chemicals and products, it must be filed in a manner readily available for use in both registration and enforcement programs. Nearly 60,000 pesticides have been registered by the Pesticides Regulation Division. To provide an IR system, an IBM system was installed in which certain registration information is coded on each registration jacket. Spaces are provided in which numbers are placed to designate the names of the active pesticide chemicals, the type of formulation (dust, wettable powder, emulsifiable concentrate, etc.), class of pesticide, accepted use, and the toxicity category of the formulation. A coding clerk transfers this information to a form entitled "Pesticide Chemicals Registered under the FIFRA" and which includes other information, such as the name and address of the manufacturer, registration number, and registration date. This form is then forwarded to the Data Processing Unit of the Agricultural Research Service where the coded information is transferred to an IBM punch card. These cards are then used in response to requests from the Division to assemble available data needed for continuing operations. The most frequent use of this coded pesticide information is in connection with operation of the five-year limitation on registrations in the Act. Every 90 days a survey is made of the products for which the five-year registration period has expired. The registrants of these products are so notified and unless they indicate that they desire that registration be extended for an additional five-year period, the registration is cancelled. If renewal is requested, it may be granted with or without such changes as may appear to be necessary.

When the Food and Drug Administration finds it necessary to reduce or cancel a tolerance for a pesticide chemical, such action will promptly be followed by a reappraisal of the registration status of many products containing this pesticide chemical by the Pesticides Regulation Division. For example, when the tolerance of 0.1 part per million for heptachlor was cancelled and the Food and Drug Administration announced that, henceforth, the tolerance would be zero, it became necessary

for the U. S. Department of Agriculture to publish a notice in the Federal Register of the cancellation of the registration of many products containing heptachlor and to notify all individual registrants involved.

Prior to publishing this notice, the Pesticides Regulation Division requested the Data Processing Division to furnish a listing of heptachlor registrants so that they could be informed of the actions being taken and provided with the necessary instructions to bring their products into full compliance with the Act.

While this IR system has been useful for such purposes mentioned, there are certain limitations and a need for revisions to increase versatility. For example, one number is used to designate all surfactants in pesticide formulations unless the surfactant is considered as an active ingredient. The number assigned to pesticide uses on tobacco is also assigned to "other field crops." Also the inert ingredients in a pesticide formulation are not coded, so under these circumstances it is not possible to determine promptly through this system the extent to which certain inert ingredients occur in the thousands of products that have been registered.

In our pharmacology staff there appears to be a need to set up an independent IR system to handle the increasing quantity of pharmacological, toxicological, and biochemical information that is rapidly accumulating.

There are three distinct areas of information which must be related to each other in review of safety. First, the toxicity evaluations must be recorded in such a manner as to be readily available for frequent review. Secondly, the toxicity must be related to patterns of use. Finally, there is a need for accurate files with regard to necessary precautionary labeling for the chemical to be effective as an IR system. All of these areas of information must be integrated in such a manner as to make it possible for review within this office. It should be rapid and efficient for the handling of several hundred actions a week. In view of the fact that other Federal groups will be assisting us in the review of pesticide products with particular reference to safety, it becomes rather important that all liaison groups use the same IR system. We are still studying available retrieval systems to determine their adaptability to our needs.

SUMMARY

A favorable decision on any application for the registration of a pesticide under the FIFRA cannot be given in the absence of adequate information to show that the pesticide can be used safely and effectively. Major problems in determining what constitutes adequate information exist. Serious problems also exist in informing prospective registrants on the type of data required and finally, the storage and recovery of accumulated information for subsequent use in the registration and enforcement programs is essential to effective operations of the Division.

ACKNOWLEDGMENT

The author is grateful to Dr. L. S. Stuart, Dr. Donald A. Spencer, Dr. Thomas T. McClure, and Mr. John S. Leary for certain information appearing in this paper.

The Patent Literature as an Information Source for Pesticide Chemists*

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Received March 9, 1964

INTRODUCTION

United States Patents issued from January 1, 1950, through December 31, 1963, and which bear on the general subject of pesticides were examined as a source of useful information for the practicing chemist. During the 14-year period, there were issued 128,134 chemical and chemically related patents which have been systematically indexed in the UNITERM INDEX TO U. S. CHEMICAL PATENTS. The data used in this paper were obtained by a computerized search of the INDEX (P. W. Howerton, "Computerized Search of the U. S. Chemical Patent Literature," in "Automation and Scientific Communication," H. P. Luhn, Ed., American Documentation Institute, 1963, p. 255).

To ensure best coverage of all pesticide patents, the following UNITERMS are subsumed under the general term "pesticide":

--Anthelminthic, nematocide	--insecticide
--bactericide	--miticide
--biocide	--phytocide, herbicide
--fungicide	

Because the INDEX is constructed from the language contained in the patents themselves, there is a certain amount of duplication between the subordinate terms and "pesticide." Furthermore, not all "pesticide" patents are

* Presented before the Divisions of Chemical Literature and Agricultural and Food Chemistry, Pesticides Subdivision, Joint Symposium on "Problems of the Pesticide Literature and Some Solutions," 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 9, 1964.