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UNITED STATES GENERAL ACCOUNTING OFFICE
WASHINGTON, D.C. 20548

RESOURCES AND ECONOMIC DEVELOPMENT DIVISION

JAN 26 1976

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B-133192

The Honorable Russell E. Train
Administrator
Environmental Protection Agency

Dear Mr. Train:

GAO has reviewed EPA's basis for determining whether safety and efficacy data submitted by pesticide registrants is complete, accurate, and reliable for registering pesticides and establishing tolerances (the maximum pesticide residues allowed in food). EPA uses safety data to evaluate the hazards a pesticide poses and to determine whether the pesticide can be used without unreasonable adverse effects on man and the environment. It uses efficacy data to determine whether the pesticide, when used as directed, will effectively control the target pest.

EPA, in determining pesticide safety and efficacy, relies primarily on tests made by nongovernmental laboratories and paid for by pesticide registrants. EPA has no program to accredit and/or inspect these laboratories to insure that they have the requisite personnel and facilities to make accurate and reliable tests.

Other Government agencies which use data from nongovernmental laboratories have ongoing accreditation/inspection programs to provide such insurance. For example, the Food and Drug Administration (FDA), which has drug-testing requirements analogous to pesticide-testing requirements, has inspected some of the same laboratories that have made health studies supporting pesticide registration. FDA has questioned the validity of studies from these laboratories because of (1) inadequate supervision and internal control of tests, (2) questionable procedures, and (3) poor recordkeeping. Because FDA has found deficiencies in some of the same laboratories EPA used, we believe that EPA should consider establishing its own accreditation/inspection program.

We made our review in the Washington, D.C., area, primarily at EPA headquarters and at FDA. We also talked to officials of other Federal agencies which rely on test

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data prepared at nongovernmental laboratories. We examined pertinent legislation and EPA regulations, records, and files relating to the use of laboratory data and to the completeness, accuracy, and reliability of such data. We also talked to and obtained information from officials of selected laboratory accreditation organizations.

EPA'S USE OF LABORATORY DATA

Under the Federal Insecticide, Fungicide, and Rodenticide Act of 1947 (7 U.S.C. 135), as amended, and the Federal Food, Drug and Cosmetic Act of 1938 (21 U.S.C. 301), as amended, EPA registers pesticides and establishes their tolerances. Generally nongovernmental laboratories under contract to pesticide manufacturers do the pesticide safety and efficacy testing required for EPA registration and tolerance setting.

EPA's proposed registration guidelines[1] require that studies "be done under the direction of qualified personnel, who are responsible for utilizing sound scientific experimental procedures adequately to determine a pesticide's toxicological hazard." The guidelines further state that "the validity of information submitted...depends on the test procedures employed and the expertise of the individuals performing the tests." However, the proposed guidelines contain no procedures for EPA to enforce these requirements by inspecting, licensing, or accrediting the participating laboratories.

EPA officials told us that EPA did not keep either a list of laboratories which made studies supporting pesticide safety and efficacy or a list of laboratories which had submitted faulty studies. We reviewed the files for the 1,199 pesticides registered during the 6-month period ended February 28, 1975, and identified 77 laboratories which recently had made studies used as a basis for registration. There were 37 laboratories which had developed safety data and 50 laboratories which had

[1]The 1972 amendments to the Federal Insecticide, Fungicide, and Rodenticide Act required that registration guidelines be completed by October 1974. As of December 1975 EPA had published proposed guidelines in the Federal Register and had received public comments thereon. An EPA official told us that the guidelines were being finalized and were to be completed in February 1976.

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developed efficacy data; 10 of the laboratories had developed both types of data.

EPA's review of safety and efficacy studies was generally restricted to reading test results and questioning (1) obvious shortcomings in the test methods, (2) conclusions which were at variance with the raw data, and (3) results markedly different from those generally expected of certain families of chemicals. EPA emphasized assessing the validity of reported results and identifying and questioning statistical variations.

EPA data reviewers expressed differing opinions of the reliability of nongovernmental laboratory data. Many believed, on the basis of personal experience, that nongovernmental laboratory data was accurate and reliable. Other officials said that reports were oversummarized, attempted to lead reviewers to favorable conclusions, and could contain false data that EPA might accept. Some reviewers believed that the market system provided an incentive for accurate data in that consumers would not continue to buy products found to be ineffective; others pointed out that consumers cannot detect the ineffectiveness of such products as germ killers or the long-term health hazards, such as cancer or birth defects, of pesticide products.

In their review of data registrants submitted, EPA reviewers have occasionally found inconsistencies, failures to follow prescribed test methods, results lacking statistical validity, and conflicting data. Many reviewers also said that fabricated studies not supported by laboratory work could pass review without detection if the data was consistent with data on similar pesticides.

EPA's limited preregistration testing had disclosed that some EPA results varied from data submitted by registrants. For example, one registrant submitted data which indicated that a sanitizer was irritating to the eye but not to the skin. After testing the product, EPA concluded that "confirmatory testing of the submitted samples of * * * [the product] significantly differ from the test results which were submitted in support of this registration." EPA's tests showed that the product caused severe eye damage and primary skin irritation. As a result, EPA required the registrant to change the signal word on the label from "Caution" to "Danger" and to add other precautionary statements to the label. Similar variances

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might be found in such safety testing as chronic-feeding studies;[1] however, EPA does not replicate these studies because it lacks the facilities.

EPA officials told us that they agreed that greater assurance was needed regarding the adequacy and accuracy of studies submitted in support of pesticide registrations and that this concern was shown in a May 1974 strategy document of plans and policies for carrying out the 1972 amendments to the Federal Insecticide, Fungicide, and Rodenticide Act. The strategy document stated that "The possibility of requiring industry to use Government certified laboratories to perform testing will be investigated as a further means of ensuring objectivity and standardization in data submissions." EPA officials told us that EPA had not taken any action in this regard because EPA's efforts had been directed to higher priority requirements mandated by the act to be completed by certain dates.

INSPECTION AND ACCREDITATION PROGRAMS REQUIRED BY OTHER FEDERAL AGENCIES

Other Federal agencies also use nongovernmental laboratories to assess the hazards of drugs and manufacturing chemicals. In its human-drug registration program, FDA requires essentially the same type of toxicity testing as EPA requires for pesticide registration. Thus for certain drugs and pesticides, analogous testing is required to determine acute (one-dose exposure) and subacute (continuous exposure generally over a 90-day period) toxicity, as well as chronic (long-term) studies, to determine a product's potential to cause cancers (carcinogenicity) or birth defects (teratogenicity) or to affect reproduction. In many cases the same laboratories do both pesticide and drug testing.

The EPA and FDA programs differ in one major respect--FDA has a program to inspect laboratories to insure the reliability of data submitted for drug registration. The objectives of FDA's inspection program are to insure that laboratories:

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[1]Studies during the lifetime of test animals involving multiple exposure to substances in their food. The study is to find a maximum level which induces no toxicological effect and to determine the nature and degree of long-term effects.

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--Have sufficient and properly maintained facilities and equipment.

--Keep complete and accurate records which allow for verification of data submitted.

--Have qualified staff.

--Follow valid test procedures.

FDA inspectors have found inadequate internal control, insufficient supervision, questionable procedures, and poor recordkeeping in several nongovernmental laboratories which test both pesticides and drugs. For example, at one drug-pesticide laboratory, FDA inspectors found that:

--The laboratory had purchased animals which were not accounted for.

--Animals' identifying numbers were changed in a record book without explanation, initials, or date.

--Data sheets and corrections thereon were not always initialed.

--Recalculations of animals' food intake for a 2-week period were not adequately explained.

The lack of accountability of animals and/or the substitution of test animals during a test could affect the test's outcome to the extent that a harmful chemical could be declared safe.

In addition to EPA and FDA, many Federal, State, and local agencies rely on other types of data prepared by nongovernmental laboratories, many of which are regulated by accreditation or inspection programs. (A number of accreditation/inspection programs and their cost are discussed in enc. I.)

One major area where the Congress recognized the need to insure high-quality laboratory data was clinical tests--tests for the diagnosis, prevention, or treatment of human diseases or impairments. The Clinical Laboratory Improvement Act of 1967 requires the Center for Disease Control (CDC) of the Department of Health, Education, and Welfare (HEW) to license clinical laboratories which receive clinical specimens that cross State lines. CDC accepts

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accreditation by the College of American Pathologists and the New York State Department of Health in lieu of a CDC site inspection. CDC, which charges a licensing fee, has licensed about 700 such laboratories. Additionally, numerous other State agencies also inspect and accredit clinical laboratories, primarily those not involved in interstate commerce. CDC said that its licensing program had improved laboratory-proficiency testing.

EPA, FDA, the Department of Agriculture, the American Industrial Hygiene Association, the American Association for the Accreditation of Laboratory Animal Care (AAALAC), and various State agencies accredit or inspect a variety of other types of testing laboratories. A 1974 contract study for EPA's Office of Research and Development on the feasibility of an environmental laboratory accreditation/inspection program credited these existing programs with (1) reducing the frequency of incorrect data, (2) correcting technical problems, (3) weeding out poorly qualified employees, (4) standardizing laboratory procedures, and (5) upgrading facilities and equipment.

As a result of this contract study, EPA is establishing an accreditation/inspection program for environmental-testing (water quality) laboratories. In addition, the Department of Commerce and the Occupational Safety and Health Administration are considering similar programs for laboratories whose data they use.

Another means of improving the accuracy and reliability of data is to require accreditation of laboratories by existing professional associations. As mentioned previously, CDC uses such an approach in licensing clinical laboratories accredited by the College of American Pathologists and by the New York State Department of Health.

We identified two organizations--one which had, and one which was considering, accreditation programs. These organizations' programs appeared to have applicability to pesticide testing. The first, the American Council of Independent Laboratories, is a voluntary association of independent laboratories in the field of physical or biological sciences. Council accreditation requires a site inspection, made by two persons selected from the membership, to insure that the laboratory is adequately equipped and organized to render reliable service in its chosen fields in accordance with the council's guidelines.

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An apparent shortcoming of the council's program is that periodic followup inspections are not required after membership has been obtained.

12 The second, the Society of Toxicology, has recognized that a program to accredit laboratory facilities and competency in making toxicological studies is needed, and the society is studying the matter. EPA input into development of such a program could insure that EPA needs will be considered. DLG 01127

13 The National Institutes of Health (NIH) also requires that the animal-care facilities of nongovernmental laboratories with which it contracts be accredited either by NIH or by a nationally recognized professional laboratory animal-accrediting body, such as AAALAC. Although AAALAC does not evaluate such aspects as test procedures and quality of test personnel and facilities, an NIH official told us that accreditation by AAALAC improves the quality of research by insuring that good animal-care procedures are followed during studies, which keeps variables at a minimum. 28

One additional factor that EPA should consider, if it determines that an EPA-operated inspection or accreditation program is warranted, is whether a fee should be charged for EPA's service. It appears that licensing or accrediting laboratories should comply with 31 U.S.C. 483a, enacted in 1951, which states that it is the sense of the Congress that an agency charge a fair and equitable fee for "any work, service publication, report, document, benefit, privilege, authority, use, franchise, license, permit, certificate, registration, or similar thing of value or utility performed, furnished, provided, granted, prepared or issued by any Federal agency * * *." CDC assesses such fees for licensing clinical laboratories, and its program might serve as a model for a similar EPA program.

ADDITIONAL CONTROL OF TEST DATA DESIRABLE

EPA's proposed registration guidelines state that "the pesticide used for toxicological [safety] testing must be the same chemically characterized product which is proposed to be or is commercially produced and used." EPA did not require chemical analysis of the pesticide being tested, and test reports submitted to EPA generally did not contain a verification by the performing laboratory of the chemical composition of the substances tested. Reports

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merely cite the receipt and testing of samples labeled by a number or product name. Examples of material descriptions are "a red-colored liquid" and "a green powder labeled Sample #1548." Occasionally disclaimers are made by the performing laboratories that the reported results are not applicable to apparently similar or identical products. One report, for example, included the statement: "This report applies only to the sample, or samples, investigated and is not necessarily indicative of the quality or condition of apparently identical or similar products." Reports such as these provide EPA with no assurance that the product which was tested is the product being registered. We believe EPA should not accept reports containing such disclaimers and should consider requiring analysis of chemicals being tested.

CONCLUSIONS

EPA relies on safety and efficacy studies by nongovernmental laboratories as the basis for registering pesticides. EPA has no program to inspect, license, or accredit these laboratories to insure that the laboratories have appropriate facilities and equipment and qualified personnel and that proper test procedures are followed. Other Federal, State, and local agencies which use such data, some of which is analogous to data required for pesticides, have found the accuracy and reliability of data from some laboratories to be unsatisfactory and consequently have their own inspection or accreditation programs.

FDA and CDC have inspection/accreditation programs for drug registration and clinical testing, respectively. It appears that poor tests in these areas would be more readily identified than poor pesticide tests. Adverse drug reactions or incorrect specimen analyses would be readily attributable to the laboratory and should have an immediate economic impact on the laboratory because the drug company or doctor would not use such laboratories further. Nevertheless the data generated from these laboratories has not been adequate, and inspection and licensing programs have been implemented.

Pesticide exposure presents equally, if not more, serious health hazards, because adverse effects from low-level exposure may not be apparent for many years. The identification of problem pesticides is further complicated because of the dispersion of pesticides, along with a

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multitude of other chemicals, in the nation's food supply and the environment. Despite the seriousness of potential problems and the almost complete reliance of EPA's pesticide registration program on safety and efficacy studies by nongovernmental laboratories, EPA has not systematically reviewed the capabilities of such laboratories or their compliance with appropriate test procedures that will reasonably insure the accurancy and reliability of test data.

We believe that EPA's acceptance of safety and efficacy studies which contain laboratory disclaimers regarding test results and do not adequately identify the chemical composition of the compound being tested prevents EPA from insuring, as required by law, that only safe and effective pesticides are registered.

RECOMMENDATIONS

We recommend that EPA determine whether an accreditation or inspection program is necessary to insure that accurate, reliable, and objective safety and efficacy data is being provided by nongovernmental laboratories. Such a determination should consider the various alternative methods available for inspection or accreditation as a basis for selecting the most cost-effective program for EPA. EPA's needs may be satisfied by:

--A joint EPA-FDA program which would avoid duplication of visits to laboratories serving both agencies.

--Accreditation by one or more private organizations.

--A combination of the foregoing.

We also recommend that EPA not accept studies containing laboratory disclaimers and consider requiring the laboratory to make a chemical analysis of the product being tested.

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We have discussed this report with officials of EPA's Office of Pesticide Programs. They told us that they agreed that EPA should review the adequacy of laboratory data submitted for pesticide registration as a basis for determining whether a laboratory accreditation or inspection program is warranted. They also said that such a study had not

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been done because of higher priority work, such as completing registration regulations and guidelines which were required by amendments to the Federal Insecticide, Fungicide, and Rodenticide Act to be completed by October 1974.

An EPA official said that pesticide studies should contain positive identification of the compound being tested and should not be qualified regarding study replicability. He said that these areas would be reviewed to determine whether EPA's proposed registration guidelines needed to be revised.

We invite your attention to the fact that this report contains recommendations to you which are set forth on page 9. As you know, section 236 of the Legislative Reorganization Act of 1970 requires the head of a Federal agency to submit a written statement on actions taken on our recommendations to the House and Senate Committees on Government Operations not later than 60 days after the date of the report and to the House and Senate Committees on Appropriations with the agency's first request for appropriations made more than 60 days after the date of the report.

We shall appreciate being informed of any action you may take on matters discussed in this report. We appreciate the courtesies and cooperation extended to our representatives during the review.

Sincerely yours,

Henry Eschwege

Henry Eschwege
Director

Enclosure

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DESCRIPTION OF SELECTED FEDERAL AND STATE LABORATORY ACCREDITATION AND INSPECTION PROGRAMS AND THEIR RELATED COSTS

Organization	HEW, Food and Drug Administration, Bureau of Foods.
Program	Approval of State milk-testing laboratories and personnel. Includes proficiency testing and inspection.
Objectives	Conformity of laboratory procedures.
Benefits	Improved precision and accuracy of data, standardization of procedures, and upgrading of facilities.
Costs	3 staff-days for each inspection.
Number of participating laboratories	65.

Organization	HEW, Food and Drug Administration, Bureau of Drugs.
Program	Inspection of drug studies in animals and humans at commercial laboratories.
Objectives	Insure that laboratories (1) have sufficient and properly maintained facilities and equipment, (2) keep complete and accurate records which allow for verification of data submitted, (3) have qualified staff, and (4) follow valid test procedures.
Benefits	Analyses of benefits not currently available.
Costs	None currently available.
Number of participating laboratories	No estimate.

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ENCLOSURE I

Organization	HEW, CDC.
Program	Licensure of clinical laboratories engaged in interstate commerce. Includes proficiency testing and inspection. Accreditation by College of American Pathologists and New York State Department of Health is accepted.
Objectives	Improvement of laboratory performance; conformity of laboratory procedures.
Benefits	Decrease of 11.5 percent in proficiency-testing deficiencies and 19 percent in number of laboratories found unsatisfactory.
Costs	Total funding, $9 million; licensing activities, $2 million; cost to laboratories, $125 plus $25 for each section inspected.
Number of participating laboratories	700.

Organization	HEW, Social Security Administration, Bureau of Health Insurance.
Program	Certification of independent clinical laboratories performing services under Medicare. Includes inspection. Regulations incorporate CDC standards.
Objectives	Improvement of clinical laboratory performance.
Benefits	Upgraded laboratory quality control and personnel.
Costs	Total funding--$3 million a year.
Number of participating laboratories	3,000.

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ENCLOSURE I

Organization	EPA, Water Quality Office, Water Supply Division.
Program	Certification of State laboratories analyzing potable water on interstate carriers. Includes inspection.
Objectives	Conformity of laboratory procedures to insure data quality.
Benefits	Improved testing procedures.
Costs	56 staff-hours for each inspection by GS-13 through GS-15 personnel.
Number of participating laboratories	50.

Organization	EPA, Methods Development and Quality Assurance Research Laboratory.
Program	Studying feasibility of certifying environmental-monitoring laboratories (water, air, and pesticides), including proficiency testing and inspection.
Objectives	Reliable data. Legal basis for refusal of data of uncertain quality and reliability.
Benefits	Not obtained.
Costs	Estimated at $750,000 a year.
Number of participating laboratories	No estimate.

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ENCLOSURE I

Organization	Department of Labor, Occupational Safety and Health Administration.
Program	Proposed accreditation of independent laboratories which test products and devices for safety. Includes proficiency testing and inspection.
Objectives	Facilitate enforcement of occupational safety and health standards.
Benefits	Proposal revoked pending resolution of questions regarding legal authority, resources required, and program standards.
Costs	No estimate available.
Number of participating laboratories	No estimate.

Organization	Department of Commerce, National Bureau of Standards.
Program	Proposed national voluntary laboratory accreditation for selected classes of technologies, initially construction materials.
Objectives	Maintain acceptable level of competence of private and public laboratories that serve regulatory and nonregulatory product evaluation needs.
Costs	No estimate available.
Number of participating laboratories	No estimate.

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ENCLOSURE I

Organization	New York Department of Health, Division of Laboratories and Research.
Program	Approval of laboratories that analyze potable water.
Objectives	Reliability of laboratory data and c nformance with minimum standards.
Benefits	Increased uniformity of data among laboratories; weeding out of poorly qualified personnel.
Costs	None currently available.
Number of participating laboratories	100.

Organization	Oklahoma Department of Health.
Program	Certification of prenatal and premarital blood-sample-testing laboratories. Includes proficiency testing.
Objectives	Maintenance of satisfactory level of performance in serological testing of blood samples.
Benefits	Increase in average proficiency-testing scores of approved laboratories.
Costs	Not obtained.
Number of participating laboratories	200.

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ENCLOSURE I

Organization	California Department of Health.
Program	Licensure of clinical laboratories, except those owned or operated by licensed physicians for work on their own patients. Includes inspection.
Objectives	Insure capability and satisfactory level of performance of facilities and personnel.
Benefits	Reduced frequency of poor (incorrect) data.
Costs	In fiscal year 1974-75, $465,199 was budgeted for 37.8 positions.
Number of participating laboratories	2,000.

Organization	AAALAC.
Program	Voluntary accreditation of laboratory-animal-care methods and facilities. Utilizes NIH's Guide for the Care and Use of Laboratory Animals and fulfills NIH requirements for grants. Participated in by the Veterans Administration. Includes inspection.
Objectives	Improved welfare and health of laboratory animals. Facilitate scientific research and testing requiring laboratory animals.
Benefits	Improvements in animal care through identification of deficiencies; 70 percent of the laboratories, initially unacceptable, improved their programs to an accreditable level.
Costs	Fee to laboratory of $100 annually. Cost varies by facilities.
Number of participating laboratories	Accredited: 275.

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ENCLOSURE I

Organization	American Industrial Hygiene Association.
Program	Voluntary accreditation of laboratories which analyze samples of airborne contaminants collected in the workplace and biological specimens of workers exposed. Includes proficiency testing and inspection.
Objectives	Improved performance and assurance of quality data.
Benefits	Improved laboratory data, selectivity in personnel hiring, and objective look at techniques and procedures.
Costs	Operated since inception under sponsorship of National Institute of Occupational Safety and Health. Annual site visit cost estimated at $350.
Number of participating laboratories	60.

Organization	College of American Pathologists.
Program	Voluntary accreditation of independent and hospital clinical laboratories. Includes inspection and proficiency testing.
Objectives	Development and implementation of high laboratory medicine standards.
Benefits	Upgraded level of performance.
Costs	Average site visit: $400.
Number of participating laboratories	12,000.

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ENCLOSURE I

Organization	Society of Toxicology.
Program	Planning to establish a working party of past presidents to prepare an outline of the goals, objectives, and means of implementing an accreditation program.
Objectives	Not obtained.
Benefits	Not obtained.
Costs	Not obtained.
Number of participating laboratories	Not obtained.

Organization	American Council of Independent Laboratories, Inc.
Program	Voluntary accreditation requiring only an initial inspection to insure adequate equipment, organization, personnel, and quality control.
Objectives	Promotion of scientific inspection, sampling, analysis, testing, consultation, development, and research.
Benefits	Not available.
Costs	Not available.
Number of participating laboratories	171.

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