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Corporate Author	
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Description Notes	Letter has subject line 2,4,5-T Rebuttable Presumption Against Registration OPP 30000/26. Leng is responding to the RPAR and encloses two of her papers. First is "Comparative Metabolism of Phenoxy Herbicides in Animals" in Fate of Pesticides in Large Animals, 1977 (not scanned), and the second is a draft of "Government Requirements for Pesticide Residue Analyses and Monitoring Studies" Chapter 11 in Pesticide Residue Analysis, January 31, 1977.

Al Young from M. Leng

1714 Sylvan Lane
Midland, Michigan 48640
July 7, 1978

(4)

Federal Register Section
Technical Services Division (WH-569)
Office of Pesticide Programs, EPA
Room 401, East Tower
401 M Street SW
Washington, D. C. 20460

Subject: 2,4,5-T Rebuttable Presumption Against Registration
OPP 30000/26

This response to the 2,4,5-T RPAR is prompted by my dedication as a scientist who is continually seeking knowledge about the effects of chemicals on man and his environment. I am submitting it as an individual who is an active member in the Division of Pesticide Chemistry of the American Chemical Society, rather than as a person who is currently employed by Dow Chemical, one of the principals in the continuing debate on the safety of this useful herbicide.

Enclosed are pertinent excerpts of two documents dealing with studies on phenoxy herbicides in humans, and with the reliability of data on residues of 2,4,5-T and its trace contaminant TCDD in foods and environmental samples.

The first paper summarizes three studies with phenoxy herbicides in humans. It includes a discussion about the fallacy of using data from studies at highly exaggerated dosage levels to predict what might happen at levels likely to be encountered from recommended uses of 2,4,5-T. (This paper was cited as reference 79 in EPA's 2,4,5-T Position Document No. 1, but only as a basis for calculating highly exaggerated residues for 2,4,5-T in meat and milk.)

The second enclosure is from my draft chapter on government requirements for pesticide residue data and monitoring studies, scheduled for publication in 1978. As indicated in this excerpt, many of the allegations of hazard from use of 2,4,5-T are based on data from studies which do not meet even minimum requirements for such investigations.

Sincerely,

Marguerite L. Leng

Marguerite L. Leng, Ph.D.

abc

cc to attached list.

M. L. Leng letter dated 7/7/78
2,4,5-T Rebuttable Presumption Against Registration
OPP 30000/26

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(46)

GOVERNMENT REQUIREMENTS FOR PESTICIDE RESIDUE ANALYSES AND MONITORING STUDIES

by

Marguerite L. Leng

Government Registration

Dow Chemical U.S.A.

Midland, Michigan

Chapter 11 in

PESTICIDE RESIDUE ANALYSIS

edited by

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Philip Ebving and James D. Winefordner, Editors

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1. INTRODUCTION

Requirements for analysis of pesticide residues have increased vastly since the 1950's when regulations were first implemented to require tolerances (maximum residue limits) for these useful chemicals in food crops intended for human and animal consumption. The evolution of changes in such requirements can be traced in reviews published between 1955 and 1971 by Gunther and Blinn (1), Fogelman (2), Harris (3), Vorhes (4), Frehse (5), Harris and Cummings (6), and Bevenue and Kawano (7).

In 1968, the U.S. Food and Drug Administration issued FDA Guidelines for Chemistry and Residue Data Requirements of Pesticide Petitions (8). These official guidelines described the studies needed at that time for obtaining analytical data suitable for establishment of tolerances for pesticides in food and feed crops and their byproducts, as well as in meat, milk, poultry and eggs.

During the early 1970's bills were passed in the U.S. House and Senate proposing major revisions in the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), resulting in passage of the Federal Environmental Pesticide Control Act (FEPCA) on October 8, 1972. Detailed regulations for implementation of Section 3 on Registration of Pesticides were finalized by publication in the Federal Register on July 3, 1975 (9).

At that time certain sections were "Reserved" for later issuance. Registration Procedures were published as regulations on September 9, 1975 (11). A preliminary draft of sections on Petitions for Tolerances (12) was made available by EPA in 1975 for comment by outside experts, but a revised version has not been issued as of this writing. Review of the draft indicated that requirements for residue data by the Environmental Protection Agency (EPA) under FIFRA as amended will be similar but more extensive than those outlined by FDA under the Food, Drug and Cosmetic Act in 1968 (8).

Proposed guidelines for studies to meet Section 3 Regulations were published in the Federal Register on June 25, 1975 along with extensive appendices outlining how the studies should be conducted (10). Final guidelines are scheduled for publication in 1977 incorporating revisions based on comments by other government agencies, industry, and any interested parties.

This chapter presents a brief outline of how certain government agencies control pesticides, of the laws under which they operate, of regulations implemented to carry out this task, and of how tolerances were established for the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) over a period of 25 years under these laws and regulations. It also provides a detailed description of current requirements for residue data based on

proposed EPA Guidelines, based in part on personal experience during more than ten years of compiling data in petitions for tolerances, including many volumes on residue studies with 2,4-D. Finally, it discusses monitoring studies for pesticide residues in raw agricultural commodities, total diet samples, and environmental samples, as well as pitfalls in interpretation of "positive" findings.

4. MONITORING STUDIES

During the 1960's, concern grew about potential long-term effects of persistent pesticides in the environment. This concern was fed in part by reports of finding residues of DDT in samples such as pelicans, walruses, and even soil far removed from where the insecticide had been used. The impact of such reports has continued long after many of the results of early studies have been refuted by more specific analytical data. Positive findings originally attributed to DDT have often been shown to be due to the presence of PCB's (polychlorinated biphenyls) (48). More recently, environmental and laboratory contamination by phthalate esters has been shown to cause responses frequently mistaken for DDT residues (49). Thus, it is imperative that analytical methods used in monitoring for pesticides are specific for the chemicals being sought and that positive findings are confirmed by secondary methods based on different principles of analysis.

4.1 NATIONAL PESTICIDES MONITORING PROGRAM

The National Pesticide Monitoring Program (NPMP) was initially designed on the basis of the minimum monitoring needed to establish baseline levels of pesticides in substrates of food and feed, humans, soil, water, air, wildlife, fish and estuaries,

Variables such as wind, rain, temperature, snow, and inversion are unpredictable and should be recorded during the sampling period.

4.4 MONITORING IN HUMANS

Concern about potential long-term effects of persistent chemicals led to the National Human Monitoring Program for Pesticides. In 1967, the Division of Pesticide Community Studies initiated a program in which adipose tissue (fat) was to be collected from postmortem and surgical specimens (50). The design provided for sampling which would yield valid data concerning pesticide incidence variation with geographic distribution, and with age, sex, and race variation of the donors.

The sampling population was drawn from sources in cities of 25,000 or more population (1960 figures) distributed among the four census regions (Northeast, North Central, South, and West), without regard for the donor's occupation. The total number of collection points (or pathologists) was 39 and each was to provide a minimum of 50 samples per year, for an annual total of at least 1950 random samples. For each collection point, the sample quota was further broken down by age and sex: 14 years and under, male and female; 15 through 49 years, male and female; and 50 years and over, male and female. Since the program objective was to reflect

the incidences in the normal (man-on-the-street) general population, samples were excluded from cases of known or suspected acute pesticide poisoning or chronic debilitating illness, and from patients who had been institutionalized for long periods.

Analyses of human adipose tissue were initially limited to the measurement of certain chlorinated hydrocarbons due to sensitivity limitations of available analytical methodology. The program originally included only DDT and its metabolites, dieldrin, heptachlor epoxide, and the isomers of BHC. As refinements of methodology progressed, additional pesticide chemicals or metabolites were added such as oxichlordane and mirex. Other pollutants such as PCB's (polychlorinated biphenyls) were added as they became identifiable.

4.5 SPECIAL MONITORING PROGRAMS

Special programs are instituted as problems arise or are suspected. Many of these are a result of industrial pollution or accidental contamination rather than from direct use of pesticides. One such example was a monitoring program for mercury, or more specifically methyl mercury, in fish and bottom sediments in the Great Lakes attributed to dumping of wastes from giant electrolytic processes. A more localized

problem was contamination of cattle and poultry in Michigan beginning in 1973 from ingestion of feed containing polybrominated biphenyls (PBB's).

Intensified programs are also put into operation when emergency use of cancelled pesticides is authorized. During recent years, EPA has taken stepwise action against DDT, mirex, aldrin and dieldrin, heptachlor and chlordane, and other chlorinated hydrocarbons are expected to follow. However, in the absence of adequate substitutes, EPA occasionally approves limited use of DDT to prevent spread of a specific pest. Similarly, EPA issued a permit in 1976 for aerial application of mirex to control fire ants on six million acres in Georgia, Mississippi, Louisiana, and Arkansas. Scientists from APHIS will monitor water, soil, sediment, invertebrates (crabs and crayfish), and vertebrates (mostly birds) to determine the fate of residues in the non-target environment. Such monitoring programs using specific methodology should provide more reliable information on the persistence of these useful pesticides in the environment.

Expansion of special programs is anticipated as EPA continues to review data for other pesticides on their list of candidates for Rebuttable Presumption Against Registration (RPAR). Several chlorinated phenols and phenoxy herbicides are included

in the list, due in part to the presence of dioxin contaminants. The most widely publicized of these is the herbicide 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), originally implicated as a teratogen in screening studies at high doses in susceptible strains of mice. The 2,4,5-T used in the first teratogenic studies by Bionetics (60) contained about 30 ppm of the highly toxic 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). This dioxin is formed during the manufacture of 2,4,5-trichlorophenol from tetrachlorobenzene at high temperatures under alkaline conditions. Current specifications are for less than 0.1 ppm TCDD in 2,4,5-T and other pesticides derived from 2,4,5-trichlorophenol, such as the herbicide silvex (2,4,5-trichlorophenoxypropionic acid) and the fungicide hexachlorophene (2,2'-methylene bis(3,4,6-trichlorophenol)).

Cancellation proceedings against 2,4,5-T were withdrawn by EPA in June 1974 pending results of extensive monitoring studies for TCDD. Analytical methods have been developed capable of detecting residues down to 10 parts per <u>trillion</u> (0.00001 ppm) or less in milk, fat, and environmental samples (61, 62). However, caution is needed in attributing positive responses at this level to the actual presence of TCDD residues due to interferences from unrelated substances in the same samples.

The TCDD monitoring program initially called for sampling of many substrates including human milk, fat, and liver.

Substrates most likely to contain residues were samples taken from range cattle maintained in areas with a confirmed history of repeated treatment with 2,4,5-T for many years, and slaughtered without the usual fattening period in a feed lot. Samples of fat from these animals were distributed to several cooperating laboratories including EPA and The Dow Chemical Company. Preliminary results were erroneously reported in 1975 to indicate "positive" results for about 50% of the initial 34 fat samples analyzed, but the findings were not consistent among the laboratories conducting the analyses. As reported by Dr. Ralph T. Ross, Chairman of the EPA Dioxin Project in June 1976 (63), only one of the 85 beef fat samples analyzed showed a positive TCDD level at 60 ppt, and two samples appeared to have TCDD levels at 20 ppt. He also stated that the analytical method is not valid below 10 ppt.

The method used in the above analyses involves use of gas chromatographic separation to remove interfering substances, in combination with high resolution mass spectrometry for quantitation. This method has also been used to analyze other monitoring samples collected by Dow. As reported by Shadoff in 1975 (64), no residues of TCDD were detected in samples of fish, water and mud from two locations in Arkansas and Texas that have a long history of treatment with 2,4,5-T

containing considerably more than the current limit of 0.1 ppm TCDD. Thus, it seems unlikely that continued use of 2,4,5-T would result in significant residues of TCDD in the environment.

Addendum, July 1978

Reports of the study by Shadoff et al. (above) and of two studies on surveillance samples of milk and beef fat were published in 1977 and 1978. Summaries of these studies are quoted below.

Summary [1] As part of a broad study to determine whether 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) is accumulating in the environment due to approved uses of 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) based herbicides, samples of fish, water, mud and human milk were collected from areas in Arkansas and Texas where 2,4,5-T herbicides are used and were analyzed for TCDD. No TCDD was detected by a GC-MS procedure with a detection limit which averaged less than 10 ppt.

Conclusion [2] Surveillance samples of milk from the states of Oklahoma, Arkansas, and Missouri were collected from cows grazing on pasture or rangeland treated with normal applications of 2,4,5-T. These samples and control samples were analyzed for TCDD by GC/MS. A detection limit of 1 ppt was achieved. With this sensitivity the control samples were indistinguishable from those from treated areas. Hence, TCDD was not found.

Summary [3] Specimens of fat taken from steers which had grazed on rangeland previously treated with 2,4,5-T herbicides were analyzed for the presence of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). A cleanup procedure resulting in a 500-fold concentration was followed by a gas chromatography-mass spectrometry detection technique. The limit of detection of TCDD (2.5 times peak to peak noise) was found to be in the 30-60 picogram range (3-6 ppt in beef fat using 10 gram samples).

None of the sixteen samples comprising two of the three studies showed any response for TCDD. In the third study, in which the animals were confined to a fenced pasture sprayed in its entirety with a 2,4,5-T herbicide, samples from three of the seven animals gave a positive response at the extremely low level of 3 to 4 ppt TCDD, which is at the detection limit.

[1] Shadoff, L.A., Hummel, R.A., Lamparski, L., and Davidson, J.H. A Search for 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) in an Environment Exposed Annually to 2,4,5-Trichlorophenoxyacetic Acid Ester (2,4,5-T) Herbicides. Bull. Environ. Contam. Toxicology 18, 478-485, 1977.

[2] Mahle, N.H., Higgins, H.S., and Getzendaner, M.E. Search for the Presence of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Bovine Milk. Bull. Environ. Contam. Toxicology 18, 123-130, 1977.

[3] Kocher, C.W., Mahle, N.H., Hummel, R.A., Shadoff, L.A., and Getzendaner, M.E. A Search for the Presence of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in Beef Fat. Bull. Environ. Contam. Toxicology, 19, 229-236, 1978.

5. INTERPRETATION OF RESIDUE DATA

Several basic principles should be applied in the interpretation of positive responses obtained in pesticide residue analyses. For example, a nanogram quantity of a pesticide in a solvent may cause a measurable peak in a gas chromatogram. However, the same quantity may not be distinguishable when superimposed on the "noisy" background obtained from extracts of a substrate. Similarly a small peak from a treated sample should not be compared directly to a large peak from a sample spiked at a considerably higher level. Recovery studies should include complete analyses of several control samples fortified at the claimed sensitivity of the method. Any "positive" responses below that should be reported as "less than" or "traces". A response below the limit of detection should be reported as "none-detected" since it is not possible to demonstrate a zero residue. For example, a residue of only 0.01 ppm DDT still represents 10^{13} molecules per gram of foodstuff (65). Above all, confirmation of residue identity is needed before instrument responses can be translated into positive values.

5.1 VARIABILITY AMONG SAMPLES

The inherent biological variation among individuals of the same species can cause differences in response during analysis which might be interpreted as positive residue

values unless numerous samples were analyzed. For example, in a recent study reported by Clark et al. (66), residues of several chlorinated hydrocarbon insecticides in fat of groups of feedlot cattle were compared to the residues in the feed given to them for 112 days prior to slaughter. Both feed and fat samples contained detectable levels of lindane, dieldrin, DDT, DDE, and DDD. Except for dieldrin, each insecticide was found at higher levels in fat than in feed. However, the levels were consistently low except for DDT and its degradation products in fat. Average values for lindane were 0.002 ppm in feed and ranged from 0.014 ppm to 0.032 ppm in fat of five groups of ten calves each given various levels of ammonium salts in addition to the feed. Average levels found for DDT were 0.083 ppm in feed and ranged from 0.324 ± 0.256 ppm in fat from Group II to 0.518 ± 0.104 ppm in Group IV. If only average values for DDT are compared, a significant difference appears to exist between Groups II and IV. However, overlap of values for individuals in the two groups shows that they are not different (i.e., 0.324 + 0.256 = 0.580 which is higher than 0.518 - 0.104 = 0.414).

5.2 SENSITIVITY VS LIMIT OF DETECTION

As discussed recently by the Federal Working Group on Pest Management, the terms sensitivity and limit of detection do

not have the same meaning (52). Sensitivity depends on the response of an instrument such as a gas chromatograph under a specific set of conditions. However, as the instrument sensitivity is adjusted to a maximum, the baseline "noise" level generally increases too. The response due to a pesticide residue can be considered significant only if the peak height at the maximum usable sensitivity is twice the peak-to-peak height of the noise on the chart. Operation of the instrument at less than maximum sensitivity may be preferable, particularly for comparative analyses in different laboratories. For example, FDA analysts set instruments to give 50% of full scale recorder deflection on injection of one nanogram of heptachlor epoxide or two nanograms of parathion to assure that each laboratory operates at the same sensitivity.

On the other hand, the limit of detection of an analytical method may be defined as the concentration of pesticide above which a given sample of material can be said, with a high degree of confidence, to actually contain the chemical analyzed. This limit of detection depends upon a number of factors in addition to the instrument sensitivity, including sample size, adequacy of extraction and cleanup, size of aliquot injected, and knowledge and experience of the analyst. Deviations in peaks or baselines caused by inadequate cleanup are more evident when the instrument is operated at maximum sensitivity. These deviations may

cast doubt on the validity of the peaks of interest in assigning positive values for specific residues.

Sutherland has reviewed the analytical limit of detectability for residues (67). For all practical purposes, the response of control samples to a specified analytical method is the sole determinant of the limit of detectability. However, these control samples must be taken from plants or animals exactly comparable to the treated samples. They must be sampled at the same time, from identical varieties of the same degree of maturity, and must have been treated in all respects the same as the treated samples except that the chemical to be determined must not have been used on them. Furthermore, the samples must be independent and normally distributed according to statistical definitions. The responses given by, or apparent residues found in these control samples will usually follow a bell-shaped distribution curve. The average of all samples analyzed will be the true mean. An old rule-of-thumb was that any uncorrected residue value greater than twice the average control represented a real residue (65). However, this is not necessarily so depending on the spread of the frequency distribution around the mean for that substrate. Hahn has recently discussed the consequences of incorrectly assuming that distribution is normal about the mean (68).

Even greater care must be taken in interpreting data for extremely low residues of highly toxic chemicals in the environment. This was demonstrated following collaborative studies on TCDD conducted as part of the EPA Dioxin Implementation Plan in 1976. Agreement was reached among scientists from EPA, USDA, Harvard, University of Utah and Dow that it takes a response of 2.5 times background noise to indicate a positive finding. Furthermore, it takes a response of 10 times background noise before quantitative values at low parts per trillion can be assigned.

5.3 INTERPRETATION OF MONITORING DATA

Unfortunately, analysts conducting monitoring studies do not have the benefit of comparisons to control samples because samples reliably free from pesticides are usually not available. In such cases, the limit of detection is based on the analytical variability for each pesticide on each substrate, generally by carrying through the entire method at least six replicate samples containing levels near the estimated limit of detection of the pesticide (52). Under these conditions, the limit of detection is considered equal to two standard deviations (approximately 95% confidence level) calculated from the replicated results. The identity of any peak larger than this should be subject to confirmation

as discussed in Section 5.4, but practical limitations preclude confirmation of most "positive" values.

Although variability among analyses of six replicates may be adequate for samples of certain species of plants or animal tissues, it may not be adequate to establish a reliable baseline for samples of soil or water from widely divergent geographical locations subjected to contamination by a great variety of chemicals. Unfortunately, some chemists do not recognize such limitations and interpret any positive response similar to that produced by a pesticide as proof that a residue is present. Furthermore, reports of monitoring studies tend to emphasize the frequency of positive responses without regard to the significance of the "residues" found.

One such report issued in 1973 was entitled Pesticides in Selected Western Streams -- 1968-1971 (69). It gave results of analyses by the U.S. Geological Survey for nine chlorinated hydrocarbon insecticides and three phenoxy herbicides in water from twenty locations in fourteen states. The authors reported "total occurrence (of phenoxy residues) reached a peak of 106 during 1968-69 and declined sharply to 54 during 1970-71. This decrease of about 50% was due to 'reduced occurrences of 2,4-D and 2,4,5-T'." Examination of the lengthy data tables revealed that traces of phenoxy herbicides

amounting to less than 0.0005 ppm (0.5 part per billion) appeared to be present in about 16% of the samples for 2,4-D and 2,4,5-T and 7% of the samples for silvex. Furthermore, four-fifths of the positive findings were at levels below 0.1 part per billion (ppb). The detected limits were listed at 0.005 µg/liter for silvex and 2,4,5-T and 0.02 µg/liter for 2,4-D (i.e., a sensitivity of 5 to 20 parts per trillion). Recoveries of 80 to 100% were claimed for validation studies but the spiking levels were not specified and may not have approached the claimed sensitivity. Furthermore, confirmatory analyses for phenoxy compounds were not mentioned although other methods or other columns were discussed for confirmation of the insecticides found.

The report also stated that 64% of the silvex occurrences were at one station in Nevada and 47% of the 2,4,5-T occurrences were in two associated sites in Arkansas and Oklahoma. In view of the localization of positive findings, it is possible that the parts per trillion residues "found" may have been due to the presence of interfering substances in samples from these locations rather than to actual residues of silvex or 2,4,5-T in the water. Unfortunately, the report has been cited as evidence of widespread contamination of water by these controversial herbicides in Western States.

Another example is a paper in the September 1974 issue of Bulletin of Environmental Contamination and Toxicology (70). A total of 13 authors summarize studies on the distribution of pesticides in randomly selected soil samples taken from diverse environments in five west Alabama counties. Pesticide residues were found in all samples examined, even soil samples from areas where records indicated that no pesticides had been applied directly. The pesticides included eleven chlorinated hydrocarbon insecticides, six nonchlorinated insecticides, and two herbicides (atrazine and 2,4,5-T). They reported finding 2,4,5-T in 24% of the samples of top soil analyzed. Examination of the data revealed that 37 samples of top soil contained no detectable residues (sensitivity not specified) and only one sample containing more than 0.1 ppm 2,4,5-T. The samples were analyzed twice by GLC using two columns. No analytical data were provided to indicate reliability for the eight samples reported as "positive" at <0.1 ppm. Unfortunately, such data are used as evidence of persistence of pesticides in the environment.

The above examples also demonstrate the pitfalls in drawing conclusions from reports which emphasize the maximum residue found or the percent "positive" samples without adequate allowance for variations in background "noise". This becomes even more important in special monitoring programs for highly

toxic chemicals at extremely low levels. An example discussed previously was the premature release of preliminary data from analyses for TCDD at levels around 10 parts per trillion in beef fat which could be construed by some as sufficient evidence that 2,4,5-T and related pesticides should be banned (63).

5.4 CONFIRMATION OF RESIDUE IDENTITY

Residue analyses without confirmatory tests provide only qualitative information. It is not safe to assume that a response similar to that produced by a known pesticide means the pesticide is actually present. Many instances have been noted in which one material masquerades as another in any one test (e.g. PCB's, phthalate esters, etc.). The certainty of identification is increased when the behavior of the unknown and the standard is the same in a number of tests.

Subscribers to Pesticides Monitoring Journal received a June 1975 issue entitled Guidelines on Analytical Methodology for Pesticide Residue Monitoring (52). The following specific guidelines on confirmation of residue identity were listed:

> Residues reported should be confirmed by tests such as TLC, element specific GC, p-value determinations, derivatization, ultraviolet photolysis, etc., in addition to EC-GC.

PCB's or other suspected complex interfering substances must be separated and confirmed.

Combinations of confirmatory tests that measure the same physical property parameters as tests that measure the same parameters as the initial analysis, although they may help to support the identification, are not the best means of doing so. If sufficient material is available, excellent identifications can be made by infrared spectrometry, particularly with the use of microcell techniques or Attenuated Total Reflectance.

Mass spectrometry (MS) or combined GC-MS is recommended for identifying or confirming identity of important residues not adequately identified by other techniques.

The methods used for confirming residue identity should always be described in the report of residue results.

Although some laboratories may not have time to confirm every residue tentatively identified by GC, confirmatory analyses should be conducted at intervals such as one in every five samples when the same residues are apparently present throughout the group. When insufficient sample is available, confirmatory analyses may be conducted on a pool of several cleaned up sample extracts.

5.5 STATISTICAL EVALUATION OF RESULTS

The Federal Working Group on Pest Management also differentiates between accuracy and precision of pesticide residue analyses (52). Accuracy involves statistical measurements that relate to the differences between the test results and the true result when the latter is known or assumed, and may be expressed as the mean error or relative error. Precision involves statistical measurements that relate to the variation among test results themselves -- i.e., the scatter or dispersion of a series of test results without assumption of any prior information as to the true result. Precision may be expressed in terms of the variance, standard deviation, relative standard deviation, range, etc. Values from single or duplicate injections of extracts from duplicate samples are more meaningful than values from multiple injections from single samples. These should be differentiated in evaluating differences among groups of data.

As noted in Section 3.1.1, pesticide residue methods are often subjected to collaborative studies through the Association of Official Analytical Chemists (AOAC). These studies evaluate specificity, repeatability, and reproducibility of independent analyses for various samples. Repeatability is a measure of how well an analyst can expect to agree with

himself from day to day, whereas reproducibility is how well analyses in one laboratory are likely to agree with results from other laboratories. The Statistical Manual of the AOAC presents excellent information on formulating and statistically analyzing collaborative studies (71).

6. CONCLUSION

The regulation of pesticides involves a complex maze of rules implemented by various government agencies in their everchanging interpretation of laws enacted and amended by the U.S. Congress to control the use of such chemicals. Two basic elements in these laws are that all pesticide products must be registered and that tolerances must be set for safe residue limits of all pesticides used in food or feed crops. Requirements for residue data in support of these tolerances are discussed in Section 3. Monitoring studies are conducted by groups within several government agencies to assure that excessive residues are not present in foods or accumulating in the environment, as discussed in Section 4. The importance of careful interpretation of residue data is discussed in Section 5 of this chapter.

Concern about the significance of monitoring data was expressed at a 1973 hearing on EPA studies of specific chemicals in estuarine and freshwater environments. At that time the agency's Hazardous Materials Advisory Committee was told that virtually all measurements of DDT in the environment were suspect due to interferences in the analyses (72). Early data did not distinguish between DDT and residues of PCB's used extensively in transformer fluids, etc. (48, 52).

Furthermore, phthalate esters used widely as plasticizers accompany DDT through virtually all clean-up procedures according to D. G. Crosby of the University of California (49). Crosby also reported that interferences have been a major factor in chemical analyses for arsenic residues, and for mercury and phenoxy herbicides such as 2,4-D and 2,4,5-T.

Responsibilities in the use and misuse of scientific data were discussed during a symposium of the American Association for the Advancement of Science (AAAS) at their national meeting in New York in 1975. It was concluded that responsibility for proper reporting of data lies with individual scientists, scientific societies, and publishers. One of the speakers, Dr. Richard W. Roberts, director of the National Bureau of Standards, estimated that at least half of the data reported in scientific literature are unusable, often because too little information has been provided for independent evaluations (73). Dr. Mary L. Good, a director of the American Chemical Society, cited four areas in need of responsible attention: determination of permissible levels of potentially dangerous materials in the biosphere, lack of information on error limits and credibility of published data, overmassage or excessive manipulation of raw data by computer techniques, and evaluation and use of computerized data banks. Also, care must be taken to

delineate between those parts of reports that are factual and can be repeated by other workers and those reflecting interpretation of the data (74).

Dr. Bernard L. Oser entitled his presentation Exaggerated Conclusions Based on Inadequate Data (75). He defined scientific data as observations and findings generally expressed in numerical or descriptive terms and stated that, even when correctly reported, "data" are not necessarily equatable with "facts". Implicit in the term "facts" are the accuracy and reproducibility of findings and the competence and integrity of those responsible for the design, execution, and interpretation of the studies. Data are often statistically manipulated or "staticulated", such as by use of average values without expressing the range or distribution around the mean. Scientists may also draw false or misleading conclusions from their own data or from that of others. This may take the form of overestimating the importance of uncorroborated findings, or as one writer expressed it, extrapolation of unproven speculations. Thus, problems arise from misuse of scientific data as well as from use of unscientific data.

Emphasis in this chapter has been on the care needed in conducting analyses for pesticide residues at sub-part-per-million

levels in a variety of substrates, of the need for adequate reporting of such residue data, and of pitfalls in interpretation of data at levels below the validated sensitivity of the method. More specificity is needed rather than "picogram" measurements as often pushed by the scientific community. Premature or unwise interpretation of data can lead to precipitous action by regulatory agencies who have to respond to public pressures from individuals or groups of persons. Unfortunately, most pressure comes from lawyers and politicians who do not comprehend the limitations of pesticide residue analyses, particularly when the identity of the residues "found" has not been adequately confirmed.

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*(No.) CRF is Title (No.) of the Code of Federal Regulations, (No.) FR is Volume (No.) of the Federal Register.