Questions On The Safety Of The Pesticide Maleic Hydrazide Used On Potatoes And Other Crops Have Not Been Answered B-133192

Environmental Protection Agency
Food and Drug Administration
Department of Health, Education, and Welfare

BY THE COMPTROLLER GENERAL OF THE UNITED STATES

COMPTROLLER GENERAL OF THE UNITED STATES
WASHINGTON, D.C. 20548

B-133192

The Honorable Julia Butler Hansen
House of Representatives

Dear Mrs. Hansen:

This is our report on questions on the safety of the pesticide maleic hydrazide used on potatoes and other crops.

There is not a consensus among researchers as to the safety of maleic hydrazide. Some researchers have concluded that it is safe, while others have concluded that it may pose a health risk to exposed populations. We are therefore recommending that additional testing and research be performed and that foods treated with maleic hydrazide be periodically tested to insure that maleic hydrazide residues do not exceed approved levels.

We made our review pursuant to your request of July 13, 1973, and subsequent discussion with your office. We are returning separately the correspondence forwarded with your request.

We are sending copies of this report to the Senate and House Committees on Government Operations and Appropriations.

Sincerely yours,

Elmer B. Staats

Comptroller General
of the United States

Contents

ABBREVIATIONS

DEA	diethanolamine
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug and Cosmetic Act
FIFRA	Federal Insecticide, Fungicide and Rodenticide Act
GAO	General Accounting Office
HEW	Department of Health, Education, and Welfare
MH	maleic hydrazide
ppm	parts per million

COMPTROLLER GENERAL'S REPORT TO THE HONORABLE JULIA BUTLER HANSEN HOUSE OF REPRESENTATIVES

QUESTIONS ON THE SAFETY OF THE PESTICIDE MALEIC HYDRAZIDE USED ON POTATOES AND OTHER CROPS HAVE NOT BEEN ANSWERED

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D I G E S T

WHY THE REVIEW WAS MADE

The Congresswoman requested GAO to provide information on the Federal Government's procedures for testing pesticides, specifically, maleic hydrazide. Some researchers have stated that this pesticide, used on potatoes and other crops, may present a health risk.

FINDINGS AND CONCLUSIONS

The maleic hydrazide formulation registered for use on potatoes and onions contains diethanolamine. It is possible that both diethanolamine and maleic hydrazide may metabolize (change by chemical process) in the plant into compounds that may pose a health risk to consumers. An Environmental Protection Agency (EPA) official advised GAO that work done to date has not completely identified maleic hydrazide or diethanolamine metabolites. (See pp. 11 to 14.)

Maleic hydrazide is used on (1) potatoes and onions to inhibit their sprouting after harvest, (2) tobacco to prevent unwanted shoots, and (3) grass, trees, shrubs, and weeds to retard their growth. It is marketed as a salt to increase its solubility and make it easier to apply. (See pp. 1 to 4.)

Assessing the health risk of pesticide residues is particularly important when a pesticide such as maleic hydrazide is involved because of its use on such widely-used consumables as potatoes and tobacco.

However, there is not a consensus among researchers as to the safety of this pesticide. Some have concluded that maleic hydrazide is safe; others have concluded that it may pose a health risk to consumers. (See pp. 8 to 10.)

EPA's opinion that maleic hydrazide is safe for human consumption appears to be based primarily on early studies indicating that sodium maleic hydrazide which is no longer marketed was not toxic to dogs and rats over 1- and 2-year feeding programs. (See pp. 16 and 17.)

Legal authority for regulating the use and marketing of pesticides is in the Federal Insecticide, Fungicide, and Rodenticide Act. On December 2, 1970, administration of this law was transferred from the Department of Agriculture to EPA.

EPA relies primarily on test data submitted by the registrant (such as the manufacturer) to show that a pesticide is safe. EPA performs little additional testing.

The Food and Drug Administration (FDA) under the provisions of the Federal Food, Drug and Cosmetic Act is responsible for regulating foods containing pesticides.

After a pesticide is registered and tolerances established, it is FDA's responsibility to insure that pesticide residues on food do not exceed approved levels.

FDA's major efforts are directed primarily to a multipesticide screening test. This does not detect maleic hydrazide residues.

An FDA official told GAO that FDA records contain no evidence that foods ever were tested for maleic hydrazide residues even though this pesticide has been used for over 20 years.

Such tests should be conducted. (See pp. 18, 19, and 20.)

There is no pesticide residue tolerance set on tobacco because it is not a food and therefore, does not come under the provisions of the Federal Food, Drug and Cosmetic Act. (See pp. 14 and 15.)

RECOMMENDATIONS

The Administrator, EPA, should determine, through additional testing and research, whether maleic hydrazide will adversely affect human health or the environment. (See p. 20.)

The Secretary, Department of Health, Education, and Welfare (HEW), should through the Commissioner, FDA, periodically test potatoes, potato products, and onions to make sure that established maleic hydrazide residue tolerances are not being exceeded.

When residue tolerances are exceeded, action should be taken to remove these products from the market. (See p. 20.)

AGENCY ACTIONS AND UNRESOLVED ISSUES

EPA believes that studies submitted in conjunction with maleic hydrazide registration are valid and have adequately demonstrated the safety of maleic hydrazide usage. EPA also believes that evidence is not sufficiently compelling to warrant commitment of EPA's limited research resources to review maleic hydrazide at present. (See pp. 20 and 21.)

GAO recognizes that conclusive evidence supporting the adverse effects of maleic hydrazide is not available. However, the questions raised in several research papers about the potential health risk of exposing individuals to maleic hydrazide indicate that such risk has not been evaluated sufficiently. (See pp. 21 and 22.)

For example, additional data is needed to determine if:

--Food containing translocated maleic hydrazide (maleic hydrazide applied to the foliage from where it is transferred throughout the plant) has adverse effects on reproduction as was noted in a study published in Germany in 1958. (See p. 11.)

--Maleic hydrazide is a mutagen (a

chemical which causes changes in inherited characteristics) in animals. (See pp. 15 and 16.)

Also, data on maleic hydrazide and diethanolamine metabolites is insufficient to determine whether they present health risks. These and other unresolved questions are discussed in greater detail on pages 10 through 16.

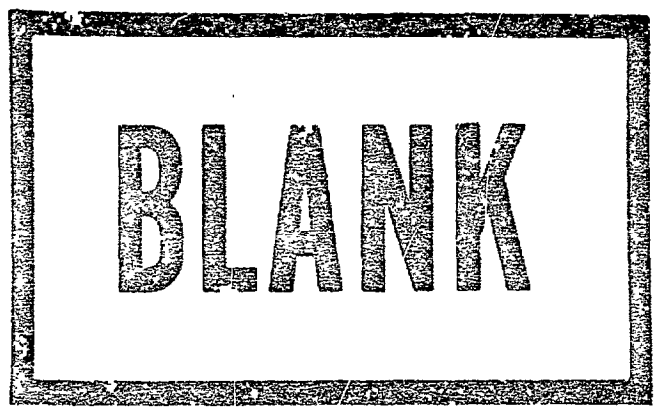
The foregoing emphasizes the need for additional research effort. EPA should require additional research on a registered pesticide when serious, unanswered questions of safety arise rather than wait until definitive adverse data is developed.

EPA can do research in-house or require the registrants to provide the data. (See pp. 21 and 22.)

FDA believes that it must concentrate its pesticide monitoring resources on a multiresidue test that will detect pesticides that pose a potentially serious threat to public health. But this test will not detect maleic hydrazide residues.

FDA will seriously consider including maleic hydrazide in its monitoring program if requested to do so by EPA.

GAO recognizes FDA's need to concentrate its monitoring activities on those pesticides presenting the greatest hazard. However, this should not preclude the periodic testing of other pesticides such as maleic hydrazide. Foods containing maleic hydrazide apparently never have been tested for maleic hydrazide residues even though maleic hydrazide has been used for over 20 years. (See p. 22.)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CHAPTER 1

INTRODUCTION

At the request of Representative Julia Butler Hansen, we obtained information on the Federal Government's procedures for testing pesticides, specifically, maleic hydrazide (MH). The request stemmed from a letter and news article submitted by a constituent indicating that MH, which is used on potatoes, may have cancer-causing properties.

CHARACTERISTICS AND USES OF MH

MH (also referred to as MH acid) is a growth regulator and herbicide used on (1) potatoes and onions to inhibit their sprouting after harvest, (2) tobacco to prevent unwanted shoots, and (3) grass, trees, shrubs, and weeds to retard their growth. It is applied to a plant's foliage where it is absorbed and translocated (transferred) throughout the plant. MH is applied to the potato plant 4 to 6 weeks before harvest and translocates to the potato itself where it remains after harvesting.

MH is relatively insoluble in water. Consequently, it is marketed as a salt formulation which increases its solubility and makes it easier to apply. The effectiveness of a formulation varies with the type of plant to which it is applied. For example, a leading MH manufacturer's representative told us that, in his opinion, a diethanolamine (DEA) salt formulation is more effective than a sodium salt formulation in inhibiting the sprouting of potatoes, whereas a potassium salt formulation is the most effective control of unwanted shoots on tobacco plants.

An MH manufacturer's representative and an official of the Department of Agriculture advised us that MH is used primarily on tobacco. The official estimated that 90 percent of the U.S. tobacco crop is treated with MH. The representative stated that MH usage on tobacco is divided about equally between the DEA and potassium formulations. He said that the second major use of MH is on potatoes and that this use is increasing because it is an insurance factor for farmers, permitting them to retain harvested potatoes

longer without fear of loss due to sprouting. He added that other growth regulators are more expensive to use because they require special fumigating equipment. Both the manufacturer's representative and the official said that other uses of MH are minor.

AUTHORITY FOR REGULATING PESTICIDES

Basic legal authority for regulating pesticides such as MH is in (1) the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) of 1947 (7 U.S.C. 135), as amended by the Federal Environmental Pesticide Control Act (FEPCA) of 1972 (7 U.S.C. 136), and (2) the Federal Food, Drug and Cosmetic Act (FFDCA) of 1938, as amended (21 U.S.C. 301). Authority for administering FIFRA was transferred from Agriculture along with the responsible organizational elements to the Environmental Protection Agency (EPA) on December 2, 1970, pursuant to Reorganization Plan No. 3 of 1970 which established EPA.

Under FIFRA, EPA registers a pesticide when the registrant provides evidence that the pesticide is safe and effective and the label contains adequate directions for use and safety precautions to protect human health and the environment. Registration is valid for 5 years and may be renewed. EPA is also required to continuously review registered pesticides to determine if they are safe and effective in light of developing scientific data.

If a pesticide remains in or on a treated food, FFDCA requires that a tolerance (the maximum pesticide residue concentration allowed in food) be established for that pesticide. The registration division in EPA's Office of Pesticide Programs establishes all tolerances for pesticide residues remaining in food either under section 408 (pesticide chemicals in or on raw agricultural commodities) or section 409 (food additives) of FFDCA. A pesticide is classified as a food additive if it is applied to processed foods or if the concentration of the pesticide increases as the raw agricultural commodity is processed. Before EPA's existence, tolerances were granted by the Food and Drug Administration (FDA) of the Department of Health, Education, and Welfare (HEW).

FFDCA generally requires that any food additives, which are not incidental additives, be declared by name on the label. FFDCA

also requires that when chemical preservatives are added, their presence must be declared on the label. Foods containing pesticides applied before harvest, however, are not required to have the pesticides' presence shown on the label. If the pesticides are applied after harvesting, only the shipping container is required to bear a label declaring the pesticides' presence.

MH REGISTRATION

MH was originally registered as sodium and DEA salt formulations in 1952 and as a potassium salt formulation in 1969. The approved registration of the sodium salt formulation was for use on potatoes and onions to inhibit sprouting. The registrant allowed the registration of the sodium salt formulation to lapse in 1967 because it was less effective than the other formulations. The approved registration of the DEA formulation was originally for controlling grass and weeds; the registration was revised in 1954, 1958, and 1959 to include use on tobacco, potatoes, and onions, respectively. The potassium formulation was registered only for use on tobacco. Presently, there are 13 companies that have registrations for MH and/or DEA and potassium salt formulations of MH.

MH RESIDUE TOLERANCES

Potatoes and onions

Because MH residues remain in potatoes and onions, pesticide tolerances are required by law. In 1953 FDA established a temporary tolerance of 10 parts per million (ppm) for MH residues in or on potatoes. Four years later a tolerance petition submitted by the original registrant was withdrawn because the petitioner could not demonstrate that MH was required in the production of potatoes and onions--the basic criterion for allowing residues to remain in food.

In 1959 an amendment to FIFRA allowed MH to meet the less stringent criterion of "useful" rather than "required." In 1960, pesticide residue tolerances of 50 ppm for potatoes and 15 ppm for onions were established under section 408 of FFDCA. These tolerance levels were based on test data submitted by the

registrant showing probable residue concentrations after treatment.

Potato chips

Concurrent with the approval of the pesticide residue tolerances, FDA established a food additive tolerance of 160 ppm for potato chips under section 409. To prevent premature sprouting, potatoes must normally be stored at a low temperature. During low temperature storage, however, the potato's starch content turns to sugar. This sugar turns an unappetizing black when the chip is fried. Treatment with MH allows higher temperature storage and the avoidance of sugar buildup.

As was the case with the pesticide residue tolerances for potatoes and onions, the food additive tolerance of 160 ppm for MH residues in potato chips was based primarily on data submitted by the registrant.

These formal tolerances and the temporary tolerance that preceded them were only for MH, not for a particular salt of MH, such as the DEA or potassium salts. An EPA official advised us that compounds such as DEA are considered inert and are exempted from residue tolerances if applied to a crop before it emerges from the soil. The official said that such compounds were exempted because residues remaining become insignificant due to the long interval between application and harvest.

Tobacco

FFDCA, the basic authority for setting and enforcing tolerances, applies only to food, food components, and chewing gum; pesticide residue tolerances are not required for nonfood consumables, such as tobacco.

SCOPE OF REVIEW

We reviewed the procedures for testing pesticides, specifically, maleic hydrazide. We made our review primarily at EPA and FDA headquarters in the Washington, D.C., area. We reviewed legislation, documents, reports, records, and files and held discussions with responsible officials. We discussed the review

with EPA, FDA, and Agriculture officials and considered their views in preparing this report. Also, we used the services of a pharmacology expert to assist us in our work.

CHAPTER 2

EXTENT OF TESTING AND RESEARCH ON MH

In registering pesticides and in establishing residue tolerances, EPA relies on test data submitted by the registrants. According to EPA officials, EPA lacks the necessary facilities to do this testing. The research on the safety of MH is not conclusive; some researchers have concluded that MH is safe while others have concluded that it may not be safe. Also, FDA has not tested food products treated with MH to determine whether they contain residues that exceed tolerance levels.

SAFETY TESTING

The primary purpose of the pesticide regulation program authorized by FIFRA is to protect the public from injury and to avoid subjecting the public to the dangers of experimentation. EPA evaluates the hazards associated with a pesticide's use to insure that only those that can be handled and used safely are registered. Hazards that are evaluated include the pesticide's degree of toxicity (poison) and whether it may be carcinogenic (causing cancer), mutagenic (causing permanent genetic changes), or teratogenic (causing birth defects). EPA also evaluates whether a pesticide could (1) affect reproduction, (2) make another pesticide hazardous, or (3) combine with other chemicals to create a compound more hazardous than any of the resultant compound's original components. Because different formulations of the same pesticide behave differently, one formulation could be safe while another could be toxic.

To minimize adverse effects on man, the registrant generally tests the pesticide on laboratory animals to determine whether it is hazardous. In 1969 a Commission (commonly known as the Mrak Commission) established by the Secretary of HEW to study pesticides and their relationship to environmental health, summarized what it believed to be minimum criteria for evaluating carcinogenic hazards:

> "(1) Food additives and contaminants should only be permitted if evidence is provided of no carcinogenic effect after adequate long-term

bioassays. The minimum requirements for such bioassays should include: Adequate numbers of animals of at least two species and both sexes with adequate positive and negative controls, subjected for their lifetime to the feeding of a suitable dose range of the test material, including doses considerably higher than would be present in food; (2) any substance which is shown conclusively to cause cancers in animals, when tested under these conditions, should be considered potentially carcinogenic for man and therefore not innocuous for human consumption. Tests which yield benign tumors will nevertheless raise the level of suspicion."

EPA is responsible for determining the safety and efficacy of pesticides before their registration. The Chief of EPA's Chemical and Biological Investigations Branch told us that the burden of proof in showing that a pesticide is safe is the registrant's responsibility and, consequently, EPA relies primarily on test data submitted by the registrant. He added that EPA does little preregistration testing because it lacks the facilities.

The Assistant Chief of EPA's Chemical and Biological Investigations Branch stated that EPA tests samples of pesticides collected from the channels of trade for safety and efficacy. He said these tests usually include a 1- or 2-week observation of the test animal after one dose of a pesticide. This test would demonstrate immediate toxicity of the pesticide but does not adequately determine the effects of long-term exposure, such as cancer and birth defects.

This official told us that EPA has never tested MH on anything but fish and it has done so only twice; MH was used in one test and the potassium formulation of MH was used in the other. He explained that the fish were placed in water containing 100 ppm of MH for 96 hours; no biological effects were noted in either case. Another official said EPA does not usually conduct tests after a pesticide is registered to support the safety of a tolerance because the burden of proof is on the registrant and EPA lacks the necessary facilities.

RESEARCH ON THE SAFETY OF MH IS NOT CONCLUSIVE

In 1963 the President's Science Advisory Committee issued a report on pesticides which recommended that the review of pesticide use be continued and, where reasonable doubt of safety is found, the pesticide's use be restricted or its registration canceled. MH research was performed at independent laboratories, universities, hospitals, and governmental research facilities by a variety of researchers in a number of countries. All but three of the studies were published in professional periodicals. We were provided copies of the reports by EPA from its files and by officials of other agencies that we interviewed.

The results of MH research have raised several questions about the safety of MH. Some independent researchers have concluded that MH is safe. Their reports concluded:

--Sodium MH was nontoxic (1955).[1]

--Sodium MH was safe (1957).[2]

--MH acid did not cause tumors (1969).[3]

--MH and DEA-MH did not increase tumor formation (1973).[4]

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[1]B. L. Oser, Maleic Hydrazide (1, 2 - dehydropyridazine 3, 6 dione), Unpublished Report by Food Research Laboratories, Inc., (1955).

[2]J. M. Barnes, et al., "The Non-Toxicity of Maleic Hydrazide for Mammalian Tissues," Nature, 180 (July 1957), 62-64.

[3]J. R. M. Innes, R. R. Bates and Others, "Bioassay of Pesticides and Industrial Chemicals for Tumorigenicity in Mice: A Preliminary Note," Journal of the National Cancer Institute, 42 (1969), 1101-1114.

[4]Brian Hunter, et al., "The Administration of Maleic Hydrazide and Its Diethanolamine Salt to Rats," Toxicology, 1 (1973), 301-307.

Other researchers have raised several hazardous possibilities. Their reports concluded:

-MH acid is carcinogenic (1965, 1968).[1, 2]

--MH (unknown formulation) causes the breakage of chromosomes in mice (1969);[3] such breakage could change inherited characteristics.

--MH may break down into a known tumor-causing compound, hydrazine, in plants (1967).[4]

--MH residues in potatoes disturbed the level of fertility of rats (1958).[5]

--MH is toxic to and retards the growth of certain amphibians (1951).[6]

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[1]F. Dickens and H. E. Jones, "Further Studies on the Carcinogenic Action of Certain Lactones and Related Substances in the Rat and Mouse," British Journal of Cancer, 19 (June 1965), 392-403.

[2]Samuel S. Epstein, et al , "Hepatocarcinogenicity of the Herbicide Maleic Hydrazide Following Parenteral Administration to Infant Swiss Mice," International Journal of Cancer, 3 (1968), 325-335.

[3]R. K. Das and C. K. Manna, "Effect of Maleic Hydrazide on the Chromosome of Mice Bone Marrow Cells," Proceedings of the 56th Indian Science Congress (1969), III, 453-454.

[4]P. K. Biswas, Oscar Hall and B. D Mayberry, "Metabolism of Maleic Hydrazide in Tea, Camellia sinensis," Physiologia Plantarum, 20 (1967), 119-824.

[5]Otto Fis hnich, Christoph Patzold and Clare Schiller, "Wachstums regulatoren im Kartoffelbau," European Potato Journal, 1 (March 1958), 25-30.

[6]V. A. Geulach and others, "The Effect of Maleic Hydrazide on the Embryonic and Larval Growth of Three Amphibians, Biological Bulletin, 101 (Dec. 1951), 285-288.

--The DEA component of DEA-MH affected reproduction and was lethal to dogs and rats (1955).[1]

EPA officials advised us that they did not believe that the two studies which concluded that MH is carcinogenic were relevant because the exposure to MH was by injection under the skin rather than by eating, the manner in which humans would be exposed. They also said that the study published in 1973, which was also an injection study and which concluded that MH and DEA-MH did not increase tumor formation, was more relevant because (1) the number of tested animals was much larger than in one of the previous studies and (2) the study was conducted with rats which are more resistant to tumor formation than mice, used in the other study.

UNRESOLVED QUESTIONS ON THE SAFETY OF MH

Impurities in MH formulations

The DEA formulation of MH which is used on potatoes and onions contains a small amount of a chemical impurity known as hydrazine. The Mrak Commission's report noted that hydrazine causes tumors.

The 1968 report[2] noted a hydrazine impurity in the MH formulation which could have caused the increased incidence of tumors in test animals. A hydrazine impurity might not have been a factor in the 1957 report[3] which concluded that MH did not cause tumors, because these researchers used specially purified MH.

EPA officials said at least a portion of the hydrazine impurity in the DEA formulation of MH could be absorbed into a potato or onion plant but research has not been done on what happens to hydrazine after it is absorbed into a plant. Thus it is not known what compounds may be created by the chemical reaction of hydrazine in the plant system or whether they are safe or harmful to those who eat treated potatoes or onions.

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[1] 1955 report; see p. 8.

[2] 1968 report; see p. 9.

[3] 1957 report; see p. 8.

Metabolites of MH

Another area EPA and the registrant have not explored is the possibility that, in a plant, MH may metabolize (change chemically) into hydrazine. On the basis of experiments using MH-treated tea plants, a research team in a report published in 1967[1] stated that hydrazine may be a metabolite of MH.

An EPA chemist stated that this study is inadequate because the researchers did not actually identify the metabolites and there is insufficient evidence to conclude that hydrazine is a metabolite of MH. An EPA plant physiologist stated that the odds are at least even that the tentative conclusions of the study would be confirmed if the test was done in accordance with good scientific methods. EPA toxicology officials said if MH changes into hydrazine in the tea plant it would probably change into hydrazine in other plants as well as in animals. An EPA chemist advised us that research on MH is incomplete and the question as to whether hydrazine is a metabolite of MH in plants has not been resolved.

A 1958 study[2] discussed the effects on animals which were fed potatoes harvested from plants sprayed with MH. It concluded:

> "Long-term feeding trials showed that if rats were maintained on a diet including tubers [potatoes] from plants sprayed with maleic hydrazide disturbances in the level of fertility occurred. No such effect was noted where the diet included tubers treated with maleic hydrazide after lifting [harvesting]."

This implies that translocated MH--MH applied to a plant's foliage before harvesting and subsequently transferred to the potato--disturbs fertility, at least in rats. EPA toxicology officials said the results of this test are suspect because (1) too few animals were tested, (2) the researchers apparently used the first generation litters in their test data (variations in first litters are very common), and (3) there is no data on how much MH or its metabolites test animals consumed.

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[1]1967 report; see p. 9.

[2]1958 report; see p. 9.

Although the study raised the question of whether maleic hydrazide caused disturbances in the level of fertility in rats, EPA did not require that a more thorough test be performed to resolve the question. A translated abstract of a 1962 Russian study[1] in EPA's files indicated that potatoes containing a normal amount of translocated MH were not toxic to dogs. The Library of Congress translated the same abstract. Its translation did not indicate whether the dogs were fed potatoes containing translocated MH or which formulation of MH was used to treat the potatoes. Also, this study did not address possible effects of MH on reproduction.

With regard to the toxic effects which were observed by feeding rats potatoes which contain translocated MH, our consultant advised us that:

> "* * *Hydrazides are commonly highly toxic substances and the strange non-toxicity of maleic hydrazide in itself is an oddity. Any chemical modification of the compound during metabolism or translocation could easily produce a very dangerous substance. * * * extensive toxicity feeding tests should be conducted with potatoes which have been exposed to maleic hydrazide under realistic conditions, to answer this question."

The DEA formulation of MH

The DEA formulation of MH was registered for use on potatoes and onions in 1958 and 1959, respectively. The registrant provided data indicating that the assay technique would detect DEA residues when DEA alone is applied to potatoes or onions. The registrant did not provide data, however, on whether the technique would detect DEA residues when DEA-MH--the marketed formulation--is applied to potatoes or onions.

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[1]K. V. Mukhorina, "The Action of Maleic Acid Hydrazide Used in Protecting Potato Fields from Weeds on Animal Organisms," Gigiena i. Toksikol Novykh Pestisidov i. Klinika Otravleni Dokl. 90 (962), English abstract presented in A. W. Mitlehner, Summary of Toxicology on Maleic Hydrazide, Bethany, Connecticut, (1971), 9-12.

EPA officials said the registrant's assay technique should detect residues of DEA when applied as DEA-MH. One official noted, however, that a test confirming whether the assay technique would detect residues of DEA applied as DEA-MH was apparently not performed. He stated that currently such tests are usually required.

EPA officials said DEA would be readily absorbed into a plant sprayed with DEA-MH and should be quickly metabolized in the plant. They also said that, to the best of their knowledge, there is no information available on what metabolites would be created.

It is not known if DEA or its metabolites can be safely ingested. One research group[1] found that rats fed 0.1 percent of DEA-MH in their diet had lower fertility rates and fewer of their offsprings survived the first 3 weeks of life. In another test the same research group fed 24 rats and 3 dogs 1.0 percent of DEA-MH in their diet; 96 percent of the rats died within 12 weeks, and all of the dogs died within 6 weeks. The researchers concluded that DEA-MH was toxic but attributed the toxicity to the DEA component.

The original registrant found that "studies indicate that diethanolamine itself is toxic, hence further experimental use of MH formulated as the diethanolamine salt is not suggested on edible crops." However, the registrant later requested and obtained from Agriculture a label change permitting the use of DEA-MH on potatoes and onions. A representative of the registrant advised us that this change was made because the registrant believed that the data indicated DEA residues were not present in the potato and eliminated the concern over using DEA-MH on food crops.

We noted, however, that when the same registrant applied for registration of DEA-MH in December 1960 for use on cranberries the petition was withdrawn because the assay techniques could not accurately determine residues of DEA-MH sprayed directly on the fruit.

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[1]1955 report, see p. 8.

After the petition for use of DEA-MH on cranberries was withdrawn, the registrant told FDA that the DEA formulation of MH was being dropped because of the registrant's inability to solve the analytical problems connected with determining DEA residues. The registrant further stated that a potassium salt of MH was being developed to replace DEA-MH. A representative of the registrant advised us that these comments were intended to apply only to DEA-MH use in cranberries.

As of September 1974, this registrant and others still produced and marketed DEA-MH. The potassium salt was developed and marketed but was registered only for use on tobacco.

MH residues in tobacco

FFDCA, the basic authority for setting and enforcing tolerances, applies only to residue tolerances for food, food components, and chewing gum. Thus a pesticide residue tolerance is not required for tobacco. According to some research studies, however, MH residues are in tobacco and tobacco smoke. In 1954, the original MH registrant reported that less than 20 ppm concentration of MH residues would remain in tobacco; 11 years later, Agriculture found residues which in some cases exceeded 500 ppm. An Agriculture official advised us that MH residues in tobacco average from 50 to 100 ppm. An Agriculture official estimated that 90 percent of the U.S. tobacco crop is treated with this pesticide. Usage on tobacco is equally divided between DEA and potassium formulations.

Agriculture has suggested that the National Cancer Institute investigate the carcinogenicity of DEA-MH residues in tobacco smoke. DEA-MH was included on the Institute's "List of Chemicals Suggested By Member Agencies of the Interagency Collaborative Group on Environmental Carcinogenesis" which was published in February 1974. An Institute official said that DEA-MH is not presently scheduled for review.

In response to our question of whether EPA sees a need to seek legislative authority to establish tolerances for pesticide residues on tobacco, EPA advised us in a letter dated September 4, 1974, that:

"Both the Department of Agriculture and the Department of Health, Education, and Welfare considered whether or not they had authority to establish a tolerance on tobacco on several occasions. The latest was in 1970 in which an EPA representative (HEW at the time) participated. They reached a well considered and deliberate opinion at that time to not seek legislative authority to set tolerances on pesticide residues on tobacco; such action, it was felt, would imply to the consumer that tobacco smoking was safe. Since tobacco itself is a carcinogen, such an implication would not be in the public interest."

Mutagenic properties of MH

The Mrak Commission's report (see p. 6) stated that exposure of individuals to mutagens may lead to cancer and to birth defects. However, the report expressed greater concern for the descendants of exposed individuals because changes caused by mutagens may lead to a wide range of abnormalities, mental retardation, physical and mental diseases, and all other inherited weaknesses and debilities to which man is susceptible. Since these effects may not be apparent until future generations, when the damage is already irreversible, the Commission recommended (1) prompt identification of chemical mutagens to which the population is exposed and (2) that pesticides with mutagenic properties be rigorously restricted or banned unless thorough and impartial study convincingly demonstrates that the benefit outweighs the risk.

The Commission's report listed MH as a mutagen in plants because of its chromosome-breaking property. An FDA official told us that the relevancy of such findings to man are questionable. He advised us, however, that there are two studies indicating that MH is mutagenic in the fruit fly. He said that properly conducted insect studies can be a satisfactory indicator of the mutagenic properties of a chemical (pesticide) in man, provided that proper testing procedures have been used. The official also stated that the long-term, MH-feeding studies performed to date would not satisfactorily address the question of whether MH is a mutagen in animals.

In commenting on this report in its letter of July 22, 1974, HEW stated:

> "* * *reports by Nasrat and Northrup indicate that maleic hydrazide possesses the potential to induce heritable gene mutations in the fruit fly (Drosophila melanogaster) (C. E. Nasrat, Nature, 207, 439, 1965: J. H. Northrup, J. General Physiology, 49, 971, 1963). Based on these observations, it appears that re-examination and additional testing of the properties of maleic hydrazide is indicated whereby recent advances in mutagenic testing would be utilized for such purposes."

Also, in August 1974 an FDA official suggested that MH be referred to the HEW Toxicology Coordinating Committee where existing literature could be reviewed and, if necessary, a testing program with proper procedures could be established to assess the safety of MH.

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EPA officials told us that the information available leads them to believe that MH residue tolerances established for potatoes, potato chips, and onions make MH safe to use. These officials stated that the results of properly conducted feeding studies involving an adequate number of animals should be given primary consideration in evaluating whether pesticides found in food cause tumors or other problems. EPA officials also stated that studies concerning possible adverse effects of DEA on animals are not pertinent because DEA, even when applied at 4.8 times the maximum recommended treatment, does not result in detectible residues in food.

Our consultant commented on the adequacy of studies made to determine the safety of MH. He advised us that:

> "* * *The possible health effects associated with the use of MH in foods have not been thoroughly studied according to up-to-date

standards. The opinions of FDA and EPA officials that MH is harmless appear to be based on two early studies indicating that MH is non-toxic when fed chronically to rats and for 1 year to dogs. However, doubts of the possible carcinogenicity or mutagenicity of MH have been raised by the results of several other investigators. More importantly, however, the diethanolamine salt of MH is being widely used on potatoes. Chronic feeding to rats and dogs indicate that this preparation is far from non-toxic at a 1.0% feeding concentration. Whether this is due to DEA itself or to DEA modification of MH toxicity, this observation demands prompt further investigation."

* * * * *

"* * *In addition DEA is a secondary amine which could react with nitrite, another food additive, or nitrate (present in well water) to form a carcinogenic alkylating agent. Chronic toxicity experiments definitely need to be done with the diethanolamine preparation."

COMPLIANCE TESTING

After a pesticide has been registered and its tolerances established, it is FDA's responsibility to insure that pesticide residues in food do not exceed approved tolerance levels. FDA, however, has not tested for MH residues in food.

FDA has two major programs to monitor the amount of pesticides in food products. One program, called the total diet study, is an information-gathering program and does not serve as a basis for regulatory action against specific products. Market baskets, each containing 117 food items, are collected 6 times a year by FDA inspectors in 4 areas of the United States. The items collected are based on a recommended diet for an adolescent male--

usually the biggest eater in the general population. The 117 food items are separated into 12 commodity groups and each composite group is blended into a homogeneous slurry--a uniform mixture of similar food commodities. The slurries are then analyzed for 60 to 80 various pesticide residues. The test does not detect MH.

The second FDA program is the pesticide surveillance program. The Deputy Associate Commissioner for Compliance informed us that this program, FDA's primary regulatory program for pesticide surveillance, is conducted on a continuing basis at all 17 FDA district offices. Samples of food commodities are collected at the grower or shipper level to provide effective regulatory action. Program objectives are:

"1. to determine the pesticide levels of individual food commodities on a geographical basis through the use of gathered intelligence on pesticide use and misuse and a statistically-based sampling plan;

2. to survey selected food commodities on a nationwide basis to obtain an overview of the pesticide residue levels in these foods;

3. to maintain surveillance of imported food commodities denying entry to those containing illegal amounts of pesticide residues; and,

4. to provide coverage of the excessive pesticide residue problem at a sampling level where compliance follow-up may be most effectively instituted and thus provide for maximum consumer protection."

An FDA official advised us that the program's current testing methods would not detect MH residues and that his review of FDA records indicated no evidence that tests had ever been performed to determine the extent of MH residues in treated food products. He explained that, normally, testing would not be performed for MH residues because FDA's efforts are directed to the multiple-pesticide screening test.

CHAPTER 3

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Accurately assessing the health risk of pesticide residues is particularly important when a pesticide such as MH is involved because of its use on such widely-used consumables as potatoes and tobacco. However, there is not a consensus among researchers as to the safety of MH.

From our review of the extent of testing and research on MH and after considering the views of the pharmacology expert we utilized, we believe that the possible health effects to individuals consuming MH in food have not been adequately studied by present-day standards. The EPA opinion that MH is safe for human consumption appears to be based primarily on early studies indicating that MH was not toxic to dogs and rats over 1- and 2-year feeding programs, respectively.

However, several researchers have raised the possibility that MH may cause cancer or mutations or may affect reproduction. In particular, the possibility that hazardous impurities in MH formulations or hazardous MH and/or DEA metabolites exist should be seriously considered.

The DEA salt of MH, which is widely used on potatoes, has proven to be far from nontoxic when fed to dogs and rats. The possible adverse effects may be due to DEA itself or to DEA modification of MH toxicity.

FFDCA authorizes the setting of tolerances in food products and the removal of those products from the market that exceed tolerance levels. MH has been marketed for over 20 years, yet FDA records show no evidence that tests have ever been performed to determine the extent of MH residues in food products. This situation takes on added significance in view of the fact that consumers cannot tell which potatoes are MH treated and which are not.

Potatoes, potato products, and onions should be periodically tested to determine whether established residue tolerance levels have been exceeded. Foods containing residues exceeding tolerance levels should be removed from the market.

RECOMMENDATIONS TO THE ADMINISTRATOR, EPA

We recommend that the Administrator, EPA, through additional testing and research, determine whether MH and its marketed formulations will adversely affect human health or the environment.

RECOMMENDATION TO THE SECRETARY, HEW

We recommend that the Secretary, HEW through the Commissioner FDA, periodically test potatoes, potato products, and onions to determine if established MH residue tolerances are being exceeded. When residue tolerances are exceeded, appropriate action should be taken to remove those products from the market.

AGENCY COMMENTS AND OUR EVALUATION

EPA

In commenting on our report (see app. I), EPA stated that:

> "The MH studies upon which the tolerances and registrations are based are valid. The fact that they are not current studies does not obviate their pertinence. These studies concern the actual residue for which the tolerance is set, i.e., MH."

* * * * *

> "No valid evidence, in the opinion of EPA scientists, has come to light since the earlier long-term exposure studies, which has demonstrated cause for alarm concerning MH tolerances. Later studies have various scientific weaknesses, such as improper routes of administration for determining human safety indices, improper documentation,

statistical inconclusiveness, or other scientific inadequacies. Registration and tolerance for present MH uses are based on soundly conceived, long-term, multigeneration reproduction tests, in which no evidence of teratological or carcinogenic effects was noted."

* * * * *

"The resources of this Agency for in-depth evaluations of registered chemicals are best directed to the most suspect compounds. Since, in our opinion, compelling evidence concerning possible adverse effects of presently registered MH products has not come to light, we intend to continue to proceed with our priority investigations of those chemicals for which such compelling evidence does exist."

We recognize that compelling evidence supporting the adverse effects of MH is not available. However, the questions raised in a number of research papers about the potential health risk of exposing individuals to MH indicated that such risk has not been sufficiently evaluated. Areas in which adequate data has not been provided include:

--The hydrazine impurity in DEA-MH and its fate in the plant.

--The products which occur when MH and DEA are metabolized in the plant and whether they can be safely ingested.

--Studies on translocated MH which would support or negate the reproduction problem noted in the 1958 study published in Germany.

--Studies on the long-term effects of DEA-MH. Long-term studies have been conducted only on the sodium salt of MH which is no longer marketed.

--Whether MH is a mutagen in animals.

The foregoing emphasizes the need for more research. EPA should require more research on a registered pesticide when serious, unanswered questions of safety arise rather than wait until definitive adverse data is developed.

With regard to EPA's statement that it does not have adequate personnel or facilities to do such research work, it is the registrants' responsibility to prove a pesticide is safe and effective. Thus, EPA can require registrants to furnish more data. Such action should not adversely affect EPA's limited resources.

HEW

In commenting on our recommendation (see app. II), HEW stated that, at the present time:

> "FDA cannot justify surveillance for MH because practical resource constraints, relative risks and the myriad of possible pesticide/food combinations force FDA to make a careful choice of the pesticides and foods which are included in its pesticide program."

HEW said FDA concentrates its pesticide-monitoring resources on a multiresidue test capable of detecting over 90 organochlorine and organophosphate pesticides, two classes of pesticides that pose a potentially serious threat to public health. HEW also stated that FDA will seriously consider including MH in the pesticide program if EPA concludes that the toxicity of MH is of such magnitude that periodic testing is needed to protect public health.

We recognize FDA's need to concentrate its monitoring activities on those pesticides presenting the greatest hazard, such as the organochlorines and organophosphates. However, this should not preclude the periodic testing of other pesticides such as MH, even though they are considered less important. Foods containing MH apparently have never been tested for MH residues even though MH has been used for over 20 years.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Mr. Henry Eschwege
Director, Resources and Economic
Development Division
U.S. General Accounting Office
Washington, DC 20548

September 4, 1974

Dear Mr. Eschwege:

In response to GAO's second draft report, "Unresolved Questions on the Safety of the Pesticide Maleic Hydrazide Used on Potatoes and Other Crops," this Agency is pleased to have the opportunity to make the following comments.

Let me first say that GAO's concern in the area of consumer protection is understandable and commendable. We most vigorously share your desire to protect the public welfare, and consider our responsibility in establishing residue tolerances a vital function toward this end. Our general procedures are based upon the understanding that there is no absolute safety level. Decisions to establish tolerances and to register products must be based upon informed judgement as to whether the preponderance of evidence justifies the registration or not. The risk involved in a pesticide's use must be weighed against the benefits derived from such use, and both human and environmental safety considerations are significant aspects of our decision-making process.

We have reviewed all of the evidence cited in the subject report regarding the safety of the current tolerances for maleic hydrazide (MH) on potatoes and onions. In the judgement of our scientific staff, there are adequate safety factors to support the present tolerances. Our findings are as follows:

1. The MH studies upon which the tolerances and registrations are based are valid. The fact that they are not current studies does not obviate their pertinence. These studies concern the actual residue for which the tolerance is set, i.e., MH.

2. Studies concerning diethanolamine (DEA) are not pertinent when considered in light of residue data on the DEA-MH products. DEA is exempted from a tolerance because the data show no detectable residue (less than 0.1 part per million) from an application rate even 4.8 times the maximum recommended treatment. The residues, if any, would probably resemble those resulting from ethylamine which is a normal biochemical metabolite in animals. Information pertaining to the effect of DEA on rats and dogs at high rates of administration would not affect the tolerance level, since the consumer is not exposed to DEA residues from the approved MH use patterns on potatoes and onions.

3. No evidence has been presented which indicates that hydrazine is a likely metabolite of MH in plants. If present, it would be likely that nitrates and/or nitrites would be produced from hydrazine. Even if hydrazine were formed, it is likely, because it is a powerful reducing agent, that such residues would be transitory only.

4. No valid evidence, in the opinion of EPA scientists, has come to light since the earlier long-term exposure studies, which has demonstrated cause for alarm concerning MH tolerances. Later studies have various scientific weaknesses, such as improper routes of administration for determining human safety indices, improper documentation, statistical inconclusiveness, or other scientific inadequacies. Registration and tolerance for present MH uses are based on soundly conceived, long-term, multigeneration reproduction tests, in which no evidence of teratological or carcinogenic effects was noted.

5. Both the Department of Agriculture and the Department of Health, Education and Welfare considered whether or not they had authority to establish a tolerance on tobacco on several occasions. The latest was in 1970 in which an EPA representative (HEW at the time) participated. They reached a well considered and deliberate opinion at that time to not seek legislative authority to set tolerances on pesticide residues on tobacco; such action, it was felt, would imply to the consumer that tobacco smoking was safe. Since tobacco itself is a carcinogen, such an implication would not be in the public interest.

6. The resources of this Agency for in-depth evaluations of registered chemicals are best directed to the most suspect compounds. Since, in our opinion, compelling evidence concerning possible adverse effects of presently registered MH products has not come to light, we intend to continue to proceed with our priority investigations of those chemicals for which such compelling evidence does exist.

In conclusion, scientific evaluation of all evidence available to date on MH by this Agency indicates that presently registered uses of this chemical continue to meet the statutory criteria for registration. Of course, there is a clear-cut procedure provided by FIFRA by which any interested party can petition the Agency to initiate registration cancellation, providing that such party is willing to take the burden of carrying its evidence forward in a cancellation hearing.

Again, I appreciate the opportunity to comment on your draft prior to its publication. I will of course be most happy to discuss the matter further if you so desire.

Sincerely yours,

Alvin L. Alm

Alvin L. Alm
Assistant Administrator
for Planning and Management

APPENDIX II

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
OFFICE OF THE SECRETARY
WASHINGTON, D.C. 20201

JUL 22 1974

Mr. Gregory J. Ahart
Director, Manpower and
Welfare Division
U.S. General Accounting Office
441 G. Street, N. W.
Washington, D. C. 20548

Dear Mr. Ahart:

The Secretary has asked that I respond to your request for our comments on your draft report entitled, "Unresolved Questions on the Safety of the Pesticide Maleic Hydrazide Used on Potatoes and Other Crops." We have enclosed (i) our response to your recommendation, (ii) some technical comments you may wish to consider before finalizing this report, (iii) excerpts of a monograph on the carcinogenicity of hydrazines and its derivatives, including Maleic Hydrazide and (iv) information concerning the Department of Health, Education, and Welfare Departmental Committee to Coordinate Toxicology for future reference.

We appreciate the opportunity to comment on this draft report.

Sincerely yours,

John D. Young
Assistant Secretary, Comptroller

3 Enclosures

DEPARTMENT COMMENTS ON THE GAO DRAFT REPORT TO CONGRESS ENTITLED "UNRESOLVED QUESTIONS ON THE SAFETY OF THE PESTICIDE MALEIC HYDRAZIDE USED ON POTATOES AND OTHER CROPS"

GAO RECOMMENDATION:

The Secretary, HEW, through the Commissioner, FDA, should initiate periodic tests to determine if established MH residue tolerances for potatoes, potato products, and onions are being exceeded. If such residue tolerances are exceeded, appropriate action should be taken to remove those products from the market.

DEPARTMENT COMMENT:

If the Environmental Protection Agency concludes that the toxicity of MH is of such magnitude that periodic testing of food for this compound is needed to protect public health, FDA will give serious consideration to including MH in the pesticide program. At the present time, FDA cannot justify surveillance for MH because practical resource constraints, relative risks, and the myriad of possible pesticide/food combinations force FDA to make a careful choice of the pesticides and foods which are included in its pesticide program.

To date, tolerances have been established for about 300 different pesticides which are used on a large number and variety of raw agricultural commodities. In addition, there are about 300 other pesticides registered by EPA, which though not permitted, may be present in food as a result of environmental contamination. FDA presently concentrates its pesticide monitoring resources on the organochlorine and organophosphate pesticide classes by employing a multiresidue method capable of detecting over 90 different such compounds in almost any type of food. These pesticides are highly toxic, and most are quite persistent in the environment and bioaccumulate in living organisms, including man. Furthermore, these classes of pesticides are used in a much wider variety of food commodities than maleic hydrazide. In short, the presence of organochlorine and organophosphate residues in the diet pose a potentially serious threat to public health.

The current approach does not preclude FDA from testing foods for other pesticides. If there is evidence or suspicion of pesticide misuse or special interest on the occurrence and levels of a certain residue, FDA can analyze foods for that particular pesticide. For

example, if EPA concludes that the toxicity of MH is a significant threat to public health, consideration would be given to including it in the FDA pesticide program.

Needless to say, if pesticide residue tolerances are exceeded, whether it be maleic hydrazide or some other pesticide, FDA would initiate regulatory action to remove the violative product from consumer channels. FDA would also consider initiating an injunction against the firm from further shipment of violative foods and invoking criminal penalties against the individuals which caused the violations.

DEPARTMENT COMMENTS ON THE GAO DRAFT REPORT TO CONGRESS ENTITLED "UNRESOLVED QUESTIONS ON THE SAFETY OF THE PESTICIDE MALEIC HYDRAZIDE USED ON POTATOES AND OTHER CROPS"

TECHNICAL COMMENTS:

[GAO note: Material has been deleted because of changes to the final report.]

It is recommended that the third paragraph of Page 22 be changed to reflect the new and improved understanding of mutagenic test systems developed since the publication of the Mrak Commission Report in 1969. While it is true that maleic hydrazide has been reported, as cited in the Mrak Commission Report, to induce chromosomal breaks and other chromosomal aberrations in a variety of plants, experts in chemical mutagenesis have become increasingly skeptical of the relevance of such observations to mammals and man. On the other hand, reports by Nasrat and Northrup indicate that maleic hydrazide possesses the potential to induce heritable gene mutations in the fruit fly (Drosophila melanogaster) (C. E. Nasrat, Nature, 207, 439, 1965: J. H. Northrup, J. General Physiology, 49, 971, 1963). Based on these observations, it appears that re-examination and additional testing of the properties of maleic hydrazide is indicated whereby recent advances in mutagenic testing would be utilized for such purposes.

APPENDIX III

PRINCIPAL OFFICIALS OF EPA AND HEW RESPONSIBLE FOR ACTIVITIES DISCUSSED IN THIS REPORT

	Tenure of office	
	From	To
EPA (note a)		
ADMINISTRATOR:		
Russell E. Train	Sept. 1973	Present
John R. Quarles, Jr. (acting)	Aug. 1973	Sept. 1973
Robert W. Fri (acting)	Apr. 1973	Aug. 1973
William D. Ruckelshaus	Dec. 1970	Apr. 1973
ASSISTANT ADMINISTRATOR FOR ENFORCEMENT AND GENERAL COUNSEL:		
Alan G. Kirk, II	Apr. 1973	Present
John R. Quarles, Jr.	Feb. 1971	Apr. 1973
ASSISTANT ADMINISTRATOR FOR WATER AND HAZARDOUS MATERIALS:		
John L. Agee (acting)	Apr. 1974	Present
ASSISTANT ADMINISTRATOR FOR HAZARDOUS MATERIALS CONTROL (note b):		
Charles L. Elkins (acting)	Oct. 1973	Apr. 1974
David D. Dominick	June 1971	Sept. 1973
ACTING COMMISSIONER OF PESTICIDES:		
Raymond E. Johnson	Dec. 1970	May 1971
DEPUTY ASSISTANT ADMINISTRATOR FOR PESTICIDES PROGRAMS:		
Dr. Henry J. Korp	Dec. 1972	Present
Dr. William M. Upholt	May 1971	Dec. 1972

	Tenure of office	
	From	To
HEW		
SECRETARY OF HEALTH, EDUCATION, AND WELFARE:		
Caspar W. Weinberger	Feb. 1973	Present
Frank C. Carlucci (acting)	Jan. 1973	Feb. 1973
Elliot L. Richardson	June 1970	Jan. 1973
Robert H. Finch	Jan. 1969	June 1970
Wilbur H. Cohen	Mar. 1968	Jan. 1969
John W. Gardner	Aug. 1965	Mar. 1968
ASSISTANT SECRETARY FOR HEALTH:		
Charles C. Edwards	Mar. 1973	Present
Richard L. Seggel (acting)	Dec. 1972	Mar. 1973
Merlin K. Duval, Jr.	July 1971	Dec. 1972
Roger O. Egeberg	July 1969	July 1971
Philip R. Lee	Nov. 1965	Feb. 1969
COMMISSIONER, FOOD AND DRUG ADMINISTRATION:		
Alexander M. Schmidt	July 1973	Present
Sherwin Gardner (acting)	Mar. 1973	July 1973
Charles C. Edwards	Feb. 1970	Mar. 1973
Herbert L. Ley, Jr.	July 1968	Dec. 1969
James L. Goodard	Jan. 1966	June 1968
Winton B. Ranking (acting)	Dec. 1965	Jan. 1966

[a]All pesticide functions in the Department of Agriculture were transferred under Reorganization Plan No. 3 of 1970 to EPA on December 2, 1970.

[b]Before July 24, 1973, the title of this position was Assistant Administrator for Categorical Programs.