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Report/Article Title Memorandum with attachments: From Alvin L. Young regarding Arsenical Herbicides discussion at Weed Science Society of America Twelfth Meeting, dated March 24, 1972

Journal/Book Title

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Descripton Notes Attachments include list of discussion participants and a draft of a paper titled, "Evaluation of Benefit vs. Potential Hazard in Environmental Toxicology" by Dr. Leon Golberg. See Item 4830 for related items

DEPARTMENT OF THE AIR FORCE
DEPARTMENT OF LIFE AND BEHAVIORAL SCIENCES
USAF ACADEMY, COLORADO 80840

REPLY TO
ATTN OF: DFLS

24 March 1972

SUBJECT: Arsenical Herbicides

TO: Gentlemen:

1. A discussion on the use of "ARSENICAL HERBICIDES" was held 10 February during the 1972 Weed Science Society of America Meetings in St. Louis, Missouri. Pertinent information was discussed on the current status of arsenical herbicides. Those in attendance felt:

a. a requirement exists for a new methodology for determination of arsenic in soil, water, and tissue.

b. a requirement exists for techniques to differentiate forms of arsenic existing in soil, water, and tissue following application of arsenical herbicides.

c. a requirement exists for bioassay data on arsenicals and for a composite list of susceptible and resistant plant species.

d. an effort should be made to keep interested scientists informed of each other's research progress. This could be done by preparing a distribution list of "SCIENTISTS INVOLVED IN ARSENICAL HERBICIDE RESEARCH."

2. A distribution list has been prepared and is enclosed. I will be happy to act as a coordinator for any of you who wish to use my services.

3. At the WSSA Meetings, Dr. Leon Golberg presented an excellent paper on "Evaluation of Benefit vs. Potential Hazard in Environmental Toxicology." I've enclosed a Xerox copy of a "draft" of his paper that was distributed by the WSSA News Release Team. Dr. Golberg's paper is to appear in WEED SCIENCE in the near future.

GOOD LUCK TO ALL OF YOU IN YOUR RESEARCH!!!!

Sincerely,

ALVIN L. YOUNG, Captain, USAF
Assistant Professor of Life Science

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DATE 15 FEB 72

OFFICER CAPT YOUNG

SUSPENSE DATE 17 FEB

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This will be a draft in preparation for a LS-280 standard.

EVALUATION OF BENEFIT VS POTENTIAL HAZARD IN ENVIRONMENTAL TOXICOLOGY *

DR. LEON GOLDBERG
SCIENTIFIC DIRECTOR
ALBANY MEDICAL COLLEGE OF UNION UNIVERSITY
ALBANY, N.Y.

* PRESENTED FEBRUARY 8, 1972
WEED SCIENCE [redacted] SOCIETY OF AMERICA
ST. LOUIS, MISSOURI

Future historians of Toxicology will view the decade from 1958 to 1968 as the last stage of a long period of steady progress under what one might call the 'Old Regime.' The year 1958 marked the passing of the (Food Additives Amendment) Food, of Drug (and Cosmetic) Act (1938) together with that famous — or infamous, depending on one's point of view — appendage ~~clause~~, the Delaney Clause ~~Amendment~~. As the requirements of the new Act threatened to swamp both government and industrial scientific resources, a variety of ingenious means were devised for achieving evaluation of safety within the limits of existing knowledge. The ensuing 10 years saw a tremendous proliferation of research and testing facilities, responding to the increasing demands and stringencies of government requirements. Basically, however, the approach to safety evaluation had not changed, even through the tragedy of the thalidomide disaster and the trauma of the Kefauver Hearings. The stakes had been raised, but the rules of the game remained essentially the same. At the time, one felt that change was in the air; in retrospect, however, it was a period of tranquility and relative stability that made possible unparalleled advances in the application of chemicals for the benefit of mankind.

Whether for better or for worse, a new era is upon us. It is a time of intensification of technical difficulties, occasioned by a de facto acceptance that safe levels do not exist for carcinogens, teratogens, nor mutagens (under any conditions of environmental exposure of man). It is a time of consideration of environmental impact of new products or processes, often on the basis of as yet untried methodology of assessment. It is a time of involvement of the public in the decision-making process, ~~up to now largely~~

~~in response to the public's self-appointed, self-proclaimed defenders and protectors~~. As Mr. Ruckelshaus himself has put it, "Sound policy making is impossible without a full exposition of all relevant thought."

With some notable exceptions, the academic scientist cringes at the prospect of such "full exposition of all relevant thought", through the medium of public hearings under conditions of adversary proceedings. It takes a special type of scientific mind to attune itself to the need for sweeping generalizations and confident dogmatic assertions, with none of the uncertainties, hesitations, admissions of gaps in our state of knowledge, nor other evidence of the scholar's misplaced humility — or, far worse, timidity. "Aggressiveness" is the quality most prized nowadays in the academic world. I recall the pithy comment by an Oxford Don, following a presentation by one such "aggressive" scientist: "He looks like a gangster; he talks like a gangster; the only question is, is he a gangster?" Nevertheless, that seems to be the paramount attribute needed for participation in sessions intended to subject scientific expertise and recommendations to what is significantly termed the "full glare of the public limelight."

Mr. Ruckelshaus has left us with little choice. "I fully understand" says he, "the scientist's desire to seek a quiet spot to contemplate and carefully work out rational solutions, as well as his distaste of the hysteria that sometimes accompanies public discussion of environmental issues. However, the demands of a free and open society will not permit such a luxury." So be it. In preparing

to meet these demands, however, it is prudent to consider what they entail.

The Anatomy of Decisions

Recent events in Environmental Toxicology have made it abundantly clear that we cannot continue much longer to muddle along, plunging from one crisis to another, without making a serious effort to put our house in order. New rules are needed as a basis for evaluating benefits as against potential hazards from environmental chemicals. The old ways of thinking were applicable to much simpler situations than those existing to-day. Benefit from the use of a chemical was often taken on trust. Potential hazard from prolonged exposure to low levels of pollutants was either not considered or assumed to be non-existent.

To-day's critical climate demands that a fresh start be made with every compound. All preconceived assumptions, whether of benefit or of safety-in-use should be discarded. The primary consideration must be a sincere concern for human welfare, and for the protection of man against the threats presented by man-made chemicals. It is a renaissance of Toxicology, an exhilarating feeling like the Spring After Silent Spring! But with the exhilaration must come a realization of the [redacted] responsibilities for providing our newfound colleagues, the public at large, with the depth of background understanding that is essential if they are to comprehend the issues at stake.

It is a curious quirk of human nature that, while few would claim to be experts in the field of mathematical astrophysics, virtually everyone feels impelled to pronounce judgments on the most complex

issues in nutrition and food science, on environmental hazards and the imminent destruction of life on earth. Attempts to oversimplify distort the facts; this is particularly true of attempts to measure benefits and risks on anything but a *relative* basis — benefits can only be assessed in comparison with available practical alternatives and risks on a scale of hazards to which we are already subject.

Scales of hazards

The extent to which Society tolerates maiming and destruction of human life is truly remarkable: 58,000 deaths annually on U.S. roads, more — many more — preventable deaths from lung cancer. Even the most trivial of life's occupations is not free from hazard; for instance the apparently simple act of swallowing food has produced hundreds of cases of bolus obstruction, not to mention many deaths of so-called "cafe" coronaries'.

There are other hazards that are more readily quantifiable. Background radiation is perhaps the one most accurately measured and found in the U.S. to range from 90 to 200 mrems/year, with a mean of 180 mrems/year. This hazard, to which all are exposed, and from which there is no escape is calculated to account in part for the 12,000 cases of leukemia annually in the U.S. alone, (about 1300 being attributed to background radiation) Also well accepted together with 56,000 other forms of cancer annually are the substantial increments of radiation exposure through medical and dental use of X-rays, though efforts are now being made to reduce these exposures. However, even the use of electronic equipment such as TV sets involves small but finite increments of radiation. If the

burning of fossil fuels is to be replaced by nuclear power, there is again a trade-off in terms of additional radiation exposure. Whatever elaborate and expensive precautions are taken to minimize this increment of hazard, a number of additional cancer deaths is entailed.

Out of the vast research effort on the biological consequences of radiation came the two concepts that underlie some of the most intractable problems connected with the regulation of the use of chemicals in the environment. The first was the idea that dose-response curves for radiation effects pass through the origin, ie. that there is no threshold below which radiation does not affect biological systems. The second derives directly from the first: namely, that radiation exposures — however small — are all additive; every little counts. These ideas have been applied to environmental chemicals that show evidence of carcinogenicity, mutagenicity and even teratogenicity in animals and lower organisms. Before proceeding to consider to what extent this 'hard-line' outlook is applicable to environmental chemicals, it should be stressed that even the field of radiation hazard has its rebels. In the induction of mammary tumors in the rat, Rossi and Kellerer claim to have demonstrated that at low levels of radiation exposure the action of radiation on more than one cell is involved, rendering it at least possible that there is a threshold.

A particularly striking example of unavoidable hazard is presented by food: pure, natural, wholesome 'organic' food. Applying no chemical fertilizer to grow it, using no chemical additive in its preparation for consumption, food may still contain at least 20 known

classes of cancer-inducing or promoting agents, the total number of recognized carcinogens probably being well in excess of 100. Expert testimony was presented at the recent Hearings on Diethylstilbestrol, to the effect that one molecule of a carcinogen is capable of causing cancer. The fact is that all mankind does not develop cancer, despite lifetime exposure to radiation, food and a host of external environmental carcinogenic influences.

Some explanations are in order as to why we consider that every molecule of carcinogen does not cause cancer. Most such compounds require to undergo biotransformation to the active proximate carcinogens. In many instances such reactions compete with other metabolic changes which render the compounds inactive as carcinogens. The balance between activation and inactivation depends on a host of factors (genetic, dietary, environmental) and is different for each carcinogen. Even when the electrophilic reactant, that constitutes the proximate carcinogen, is formed, there is a considerable chance that it will react with those tissue nucleophiles which will prevent it from exercising its carcinogenic potential. Anticarcinogenic action may involve competition between carcinogenic polycyclic aromatic hydrocarbons and structural analogs that are non-carcinogenic

From these considerations it follows that there is a scientific basis for believing that low exposures to carcinogens may be harmless. To demonstrate that this belief is well-founded is a problem that still confronts us. The practical difficulties are so great that many consider them unsurmountable. Weinberg has coined the term 'trans-scientific' for such issues, ie. incapable of scientific solution. I do not concur with this pessimistic outlook. For example,

the current WHO 5-Center (World Health Organization) study of DDT carcinogenesis is showing some satisfactory dose-response relationships and may even reveal the existence of a threshold. The NCTR at Pine Bluff is intended to pursue similar objectives. Above all, I am naive enough to emphasize that the final and unequivocal answer will come, not from megamouse experiments, nor the computer printouts of statisticians, but from sufficient understanding of the underlying mechanisms of hepatoma development that will permit us to establish a firm sequence of events in relation to the levels and other conditions of exposure needed to elicit those events.

The Pathology of Decisions

Even in our present state of knowledge we should be in a position to rank carcinogenic hazards as major or minor and to conclude that some minor risks have such low potential for harm that we need afford them only a low priority for consideration. An example may be found in the antithyroid agents that, under conditions of continuous exposure, can bring about thyroid hyperplasia and ultimately thyroid carcinoma in rats. Even an iodine-deficient diet causes thyroid cancer in the rat. These antithyroid agents are not necessarily the products of the chemical laboratory. They occur in plentiful variety in natural foods, encompassing the glucosinolates of *Brassicae*, the isothiocyanate mustard oils and the liberal endowment of alkyl disulfides and monosulfides in *Allium* species like onions and

garlic. Since these antithyroid compounds act at different points in the biosynthetic pathway of thyroid hormone, each compound potentiates the action of the others.

When, therefore, a thiourea derivative like ETU (ethylene thiourea) comes up to expectations and produces thyroid hyperplasia and thyroid carcinoma in the rat, the proper question to ask is not: how can we allow trace residues of a carcinogen on food crops; the proper question is: does a residue of a few ppb resulting from the use of bisdithiocarbamate fungicides on crops constitute a greater carcinogenic hazard than a slice of raw onion on your hamburger or an exotic whiff of garlic exhaled by your girl friend? In place of this logic we have the inexorable response that a carcinogen is a carcinogen is a carcinogen.

I could continue to multiply examples, but perhaps I have made my point: that in order to assess hazard realistically a substantial background of knowledge and understanding is essential. Facts cannot be taken simply at their face value, least of all data forthcoming from animal experiments. By every instance in which reason and judgment are abrogated the cause of progress is set back another step. Not only lawyers and environmentalists, but even some scientists display a passionate attachment for the Delaney Clause, which denies judgment and abolishes interpretation. The hoped-for extension of this Clause to cover mutagenesis, teratogenesis and other so-called "irreversible" long-term effects would be a further crushing blow to those of us who feel very strongly that the fruits of Technology merit a realistic scientific appraisal.

A further development that is now proposed gives any individual or organization believing that use of a particular pesticide raises a "substantial question of safety" the right to request action by the Administrator of EPA to bar further sales. Suspension, cancellation or denial of registration are involved. Federal pesticide hearings would be open to TV and radio coverage! If I were an adversary who under "appropriate safeguards to prevent undue disruption"

believed that my mission was to prevent the introduction of new chemicals and (to ensure) suspension of the use of old ones, my course of action would be clear. There never has been any chemical brought into any use — be it food additive, drug, pesticide etc — for which one cannot readily devise a long list of missing information, tear to shreds the existing evidence on the basis of real or contrived imperfections, and, without the exercise of very much ingenuity, concoct a case for imminent hazard to human health resulting from exposure to the chemical. This tactic was strikingly successful with NTA, so much so that it will take years of work to deal with all the red herrings (that were raised) and to establish NTA as safe and effective under its conditions of intended use, as we have known all along that it is. In the case of 2,4,5-T the questions raised about dioxins are in most cases valid and important, but it must be recognized that fresh issues (or variations on old themes) can continue to be put forward for the remainder of the century. By the use of such tactics any product can be driven off the market.

(X) One more example must suffice. According to the National Cancer Institute Report to the Surgeon-General "Chemicals must be considered potentially guilty unless and until proven innocent". Yet the same Report states that bioassays are incapable of detecting

carcinogenic effects below the 10% level and therefore negative data are grossly inadequate to give assurances of safety for man. Hence it is not only possible but justifiable to challenge the result of any test for carcinogenesis that gives negative results on the following grounds: ① too few species used ② wrong strains ③ too few strains ④ lack of true control ⑤ use of the control with strain for which it is not true ⑥ too few animals at the start ⑦ too few animals surviving at the finish ⑧ animals sacrificed too early ⑨ animals sacrificed too late ⑨ inadequate levels of administration ⑩ inadequate number of rates of administration.

I have hardly dared touch on the subjects of teratogenesis (in hen's egg!) and least of all on mutagenesis — for which all are busy testing, in the hope that something useful will emerge.

We must face the fact that many of our present procedures in Toxicology leave much to be desired. Government authority tries to fashion regulations for whose purposes tests are needed that are sharp precise scalpels — when what we have (in many instances) are rather blunt 19th century instruments, anachronisms that have survived to the present day. Toxicology is not entirely an exact science, though we try hard to make it so,

as far as possible. Despite the Delaney Clause, despite Mr. James Turner its fervent admirer and would-be begetter of Turner Clauses — despite all this, we cannot separate interpretation and judgment from the process of ascertaining the scientific facts because we are always working with fragmentary knowledge. This is not Physics or Chemistry. We almost never know the mechanism of what is happening; we dare not guess far beyond the conditions of our experiment in animals, yet we have to extrapolate to man in an effort to assess likely hazard.

The theme of this meeting is: A Positive Concern for Society. The question we must ask ~~[illegible]~~ is the following: does a genuine concern for Society and for the Environment mean a denial of the genuine benefits that chemicals have brought and are bringing to our way of life? Do we have to destroy this country's leading position in world technology in order to protect Society?

We have lived through many panics in recent years; the DDT—photosynthesis hoax, the greenhouse effect, the melting of polar ice caps, the Stringlass reduction in the fall in infant mortality due to atom

* U.S. GOVERNMENT PRINTING OFFICE: 1971-NIH 72 315/446 O46

bomb tests, and many other cries of doom. It would be more profitable, instead of becoming exercised over issues like this, if we tried to find room for genuine improvements:

cf. drug release, bioavailability, increasing sophistication, enzymes in detergents, encapsulation, and CONTROLLED RELEASE PESTICIDE-POLYMER COMBINATIONS.

We should welcome the new social character of science but not expect the impossible from it. The best protection we can give the Environment is to scrupulously fair to man too, which means weighing benefits and risks honestly and objectively.