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Report/Article Title Memorandum: From Sherrill G. Laney, Assistant for Occupational Safety and Health, USAF, regarding attached Minutes of the DHEW-CCREP Sponsored Meeting on 2,4,5 -T/Dioxins and 2,4-D of August 24 ,1979, dated October 11, 1979

Journal/Book Title

Year 1979

Month/Day

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Description Notes

DEPARTMENT OF THE AIR FORCE
WASHINGTON 20330



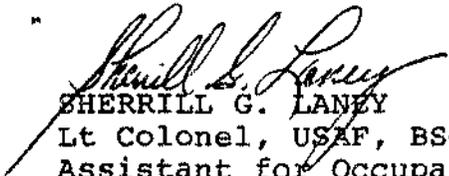
OFFICE OF THE ASSISTANT SECRETARY

October 11, 1979

MEMORANDUM FOR COLONEL MABSON, USAF/OEHL
COLONEL LATHROP, USAFSAM/EK
MAJOR BROWN, AF/SGES

SUBJECT: Minutes of the DHEW-CCREP Sponsored Meeting on
2,4,5-T/dioxins and 2,4-D

The attached was provided by Mr. Bob Berenson, Domestic Policy Staff, White House, on October 10, 1979. It appears HEW is considering the universe of Dioxins. It would also appear that HEW has plans to use Air Force data. It would likewise appear proper for the Air Force to be a party to these deliberations if possible. Suggest AF/SGES contact Dr. Shapiro and arrange for an invite to future 2,4,5-T/Dioxins and 2,4-D DHEW-CCREP meetings.


SHERRILL G. LANEY
Lt Colonel, USAF, BSC
Assistant for Occupational
Safety & Health, SAF/MIQ

Attachment

Minutes of the DHEW-CCERP Sponsored
Meeting on 2,4,5-T/dioxins and 2,4-D

Friday, August 24, 1979, 9:00 A.M.

Humphrey Building, Room 729-G, Washington, D. C.

Summary

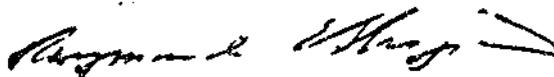
1. Mutagenicity studies will be initiated with these chemicals as well as male reproductive studies, as soon as experimental materials are obtained and space becomes available.
2. Chlorinated dibenzofurans have been found in Agent Orange. This expands the scope of impurity analyses and testing that may be required.
3. We need to further consider the possibility that the 2,4-D component of Agent Orange may be a contributing factor to some of the symptoms reported by exposed Vietnam veterans.
4. NIOSH studies in this area were described.
5. The DHEW should make every effort to obtain the Air Force protocol on their proposed study of a select cut of Air Force veterans and personnel exposed to Agent Orange in order to comment on it. In addition, we should ascertain whether DoD has the type of data that DHEW will need for their epidemiologic studies relative to these questions.
6. Analytical capabilities for the above chemicals and their impurities must be evaluated and expanded if necessary and possible in order to properly back up proposed studies.
7. Dr. Selikoff reported on his studies of workers at the Vertek 2,4,5-T plant in Jacksonville, Arkansas.
8. Dr. Selikoff then reviewed his exploratory discussions with the Bronx Veterans Administration Hospital with respect to a study of Vietnam veterans. This study appears feasible and has the support of the Veterans Administration in Washington.
9. It was agreed that there was a need for a uniform protocol in this area so that subsequent studies could be better cross compared. Dr. Lemen, NIOSH, will collate all thoughts that those may have on this area and send them to Dr. Rall.

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10. Dr. Suskind reported on his Department's contract study concerning the Monsanto Chemical Company's 2,4,5-T plant in Nitro, West Virginia.

11. All participants were asked by Dr. Rall to send the Executive Secretary, DHEW-CCERP, any pertinent references or articles that the entire group might wish to read.

Prepared by:



Raymond E. Shapiro, Ph.D.
Executive Secretary
DHEW Committee to Coordinate
Environmental and Related Programs

September 12, 1979

Address: National Institute of Environmental
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P. O. Box 12233
Research Triangle Park, NC 27709

Minutes of the DHEW-CCERP Sponsored
Meeting on 2,4,5-T/dioxins and 2,4-D

Friday, August 24, 1979, 9:00 A.M.

Humphrey Building, Room 729-G, Washington, D. C.

The meeting was chaired by Dr. Rall, Chairman of the DHEW-CCERP, and is a follow-up to the July 10, 1979 meeting on this same subject. The list of attendees and agenda are attached (attachments A and B). Pre-meeting mail outs are included in attachment C.

With respect to mutagenicity studies with these compounds, Dr. Zeiger concluded that more work is needed with these chemicals. There will be a teratogenicity report from Dr. Zeiger at a later date.

Dr. Moore told the group that NIEHS will do the male reproductive studies in rodents when space is available at NIEHS. The study initially will be a "gemisch" approach. If this is negative, one does not have to worry about the fact we used a mixture. If it is positive, one would need an additional study to separate out which chemical(s) produced which effect(s).

There then ensued a discussion of determining and validating the right animal model(s) to look for different effect(s) produced by those chemicals that would be relevant to what happens in man.

Dr. de Serres was not present to give an updated report on possible chromosome breakage studies. He has been asked to comment on this matter (attachment D).

Dr. Kimbrough then gave us further details on the presence of chlorinated dibenzofurans in Agent Orange. She gave us two references:

- (1) Rappe et al., Chemosphere, 7:431-438, 1978; and
- (2) Huckins et al., J.O.A.C., 61:32-37, 1978.

These papers reported the presence of furans and dioxin isomers in Agent Orange. The TCDD levels were low and the other dioxin isomers were not identified. It was felt that this work should be repeated. Dr. Kimbrough also mentioned that some dichlorodioxins had been found in 2,4-D. Dr. Kimbrough recommended that we might want to consider analyzing Agent Orange samples for furans and dioxins. Professor Selikoff noted that Al Young of the Air Force is supposed to have a complete set of samples of all Agent Orange purchases by the Air Force. One may not be able to say whether or not each purchase was used in Vietnam. We may be able to obtain this information about these samples. This would then broaden any analytical discussions in the future concerning these chemicals in this new contaminant area.

Dr. Moore then noted that with respect to the Seveso incident, no one has looked for or discussed furans. Professor Selikoff then made two observations: (1) if there were furans in Agent Orange, then we might want to look for furans in the liver tissue of Vietnam veterans possibly exposed to Agent Orange; analogous to the Yusho incident in Japan where furans were in the PCB-contaminated rice cooking oil; and were subsequently found in liver tissues of those exposed; and (2) we might want to look for furans in the 2,4,5-T that was used in Vietnam until 1969 when the program there was stopped (Drums of this pre-1969 produced material apparently are available.).

These discussions reenforced the decision to consider furans as a possible contaminant of Agent Orange.

The next item discussed was a survey of the literature with respect to neurological and muscular effects related to exposure to 2,4-D. Since our meeting of July 10, Dr. Falk sent Dr. Rall a memorandum on this subject (attachment E). Dr. Renate Kimbrough then reviewed this same subject area and she supplied a summary of her review (attachment F). The discussion of Dr. Kimbrough's review produced a consensus that we need to further consider the possibility that 2,4-D exposure may be a contributing factor to some of the symptoms reported by Vietnam veterans exposed to Agent Orange. The possibility and/or need of developing appropriate animal models to do this research was also discussed. Also discussed was how ongoing projects might have some add ons directed towards these questions. Dr. Robbins noted that NIOSH is looking at workers in a plant where only 2,4-D is being produced. It was felt that other worker groups having 2,4-D, alone, exposures should be identified if at all possible.

During the discussion of the above subject it was noted that up until 1969 almost everyone in the United States was exposed to 2,4,5-T as it was widely used on lawns and gardens. Since 1969, 2,4-D is the widely used pesticide for these purposes. Dr. Falk's memorandum of September 6 (attachment G) indicates the composition of the various herbicide mixtures used in Vietnam.

Dr. Halperin then summarized NIOSH's efforts in this area. This was based on his memorandum included in attachment C.

One of the questions posed at our last meeting was whether or not there were any verifiable cases of chloracne among Vietnam veterans as determined by the Veterans Administration. This question has been answered in the Science article of August 24, 1979 (attachment H).

There then ensued a discussion of the proposed Air Force protocol of an epidemiological study of possible effects in Air Force personnel and veterans exposed to Herbicide (Agent) Orange in Vietnam. Apparently only Dr. Suskind had read the protocol and his version dated back to last June. Various possible problems and defects with both the protocol and its execution were discussed. An integral part of this discussion revolved around the question as to whether or not DoD had good enough records with respect to the Vietnam veterans and their possible exposure to Agent Orange in terms of questions that DHEW might pose with respect to epidemiologic studies in this area. It was agreed to try and obtain a copy of the protocol for DHEW comment as well as explore the ability of DoD to supply the needed data to DHEW. Attachment I gives the Federal Register announcement concerning a closed meeting to discuss the proposed Air Force study. A call to Commander Halverson by Dr. Shapiro elicited the comment that everything will be released to the public when the study is completed. This point was not explored any further.

The next item discussed was the general analytical capabilities to do the necessary dioxin, and possibly furan, analyses needed to back up the ongoing and planned animal and epidemiologic studies. The consensus emerged that all known competent laboratories in these areas were "saturated" with work. Dr. Rall asked for a list of these laboratories and Dr. Liddle promised to provide such a list. It was estimated, with respect to dioxin analyses, that a laboratory could turn out 5-10 samples per week at an estimated cost of \$500-1,000 per sample. It was noted at this point that without the necessary analytical support, the research program would be slowed down accordingly. Various approaches to resolve this issue were discussed. It was agreed that this matter should be explored further.

Dr. Selikoff then reported on his studies at the Vertek 2,4,5-T plant in Jacksonville, Arkansas. They have examined 195 individuals, 80 of them current workers, while the remainder were employed previously. Immunological studies will be done on 20 individuals. Three-fourths of these 20 had no immunological changes; of the remaining five, four had B and T cell changes while two had immunoglobulin changes. In addition, 12 individuals associated with the manufacture of pentachlorophenol (PCP) in a different plant in Jacksonville, Arkansas, were also examined. PCP also contains dioxins impurities. Some chloracne was seen in this group as well as among the 2,4,5-T workers. Among the PCP plant workers, some skin cancers were seen. This may have resulted from creosote exposure of these workers. In addition, with respect to immunologic factors, five of seven showed B and T cell changes, while four of seven showed immunoglobulin changes. It should be noted that PCP contains the higher chlorinated dioxins than the TCDD that we usually consider. These results open up the possibility that these higher chlorinated dioxins may have a possible human toxicity that has not been considered heretofore.

Dr. Selikoff then reviewed his thoughts and efforts on designing and executing a study of Vietnam veterans. He has initiated discussions with the Bronx Veterans Administration Hospital in New York City. They have pledged their support to Dr. Selikoff for a study that he may design. The Veterans Administration in Washington has also indicated that they support and will assist in this proposed collaboration between their Bronx Veterans Administration Hospital and Dr. Selikoff. In June, 1979, 252 veterans coming to the admittance office could have been in Vietnam. Few of these were admitted; and three of them asked for herbicide (Agent Orange) evaluation. In a survey of 1,300 new patients, 350 of them served in Vietnam, 950 elsewhere. This latter group could serve as controls. They anticipate that in one year there will be 15,000 new patients, 4,000 having served in Vietnam and 11,000 elsewhere. The 4,000 Vietnam veterans will be divided into two groups: (1) those likely to have been exposed, and (2) those less likely to have been exposed. Therefore, there will be a total of three veteran's groups in this study; and each group should have an adequate population base to conduct a good study. This proposed design and its improvement as well as possible problems in subsequent data interpretation was then discussed; including the possibility of adding other hospitals in order to increase the numbers in each group. During this discussion, it was agreed that there appeared to be a need for a uniform protocol including a uniform medical examination, laboratory workup, case history, etc. in order that there may be good cross comparisons among the various future studies in this area. It also was agreed that this ad hoc Subcommittee could serve as the focal point to develop a clinical protocol for use by all. Following Dr. Robbins' suggestion, Dr. Lemen, NIOSH offered to collate all thoughts that those present may have on this subject area and send them to Dr. Rall.

Dr. Suskind then reported on his Department's contract study dealing with Monsanto Chemical Company's 2,4,5-T plant in Nitro, West Virginia. This plant produced 2,4,5-T from 1943 to 1968 or 1969. In March, 1949, there was a runaway reaction in a kettle containing an intermediate used in the manufacture of 2,4,5-T. There were 122 individuals involved. Chloracne was reported among those exposed as well as transient hepatotoxicity. In addition, there were neuromuscular and other systemic effects reported. As controls, there were 116 individuals who did not have any contact with the building in 1949 when the explosion took place or joined the work force after 1949.

Thirty-six individuals were examined in 1953-1954. In 1977, a retrospective study was started of 122 individuals associated with exposure from this 1949 explosion. As of December, 1978, 32 had died and 90 were alive. Death certificates were obtained for the 32 who had died. There is one nurse, who is still alive, who has chloracne. She had treated those who came to see her. The relative risk from all

deaths is: 0.69 observed, 0.46 expected. There were nine deaths resulting from malignancies; whereas 9.04 would be expected. A further breakdown gives: (1) 5 lung cancers observed, 3.02 expected; (2) 3 lymphomas, 0.88 expected; and (3) 1 other malignancy (I did not get the type.), 0.15 expected. The question was raised that the expected values seemed high*. Both groups, 122 exposed to the explosion and 116 not so exposed, all had chloracne in the past; as well as other symptoms. There were 15 coronary deaths among the 122 exposed to the explosion. Dr. Suskind remarked that appearance of skin disease is a definitive marker to indicate exposure. He felt that if an individual does not have skin disease then he is not in imminent hazard of disease. The subsequent discussion brought out the point that chloracne is a marker, only. Individuals have been seen in other exposure situations who have chloracne and upon examination, appear healthy.

The retrospective study involves three groups: (1) those acutely exposed (explosion), (2) those not acutely exposed; and (3) those never exposed; i.e., not involved with 2,4,5-T production but in the plant someplace. Each participant was given a 25 page, one hour interview as well as a medical and clinical workup. Skin biopsies were taken but these were for histopathological examination and not for dioxin analyses. Dr. Suskind noted that in those cases where chloracne persisted with time up until today, then other marked changes also were seen that were not usual for their age group.

There then ensued a discussion of measuring dioxins in tissue samples of heavily exposed individuals, including expressed sebum. In addition, we still don't know if it is stored in the fat of people. Dr. Moore remarked that to his knowledge there were only three human cases of measured dioxins in man. He also suggested the the best time to look for dioxin in man is right after a significant human exposure. If one cannot find dioxin at this point in time, then there is no need to analyze samples taken; e.g., five years after exposure. Various

*With respect to the expected lymphomas, Dr. Suskind wrote to Dr. Rall on August 31:

"When I discussed the mortality experience of workers to TCDD following the run-away reaction at Nitro, March 1949, you expressed some doubt about the accuracy of the expected mortality rate for lymphomas. I quoted the Monson program figure of expected frequency of 0.88. I have reviewed that information and my quotation was accurate. An additional interesting bit of information is that the expected rate for West Virginia is 0.83."

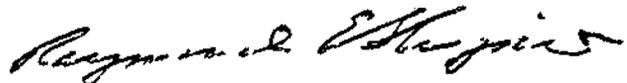
members mentioned having samples taken in the appropriate time frame that could be analyzed. While not taken up at this time, this brings us back to the analytical capabilities discussion which took place earlier in the meeting.

Dr. Rall then asked that those present send to Dr. Shapiro (National Institute of Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, NC 27709) any review articles, references and hard copy of any material that is germane to the questions being considered by this group.

Dr. Rall closed the meeting by remarking that the scheduling of a meeting should not be left entirely to his discretion. Anytime someone has something significant to report to the group, they should let him know so that he could schedule a meeting.

The meeting adjourned at 11:35 a.m.

Prepared by:



Raymond E. Shapiro, Ph.D.
Executive Secretary
DHEW Committee to Coordinate
Environmental and Related Programs

September 12, 1979

Address: National Institute of Environmental
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Attachments

Addendum

While not a part of this meeting, these minutes also serve as a means of sending you additional material in order that this package be as complete as possible. These include:

- (1) Note to the Secretary from the Office of the Assistant Secretary for Health, dated August 13, 1979, with respect to Agent Orange (attachment J)
- (2) Summary of Mutagenicity and Teratogenicity Literature (attachment K)
- (3) Activities with Respect to Mutagenicity Testing (attachment L)
- (4) List of Dioxin - Reviews from Dr. Suskind (attachment M)
- (5) Dr. de Serres' Reply to Attachment D (attachment N)

Attendees

Meeting on 2,4,5-T/dioxins and 2,4-D

Friday, August 24, 1979, 9:00 A.M.

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