Statement by
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The Dow Chemical Company

before the
Subcommittee on Energy, Natural Resources, and the Environment
of the
Senate Committee on Commerce
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Mr. Chairman,

I am Julius E. Johnson, Vice President and Director of Research and Development of The Dow Chemical Company, Midland, Michigan. I also served as a member of the Secretary's Commission on Pesticides and Their Relationship to Environmental Health, May 8, 1969 to November 7, 1969, Chairman - Emil M. Mrak. I have with me George Lynn - Director of Government Regulatory Relations of The Dow Chemical Company.

V. K. Rowe - Director of the Dow Toxicological Laboratory and Etcyl Blair - Director of Dow Agricultural Chemical Research - are also present to assist if necessary.

This statement is concerned with the herbicide 2,4,5-trichlorophenoxyacetic acid, which has often been referred to as 2,4,5-T and the chemical intermediate 2,4,5-trichlorophenol used in the manufacture of 2,4,5-T.

An announcement was issued October 29, 1969, by Dr. Lee Dubridge of the Office of Science and Technology which referred to birth defects observed in tests by the Bionetics

Laboratories using 2,4,5-T in various dosage ranges in mice and rats. This announcement preceded the final report of the Panel on Teratology to the Mrak Commission appointed by Secretary Finch which, since May 8, 1969, had been reviewing the effects of pesticides upon health and the quality of environment. At the time (October 29, 1969) members of the Mrak Commission had not seen the Bionetics report on teratology.

Following the announcement by the Office of Science and Technology, I became particularly concerned because Dow is a manufacturer of this herbicide. Consequently, I made a diligent effort to trace the source of samples used and learned that the 2,4,5-T sample came from the Diamond Alkali Company (which no longer makes 2,4,5-T). Moreover it was learned that 2,4,5-trichlorophenol also tested by the Bionetics Laboratory came from Coleman Mathison Bell who had obtained the sample from McKesson Robbins who in turn had procured it from The Dow Chemical Company. 2,4,5-trichlorophenol is used as an intermediate in the manufacture of 2,4,5-T. Hence, the quality of 2,4,5-T is related to the quality of its intermediate 2,4,5-trichlorophenol. The chemical process used by Dow for manufacture is as follows:

1,2,4,5-tetrachlorobenzene is hydrolyzed in a solution of methanol and sodium hydroxide in water to form sodium 2,4,5-trichlorophenate. This is in turn reacted with sodium monochloroacetate to form sodium 2,4,5-trichlorophenoxyacetate. The solution is acidified to precipitate and recover the 2,4,5-trichlorophenoxyacetic acid.

Since 1950 we have been keenly aware of the possibility of a highly toxic impurity being formed in 2,4,5-trichlorophenol as a side reaction under conditions of elevated

processing temperatures. The most sensitive toxic reaction observed in humans to this impurity was manifested by a condition known as chloracne, a skin disorder mostly prevalent on the face, neck and back. It is similar in appearance to severe acne often suffered by teenagers. We also knew that if the impurity was present in the 2,4,5-trichlorophenol it could be carried forward to the end product, 2,4,5-T. It is not formed during the manufacture of Dow 2,4,5-T from the 2,4,5-trichlorophenol, nor does it form on storage even at high temperatures. To avoid the impurity in 2,4,5-T it is necessary to keep it out of the 2,4,5-trichlorophenol.

Our early control test was a bioassay. This consists of applying a solution of the material to the inner surface of a rabbit's ear and observing for the typical skin response described in a paper published in 1941 by Dow scientists. I wish to insert in the record at this point the paper entitled "The Response of Rabbit Skin to Compounds Reported to have caused Acneform Dermatitis," by E. M. Adams, D. D. Irish, H. C. Spencer, and V. K. Rowe, published in Industrial Medicine, January 1941.

As early as 1944 we were monitoring the oils removed as impurities from the 2,4,5-trichlorophenol process by the rabbit ear test. It is in these waste oils that the impurities are concentrated.

In late 1964 some workmen developed chloracne and our bioassay program showed that the chloracne potential of the waste oil from 2,4,5-trichlorophenol process was building up to a danger point. This came about from operating changes made to improve production capacity. Exposure to this waste oil was the cause of the acne in the workmen. (This waste is routinely distroyed by incineration at high temperature.)

The plant was summarily shut down. Bioassays of Dow 2,4,5-trichlorophenol and 2,4,5-T being produced at this time were negative. We confirmed that the principal offending impurity was 2,3,7,8-tetrachlorodibenzo-p-dioxin. Technology had advanced by early 1965 to the point where we were able to develop a gas chromatographic method for the tetrachlorodibenzo-p-dioxin with a sensitivity of 1 ppm in 2,4,5-trichlorophenol and 2,4,5-T. I wish to insert in the record at this point a paper entitled "The Determination of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in 2,4,5-trichlorophenoxyacetic acid by Gas-Liquid Chromatography", by The Dow Chemical Company.

The 2,4,5-trichlorophenol plant was re-designed to ensure, insofar as possible, the production of a product containing a minimum of the tetrachlorodibenzo-p-dioxin. By so doing we were able to control the quality of Dow 2,4,5-T.

By May 1965 we had the technology to establish a manufacturing specification of no detectable 2,3,7,8-tetrachlorodibenzo-p-dioxin in 2,4,5-trichlorophenol and 2,4,5-T, using an analytical method sensitive to 1 ppm. While the plant was being rebuilt, we purchased 2,4,5-trichlorophenol and 2,4,5-T on the basis of this specification. The new plant came on stream in 1966 and since that time Dow 2,4,5-trichlorophenol and 2,4,5-T have met this specification, and most has contained less than 0.5 ppm of the 2,3,7,8-tetrachlorodibenzo-p-dioxin.

When the difficulty was encountered in 1964 we notified: The Michigan Department of Health, The Institute of Industrial Health, University of Michigan, and various other health oriented individuals in private medicine and industry.

In addition we called a meeting which was held in March 1965 to notify other manufacturers of 2,4,5-T of the difficulties encountered. We described to them the nature of the health hazard and shared our test procedures and analytical standards.

With this background--and firsthand experience--it was only natural that my associates and I would inquire about the identity of the sample used for the Bionetics tests. The 2,4,5-trichlorophenol tested was Dow material and the 2,4,5-T was a Diamond Alkali sample. It is important to emphasize that 2,4,5-trichlorophenol was reported to show no significant increase of anomalies by the Bionetics Laboratory, but the sample of 2,4,5-T did display a significant increase of anomalies. This prompted examining our past records of tests run in 1964. The records of analytical determinations of different supplies showed that samples of Diamond Alkali 2,4,5-T in fact did contain tetrachlorodibenzo-p-dioxin up to levels of 16 ppm. It should be emphasized at this point that Diamond Alkali has since stopped manufacturing 2,4,5-T.

I presented the essence of the above information to the Mrak Commission November 7, 1969 and showed pictures of the chloracne observed in humans and pictures illustrating the rabbit ear test. Moreover, I stated that the Bionetics test with 2,4,5-T may have been complicated by an impurity in the 2,4,5-T. I further emphasized the importance of tests using procedures recognized among experts as being valid and meaningful; the importance of representative materials which could be better obtained by consultation with industry; and the importance of knowledge of composition and purity of the materials tested. These points were made in the course of writing the final draft of recommendations of the Mrak Commission.

In view of our knowledge of the low mammalian toxicity of 2,4,5-T and the absence of reports of increased incidence of birth defects in cattle or sheep grazing rangelands sprayed with 2,4,5-T, we found it difficult to believe that any practical hazard existed from the registered uses of 2,4,5-T. It became important to gain additional evidence as soon as possible as to whether (1) the sample of 2,4,5-T tested by Bionetics was contaminated with 2,3,7,8-tetrachlorodibenzo-p-dioxin, (2) if so, could the tetrachlorodibenzo-p-dioxin itself be responsible, and (3) would 2,4,5-T of a specification made by Dow cause similar birth abnormalities.

I asked Dr. Dale Lindsay of FDA if a conference could be arranged with appropriate individuals in DHEW to discuss protocols for tests which would be acceptable to their scientists. Dr. Lindsay asked Dr. McLaughlin of FDA to arrange a meeting which was held November 25, 1969. Present at this meeting were:

Dr. I. Mitchell and Dr. R. Bates of the National Cancer Institute;

Dr. J. McLaughlin, FDA;

Dr. J. E. Johnson, Mr. D. D. McCollister, Dr. V. B. Robinson, and Mr. V. K. Rowe of Dow.

I requested that Dr. Mitchell identify the test procedure by which we could re-examine 2,4,5-T and the suspected contaminant. Dr. Mitchell replied that tests with Sprague-Dawley rats would be the best procedure for reconfirmation and further stated that, for the purpose, it would be superior to a test with mice. I offered to underwrite the cost of confirmatory experiments in the laboratories

of the National Institutes of Health, in the laboratories of a third party (independent of government or Dow) or in the Dow laboratories open to observation at any time by personnel of the Department of HEW. Dr. Mitchell stated that he would have confidence in the work if it were done in Dow laboratories. We agreed to repeat the Bionetics work with Sprague-Dawley rats using Dow 2,4,5-T of regular production grade. If this study yielded positive results the Bionetics results would be confirmed. If the results were negative it would be necessary to run further tests on graded levels of the contaminant and on refined 2,4,5-T. It was agreed that Dow would provide samples of 2,4,5-T and 2,3,7,8-tetrachlorodibenzo-p-dioxin to the National Institute of Environmental Health Science laboratories at Research Triangle, North Carolina. Moreover--Robinson and Rowe of Dow would visit the NIEHS laboratories in order to confer with them concerning the details of the test methods to be used.

On December 1, 1969 I met with Dr. DuBridge and Dr. Buckley of the OST to apprise them of the possibility of a contaminant in the sample tested by Bionetics and also the information known to Dow. At this meeting the same points were discussed as presented to the Mrak Commission. (see above) The plan for additional testing as discussed with Drs. McLaughlin, Bates and Mitchell of DHEW was also presented.

Dr. DuBridge stated that he would be interested in further information as it developed and was willing to consider new evidence when it was available. I promised to report the results of our work. Information has been supplied primarily through Dr. Burger of the OST.

On December 11, Dr. V. B. Robinson and V. K. Rowe met with Drs. Falk, Courtney and Gaylor at the Research Triangle and discussed with them the design of a teratological study to be conducted on Dow regular production 2,4,5-T. Agreement on the design of the experiment was easily achieved and was followed in our studies.

At this meeting Dr. Courtney of the NIEHS Laboratory provided a two gram sample of the 2,4,5-T used by the Bionetics Laboratory. This sample was examined at Dow with the following results:

1. Rabbit ear tests showed a positive reaction characteristic of the contaminant.

2. Analysis by gas liquid chromatography indicated the presence of 27± 8 ppm of 2,3,7,8-tetrachlorodibenzo-p-dioxin.

In late December Dr. Burger of the OST requested a review of the chemistry of 2,4,5-T production to be presented to Dr. Baldeschweiler, a consultant of the agency. The information for this report was organized by Dr. Blair of Dow and presented at a meeting with the OST on December 29, 1969 in Washington.

By January 12, 1970, we had made enough progress in the teratological study in rats with Dow production grade 2,4,5-T to make a report to Dr. Egeberg, Assistant Secretary for Health and Scientific Affairs, HEW. Copies were sent to other involved persons in DHEW and USDA. This report showed that the Dow 2,4,5-T of regular production grade did not cause birth defects as determined by gross examination of fetuses. The dosage levels used were selected in consultation with Drs. Falk, Courtney, and Gaylor of NIEHS.

Furthermore, we were able to report to Dr. Egeberg that a pilot study with pregnant rabbits fed the same 2,4,5-T had not caused birth defects. Dr. H. L. Richardson, pathologist, FDA, observed the results of both of these tests.

These preliminary observations were followed by the more time consuming microscopic examinations of the tissues and detailed skeletal examinations. This work confirmed the preliminary findings.

The final report of the study was presented before the Society of Toxicology in Atlanta, Georgia on March 17, 1970. I wish to insert into the record at this point an abstract of this report entitled "Teratogenic Study of 2,4,5-trichlorophenoxyacetic Acid in the Rat" by J. L. Emerson, D. J. Thompson, C. G. Gerbig and V. B. Robinson, The Dow Chemical Company.

In accordance with the plan discussed with the DHEW in December, as soon as the preliminary results of the 2,4,5-T study on rats indicated no fetal anomalies, we proceeded to conduct a teratology study in rats with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Dosages were used which bracketed the levels of the contaminant which were given inadvertently to the rats in the Bionetics study. The results of this experiment indicated that a high level of maternal and fetal toxicity was associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. Dr. H. L. Richardson of FDA and Dr. C. T. G. King, National Institute of Dental Research, NIH, participated in the observations made on these animals at necropsy at the Dow Laboratories in Midland.

We concluded that the presence of the tetrachlorodibenzo-p-dioxin in the sample tested in the Bionetics Laboratories could well have accounted for the observations reported

and attributed 2,4,5-T. At this point I wish to insert into the record an abstract of the report as presented to the Society of Toxicology, March 17, 1970, Atlanta, Georgia, entitled "Teratogenic Study of 2,3,7,8-Tetrachlorodibenzo-p-dioxin in the Rat" by G. L. Sparschu, F. L. Dunn and V. K. Rowe, The Dow Chemical Company.

The detailed results of these tests were also presented by Dow personnel to the scientists of FDA, NIH, NIEHS, in Washington on February 24, 1970.

In addition to our investigations with laboratory animals, we have also utilized the medical records of Dow employees accumulated throughout their Dow careers.

Our physicians have made an in-depth evaluation of the health of 130 male employees who have been exposed to 2,4,5-T in manufacturing operations for from six months to approximately twenty (20) years. From the medical data available, over fifty (50) clinical parameters were selected for statistical evaluation. The control population for this evaluation consisted of 4,600 other individuals for whom similar data were available.

After careful study of this information, it was the conclusion of our medical staff that there was no evidence that exposure to 2,4,5-T had resulted in adverse effects.

It is our belief that the adverse effects reported by the Bionetics Laboratories were the result of a contaminant (2,3,7,8-tetrachlorodibenzo-p-dioxin) and were not caused by 2,4,5-T.

Moreover it is our belief that 2,4,5-T produced under specifications requiring less than 1 part per million

of 2,3,7,8-tetrachlorodibenzo-p-dioxin present no practical hazard when used in accordance with good agricultural practices.

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Since the petition requesting a finite tolerance for 2,4,5-T residues on foods was a key point in the October 29th announcement by the OST, it is in order to describe its history and present status.

2,4,5-T and other similar phenoxy herbicides, are manufactured by several companies. Since these are not proprietary compounds, an Industry Task Force on Phenoxy Herbicide Tolerances was established by the National Agricultural Chemicals Association. The members of this Task Force were the major producers of phenoxy herbicides, including 2,4,5-T. The objective of this Task Force was to pool all of the information available among the various companies and to provide resources to generate additional information to meet present day requirements of the USDA and the FDA. The petition for negligible residue tolerances of 2,4,5-T was submitted by the Industry Task Force in December of 1967. In April of 1968, FDA responded to this petition stating that information was needed on metabolism together with more up-to-date residue data on certain food crops. The Task Force has since been gathering the additional data requested.

2,4,5-T was registered by USDA in an era when an FDA residue tolerance in food crops was not required if a showing could be made that no residue would result at harvest. On April 13, 1966, the Secretaries of Agriculture and Health, Education and Welfare implemented a change in policy which required the establishment of a formal finite residue tolerance at a negligible level in lieu of the no-residue registration procedure. 2,4,5-T was one of

scores of pesticides for which a negligible residue tolerance petition was required. The new policy also provided for extensions of registrations--until December 31, 1970--to provide time to gather additional data if needed in order to meet up-to-date requirements of FDA.

At the time of the October 29 announcement by the Office of Science and Technology, FDA was still awaiting the additional residue data in order to proceed with the processing with the petition. As the end of December approached it became apparent to the Industry Task Force that all of the residue data would not be ready in time for a decision before January 1, 1970; furthermore, the additional teratological studies designed to help evaluate the meaning of results of the Bionetics Laboratories would not be completed by January 1, 1970. It was understandable that FDA would be unwilling to grant a tolerance until more evidence was available; therefore, the Industry Task Force, according to the provisions afforded in the FDA Regulations, withdrew the petition without prejudice to future filing. At the same time the Task Force requested the USDA to continue the extension of the registrations of 2,4,5-T. This extension was requested by the Industry Task Force founded on the conviction that there was no imminent hazard from the continued use of 2,4,5-T. In response to this request the USDA has extended the registrations to January 1, 1971. The Industry Task Force will re-file the petition for tolerances in advance of this date.