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ROWE, V.K. 1980

Human
TCDD
Chlorzene
Kligman
Study

BEFORE THE
ENVIRONMENTAL PROTECTION AGENCY
OF THE UNITED STATES OF AMERICA

In Re:	)	FIFRA Docket
	)	Nos. 415, et al.
The Dow Chemical Company, et al.	)	

DIRECT TESTIMONY OF DR. V. K. ROWE

(Exhibit 865)

Date Served: October 30, 1980

Scheduled Appearance Date: November 13, 1980

TABLE OF CONTENTS

DIRECT TESTIMONY OF V. K. ROWE

I. QUALIFICATIONS.

My name is V. K. Rowe. I am currently a consultant to the Vice President for Health and Environmental Sciences at The Dow Chemical Company, having retired from full-time duties in 1979. After receiving my A.B. degree from Cornell College, I received my M.S. degree in biochemistry from the State University of Iowa in 1938. I also was awarded an Honorary Doctor of Science degree by Cornell College in 1971. I joined the Biochemical Research Laboratory at Dow in 1937 and have remained with the company since that time.

In 1954, I was named director of the Toxicological Research Section of the Biochemical Research Laboratory. In 1964, I became an Assistant Director of the Biochemical Research Laboratory. The department of Biochemical Research became the department of Chemical Biology Research in 1970 where upon I was made director of Toxicology Research and Industrial Hygiene for the department. One year later, in 1971, I became an Assistant Director of the Department. In 1973, I was designated as Director of Toxicological Affairs and Health and Environmental Research for the Dow Chemical Company, a position which I held until my retirement.

I am a Charter Member of the Society of Toxicology which was formed in 1961, and have served on its Council and

as its President during the year 1966-67. I have been a member of the American Industrial Hygiene Association since its beginning in 1939 and was a Director from 1956-1959. I served as President of the American Academy of Industrial Hygiene in 1973-74. I was a member of the National Academy of Science, National Research Council, Committee on Toxicology from 1964 to 1972 and, was liaison representative of the Society of Toxicology to the National Academy of Sciences, National Research Council.

I was an associate editor of the American Industrial Hygiene Journal from 1963-1964, and a member of the editorial board of the Journal of Toxicology and Applied Pharmacology for three years from 1967-1970. In addition, I have served as a member of committees sponsored by the Environmental Protection Agency, the Occupational Safety and Health Administration, and the National Cancer Institute.

In 1976, I received the Society of Toxicology Merit Award. The American Industrial Hygiene Association presented me with the Donald E. Cummings Memorial Award in 1979.

I have published over 75 scientific articles during my long career as a toxicologist and industrial hygienist. A copy of my curriculum vitae is submitted as Exhibit 865-c.v.

II. SUMMARY OF TESTIMONY.

My testimony sets forth the results of studies, including those performed on animals by Dow, and those performed for

Dow by an independent consultant, in which the chloracnegenic potential of 2,3,7,8-TCDD was tested. In order to put these studies in perspective, I have briefly described the circumstances leading up to the latter study, including in particular Dow's efforts to detect potential chloracnegenic problems by use of the rabbit ear bioassay.

III. DOW's EARLY EXPERIENCE WITH IDENTIFYING CHLORACNEGENS.

Dow began the manufacture of 2,4,5-T in 1950. Before marketing the herbicide, we conducted tests on animals which showed that there were no unusual hazards associated with the handling and use of commercial 2,4,5-T. Further toxicological testing, done on several animal species, during the early 1950's, produced comparable results for various 2,4,5-T derivatives. The results were published in 1954. (Ref.1).

In the course of this toxicity testing, we examined the chloracnegenic potential of 2,4,5-T. As discussed in greater detail in the testimonies of Drs. Reggiani and Crow, chloracne is a skin disease characterized by an eruption of blackheads in a highly distinctive pattern. Because earlier testing had indicated that the 2,4,5-trichlorophenol processes yielded chloracnegens, we were aware of the possibility that 2,4,5-T might also contain chloracnegenic compounds.

We tested the chloracnegenic potential of 2,4,5-T by the rabbit ear bioassay. This means of testing for chloracnegens was first described in an article which I co-authored

with three other Dow scientists in 1941. (Ref. 2). In that study, we applied five known human chloracnegens to the inner surface of the rabbit ear. In each case, we obtained a positive response, characterized by epithelial hyperplasia, thickening of the surface of the ear, enlargement of hair follicles, and in severe cases, heavy, crusty induration. Chemicals not suspected of being chloracnegens did not give a positive response when tested in the rabbit ear. For this reason we concluded that the rabbit ear bioassay could serve as a screen for chloracnegenic compounds.

In our premarket testing of 2,4,5-T, we found that our product did not produce chloracne by the rabbit ear test. This led us to conclude that 2,4,5-T (at least as manufactured by our process) was probably not a human chloracnegen, a fact that was borne out by our plant experiences.

IV. THE 1964 CHLORACNE OUTBREAK.

Despite our early success in preventing chloracne among our workers, in 1964, following changes in the reaction process, many of the workers in our 2,4,5-trichlorophenol plant (not the 2,4,5-T plant) developed chloracne. The plant was shut down immediately and the Michigan Department of Health, the Institute of Industrial Health, and others were notified of the problem. The rabbit ear bioassay was negative for the 2,4,5-trichlorophenol and 2,4,5-T then being manufactured, but was strongly positive for the 2,4,5-trichlorophenol manufacturing wastes.

In all, 49 workers developed chloracne as a result of these process changes. Careful medical surveillance of the workers in the trichlorophenol plant revealed no symptoms other than chloracne. Dow monitored these workers for many years and has published a report of their mortality experience discussed in detail in Dr. Cook's testimony.

Shortly after the 1964 chloracne outbreak, we were able to isolate the chemical impurity 2,3,7,8-TCDD as the probable cause of the chloracne. This confirmed previous work done by investigators in Germany. (Ref. 3).

V. RESEARCH SUBSEQUENT TO THE 1964 CHLORACNE OUTBREAK.

We were understandably concerned about the outbreak of chloracne at our plant, and took steps to prevent its recurrence. This included an intensive program to improve our analytical capabilities for TCDD. But until analytical capabilities could be improved, the rabbit ear bioassay remained our best monitoring device for TCDD. Consequently, we decided that it would be useful to have at least a rough idea of how the chloracne sensitivity of rabbits to TCDD compared with that of man. At this point, we knew that 0.2 µg was without effect on the rabbit ear; 0.5 µg caused a marginal effect; 1-2 µg usually caused a positive response; and 4-8 µg usually caused a severe response.

To help answer this question, I contacted Dr. Albert Kligman, Professor of Dermatology at the University of

Pennsylvania, who had participated in testing the safety of various chemicals and drugs in volunteers from a prison in Lewisburg, Pennsylvania. Dr. Kligman agreed to test the chloracnegenic potential of TCDD in humans under his existing program.

I took steps to assure that signed consent forms were obtained from each prisoner volunteering to participate in the study and also wrote a highly conservative protocol to be followed by Dr. Kligman in carrying out his experiment. (Exhibit 866).

According to my protocol, the initial dose was to be 0.2 µg, a dose which did not produce positive responses in the rabbit ear. Only when the results of that dose were evaluated was the next dose to be administered. Each new dose was to be approximately doubled, up to a dose of 8 µg. In addition, the protocol required that careful observations, including clinical monitoring, be carried out for each subject. I should point out that in 1965, when the protocol was written, no tests of the chronic effects of TCDD had been conducted.

The first set of tests, carried out in accordance with my protocol, was performed during late 1965 and early 1966. The results were described in a letter from Dr. Kligman dated May 11, 1966 and summarized in a longer report of June 22, 1966. Dr. Kligman reported that the subjects were divided into 6 separate groups of 10 each. The first group

was studied in two phases: initially, a single dose of 0.2 μg was administered; after a two week interval, the same total dose (0.2 μg) was administered to the same skin site, in two daily doses of 0.1 μg. In half the subjects, the dose was administered to the forehead, in the other half the dose was administered to the mid-back region. The application site was covered for 24 hours by a 2" gauze square.

One week after the single dose, and 3-4 days after the final daily dose, clinical tests were performed on each subject. These tests included CBC (hematology test), BUN and creatinine clearance (kidney function tests) and SGOT and alkaline phosphatase (liver function tests). At the end of each phase, the subjects were examined by an internist for signs of systemic illness. The skin was examined weekly for six weeks after the last dose.

Following the medical examination of the subjects in Group 1, the same procedure was repeated for Group 2, except the initial dose was 0.5 μg, followed by subsequent total dose of 0.5 μg administered in daily applications of 0.1 μg. Taking the initial and daily doses together, the total dose in Group 2 was 1.0 μg. The same procedure was used for all the remaining Groups at the dosage levels presented in Table 1.

TABLE 1

	Single dose	Dose Administered .1 µg/day	Total dose
Group 1	.2	.2	.4
Group 2	.5	.5	1.0
Group 3	1.0	1.0	2.0
Group 4	2.0	2.0	4.0
Group 5	4.0	4.0	8.0
Group 6	8.0	8.0	16.0

In his report, Dr. Kligman concluded that "there was not the slightest evidence of acne, either on the forehead or the back." Moreover, the results of the laboratory tests showed that each of the clinical parameters tested fell within the normal range, and "was not harmful to the subjects."

Dr. Kligman's experiments indicate that man is "far more resistant to acnegenic substances than the rabbit ear," but they provided no indication of the threshold dose level that would produce chloracne in humans. Accordingly, I indicated to Dr. Kligman that Dow would fund a continuation of his studies.

In January of 1968, I was surprised to receive a letter from Dr. Kligman reporting new results. Ten subjects were given 0.05 ml of a 1% TCDD preparation in alcohol chloroform every other day for one month. The solution was applied to one square inch of the back and covered by non-occlusive

gauze. At this dose, 8 of the 10 subjects developed chloracne lasting 4-7 months. Each week for six weeks, urinalysis, CBC, BUN, SGOT, alkaline phosphatase and creatinine clearance tests were performed. The results of all these tests were within the normal range and there was no evidence of toxicity or illness, other than the chloracne, among any of the subjects.

The results Dr. Kligman reported are relevant both for ascertaining the relative sensitivity of rabbits and man to the chloracnegenic effects of TCDD and, to a lesser extent, for determining the threshold dose that produces chloracne in man.

The total dose given by Dr. Kligman to the 10 prisoners in this experiment was around 7,500 µgs of TCDD. Much of the TCDD was in suspension rather than solution, a circumstance that is relatively common when solubility is limited. Although no description of the handling of the 50/50 chloroform alcohol suspension was provided, normal practice would have been to shake the liquid, and, therefore, all, or nearly all of, the dose would have been applied.

Unfortunately, Dr. Kligman's latter experiment does not permit the definition of a threshold exposure for the induction of chloracne by TCDD in man, as was my purpose in initiating the study. It does show, however, that the threshold dose for chloracne lies somewhere between 16 µg and 7500 µg and that even with this huge dose no clinical evidence of adverse systemic effects was detected.

Notwithstanding these limitations, I felt it necessary and appropriate to present the results of Dr. Kligman's experiments, because, as I understand it, the purpose of these hearings is to consider all of the available information on the possible health effects of 2,4,5-T silvex and TCDD.

V. K. Rowe

EXHIBITS

866 Kligman, A.M., Letters and data concerning the Chloracnegenic potential of TCDD in humans.

REFERENCES

1. Rowe, V.K. and Hymas, T.A., "Summary of Toxicological Information on 2,4-D and 2,4,5-T Type Herbicides and an Evaluation of the Hazards to Livestock Associated with Their Use," Am. J. Vet. Res., 622-629 (October, 1954).

2. Adams, E.M., et al., "The Response of Rabbit Skin to Compounds Reported to Have Caused Acneform Dermatitis," Indust. Med., 10: Ind. Hyg. Sec., 2 at 1-4 (1941).

3. Kimmig, J. and Schulz, K.H., "Occupational Chloracne Caused by Aromatic Cyclic Ethers," Dermatologica, 115 at 540-546 (1957).

CERTIFICATE OF SERVICE

I HEREBY CERTIFY that copies of the foregoing Direct Testimony (and Exhibit) of Dr. V. K. Rowe were hand delivered or mailed first class postage prepaid on October 30, 1980, to the persons on the attached list.

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