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UNITED STATES OF AMERICA

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BEFORE THE

ENVIRONMENTAL PROTECTION AGENCY

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In the Matter of the Hearing of::

2,4,5-T and SILVEX : Docket Nos. 415, et al

The Dow Chemical Company, et al :

----- X

(This volume contains pages 16875 through 17065)

Room 2409  
Environmental Protection Agency  
Headquarters  
401 M Street, Southwest  
Washington, D. C.

Thursday, November 13, 1980

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The hearing was convened pursuant to adjournment,  
at 9:00 a.m., before Administrative Law Judge Edward B.  
Finch, when were present the following:

ON BEHALF OF THE ENVIRONMENTAL PROTECTION AGENCY:

- DOROTHY PATTON, ESQ. Office of General Counsel
- KARL BAYER, ESQ. Office of General Counsel
- MICHAEL WINER, ESQ. Office of General Counsel
- ANDREW G. GORDON, ESQ. Office of General Counsel

T5/S1 -1 1 JUDGE FINCH: We will resume the hearing.

2 Mr. McConnell.

3 MR. McCONNELL: Good afternoon, Your Honor.

4 Our next witness is Mr. V. K. Rowe, Mr. Rowe  
5 is the former director of Toxicological Affairs and Health  
6 and Environmental Research at Dow. He retired from Dow  
7 in 1979, but he is still active as a consultant.

8 Mr. Rowe was a charter member of the Society  
9 of Toxicology, and is a past president of the Society.  
10 He has, in addition, served on advisory committees for  
11 EPA, for OSHA and with the National Cancer Institute.

12 Mr. Rowe.

13 Whereupon,

14 V. K. ROWE

15 was called as a witness and, having first been duly sworn,  
16 was examined and testified as follows:

17 JUDGE FINCH: Are there any additions or  
18 corrections to your statement?

19 THE WITNESS: Yes, I have one minor one, in  
20 the educational section there, my Master's Degree was  
21 awarded in 1938, instead of '37.

22 JUDGE FINCH: Well, we want to make that change  
23 then, where does it appear?

24 THE WITNESS: It's in my CV.

25 JUDGE FINCH: Oh, in the CV.

NEAL R GROSS

5 1 Q And would he be one of the people that may have  
2 informed you that the careful medical surveillance was  
3 being conducted?

4 A I suspect that that is the case, but I cannot  
5 be certain.

6 Q Do you remember what he told you, or what you  
7 were told by people in the meetings?

8 A Simply that these people were being followed on  
9 a periodic basis.

10 Q You were not informed as to the tests that were  
11 actually being conducted on these workers, were you?

12 A I can't testify to that on a personal basis, no.

13 Q Let's turn to the next section of your witness  
14 statement. On page 5, which is entitled "Research Sub-  
15 sequent to the 1964 Chloracne Outbreak".

16 A (Perusing documents.) Yes.

17 Q This section of your testimony discusses  
18 experiments conducted by a Dr. <sup>Albert</sup>~~Alfred~~ Kligman, which were  
19 initiated and funded by Dow Chemical Company, is that  
20 correct?

21 A That's right.

22 Q In these experiments varying doses of 2,3,7,8-  
23 TCDD were dermally applied to the forehead and back of  
24 human subjects incarcerated at a prison at Holmesburg,  
25 Pennsylvania, is that correct?

6  
1           A     The test procedures were as you describe,  
2 whether incarcerated is a proper word, I don't know, I  
3 presume it is.

4           Q     They were prisoners, is that correct?

5           A     That's my understanding.

6           Q     You state, at the beginning of the bottom of  
7 page 5 that you contacted Dr. Albert Kligman and then at  
8 the top of page 6 you state, "Dr. Kligman agreed to test  
9 the chloracnegenic potential, TCDD in humans, under his  
10 existing program", is that correct?

11          A     Yes.

12          Q     Would it be fair to say that you were the Dow  
13 representative who initiated contact with Dr. Kligman,  
14 and requested that he conduct experiments in which human  
15 subjects would be dermally exposed to TCDD?

16          A     Yes.

17          Q     Now, Dr. Kligman conducted two separate sets  
18 of tests in which he applied TCDD to the skin of these  
19 human subjects, is that correct?

20          A     You are talking about two different tests?

21          Q     Two different sets of experiments.

22          A     Well, there was one experiment to start with and  
23 then there was a subsequent experiment that he conducted,  
24 yes.

25          Q     Did you not design the protocol for the first

-17  
1 set of tests conducted by Dr. Kligman in which the re-  
2 searchers applied a range of doses of TCDD to the backs  
3 and the foreheads of 60 human subjects?

4 A Yes.

5 Q Was there a different protocol for the second  
6 series of tests which Dr. Kligman conducted?

7 A Well, not to my knowledge, that was his protocol.  
8 I did not know that this second experiment was to be done  
9 the way it was done.

10 Q On page 8 -- let's turn to page 8.

11 A (Perusing documents.) Yes.

12 Q In the second full paragraph on that page, near  
13 the bottom of that page, at the bottom of that paragraph,  
14 you state, "Accordingly, I indicated to Dr. Kligman that  
15 Dow would fund a continuation of his studies" and then you  
16 go on to say, "In January of 1968, I was surprised to  
17 receive a letter from Dr. Kligman reporting new results".

18 Could you explain to us what you mean by  
19 "surprised"?

20 A Yes. As much of the first protocol had yielded  
21 absolutely negative results, we did agree, at his request,  
22 to fund a continuation, but I assumed it would be following  
23 the same progression that I had outlined in the first  
24 instance. Unfortunately, that was never confirmed in  
25 writing. And the next I heard from it was that the results

18 1 that he reported to me.

2 Now, each of these steps takes a considerable  
3 period of time. If you will look at the protocol, because  
4 I was very concerned that we approach this very cautiously.  
5 And raise the dosage in increments so as not to exceed a  
6 level which would produce a threshold response.

7 The reason for that was that in our studies on  
8 animals we had determined that concentrations of chloracne-  
9 gens which produced an effect in humans, essentially always  
10 produced an effect in the animals.

11 And if the animal work was not positive, we  
12 never had a material that cause injury in humans.

13 Now, so what we wanted to do and what we felt  
14 we should do was to attempt to determine the relationship  
15 between the sensitivity of the rabbit's ear to that in  
16 humans. After we had identified the material had <sup>quantitative</sup> ~~quantitative~~  
17 -- it measured quantitatively, we determined that a certain  
18 dosage level was the minimum required to produce an effect  
19 on the rabbit's ears.

20 But our evidence from practical experience had  
21 indicated that the human was much more resistant, but we  
22 didn't know how much more resistant. And we were very  
23 concerned about what the margins of safety would be.

24 So, therefore, the purpose of this study was to  
25 incrementally increase the dosage, so that we would be able

-19 1 to find out what that figure was.

2 Q You indicated to Dr. Kligman that Dow would  
3 continue its funding of the studies, is that correct?

4 A That's right.

5 Q And yet you assumed -- you said that you assumed  
6 that he would continue to follow the protocol that you had  
7 given him, is that correct?

8 A Yes.

9 Q Between the time you received the results of  
10 Dr. Kligman's first series of tests, in May and June of  
11 1966; and the time that you received his letter in which  
12 he stated he had conducted a second set of tests, did you  
13 have no contact with Dr. Kligman concerning this second  
14 series of tests?

15 A I had none.

16 Q You mean you had said that Dow would continue to  
17 fund this study, and yet you did not bother to even con-  
18 tact Dr. Kligman to see what he was doing.

19 MR. McCONNELL: Your Honor, I think that question  
20 may be a little argumentative.

21 JUDGE FINCH: I think it is, too. He said he  
22 did not.

23 You can answer the question did you have any  
24 contact between the time you got the results?

25 THE WITNESS: If I did, I have no knowledge of

1 it. I don't believe I did,

2 BY MR. GORDON:

3 Q Does Dow normally fund studies and then not pay  
4 attention to what is being done with the money it grants?

5 A Well, it depends on what the situation is, this  
6 was a contract with the university and with a professional  
7 dermatologist who had conducted the first series of protocols,  
8 he knew what my philosophy, with respect to testing was.  
9 And it takes so much time between tests, that if you  
10 proceed according to the protocol, that I had designed,  
11 that I didn't feel it was necessary, and I didn't ask him  
12 about it.

13 As I said, it was a total surprise when the  
14 report came as it did.

15 Q Well, you say that Dow and yourself were con-  
16 cerned with the margins of safety, what was the highest  
17 dose level given -- applied to the skins of the prisoners  
18 in the first set of tests?

19 I believe you can find the answer to that on  
20 page 8, in Table 1.

21 A Yes, that's right, the total dose that was given  
22 was 16 microgram/kg -- per person.

23 Q What was the total dose given in the second set  
24 -- second series of tests that Dr. Kligman had conducted,  
25 in which Dow funded?

1 A 7500 micrograms,

2 Q So, Dr. Kligman went from 16 micrograms to

3 7500 micrograms, is that correct?

4 A . That's what he says he did.

5 Q So, he increased the dosage somewhere in the  
6 neighborhood of 5,000 orders of magnitude?

7 A No, it would be closer to 40 to 50, 45 perhaps,  
8 something like that, wouldn't it?

9 Excuse me, I will make a calculation.

10 JUDGE FINCH: That's all right, wait until you  
11 get another question, unless you want him to.

12 BY MR. GORDON:

13 Q Would you work that out for us, please?

14 A Yes. You are closer to right, it's about 470.

15 MR. McCONNELL: Your Honor, if we might have a  
16 clarification on the question, was that phrased in terms  
17 of the magnification of the dose, or the order of magnitude  
18 of difference?

19 MR. GORDON: Magnification, I'm sorry, I used  
20 the wrong terminology.

21 THE WITNESS: It's the difference between 16  
22 and 7500, and if you divide 7500 by 16, you come out close  
23 to 470.

24 BY MR. GORDON:

25 Q Well, when you wrote the protocol for the first

1 series of tests, you increased the dosage for each group  
2 at what you would term a conservative amount, is that  
3 correct?

4 A That's right.

5 Q Would you call the increase that Dr. Kligman  
6 conducted in the second of tests a conservative increase?

7 A No, sir, I wouldn't.

8 Q Did you -- had Dow ever funded studies by Dr.  
9 Kligman previous to the ones that are discussed in your  
10 testimony?

11 A I can't answer that, I don't remember doing any  
12 of it myself, but Dow Chemical Company is a very large  
13 corporation and it could have been done by the medical  
14 department, or somebody, and I might not have known about  
15 it. Not to my knowledge.

16 Q So, to your knowledge, Dow had no prior experience  
17 with overseeing Dr. Kligman's studies, is that correct?

18 A I believe that is correct.

19 Q So, upon what basis did you determine that it  
20 was not important to oversee the second series of tests  
21 which he was going to conduct?

22 A I guess only that he was a professor of derma-  
23 tology at the University of Pennsylvania, and we had  
24 reasonable confidence that he would proceed in a manner  
25 consistent with our original protocol.

1 UNITED STATES OF AMERICA

2 - - - 8:17:41

3 BEFORE THE

4 ENVIRONMENTAL PROTECTION AGENCY

5 - - -

6 ----- X

7 In the Matter of the Hearing of: :

8 2,4,5-T and SILVEX : Docket Nos. 415, et al

9 The Dow Chemical Company, et al :

10 ----- X

11 (This volume contains pages 17066 through 17238)

12  
13 Room 2409  
14 Environmental Protection Agency  
15 Headquarters  
401 M Street, Southwest  
16 Washington, D. C.

17 Friday, November 14, 1980

18 - - -

19 The hearing was convened pursuant to adjournment,  
20 at 9:05 a.m., before Administrative Law Judge Edward B.

21 Finch, when were present the following:

22 ON BEHALF OF THE ENVIRONMENTAL PROTECTION AGENCY:

23 DOROTHY PATTON, ESQ. Office of General Counsel

24 KARL O. BAYER, ESQ. Office of General Counsel

25 ANDREW G. GORDON, ESQ. Office of General Counsel

1 Q Was Dow not interested at all in seeing those  
2 results?

3 A We accepted the statements that he and his in-  
4 ternist made.

5 Q Does Dow normally, when they contract out to  
6 outside experimenters, do they normally not bother to  
7 acquire the results of the test that the experimenter  
8 performed?

9 A It generally depends on the -- and we, incident-  
10 ally contract out very little work -- but it depends on  
11 what the purpose of that work is, where it is going and  
12 what the ultimate end is to be. Monitoring of laboratory  
13 work by consulting laboratories, in the time when this was  
14 done, was not done to the extent that it was done under  
15 the present GLPs, where every data point has to be monitor-  
16 ed.

17 In those days we usually took what we considered  
18 to be competent people and expected them to conduct their  
19 studies in the normal course of their investigations. And  
20 Dr. Kligman was a professor of dermatology, he is an M.D.,  
21 he did lots and lots of skin work in those days. And these  
22 are his results, we did not question his reporting.

23 Q In the second series of tests which is discussed  
24 in Dr. Kligman's January 23rd letter, he reports that eight  
25 of the 10 subjects developed chloracne. Did not Dow want

1 to see the clinical tests that were conducted on these  
2 eight subjects who did develop chloracne?

3 A I guess we really didn't think that it was  
4 necessary to see them.

5 Q Why did you think it was not necessary to see  
6 the results of these clinical tests which were conducted  
7 on eight human subjects which had developed chloracne?

8 A Well, in retrospect I will say it would have  
9 been nice to have seen them. But in those days we took  
10 their words that they had -- we had seen lots of chloracne,  
11 it wasn't a new phenomenon to us.

12 Q So for these human beings you are saying in  
13 retrospect, it would have been nice to see the results of  
14 these clinical tests?

15 A I think so, from a curiosity point of view.

16 Q Just for curiosity's sake? You were not  
17 interested in the health of these eight human beings?

18 A Well, of course we were --

19 Q Then why did you not ask to see the clinical  
20 results of the tests.

21 MR. McCONNELL: I don't believe Mr. Rowe had  
22 finished his answer there, if I am wrong, I will apologize.  
23 But it sounded to me like he was going to say something  
24 more.

25 THE WITNESS: I was only going to say that  
NEAL R. GROSS

1 follow-up on the health status of these three individuals?

2 A I do not.

3 Q Do you know whether Dow or Dr. Kligman has ever  
4 conducted a follow-up survey of the health status of the  
5 human subjects exposed to TCDD in Dr. Kligman's tests?

6 A Not to my knowledge, I do not know that he has,  
7 no. I have no knowledge of that.

8 Q Do you know whether Dow has conducted such a  
9 follow-up study?

10 A Dow has not.

11 Q Dow has not?

12 A Right.

13 MR. GORDON: Could I have just one moment, Your  
14 Honor?

15 JUDGE FINCH: Sure.

16 MR. GORDON: I am going to provide the witness,  
17 and Counsel with Exhibit No. 15, entitled, "Results of the  
18 Two-Year Chronic Toxicity and Oncogenicity Study on 2,3,7,8-  
19 Tetrachlorodibenzo-p-dioxin, TCDD in Rats" by Kociba, et  
20 al.

21 MR. McCONNELL: Did you say Exhibit 15 or  
22 Exhibit 13? I believe this is Exhibit 13.

23 MR. GORDON: Oh, I meant to say 13, yes.

24 BY MR. GORDON:

25 Q Are you familiar with this document, Mr. Rowe?

1           A     I am generally familiar with it, not in detail  
2 because I am not a pathologist and I certainly don't in-  
3 tend to get into pathology.

4           Q     Let's look at the abstract on the first page,  
5 in the seventh line from the top, does it not state that  
6 "Ingestion of 0.1 <sup>ug</sup>mg/kg/day caused an increased incidence  
7 of hepatocellular carcinomas and squamous cell carcinomas  
8 of the lung, heart, palate, nasal turbinates, or tongue,  
9 whereas a reduced incidence of the pituitary, uterus,  
10 mammary glands, pancreas and adrenal gland was noted"?

11          A     Yes.

12          Q     After you became aware of the oncogenic effects  
13 of TCDD reported in the Kociba Study, did you or Dow con-  
14 sider whether the human subjects you had exposed to TCDD  
15 had developed cancers in the years subsequent to the con-  
16 duct of the study?

17          A     We have not followed up on that.

18          Q     Did you consider whether the human subjects had  
19 developed cancers from the study in 1966?

20          A     I don't remember entering into any discussions  
21 on that subject.

22          Q     Well, you had entered into no discussions as  
23 to whether these human subjects had developed cancer, but  
24 had you considered that they might have developed cancer  
25 on your own?

July 9, 1965

Albert M. Kligman, M.D., Ph.D.  
Department of Dermatology  
Hospital of the University of Pennsylvania  
36th and Spruce Streets  
Philadelphia 4, Pennsylvania

Dear Dr. Kligman:

I am sending you under separate cover a small amount of 2,3,7,8-tetrachlorodibenzo-p-dioxin. This is the material which is a potent acnegen and is highly toxic. I have checked back on our figures and find that the single dose oral LD<sub>50</sub> for rabbits is in the neighborhood of 100 micrograms/kilogram, and we had one animal die which had received a single dose of 16 micrograms/kilogram. It is safe to say, however, that doses of 0.5 to 1.0 mg/kg are always fatal, although deaths may be delayed for 10 to 20 days post treatment. The typical clinical picture is severe liver and kidney injury.

In regard to the skin response on rabbits, we have attempted to quantitate this by applying 0.1 ml of test solution to one to two square inches of the surface of the inner face of the rabbit ear. We find that when the total dose does not exceed about 0.2 of a microgram of the acnegen, no follicular prominence or epithelial hyperplasia develops. When the total dose is about 0.5 of a microgram on this area, the response is marginal; 1 to 2 micrograms almost always produces a response, and 4 to 8 micrograms usually produce a severe response. We have not as yet been able to quantitate the dose required to cause 50% mortality from skin exposure, but we are sure it is well above the total dosages noted above.

In view of this information, it does not seem probable that the dosages shown in the accompanying suggested protocol for the human work would be likely to constitute any serious systemic hazard because the dose on a per kilogram basis would be far below that which produces any significant effect systemically in the rabbit. I might add that the rabbit is far more sensitive than the rat to this type of compound. Nevertheless, the seriousness of the consequences that might develop from testing with this type of compound require that we approach the matter in a highly conservative manner. It

July 9, 1965

is with this thought in mind that I have developed the attached protocol. The number of persons per experiment is your decision; I would suggest two as a starter. When applications are repeated, I would like to have them made on consecutive days, if it is convenient to do so. Although the time required to conduct these experiments will require several months, I believe it is the safe way to proceed, using a few people at a time with careful observations on each. The observations are to be made at your discretion, but I would urge routine SGOT's and alkaline phosphatases as a minimum.

There is another item upon which comment should be made. I have indicated in the suggested protocol that a two week observation period should be used prior to starting the next series of experiments. This is because our experience with both animals and man indicates that there is an induction period. In a few instances, we believe an eruption in the human has developed four to six weeks post exposure. Also, we have had a few serious flare-ups which have developed within a matter of days, post exposure. I have compromised on a two-week observation period, but of course, any treated individual should be watched for at least two months post test.

You asked about materials in which this test substance is soluble. I have indicated it is quite soluble in chloroform and benzene and slightly soluble in alcohol. I believe that a solution in 50/50 alcohol and chloroform would be quite appropriate for your work. In regard to covering the exposed area, I would suggest that when the treated area has dried that it be covered lightly with a gauze simply to keep the material from being brushed away or having a person contaminate his hands or clothing inadvertently.

I hope I have answered your questions, but if you have any others, please do not hesitate to contact me.

Sincerely yours,

V. K. Rowe  
Biochemical Research Laboratory  
1701 Building

VKR/jd

Attach.

cc: Medical Department:  
Gordon, Holder, Kramer  
J. E. Peterson  
L. Silverstein  
H. R. Hoyle  
V. K. Rowe (2) —  
TC6.25-66681-7

TO DETERMINE THE ACNEGENIC POTENTIAL OF  
 2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN  
 AND TO STUDY THE PATHOGENESIS  
 OF CHEMICALLY INDUCED ACNE

Volume/Application = 0.04 ml.

Area Treated - Approximately 1 square inch

Solvent - 50/50 Chloroform and Ethanol

<u>Test Solution</u>	<u>ug/ml</u>	<u>ug/0.04 ml</u>
A	2.5	0.1
B	12.5	0.5
C	25.0	1.0
D	50.0	2.0
E	100.0	4.0

Label all solutions with appropriate warnings as: Danger! This material is extremely toxic.

Handle with special care to prevent inadvertent contamination of laboratory equipment (tables, papers, desks, etc.) or otherwise "clean" facilities.

<u>Experiment Number</u>	<u>Total Dose/Test Site</u>	<u>Number of Applications</u>	<u>Solution</u>
1	0.2	2 <i>in same leg</i>	A - 25
2	0.2	2	A - 25
3	0.5	1	B - 12.5
4	0.5	5	A - 25
5	1.0	1	C - 25
6	1.0	1	B - 12.5
7	2.0	1	D - 50
8	2.0	4	B - 12.5
9	4.0	1	E - 100
10	4.0	2	C - 25
11	8.0	2	E - 100
12	8.0	2	C - 25

January 23, 1968

Mr. V. K. Rowe  
Biochemical Research Laboratory  
1803 Building  
The Dow Chemical Company  
Midland, Michigan 48640

Dear V. K.:

This note is a follow-up to my report of July 8, 1966. In that study, you will recall that 6 groups of healthy adult subjects received small and increasing doses of tetrachlorodibenzo-p-dioxin. We followed a specific protocol laid down by you. Unfortunately, not a single subject developed acne nor was there any evidence of toxicity.

This encouraged me to proceed more vigorously. We then assembled a new panel of 10 subjects and applied 0.05 ml of a 1% solution in alcohol chloroform to a one inch square on the back. These applications were made every other day for one month. The treated sites were covered with a non-occlusive gauze square. Each week for 6 weeks, the following laboratory tests were done: Urinalysis, CBC, BUN, SGOT, Alkaline phosphatase, and Creatinine clearance.

Clearly, this exposure was immensely greater than the former one. 8 of 10 subjects showed acne form lesions usually beginning 3 to 4 weeks. This began as with a typical development of comedones. In 3 instances, the lesions progressed to inflammatory pustules and papules. These lesions lasted for 4 to 7 months, since no effort was made to speed healing by active treatment. Biopsies were obtained in 5 instances at various stages. The histologic and clinical manifestations were in every way comparable to classical chloracne. The lesions were indistinguishable from those obtained by Dow 6X and Halowax.

In no instance was there laboratory or clinical evidence of toxicity. The subjects remained well throughout the study.

January 23, 1968

These results implement the conclusions formerly drawn, namely: it is much more difficult to induce acne in the human than in the rabbit ear. The process begins more slowly and the doses required are very much greater. However, unlike the rabbit ear, the comedones often become inflammatory. It is a certainty that the rabbit ear is exceptionally sensitive to acneigenic chemicals and is an excellent system for the detection of such chemicals. Finally, it may be said that chloracne closely mimics acne vulgaris. The only difference is the paucity of anaerobic organisms in the comedo. One may conclude that bacteria are not very significant in the pathogenesis of chloracne.

Very sincerely yours,

  
Albert M. Kligman, M. D.

AMK/kif



THE DOW CHEMICAL COMPANY

MIDLAND  
December 28, 1964

D. D. Irish  
E. M. Adams  
H. R. Hoyle  
H. H. Gay  
H. L. Gordon  
P. B. Holder  
C. G. Kramer  
M. B. Lilly  
R. D. Stewart  
D. J. Kilian

RESEARCH ON CHEMICAL ACNEGENS USING HUMAN SUBJECTS

As a result of our discussion with Dr. Albert M. Kligman, Professor of Dermatology at the University of Pennsylvania, when he visited us on December 11, 1964, Dr. Kligman has drawn up a proposed program for a basic study on acne. As I am sure you are all aware, one of our basic problems is to learn how to correlate the response observed in humans with that observed in rabbit ears. We need to know of the quantitative as well as of the qualitative relationships between the sensitivity of the rabbit and man. Aside from this quantitative aspect, we also need to know something about the basic changes that occur in the skin in response to given acnegens. What is the effect of these materials upon the microflora of the skin and what, if any, treatments can be instituted to alleviate the condition once it begins to develop? Dr. Kligman is very desirous of searching for the answers to these questions. It would be our intention to correlate his work on humans with rabbit work done here with exactly the same compositions, thereby hopefully establishing quantitative and qualitative relationships.

I should like to have opinions from each of you relative to the merits of Dr. Kligman's proposal. If the consensus is that such a project would be worth the anticipated expenditure, I shall attempt to obtain authorization to proceed.

If any of you have any questions, I will be glad to try to answer them.

V. K. Rowe  
Biochemical Research Laboratory  
1701 Building  
ME 6-2376

VKR/jd

MIDLAND  
March 4, 1965

L. C. Chamberlain  
Director of Independent Laboratories  
Executive Research  
566 Building

C. O. Hutchenreuther  
Chemicals Production  
258 Building

REQUEST FOR AUTHORIZATION FOR \$10,000 FOR RESEARCH ON  
CHEMICAL AGENTS USING HUMAN SUBJECTS

Attached is a copy of a letter dated December 24, 1964, addressed to a number of persons who at that time I thought would be interested in the subject. Attached to this letter is an outline of a proposed study, an estimate of the cost of such a study, and a copy of a letter from Dr. Kligman which relieves the Company of any liability which may be incurred by Dr. Kligman's experimental work and which is acceptable as far as Mr. O'Connor of the Dow Legal Department is concerned.

This program has been discussed with all of the addressees of my letter of December 24th, and also with Mr. Hutchenreuther, Mr. Georgan and Dr. Trapp. All have agreed that this would be a desirable project to support.

In view of the fact that this work is of direct interest to the chloracne problem and because it is research in nature and the results are expected to be useful in other applications, I suggested that the cost be split evenly between our laboratory and Mr. Hutchenreuther's production unit.

I should like to have the approval of each of you so that I can get the program under way. If you have any questions I would be glad to discuss them with you.

V. K. Rowe  
Biochemical Research Laboratory  
1701 Building  
ME 6-2376

VER/jd

cc: E. A. Adams  
E. R. Boyle  
E. E. Gay, M.D.  
J. M. O'Connor  
Authorization Book  
V. K. Rowe (2)  
Correspondence

ALBERT M. KLIGMAN, M. D., PH. D.  
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EVERETT 2-1000  
EXTENSION 111

Mr. V. K. Rowe  
Biochemical Research Laboratory  
1701 Building,  
The Dow Chemical Company  
Midland, Michigan

March 2, 1965

RECEIVED  
MAR 5 1965  
Biochem, Res. Lab.

Dear Mr. Rowe: —

This letter will indicate that The Dow Chemical Company is released from liability in case of adverse effects developing in human volunteers in the course of certain studies in which The Dow Chemical Company is interested. I assume full responsibility for any liabilities which may arise in connection with human testing. I might add that we have never encountered a problem in this respect. These are the terms which are obtained in all of our contracts with industry.

Very sincerely yours,

Albert M. Kligman, M.D.

AMK/a