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February 20, 1994

To: Dioxin/PCB Nerds

Re: Early industry knowledge of dioxin

(see attached Monsanto memos: 6/12/56 Elmer P. Wheeler to R. Emmet Kelly, notes of meeting with BASF scientists [C15579-C15581]; attached undated Elmer P. Wheeler notes of meeting with Raymond Suskind, L.C. Weger [Monsanto], and H. Oettel [BASF] titled "Conference at Kettering Laboratory" [C15582-C15586])

Many of us have suspected for some time that the chemical industry was aware of chlorinated dioxins and furans earlier than has been acknowledged. The attached documents confirm that suspicion for Monsanto, BASF, and Dow.

To our knowledge, these documents -- or related materials from the same time period -- have not been produced in either PCB cases or the Agent Orange litigation (alert us, please, if you know otherwise!). These two memos came to light only in cases brought against Monsanto by its Nitro, W.Va. workers (Bogges, Adkins, et al) and by people exposed to the Sturgeon, Mo., railroad spill of Monsanto's orthochlorophenol (e.g., Kemner, et al).

These documents set back Monsanto's and BASF's -- and probably Dow's -- knowledge not only of the identity, structure, and extreme toxicity of chlorinated dioxins and furans, but also of their probable presence as contaminants of PCBs, chlorinated naphthalenes, and all chlorophenol products (e.g., Agent Orange).

The significance of the memos may have been overlooked previously because they refer to dioxins and furans by their archaic names: "chlorinated diphenylene dioxide" (chlorinated dioxin) and "chlorinated diphenylene oxide" (chlorinated furan). The crude drawing of a PCDF on page C15580 is unmistakable. References to the diphenylene oxides (furans) occur in the literature back to 1934, and to the diphenylene dioxides (dioxins, 2,6-DCDD) back to 1941; after 1957, the word "dioxin" replaced "diphenylene dioxide". (Huff, J.E., & J.S. Wassom, "Chlorinated Dibenzodioxins and Dibenzofurans" (1973) Environmental Health Perspectives #5, pp. 283-312) (cross-referencing modern and archaic nomenclatures for various dioxins and furans).

Monsanto has repeatedly asserted that it had no reason to suspect dioxin or furan contamination of PCB products until the late 1960s and early '70s. The first memo, however, put Monsanto on notice in 1956 that these impurities "can show up in the production of any chlorinated phenols and is probably responsible for any chloracne which has been due allegedly to chlornaptha-

lenes, pentachlorphenol, chlorinated biphenyls [PCBs], etc." (p. C15580) The same paragraph refers to "the most potent chloracnogen" as a compound similar to chlorinated diphenyl oxide (furan) "but probably with additional oxygen atoms in the molecules" -- i.e., dioxin -- and refers to a similar conclusion by Don Irish at Dow and communications with him.

The 1956 memo notes Wheeler's recommendation that further exchange of information be conducted directly with Dr. Suskind (subsequent author of published studies of Nitro workers) with carbon copies of any correspondence sent to Monsanto. (There is also a tantalizing reference to "Mr. Weger's excellent 'History of Chloracne'" with covering memo dated May 15, 1956.)

The second memo, apparently also written by E.P. Wheeler, is an undated record of a conference at Kettering Laboratory (Suskind's lab) attended by Suskind, Oettel (BASF), Wheeler, and Weger (both of Monsanto). It appears to have been produced as an attachment to the 1956 memo, although there is some controversy over its date of origin (Dr. Roush, Monsanto medical director, testified that it is a 1956 memo; Dr. Suskind, however, claimed in testimony that he had correspondence suggesting the meeting took place in 1960. Given the nomenclature of the dioxins and furans discussed in the memo, and Suskind's well-documented contradictions on other matters, Roush's testimony on this point is probably the more accurate, particularly as it is unlikely that Oettel would have waited four years after the first memo to communicate with Suskind; the human experiments discussed in the memo were done by Suskind in 1955).

Of interest in the second memo is the recognition by both Suskind and Oettel that chloracne "may be systemic in origin," and Suskind's statement that "in the Monsanto cases the skin problem was not disabling but the many other symptoms such as vertigo, aching muscles, dyspnea [labored breathing] and headaches were." (pp. C15584-85) Also significant is that at this meeting, BASF reported acutely lethal toxicity to rabbits of TCDF (tetrachloro diphenylene oxide) at 0.1 mg per kilogram and TCDD (tetrachloro diphenylene dioxide) at 0.005 mg per kilogram (100 and 5 parts per billion respectively), as well as evidence that Dow's rabbit ear patch test was an unreliable indicator of TCDD contamination.

These discoveries predate by a year Kimmig & Schulz's report of TCDD's apparently independent discovery. The primary importance, beyond demonstrating a cover-up of dioxin and furan contamination of PCBs for more than a decade by Monsanto, is that the documents provide a basis for imputing the companies knowledge of horrendous effects in trichlorophenol workers to a broad class of chlorinated chemicals, an important fact for failure to warn, failure to test, fraud, and punitive damage legal theories of recovery. (For example, Monsanto did not attempt to analyze its PCB products for dioxins or furans until the 1970s, sixteen years after the 1956 meeting with BASF.)

From MONSANTO CHEMICAL COMPANY
At St. Louis, Mo.

: Mr. H.K. Nason-M.O. 317
Mr. R.E. Soden-Nitro
Mr. L.C. Weger-Nitro

Date June 12, 1956

To Dr. R. Emmet Kelly
At Medical Dept.

Reference Nitro

Subject CHLORACNE CASES AT BADISCHEN ANILIN DUE TO TRICHLORPHENOL

Persons Present: Dr. H. Oettel
Dr. H. T. Hofmann
A. Palm (Ph.D.)
W. Soenksen (Plant Supt., part-time)

On the 17th of November, 1953, Badische was producing a batch of trichlorphenol from tetrachlorbenzene when the process exceeded control pressure and temperatures similar to our incident at Nitro. No one was injured at the time. Within one week, as clean-up was being carried out, the first cases of chloracne developed. Fifteen or sixteen cases (6 serious) developed within the next 1-2 months and additional cases showed up during the next 10-12 months until there was a total of 50-60 cases.

I did not see our most severe Nitro cases nor have I seen photographs of these cases. The photographs of the worst Badische cases show horrible skin eruptions with nearly blister-like welts and some ulceration where infection ensued. Areas involved included the face, neck, arms, and upper half of the body. It is my impression that their severe cases were much worse than ours. In addition to the skin manifestations, their men reported all the additional symptoms as experiences in our workers, i.e, fatigue, vertigo, loss of libido, painful joints, etc.

About ten days following the incident, and after initial clean-up, Dr. Oettel was asked to expose animals to the workroom atmosphere. Rabbits (in open wire cages) were placed in the operating area for 24-48 hours. There were no obvious symptoms which developed in the animals until one week after exposure - when they died. Autopsy showed liver necrosis. Oettel thought there might be virus infection or some other cause for death until he exposed additional animals in the department, others in cages suspended inside the "decontaminated" autoclave, and some in the adjacent department. All died within 1-2 weeks following exposure. Subsequently, animals placed in the cages which had previously been in the department died of liver necrosis.

A thorough systematic investigation has isolated impurities in the trichlorphenol process (or residues) which will cause the same effects in rabbits. Liver necrosis will develop in rabbits at the following doses of the indicated materials:

15-20 mg. of pentachlor naphthalene
1 mg. of chlorinated diphenyl oxide
0.1 mg. of residue from trichlorphenol distillation
0.01 mg. of residue fraction from trichlorphenol (above 230°C)

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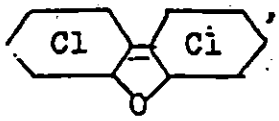
C15579

Dr. Oettel believes that the most potent chloracnogen is a compound somewhat similar to chlorinated diphenyl oxide, 

, but probably with additional oxygen atoms in the molecules. He has corresponded with Don Irish at Dow who either reached the same conclusion independently or, in mentioning the potential of chlorinated diphenyl oxide, influenced Oettel's reasoning. Oettel believes, further, that this impurity can show up in the production of any chlorinated phenols and is probably responsible for any chloracne which has been due allegedly to chlornapthalenes, pentachlorphenol, chlorinated biphenyls, etc.

Dr. Oettel has no faith in any animal skin tests for isolating chloracnogens. He was very interested in Kettering's work and was not aware of the publication referred to in Dr. Suskind's first report and which describes the cyclic skin development in new-born rats. (Reference: Parnell, J.P.: Postnatal Development and Functional Histology of the Sebaceous Glands in the Rat, Am. J. Anat., 85:41, 1949). He is convinced that the Bromsulphalein test reported in the attached reprint is significant. In this regard, Badische routinely uses this test on each batch of trichlorphenol which they now purchase from Bayer, and refuses to accept material which fails to pass the animal tests. (I also learned at Bayer that they have experienced chloracne during the production of trichlorphenol but "have now licked the problem" according to Dr. Hansen (chemist - Research Director At Elberfeld).

Badische has been able to reproduce in the laboratory the conditions which lead to the incident such as theirs and ours at Nitro and was quite surprised that we had not been able to do so. I was not given the Nitro process information, i.e., temperatures and pressures, but if I had had this information I am sure that I could have obtained Badische's. One of their chemists, a Dr. Palm, sat in on our discussions and was prepared to go into details. He did mention that "with 3 mols of trichlorphenol, methyl alcohol, and alkali, and a temperature of 180°C" the process gets out of control. His remarks are in quotes because he does not speak English and I'm not certain of his remarks.

Dr. Oettel would be very happy to receive samples of any of our materials for investigation. He would like particularly:

(1) Samples of any of the materials involved in our 1949 incident including tetrachlorbenzene, trichlorphenol, or Na salt and any residues from the autoclave or material cleaned from the equipment and structural members.

(2) Trichlorphenol (or Na salt) from regular production.

(3) Any samples from raw materials, intermediates, and final product which may have been involved in our cases which developed during our normal 2,4,5-T production in the years following the initial incident.

He would be happy to exchange freely any and all information with us and Kettering. It was my suggestion that this be direct with Dr. Suskind to eliminate "third parties." He would routinely send carbons of any correspondence to us and we could request Dr. Suskind to do likewise. It is my opinion that this might save unnecessary duplication of effort and expense. In addition, Kettering might obtain valuable information to further their investigation involving human volunteers.

I left with Dr. Oettel copies of the following:

(1) The five (5) reports from the Industrial Hygiene Foundation which discuss their rabbit ear tests.

(2) Kettering's report - "Clinical and Environmental Survey at Nitro, 1953."

(3) Kettering's report - "Environmental Survey Carried Out In Building 30, Monsanto Chemical Company at Nitro, February 2, 1955."

We reviewed thoroughly Mr. Weger's excellent "History of Chloracne" which he sent to me with covering memo dated May 15, 1956, and which included descriptions of Kettering's reports on their human and animal research. I did not give Dr. Oettel a copy of this account because I did not have permission to do so. As a result of my visit, it may be desirable to edit this report somewhat and add further process information before forwarding this to Badische.

Any specific recommendations are implied in the above narrative account of my visit to Badische and must be based on an agreement that full and complete exchange of information with Badische is desirable and possible.

EPW

Elmer P. Wheeler

EPW:dh

Attachment

## CONFERENCE AT KETTERING LABORATORY

PRESENT:
R. R. Suskind M.D. - Kettering Laboratory Cincinnati, Ohio
H. Oettel M.D. - B.A.S.F. Ludwigshaven, Germany
E. P. Wheeler - Monsanto
L. C. Weger - Monsanto

This conference was arranged to share information between Badische, Monsanto and the Kettering Laboratory on chlor-acne. In the case of both Badische and Monsanto, the incident of chlor-acne followed the violent decomposition of a batch of trichloro-phenate in process. The Monsanto incident occurred March 8, 1949 and the German incident in December, 1953. Both cases were followed in a period of days or weeks by an outbreak of chlor-acne of epidemic proportions.

Following the Monsanto incident Dr. Suskind and the Kettering Laboratory have done extensive studies into the problem. Dr. Suskind reviewed, in some detail, work and studies which were carried out. In the beginning, Dr. Suskind related tests and studies made on four of the more severe acne cases and presented pictures of the individuals involved together with photo micrographs of skin biopses showing acne lesions. Dr. Oettel presented similar photographs and photo micrographs of German cases which compared very closely with those from Monsanto. It appeared that the German cases may have been more severe with regard to the skin disturbances. It was also apparent that the residual scarring was a good deal more pronounced.

Dr. Suskind described in some detail, animal tests continued by skin application and by inhalation using both sodium TCP and 245T on a

variety of animals including rabbits, rats (adult and baby), cats, dogs and guinea pigs, etc. While in many of the experimental animals evidence of toxicity was manifest, there was no chlor-acne developed. Dr. Suskind and Dr. Oettel both agreed that the so called "rabbit ear test", as developed and described by Messrs. Adams, Irish, Spencer and Rowe, is unrealistic and non-reproduceable. Since none of the very extensive animal experiments were successful in the production of acne, a decision was made to employ human volunteers in an attempt to find a means of evaluating the acnegenic potential of various process materials.

In the first of these experiments, Halowax 1014 (a known acnegen) was chosen as a control. This was applied as a 20% application in "plastibase" an ointment essentially consisting of 5% Polyethylene in mineral oil. Halowax in this experiment was compared to 245T and both materials were applied to the forearm of the human volunteers and kept in contact with the forearm on a continuous basis. Extensive liver function tests were conducted every other day and the volunteers were examined daily by a qualified physician who was particularly mindful of possible liver changes. In 2 to 3 days, redness developed in the Halowax exposures and in 10 days there were some follicular changes terminating in actual lesions. There was no evidence of skin changes in the 245T exposures. Acne was produced only locally in the sight of exposure in every case, that is, there was no systemic change. (At other hospitals with large scale tests, using Halowax, acne was produced in all cases except people above the age of 70. In no case was there any change in liver functions.)

In a later series of experiments, Dr. Suskind described how three materials submitted by Monsanto were compared with Halowax using the technique described above. The materials from Monsanto were all sodium triphenolate prepared as follows:

1) Normal sodium TCP from a plant operation
2) Sodium TCP made from distilled triphenol
3) Sodium TCP made from trichlorophenol purified by the Diamond Alkali technique (dilution, filtration, precipitation and washing)

In this experiment acne was produced in the Halowax control cases and in the cases exposed to the normal plant produced sodium TCP; no acne developed in the cases exposed to the treated TCP samples in the concentrations used.

Dr. Suskind stated that the evolution of chlor-acne is very similar to Acne Vulgaris. Dr. Oettel and Dr. Suskind agreed that massive doses of Vitamin A (100,000 units per day) are effective in Acne Vulgaris. Vitamin therapy was unsuccessful in the Monsanto cases. Dr. Oettel was of the opinion that treatment was too late and stated that they have found that massive doses given in the very early signs of chlor-acne have often resulted in complete clearing of symptoms in 2 to 3 weeks.

Dr. Suskind stated that there is evidence that people develop acne from inhalation or ingesting of Halowax and Dr. Oettel agreed that acne need not come from percutaneous absorbtion but also may be systemic in origin. Dr. Suskind stated that in the Monsanto cases the skin problem was not disabling but the many other symptoms such as vertigo, aching muscles,

dyspnea and headaches were. In close checking the varying secondary symptoms (once termed bizarre) it developed that all of the typical symptoms were common to both the German and Monsanto cases with the exception of dyspnea and intolerance to cold.

Dr. Oettel stated that materials such as Halowax and trichlorophenol are not in themselves acnogenic but that the offending contaminant is an "oxidate". Residues from the Badische decomposition have been extracted and elemental analyses made of the extracts (carbon, hydrogen, chlorine, oxygen). Following this, a series of oxygen bearing, chlorine bearing ring hydrocarbons were synthesized and checked for animal toxicity, using rabbits. Comparative acute toxicity of four of the compounds are as follows:

1) triphlorophenol - greater than 1 gram per kilogram
2) tetrachloro naphthalene - 50 mg per kilogram
3) tetrachloro diphenylene oxide - 0.1 mg per kilogram
4) tetrachloro diphenylene dioxide - 0.005 mg per kilogram

The latter compound (also called tetrachloro diphenyl dioxane) checks more closely by elemental analysis with the extract of the residues from the decomposition. Dr. Oettel is convinced that this is the active agent. They have developed a liver function test for rabbits which involves a micro determination of Bromsulphalein retention. This is used as a control test on purchased trichlorophenol (feeding 1 gram of the sample per kilogram of body weight to each of three rabbits). If there is no more than 5% of BSP retention in 5 days, the material is approved for processing. Dr. Oettel stated positively that there had been no cases of chlor-acne in the 245T synthesis operation.

In a later conversation while returning to St. Louis, it developed that the 1953 decomposition at Badische Works did not occur early in the hydrolysis as in the case of both Monsanto and Diamond Alkali, but was in the stripping of excess methanol following the hydrolysis when the batch was dehydrated and decomposed. The decomposition pressure was relieved through normal pressure relief devices and the autoclave was also left full of a mass of coke so hot that it was "gleaming". Badische has been able to reproduce the decomposition of NA-TCP by dehydration in the presence of iron. (This appears to still leave unexplained the type of decomposition experienced by Monsanto and Diamond Alkali.)

Badische no longer produces TCP but purchases trichloro-phenol from Bayer and uses the BSP test for acceptance or rejection of each lot. Bayer professes to have had no chlor-acne but Dr. Oettel doubts their veracity. Dr. Oettel stated that Boehringer in Ingelheim, Germany had a slight decomposition in sodium TCP production and have had many cases of chlor-acne for many years. Their trichloro-phenol gave high results (positive) by the BSP tests.

Dr. Oettel volunteered to run BSP tests for Monsanto on samples which we might forward to him. Mr. Weger agreed to have responsibility for following up on this work.