

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

Reference

At Medical Dept.

Subject

Nitro
**CHLORACNE CASES AT BADISCHE 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 trichlorophenol from tetrachlorobenzene 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 experienced in our workers, i.e., fatigue, vertigo, loss of libido, painful joints, etc.

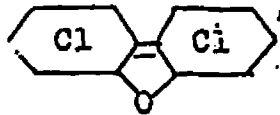
About ten days following the incident, and after initial clean-up, Dr. Oettel was asked to expose animals to the workroom atmosphere. Rabbits (in open wire cages) were placed in the operating area for 24-48 hours. There were no obvious symptoms which developed in the animals until one week after exposure - 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 trichlorophenol 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 trichlorophenol distillation
- 0.01 mg. of residue fraction from trichlorophenol (above 230°C)

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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, pentachlorophenol, 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 trichlorophenol 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 trichlorophenol 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 trichlorophenol, 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 tetrachlorobenzene, trichlorophenol, or Na salt and any residues from the autoclave or material cleaned from the equipment and structural members.
- (2) Trichlorophenol (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.

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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

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Attachment

RECEIVED
MAY 17 1956
U.S. DEPARTMENT OF HEALTH
AND HUMAN SERVICES

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