March 4, 1976

Wesley Mueller
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Dear Wes:

I'm enclosing some of the information you requested on the status of vinyl chloride emissions, toxicity, etc. I have deliberately taken these chiefly from two sources:

"Scientific and Technical Assessment Report on Vinyl Chloride and Polyvinyl Chloride" (EPA-600/6-75-004), June, 1975, and

"Toxicity of Vinyl Chloride", New York Academy of Sciences, 1975, edited by Dr I J Selikoff and E C Hammond.

(These sources are by no means "industrially oriented".)

As you may know, I was present at the New York Academy of Sciences program, as well as the OSHA hearings on vinyl chloride, and have had continuing access to EPA drafts prior to the proposed regulation. I'll draw on my notes from these sessions to amplify and interpret (as well as I can) the significance of some of the data.

First of all, at what concentration have carcinogenic effects of vinyl chloride been demonstrated? Studies conducted by P L Viola and his coworkers (published in 1970 and 1974) show oncogenic activity of vinyl chloride in Wistar rats exposed four hours per day, five days a week, for twelve months at concentrations of 500 ppm or higher. No such activity was noted at a concentration of 50 ppm. (Two hundred rats were exposed at these conditions). It is important to note that liver angiosarcomas developed in four of 150 rats at the 500 ppm level and that, from the results of all test animals at all concentrations tested, Dr Viola concludes "that almost all tissues and organs are sensitive to this carcinogen."

Longer studies conducted by C Maltoni and associates (conducted for 135 weeks) showed the development of a liver angiosarcoma in one rat at the end of the test. This rat was still living at the end of the test and was sacrificed. (My notes show that Dr Maltoni's off-the-cuff remark indicated that the 135 weeks corresponded to more than 80 years in a human life, and I have learned subsequently that all the control rats except one had died from old age at this time). As contrasted to the latency period of 135+ weeks at 50 ppm, data for concentrations of 250, 500, and 2500 ppm show latency periods of 79, 81, and 78 weeks. This may well be a significant point when we consider the possible existence of a "harmless" level.

In a subsequent study with mice, Keplinger, et al of Industrial Bio-Test Laboratories reported the finding of two liver angiosarcomas in 600 mice exposed to 50 ppm of vinyl chloride, seven hours per day, after eight months exposure. This test, sponsored by industry as were the Viola and Maltoni studies, was still continuing and the final report is not yet published. In the same studies, in one hamster, exposed to 2500 ppm VC, one angiosarcoma "may have been observed." No indications of such at 50 or 200 ppm had been noted.

In so far as human oncogenic or teratogenic effects are concerned, as of June, 1975, fifteen cases of liver angiosarcoma attributed to vinyl chloride have been confirmed. The average latency period is 15-18 years. Two other cases are extremely questionable in so far as their relationship to vinyl chloride is concerned. Even so, as Dow has pointed out, the mortality rate from VC for workers exposed twenty years or more is essentially that to be expected from traffic accidents, even though the workers in this group were exposed in the past to extremely high levels of vinyl chloride--generally in excess of 500 ppm and quite frequently more than 2000 ppm. In this same period of time (1961-1974) a total of 280-300 total deaths from liver angiosarcoma occurred. (It is important to note that agents other than vinyl chloride are known to cause liver angiosarcomas indistinguishable from those caused by VC.) Certain arsenic compounds and nitrosamines, for example, fall into this category. (The predilection for coupling liver angiosarcoma with vinyl chloride is making it very difficult to explain the recent discovery of three liver angiosarcomas in a small town in Wisconsin whose only industry deals with lumber and wood-working). In general, though, and I quote from p. 12 of Dr Baetjer's paper, "In those cases where the normal metabolic processes of the body rapidly change a carcinogenic chemical into a non-carcinogenic compound, it would seem that low concentrations could be tolerated. This appears to be the case with vinyl chloride." Moreover, it is the judgment of two highly qualified specialists, Dr Hans Popper and Dr Irving Selikoff, both of Mount Sinai, expressed in the NYAS meeting and the OSHA VC hearing respectively, that the progress of the angiosarcomas can be halted by lowering or removing exposure to VC while in the pre-malignant stage, with essentially no ill effect to the person involved.

With respect to the two cases of liver angiosarcoma originally reported in persons "exposed" to VC through PVC fabrication (not production), it is important to note that these are cases 5 and 6 of the Connecticut data. At the OSHA hearing, the Director of NIOSH himself expressed skepticism that the accountant's disease was caused by VC in the fabrication plant, since he had worked for the company such a relatively short time and stated that NIOSH was looking to see where else he had been exposed to VC! (Note the obviously erroneous presumption that all liver angiosarcomas are caused by VC). The accountant, by the way, usually visited only the office of the plant and that only once a week.

The electrical worker's case is also interesting--and disproven by the subsequent findings of the National Cancer Institute. Despite the fact that measurements showed no vinyl chloride present in his normal workplace, NIOSH persisted in insisting this was a VC-related death until the NCI finding.

In so far as "neighborhood" cases are concerned, to date all have been disproven. The one Connecticut case (number 7) is the only one where the angiosarcoma is indistinguishable from those of VC-PVC workers. Yet this man, as you will note, moved to the vicinity of the fabricating plant from New York City in 1973, and died in May of the same year. Indeed, his initial symptoms appeared while he was still a New York resident. The Niagara area case, which is still quoted in some areas, was disproven long ago, again by NCI study of liver samples. (By the way, it is my understanding that both of these cases had a history of large alcohol usage).

Now we come to the question of a no-effect level. I've already indicated that Dr Baetjer and Dr Selikoff have given statements which indicate that they accept this concept, though obviously neither can fix such a level. These beliefs are consistent with the theory of Hefner, et al, of Dow whose preliminary studies are reported in the NYAS Annals and whose subsequent studies have strengthened their faith in their preliminary conclusion. These workers believe that lesser levels (< 200 ppm) of vinyl chloride are detoxified by the liver in a non-carcinogenic pathway, but that at higher levels there exists a "spill-over" mechanism leading to carcinogenic effects. This theory would also predict that excessive "challenge" of the liver function by other factors could lower the breakpoint for a spill-over effect to occur.

The above theory is certainly consistent with our knowledge of the human cases. The three Niagara Falls workers whose death is attributed to VC all suffered impairment--alcoholism, gross obesity, and diabetes. I have been told that this is also true of all the B F Goodrich cases, with one possible exception.

In so far as vinyl chloride exposure causing excess birth defects in areas in which PVC plants are sited is concerned, one must note that a great deal has been made of Dr Peter Infante's report of excess birth defects in certain Ohio communities. Dr Infante was asked at a New York Academy of Sciences meeting in the spring of 1974 as to whether or not he had similar statistics covering a time period before the PVC plants began operation. He replied that he did, but had not worked them up yet. Judging from recent reports, he still has not done so.

Meanwhile, the Center for Disease Control investigated the cases involved. The EPA document states: "A subsequent study by the Cancer and Birth Defects Division of the Center for Disease Control confirmed a moderate increase in CNS malformations in Painesville, Ohio, but could not establish any association between cases and vinyl chloride exposure". In fact, there were 14 such cases, but in none had either parent either worked in or lived within two miles of a PVC plant. Unfortunately, the CDC study seemingly is being ignored by individuals such as Dr Infante and Dr Maggoner of NIOSH who persist in quoting Infante's study as evidence of the teratogenic effect of vinyl chloride.

Finally, we arrive at the question of what vinyl chloride levels have been detected in neighborhoods adjacent to VC or PVC plant locations.

In June of 1974, EPA conducted a 6-day survey in the Niagara Falls area to determine the concentration of VC in the atmosphere. These were conducted while the old plant was still in full operation, emitting 2-5 lbs of vinyl chloride per 1000 lbs PVC processed in the driers, and while tremendous air circulation was being used to reduce the VC concentration in one building housing roughly 40% of the production--a VC concentration which nevertheless showed a "normal" range of 8-15 ppm. The values EPA obtained in this study are shown on pages 34-36 of the EPA document.

These data show that the highest concentration detected was 40 ppb (0.040 ppm) while the medians were 7.7, 3.0 and 4.3 ppb (0.0077, 0.0030, and 0.0043 ppm). These values are lower, by factors of 30-80 than the OSHA-permitted workplace exposure averaged for a 168 hour week ($\frac{1 \text{ ppm} \times 40 \text{ hrs}}{168 \text{ hrs}}$ = 0.238 ppm or 238 ppb).

COVER — From what I know of our present operations at Niagara Falls, I would expect a repeat study to show levels 5-10 times less than those initially observed.

Wes, I hope this is an adequate summary for your purposes. I regret that I could not copy all the documents completely, but the references are there if you wish to acquire them.

Sincerely,

William L. Cox

Manager,
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RESEARCH DIVISION

William L Cox.
bss

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Enclosures