III. HAZARDS OF VINYL CHLORIDE

Vinyl chloride (chloroethene), Chemical Abstracts Service Registry No. 75015, previously had an OSHA standard of 500 ppm because its known toxic effects were thought to be relatively insignificant. Studies reported during the 1960's provided evidence of additional health hazards, prompting the American Conference of Governmental Industrial Hygienists (ACGIH) in 1971 to reduce the threshold limit value (TLV) from 500 ppm ceiling to 200 ppm time-weighted average. As a result of reports of liver cancer deaths among employees at the B. F. Goodrich Chemical Company, OSHA issued an emergency temporary standard of 50 ppm ceiling on April 5, 1974. To date, 24 cases of angiosarcoma have been reported among vinyl chloride workers, including 15 in the United States.

1. SAFETY HAZARDS

Vinyl chloride (VC) is a flammable gas with a boiling point of approximately - 14°C. It has been used as a refrigerant and as an extraction solvent for heat-sensitive substances because of its high vapor pressure. However, the substance's high flammability, acute toxicity, and readiness to polymerize made these uses undesirable. Handling of vinyl chloride presents a substantial hazard, since it is normally gaseous at room temperature and can form explosive mixtures with air. The lower explosive limit is 3.6 percent by volume in air (36,000 ppm); the upper explosive limit is 26.4 percent by volume in air (264,000 ppm). VC is normally stored or transported in liquid form under

pressure, with safety blow-off valves usually provided as a precautionary measure to guard against pressure buildup.

2. ACUTE EFFECTS AND TOXICITY OF VINYL CHLORIDE[2,3,4,5]

Most early studies involving acute exposure to vinyl chloride focused on its narcotic and anesthetic characteristics. In the 1930's, vinyl chloride was considered suitable for supplementary narcosis because of its slight toxicity, wide range of effect, low concentration in the blood stream, and rapid elimination. Several animal studies were conducted to determine appropriate narcotic concentrations. The range for anesthetic effect in animals, generally between 7 and 10 percent by volume in air, is also assumed valid for humans. Dangerous effects appear above 12 percent, and fatalities occur in test animals at concentrations between 20 and 40 percent by volume in air.

Tests on human subjects at concentrations at and below 2 percent by volume in air (20,000 ppm) revealed symptoms such as dizziness, lightheadedness, nausea, dulling of vision and hearing, and headaches which often persisted for short periods of time. Recovery from these symptoms was rapid under test conditions. The gas does not provide adequate warning of its presence by any odor or irritant action. It does, however, produce symptoms of dizziness and disorientation in advance of harmful effects, except when it is present in exceedingly high concentrations.

Two fatalities from vinyl chloride poisoning were reported in the literature.

Few pathologic and histologic studies were performed in the early experiments dealing with acute exposure to VC. In fact, these studies seem to have been somewhat perfunctory. Subsequent investigations established definite evidence of cardiac irregularities, such as sinus arrhythmia (the gradual waxing and waning of the pulse rate), tachycardia (excessively fast heart beat), and bradycardia (abnormally slow heart beat). These particular results seem to have led to the conclusion that VC is unsuitable for narcosis and anesthesia in man. Later studies on animals showed evidence of pulmonary congestion and congestion of the liver and kidneys after short periods of exposure to VC. Studies involving longer exposures (3-6 months) validated the previous studies, showing some evidence of pneumonia, lung lesions, increases in liver to body weight ratios, decreases in spleen to body weight ratios, and mixed changes in kidney weight.[5]

These studies marked the end of research into the acute effects of VC and the beginning of research into chronic effects.

3. CHRONIC AND LONG TERM EFFECTS OF EXPOSURE TO VINYL CHLORIDE

Fifteen years ago, little was known or suspected about either the chronic or the long-term effects of exposure to vinyl chloride. Since that time, VC has come under steadily increasing scrutiny

as evidence of its deleterious health effects mounted. Research efforts of this period can be divided into three areas: (1) those brought about by the persistent appearance of an effect on liver function and involving the examination of the substance's chronic effect on liver function; (2) those delving into the nature and etiology of acroosteolysis; and (3) those involved with the carcinogenic potential of vinyl chloride.

(1) Chronic Toxicity from Exposure to Vinyl Chloride[6,7,8]

The acute toxicity studies of exposure to vinyl chloride repeatedly gave evidence of an effect on liver function, but the brevity of exposure and apparent reversibility of damage precluded attaching much significance to these results. When an investigation was finally conducted to determine the effect of longer-term exposure at lower concentrations, micropathologic changes and increased liver weight were clearly identified in several animal species. In a study[8] designed primarily to indicate the value of a technique correlating clinical and environmental measurements, statistically significant alterations were found in clinical liver tests using measurements of beta-protein, bromsulphalein, and the icterus index among workers exposed for several years to vinyl chloride.

These animal and human studies were not accorded much importance, because of the belief that liver functions would return to normal when exposure to VC ceased. Reports of diseases of the liver, skin, and other organs and studies of hypertension,

vascular lesions, nervous system injuries, kidney damage, and scleroderma (hardening of the skin) were similarly given little weight. More recently, evidence[6] of lung changes and neurologic damage has come to light. When vinyl chloride was implicated as a cause of liver angiosarcoma, several clinical studies were initiated to determine the presence of pathologic abnormalities among workers. One study [20] made a comprehensive examination of workers in a polyvinyl chloride plant which had been in operation since 1946. The results of this study provided some evidence of peripheral vascular disease, enlargement of the liver and spleen, increase of alkaline phosphatase levels, and pulmonary disease. So far, the only significance that can be attached to these results is that evidence of liver dysfunction may have represented the first stages of angiosarcoma. Further clinical studies are required before the full significance of such abnormalities can be appraised.

(2) Acroosteolysis[6,9,10,11,12,13,14,15]

In the middle 1960's, reports emerged of a disease which appeared among workers involved in the polymerization of vinyl chloride. This disease, the "hand problem" or occupational acroosteolysis, is marked by soreness and tenderness of the fingertips. In some cases, it is accompanied by Raynaud's phenomenon (blanching and numbness of the fingers) and by skin lesions. In most cases no symptomatic complaints were registered; presence of the disease was found only through X-ray examinations

of the hands, which indicated osteolysis of the fingers (i.e. the destruction of bony tissues).

As a result of these initial findings, an extensive epidemiologic, industrial hygiene, and clinical study of occupational acroosteolysis was performed in the late 1960's.[12,13,14] Since the disease had been found only among workers engaged in various phases of vinyl chloride and polyvinyl chloride manufacturing, the study focused only on these industries with the purpose of identifying the loci of the disease. This study found that workers who developed acroosteolysis had been involved at one time or another in manually cleaning reactors used in polymerization. The study also suggested that unreacted vinyl chloride was the cause of the disease, although the precise etiology could not be delineated. Generally, it was found that the incidence of acroosteolysis was substantially reduced by the introduction of more automated cleaning of the reactors.

In a later study of acroosteolysis, a more detailed examination of workers was undertaken.[15] Although soreness and cold sensitivity in the fingers were generally the only symptoms identified in the earlier clinical studies, the workers involved in this study also indicated general complaints of excessive tiredness, forgetfulness and slowing down, dizziness, nausea, increased perspiration and upper abdominal pain. Studies of X-ray results were consistent with the earlier findings. Detailed internal

examinations showed many abnormalities, including light to serious thrombocytopenia (small number of platelets in the circulating blood); enlargement of the spleen; toxic liver damage; ventilation blockage; circulatory obstruction; and skin and bone alteration. Although these symptoms have not yet been assigned to a known syndrome nor have their pathogeneses been elaborated, the evidence at this point strongly indicates that vinyl chloride is the etiologic agent.

(3) Carcinogenicity of Vinyl Chloride [6,9,16,17,18,19,21]

Evidence that vinyl chloride has a carcinogenic effect first arose from a study designed to examine more fully the nature of acroosteolysis. The first observations of tumors were reported by Viola in 1970. He exposed Wistar rats to 3 percent (30,000 ppm) concentrations of vinyl chloride for a period of 12 months.[17] In these experiments, skin, lung, and bone tumors were observed. While these results were statistically valid, they were not viewed with alarm, since the concentration of VC was near the explosive limit and was not likely to be found in industrial situations. Nonetheless, Viola's results did indicate the need for an extensive investigation into the type and degree of VC's carcinogenic potential, with special attention to experimental conditions.

On January 22, 1974, the National Institute for Occupational Safety and Health (NIOSH) was informed of three deaths from liver angiosarcoma among workers at the B. F. Goodrich Company in

Louisville, Kentucky. Since then, a total of 18 cases of liver angiosarcoma among PVC production workers and one case among VC monomer production workers have been identified Thirteen of these cases occurred in the United States: seven at the B. F. Goodrich plant in Louisville, Kentucky; three at the Goodyear plant in Niagara Falls, New York; two at the Union Carbide plant in South Charleston, West Virginia; and one at the Firestone plant in Pottstown, Pennsylvania. In addition, three other cases of angiosarcoma have been identified as possibly resulting from vinyl chloride exposure: two workers in PVC fabricating plants and a person who lived within two miles of a fabricating plant developed angiosarcomas. The significance of these last three cases is still somewhat in doubt.

1. Results in Animal Studies

Subsequent to Viola's work, studies by Cesare Maltoni and by the Industrial BIO-TEST Laboratories were initiated to define more completely the carcinogenic hazards of vinyl chloride. At OSHA's public hearing on February 15, 1974, Maltoni[19] indicated that liver angiosarcoma had been observed in Sprague-Dawley rats exposed to VC concentrations as low as 250 ppm. On April 15, 1974, OSHA was informed that BIO-TEST had observed two cases of angiosarcoma in mice exposed to 50 ppm. In testimony[22,23] presented at the public hearing on June 25, 1974, further results from Maltoni showed angiosarcoma at 50 ppm in rats.Later results from BIO-TEST revealed angiosarcoma in hamsters. In all these animals, the following types of tumors were observed: Zymbal

gland carcinomas, liver angiosarcomas and angiomas, kidney nephroblastomas, skin carcinomas, intra-abdominal angiosarcoma, subcutaneous angiopericitoma, pulmonary tumors, mammary carcinomas, and liver fibroangiomas. The angiosarcoma observed in the test animals was of the same morphological type as that observed in the B. F. Goodrich workers. This provided the first clear evidence that vinyl chloride was probably the etiologic cause of liver angiosarcomas among vinyl chloride workers.

Having established the causative effect of VC, the next stage of the animal studies involved determining the dose-response relationship between vinyl chloride and liver angiosarcoma and the appearance of other tumors. The results of one of Maltoni's experiments revealed the following incidence of angiosarcoma in Sprague-Dawley rats following 52 weeks of exposure and 135 weeks of observation:

Dose (ppm)	Angiosarcomas Positive/Total
0	0/68
50	1/64
250	4/67
2,500	13/74
6,000	14/72
10,000	9/69

These results can be fitted to several models to determine risk level (the level of exposure that would be expected to induce one case) and response rate (the number of cases that would be expected at a particular level of exposure). The use of the

probit and logit models, based on different mathematical representations of the data, was demonstrated at the public hearing of June 25, 1974.[24] At their present stage of development, however, they are only hypotheses as to the form of the actual dose-response relationship. The selection of a "most appropriate" model or discovery of a scientifically verifiable safe level must await experimental verification. The results of the applications are given in Tables 1 and 2. Table 1 (risk levels) shows the level of exposure to vinyl chloride in parts per billion (ppb) that would induce liver angiosarcoma in Sprague-Dawley rats at the indicated risk level. Thus, for example, the first entry in the top line indicates that at an exposure of 225 ppb, 1 rat in 100,000 exposed would be expected to contract liver angiosarcoma. Table 2 (response rates) shows the probability that a single Sprague-Dawley rat would exhibit liver angiosarcoma at a given dose level. Thus, the first entry in the top line shows that 0.028 or 2.8 percent of rats exposed to 50 ppm would be expected to contract liver angiosarcoma. The table includes levels below those at which animal experiments have hertofore been performed, such as 25, 10 and 1ppm.

The results of these studies have only slightly advanced the understanding of the carcinogenicity of vinyl chloride. They highlight the many unknowns that need to be clarified before a definitive extrapolation to humans can be made. The results to date, along with the human experience, suggest the existence of a long latency period. In fact, they indicate the possibility

TABLE 1

Extrapolated 'Safe' Dose Level (ppb) Using Maltoni's Liver Angiosarcoma Data*
(99% Assurance Level)

	Risk Level			
Extrapolation Model	10^{-5}	10^{-6}	10^{-7}	10^{-8}
Probit (Slope = 1, Mantel-Bryan)	225	73	26	10
Logit (Slope = 3.454)	553	119	26	5.5
Logit (Slope = 2.303) and "One-hit"	21	2.1	0.21	0.021

* Only the data up through dose level 500 ppm, but not higher, were used since the response curve flattened out at higher levels.

TABLE 2

Estimated Response Rates: Liver Angiosarcoma
(99% Upper Confidence Limit)

	Dose (ppm)			
Model	50	25	10	1
Probit (Slope = 1)	0.028	0.013	0.0044	0.00015
Logit (Slope = 3.454)	0.0085	0.003	0.0008	0.00002
Logit (Slope = 2.303) and "One-hit"	0.02	0.0071	0.0018	0.00006

that, at low dosage levels, the onset of cancer may not occur during the average lifespan of humans. Many of the experimental animals did not exhibit angiosarcoma until late in their lives, and many died, not as a result of the angiosarcoma, but from other causes. Further, the results of these studies suggest that differences between species have an effect upon the incidence of angiosarcoma. This however does not mean that man is necessarily less sensitive than the animals tested. A conservative view is that man is probably at least as sensitive as the rat. Although the rat has a shorter lifespan than man, the rat's metabolic rate is more rapid than man's--thus it could be construed that the rat exhibits a proportionally accelerated version of the possible response in man. These studies also demonstrate that different organs and sites in the body are susceptible to vinyl chloride carcinogenesis at different rates, with the possibility that the angiosarcoma may not actually be the most significant effect. The relative importance of vinyl chloride's various effects still needs to be adequately delineated.

Another area which demands further study is the effect of vinyl chloride on unborn children. In Maltoni's experiments, two subcutaneous fibrosing angiosarcomas were observed in offspring of Sprague-Dawley rats exposed to 6,000 and 10,000 ppm. The significance of these findings is as yet unclear. However, this result does indicate that vinyl chloride appears to have a parent-teratogenic effect, a phenomenon which is common to other carcinogens. Further study into this problem is clearly required to determine

whether additional precautions should be taken to protect pregnant women from exposure to vinyl chloride.

In regard to the mechanism of vinyl chloride once it enters the body, it has been suggested that VC is not the ultimate carcinogen.[25] Preliminary results from an ongoing study indicate that up to a level of approximately 200 ppm vinyl chloride is metabolized by alcohol dehydrogenase. Above this level, it is apparently metabolized by microsomal oxidases. It has been suggested that metabolism through the microsomal oxidases route may produce the ultimate carcinogen. However, since this action can occur at levels below 200 ppm, this does not preclude the possibility that VC is carcinogenic at low doses.

2. Exposure Level for Humans

The most definitive way to establish a "safe" dose level for humans is to examine the data on past exposures and relate it to the occurrence of angiosarcoma. However, data is not available, and the available evidence on the possible effects of exposure can be consideredas only tentative and preliminary.

In view of the relative scarcity of angiosarcoma in the U.S. population, the relationship of the cases identified to date and vinyl chloride exposure shown in Table 3 presents strong evidence that VC is a human carcinogen. This data also shows that the time lapse from the initial VC exposure to diagnosis of angiosarcoma ranged from 11 to 36 years, with an average of 21 years, suggesting the existence of a latency period for the cancer.

TABLE 3

CONFIRMED CASES OF LIVER ANGIOSARCOMA AMONG WORKERS EXPOSED TO VINYL CHLORIDE OR POLYVINYL CHLORIDE

COUNTRY	CASE #	BIRTH DATE	1st VC or PVC EXPOSURE	DX ANGIO-SARCOMA	AGE AT DX	YRS 1st EXP TO DX	TOT YRS EXP	DATE OF DEATH
			VC MONOMER PRODUCTION WORKERS					
Sweden	02	11-27-11	00-00-45	05-15-72	61	27	23	08-16-72
			POLYMERIZATION WORKERS					
United States	01	00-00-22	12-09-48	03-00-71	49	22	16	03-03-73
United States	02	00-00-34	11-15-55	05-00-70	36	14	13	09-28-71
United States	03	00-00-15	11-28-45	12-00-73	58	28	28	12-19-73
United States	04	00-00-24	07-06-52	08-00-67	43	15	15	01-07-68
United States	05	00-00-12	06-19-44	04-00-64	52	20	18	04-09-64
United States	06	00-00-29	01-17-62	02-00-74	45	12	12	ALIVE
United States	07	05-03-22	08-00-44	00-00-68	45	24	18	03-23-68
United States	08	05-06-20	10-07-46	08-00-61	41	15	15	08-29-61
United States	09	00-00-31	05-28-45	03-01-74	43	29	17	ALIVE
United States	10	08-16-13	06-00-51	05-00-68	55	17	17	05-10-68
United States	11	05-27-09	10-14-46	03-00-70	61	23	23	03-16-70
United States	12	11-17-18	09-13-49	05-00-69	50	20	15	05-02-69
United States	13	12-01-21	08-19-44	05-00-74	53	30	30	ALIVE
W. Germany	01	07-26-31	10-14-57	00-00-71	40	14	14	12-14-71
W. Germany	02	06-04-30	10-01-57	00-00-69	39	11	11	01-25-69
Great Britain	01	00-00-01	00-00-46	12-00-72	71	26	20	12-00-72
Norway	01	12-23-15	03-00-50	12-20-71	56	22	21	01-04-72
Sweden	01	06-23-27	08-14-51	02-00-70	43	19	18	10-20-70
			SECONDARY MANUFACTURING					
United States	14	00-00-13	08-18-38	06-00-73	60	36	00	07-03-73
United States	15	00-00-25	00-00-00	07-00-72	47	00	00	02-15-73

Note: '00' indicates unknown date
DX = Diagnosed

The exact exposure levels of VC experienced by the workers who were stricken with angiosarcoma are not known. However, evidence presented at the public hearing

indicated that, at least for the U.S. cases, exposures during the 1940's and 1950's were estimated by industry to be extremely high, frequently over 1000 ppm and commonly in the 100 ppm range. This would seem to indicate that VC carcinogenicity for humans might only occur as a result of high exposure levels. On the other hand, two cases of angiosarcoma that occured in U.S. workers conflict with this hypothesis. One worker was first exposed in 1962 and since that time worked in areas where the exposure levels averaged below 200 ppm TWA. The other case worked in an extruding operation and was probably never exposed to a level above 50 ppm (with TWA's much lower). These two cases cast doubt on the existence of a "safe" level for humans.

At this time, a major epidemiologic study of the relationship between VC levels and carcinogenicity is the Tabershow/Cooper study[26] of 8384 vinyl chloride workers employed in 35 domestic VCM and PVC plants. Workers, employed for at least one year in a job involving vinyl chloride exposure, were subjectively classified according to an index representing their relative exposure level. Results were analyzed for the overall study population according to the estimated levels of exposure, the durations of exposed employment, and the values of the exposure index.

The primary finding of the study was that those exposed to vinyl chloride did not suffer a statistically significant mortality rate increase over what would be expected in a comparable U.S. male population. Other important findings were that cancers of the liver (primarily angiosarcoma), the respiratory system, the brain, the lymphatic system, and unknown primary sites occurred most frequently in those members of the study population who suffered the greatest exposure. Even though these excesses were not statistically significant, the findings warranted further study.

The results of this epidemiologic study do not definitively establish the case for or against VC carcinogenicity. The tentative conclusion of an increased number of malignant neoplasms with VC exposures raises the possibility that vinyl chloride has a more wide-ranging effect than liver angiosarcoma alone.

Further study and analysis of this data seem warranted, such as by the further development of worker histories and by the analysis of each plant by exposure levels, months of employee exposure, length of time since exposures cease, and ages of the workers. Such an investigation might include the development of a population of chemical workers with which to compare the subset of vinyl chloride workers. In addition, an epidemiologic study of workers from compounding and fabricating plants might be useful.

In viewing any epidemiologic data, conclusions drawn have to be tempered by the consideration that the full effects of past exposures among workers may not have yet surfaced because of the latency period associated with VC carcinogenesis. Other unknown factors include the effects of single or intermittent exposures at high or low levels and the effects of small differences in exposure level (such as between 15 and 25 ppm) on the onset of cancer.

NOTES

1. C. A. Brighton in N. M. Bikales, ed., Encyclopedia of Polymer Science and Technology, Vol. 14, Interscience Publishers, a division of John Wiley & Sons, Inc., New York, 1971, pp. 305-320.

2. K. B. Lehmann and F. Flury, Toxicology and Hygiene of Industrial Solvents, J. Springer, Berlin, 1938, p. 130 (As translated by E. King and H. F. Smyth, Jr., 1941, pp. 143-144).

3. W. F. Von Oettingen, The Halogenated Aliphatic, Olefinic, Cyclic, Aromatic, and Aliphatic-Aromatic Hydrocarbons Including the Halogenated Insecticides, Their Toxicity and Potential Dangers, Public Health Service Publication No. 414, U.S. Department of Health, Education, and Welfare, Washington, D.C., 1955, pp. 195-197.

4. E. Mastromatteo, A. M. Fisher, H. Christie, and H. Danziger, "Acute Inhalation Toxicity of Vinyl Chloride to Laboratory Animals," American Industrial Hygiene Association Journal, Volume 21, No. 5, October 1960, pp. 394-398.

5. D. Lester, L. A. Greenberg, andWW. Robert Adams, "Effects of Single and Repeated Exposures of Humans and Rats to Vinyl Chloride," American Industrial Hygiene Association Journal, May-June 1963, pp. 265-275.

6. Statement of Dr. Irving J. Selikoff, Mt. Sinai School of Medicine, at OSHA hearing on February 15, 1974.

7. T. R. Torkelson, F. Oyen, and V. K. Rowe, "The Toxicity of Vinyl Chloride as Determined by Repeated Exposure of Laboratory Animals, "American Industrial Hygiene Association Journal, Volume 22, No. 5, October 1961, pp. 354-361.

8. C. G. Kramer, and J. E. Mutchler, "The Correlation of Clinical and Environmental Measurements for Workers Exposed to Vinyl Chloride," American Industrial Hygiene Association Journal, Volume 33, No. 1, pp. 19-30.

9. Statement of Anton Vittone, Jr., B. F. Goodrich Chemical Company, at OSHA hearing on February 15, 1974.

10. Statement of Peter Bommarito, President, United Rubber, Cork, Linoleum, and Plastic Workers of America, at OSHA hearing on February 15, 1974.

11. R. H. Wilson, W. E. McCormick, C. F. Tatum, and J. L. Creech, "Occupational Acroosteolysis, Report of 31 Cases," The Journal of the American Medical Association, Volume 201, No. 8, August 21, 1967, pp. 83-87

12. B. D. Dinman, W. A. Cook, W. M. Whitehouse, H. J. Magmuson, and T. Ditcheck, "Occupational Acrossteolysis: I. An Epidemiological Study," Archives of Environmental Health, Volume 22, pp. 61-73, January 1971.

13. W. A. Cook, P. M. Giever, B. D. Dinman, and H. J. Magmuson, "Occupational Acroosteolysis: II. An Industrial Hygiene Study, "Archives of Environmental Health, Volume 22, pp. 74-82, January 1971.

14. V. N. Dodson, B. D. Dinman, W. M. Whitehouse, A. M. M. Nasr, and H. J. Magnuson, "Occupational Acroosteolysis: III. A Clinical Study, "Archives of Environmental Health, Volume 22, pp. 83-91, January 1971.

15. S. Juhe, C. E. Lange, G. Stein, and G. Veltman, "On the So-called Vinyl Chloride Disease," Deutsche Medizinsche Wockenschrift, 98 (43), pp. 2034-2037, English translation, 1973.

16. P. L. Viola, "Pathology of Vinyl Chloride," Medcinia del Lavoro, Volume 61, No. 3, pp. 174-179, March 1970.

17. P. L. Viola, "Carcinogenic Effect of Vinyl Chloride," Presented at the Tenth International Cancer Congress, Houston, Texas, May 22-29, 1970.

18. P. L. Viola, A. Bigotti, and A. Caputo, "Oncogenic Response of Rat Skin, Lungs, and Bones to Vinyl Chloride," Cancer Research, Volume 31, pp. 516-522, May 1971.

19. Statement of Cesare Maltoni, Instituto di Oncologia, Bologna, Italy, at OSHA hearing on February 15, 1974.

20. Statement of Irving J. Selikoff, Mount Sinai School of Medicine, at OSHA hearing of June 25, 1974.

21. Statement of Marcus M. Key, National Institute for Occupational Safety and Health, at OSHA hearing of June 25, 1974.

22. Statement of Daniel P. Boyd, Occupational Safety and Health Administration, at OSHA hearing of June 25, 1974.

23. Statement of M. L. Keplinger, Industrial BIO-TEST Laboratories, at OSHA hearing of June 25, 1974.

24. Statement of Marvin A. Schneiderman, National Cancer Institute, at OSHA hearing of June 25, 1974.

25. Statement of Perry Gehring, Dow Chemical Company, at OSHA hearing of June 25, 1974.

26. "Epidemiological Study of Vinyl Chloride Workers," Tabershaw/Cooper Associates, Inc., Berkeley, California, May 3, 1974 (Submitted to the Manufacturing Chemists Association, Washington, D.C.) (Reproduced as Exhibit 20J of the OSHA hearing of June 25, 1974).

IV. OCCUPATIONAL EXPOSURE TO VINYL CHLORIDE

An assessment of the health hazard from exposure to vinyl chloride must include an estimate of the number of workers exposed, a determination of their past and present exposure levels, and an appraisal of the number of workers who may be expected to contract liver angiosarcoma or other forms of cancer as a result of these exposures. A full characterization of employee exposure to vinyl chloride, however, cannot be accomplished at this point since very little information is available concerning the levels to which workers have been exposed in the past. A reliable model to predict the expected number of cases cannot be formulated because of the lack of data on past exposures and of the mechanism of vinyl chloride carcinogenesis. Consequently, this chapter only attempts to describe the primary potential sources of occupational exposure to vinyl chloride.

Vinyl chloride (VC) is used primarily in the production of polyvinyl chloride (PVC), a thermoplastic resin which has application in a host of products for consumers and industry. The conversion of the VC monomer into a polymer or copolymer is an incomplete process, i.e., not all of the monomer is reacted. Furthermore, despite the fact that the process of stripping removes most of this monomer from the polymer resin, it only partially accomplishes this function. Consequently, residual monomer is usually entrapped in polymer and copolymer formations, and often escapes -- thus posing a workplace hazard in both

PVC and VC plants. The VC content and form of the polymer determine the rate at which VC separates, and the extent of exposure that will occur. Even after the polymer has been fused into a product which will undergo no further heating in bulk (at least to melting temperatures), escape of the vinyl chloride may still occur because of migration to the surface. The OSHA proposed regulation excludes companies using fabricated products since no facts are available to show measurable emissions from fabricated products.

Manufacturing processes involving VC or PVC (containing entrapped monomer) fall into five distinct categories. Figure 1 presents a schematic which shows the interrelationship of these process stages. These are:

- o Production of vinyl chloride monomer;
- o Production of polyvinyl chloride homopolymer or copolymer;
- o Compounding of PVC homopolymers or copolymers with plasticizers, stabilizers, lubricants, fillers, pigments, and other additives;
- o Processing of compounded PVC into finished or semi-finished products; and
- o Fabrication of finished products from intermediate stock.

The fourth stage may yield finished products or semi-finished products used in the fifth stage. Since companies in the fifth stage will not be regulated, this report will examine only the first four stages to estimate the number of workers exposed and

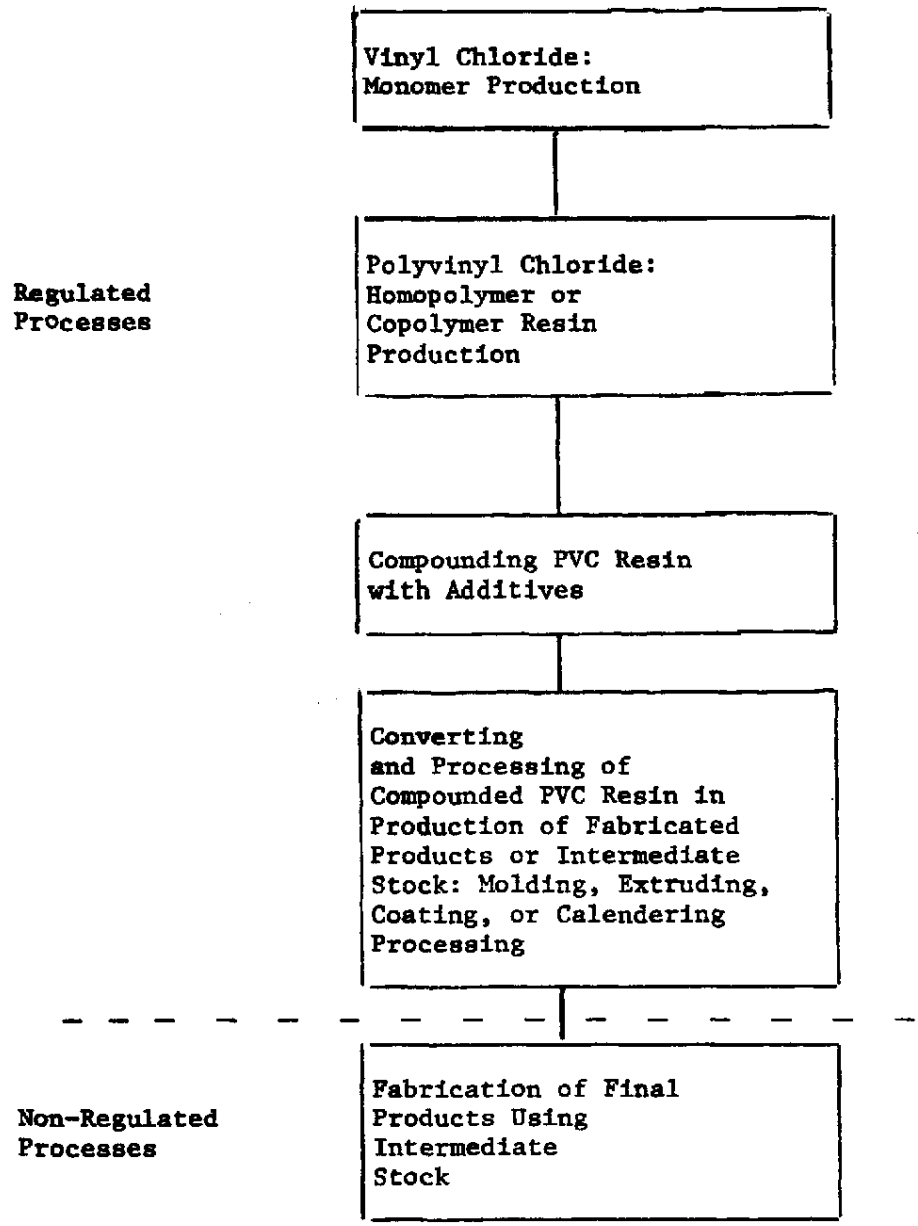


Figure 1. Manufacturing Processes Involving Vinyl Chloride or Polyvinyl Chloride

the level of their exposure to vinyl chloride.

1. PRODUCTION OF VINYL CHLORIDE

Vinyl chloride first attained commercial significance during the 1930's after the discovery that PVC could be processed and converted into a rubber-like product. The ready availability of natural rubber limited development of VC manufacture prior to the outbreak of World War II. When the war cut off supplies of natural rubber, production of vinyl chloride for PVC, as a rubber substitute, was initiated on a large scale. Developments since that time have made vinyl chloride one of the most important starting materials of the plastics industry.

(1) Process Descriptions[1,2,3,5,6,7]

Vinyl chloride is presently produced by 10 companies in 15 plants in the United States (including Puerto Rico), as shown in Table 1. The substance was initially produced by the caustic hydrolysis of ethylene dichloride, subsequently by the pyrolysis of ethylene dichloride to vinyl chloride and hydrogen chloride, and still later by the hydrochlorination of acetylene.[19] Most recently, a newer process involving the oxychlorination of ethylene has become increasingly prominent in VC production, so that presently 13 plants, with almost 92 percent of the capacity, are using the ethylene route.

Hydrochlorination of Acetylene - In this process, also known as the balanced process, vinyl chloride is produced by the hydrochlorination of acetylene, usually with mercuric chloride as the catalyst. A flow diagram for this process is

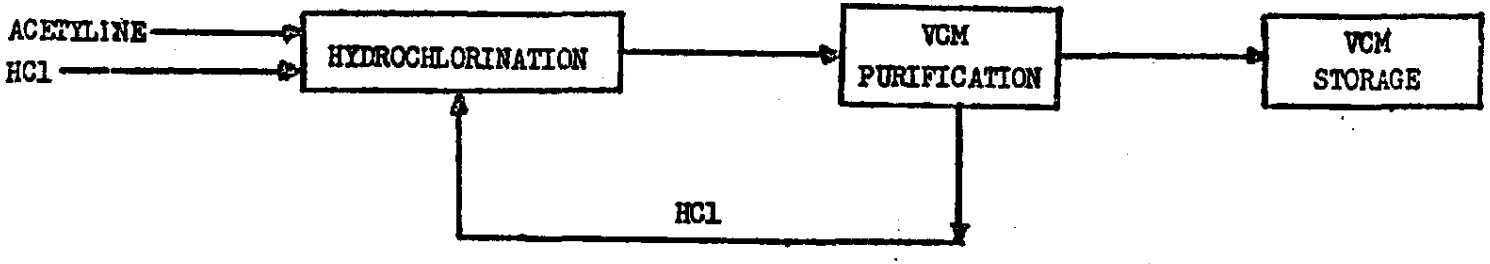
Table 1

Vinyl Chloride Monomer Producers

Company	Location	Nominal Capacity (MM lb.)	Process
Allied Chemical Corporation	Baton Rouge, La.	300	Direct and oxychlorination
American Chemical, Inc.	Watson, Calif.	170	" "
B. F. Goodrich Chemical Company	Calvert City, Ky.	1,000	" "
Continental Oil Company	Lake Charles, La.	625	" "
Dow Chemical Company	Freeport, Texas	180	Direct chlorination
	Oyster Creek, Texas	700	" "
	Plaquemine, La.	340	" "
Ethyl Corporation	Baton Rouge, La.	270	Direct and oxychlorination
	Houston, Texas	150	" "
Monochem, Inc.	Geismar, La.	350	Acetylene
PPG Industries	Lake Charles, La.	300	Direct and oxychlorination
	Guayanilla, P. R.	500	" "
Shell Chemical Co.	Deer Park, Texas	840	" "
	Norco, La.	700	" "
Tenneco Chemicals, Inc.	Houston, Texas	255	Acetylene
		6,680	

Sources: See Bibliography, references 1, 2, 3, 4.

FIGURE 2. MANUFACTURING OF VCM BY DIRECT CHLORINATION OF ACETYLENE



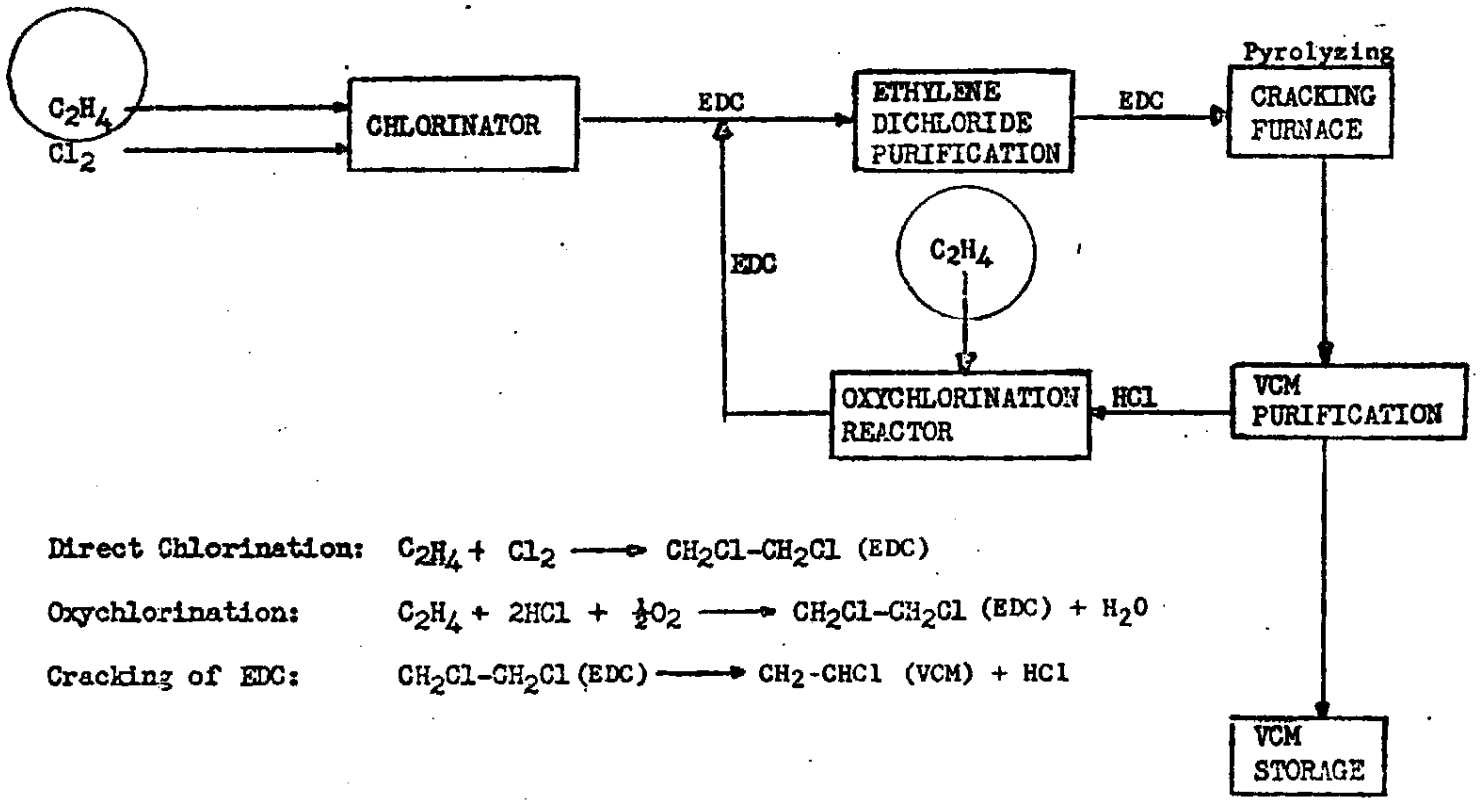
$$CH{\equiv}CH + HCl \longrightarrow CH_2{=}CHCl$$

shown in Figure 2. Acetylene and hydrogen chloride are first passed through a drying tower and then mixed in a chamber packed with activated charcoal. This mixture is passed through several hundred vertical tubes in which the catalyst is packed. The temperature of these tubes is limited to ranges which permit the reaction to take place. The product gases are then fractionally condensed, and the liquid condensate fractionally distilled to obtain vinyl chloride. The VC is finally purified by caustic scrubbing. Most of the variations in this process arise from the use of different catalysts or mixtures of catalysts. Use of this route in the United States has been declining due to the reduced availability of acetylene feedstocks.

Oxychlorination of Ethylene - Ethylene can be directly chlorinated to produce vinyl chloride; however, difficulties with this technique have led to VC production from ethylene through the intermediate formation of 1,2-dichloroethane (also called ethylene dichloride) a process used by several plants in the United States, Japan, and Europe. A schematic of this process is shown in Figure 3. There are several variations of this process which have demonstrated commercial feasibility. Differences among these generally arise in the amount of recycling or in the materials used as catalysts.

The EDC comes from two sources: chlorine combined with ethylene in a liquid phase reaction with a dissolved catalyst

FIGURE 3.. MANUFACTURING OF VCM BY DIRECT CHLORINATION AND OXYCHLORINATION



Direct Chlorination: $C_2H_4 + Cl_2 \longrightarrow CH_2Cl\text{-}CH_2Cl$ (EDC)

Oxychlorination: $C_2H_4 + 2HCl + \frac{1}{2}O_2 \longrightarrow CH_2Cl\text{-}CH_2Cl$ (EDC) $+ H_2O$

Cracking of EDC: $CH_2Cl\text{-}CH_2Cl$ (EDC) $\longrightarrow CH_2\text{-}CHCl$ (VCM) $+ HCl$

(in a chlorinator) and ethylene combined with hydrogen chloride and oxygen in a vapor phase reaction with a catalyst (in an oxychlorination reactor). The crude EDC from these two units is then purified by distillation. The final operation involves the thermal cracking (pyrolysis) of this EDC to form vinyl chloride and anhydrous hydrogen chloride. The resulting effluent is then separated by fractionation. The vinyl chloride is stored, the hydrogen chloride is passed back to the oxychlorination unit, and unreacted EDC is recycled.

(2) Worker Exposure[3,8,9,10,11]

Since vinyl chloride is produced in outdoor plants, the build-up of the substance in the workplace is less than that observed during the subsequent process stages involving the monomer or polymer. The job categories of workers at VC production plants are shown in Table 2. No data is currently available showing the number of people nationwide who are employed in each category. At the OSHA hearing on February 15, 1974, the Manufacturing Chemists Association estimated that 1,500 people work in monomer production. However, since monomer plants differ significantly in age, type, and degree of automation, it is not possible to validate this number. For example, PPG Industries states that it employs between two and four workers per million tons of stated capacity. Based on this figure, the number of workers in monomer plants would be estimated at 1,700 to 3,300. However, it is not possible to characterize such plants for the purpose of categorizing workers

Table 2

Job Categories of Workers

Vinyl Chloride Plants

Control Operator	Material Controller
Distillation Operator	Millwright
EDC Operator	OXY Operator
Electrician	Pipefitter
Instrument Technician	Quality Control Specialist
Laboratory Technician	Sample Man
Laborer	Shift Supervisor
Loading Operator	Tank Farm Operator
Maintenance Worker	VCM Operator

according to exposure levels. As a result, exposure data can only be addressed in general terms, until a comprehensive survey of the industry can be conducted.

An estimate of the number of workers in each job classification is necessary for any characterization of the total hazard of vinyl chloride production, since data presented to OSHA has indicated different peak and time-weighted-average concentrations for the various categories. The major sources of exposure under normal conditions are judged to be:

- o Sampling and analysis of vinyl chloride for quality control;
- o Loading of vinyl chloride for shipping;
- o Entry of vinyl chloride containing vessels for maintenance and repair work; and
- o Leaks of vinyl chloride in the process area.

Some sampling data indicate peak concentrations over 200 ppm for laboratory technicians, over 150 ppm for loading operators, and near 50 ppm for quality control specialists. Time-weighted-averages generally fall well below 50 ppm. Since these results were obtained prior to the emergency temporary standard, they possibly do not represent current levels of exposure to vinyl chloride. Thus, this information should be viewed only as indicative of the categories of workers where high exposures to VC may occur.

2. PRODUCTION OF VINYL CHLORIDE POLYMER AND COPOLYMER RESINS

Virtually all vinyl chloride produced in the United States and not exported is used to manufacture either vinyl chloride homopolymers or vinyl chloride copolymerized with such monomers as vinyl acetate, vinylidene chloride, and acrylates. Generically, these homopolymers and copolymers are known as polyvinyl chloride (PVC) resins. They are generally found in the form of powders which, after being compounded with a variety of additives, are processed to produce a large variety of plastic or resinous end products. Table 3 lists the 22 companies and 37 plants in the United States who produce the homopolymer resin, as well as the capacity of each plant.[19] Additional plant openings and the expansion of present plants that are currently planned are estimated to add to the capacity by approximately 2,000 million pounds.[19]

Most commercial resins have molecular weights between 30,000 and 120,000, the weight being a determinant of the resin's processing and performance characteristics. These characteristics are also affected by the specific additives with which the resins are compounded. Since theoretical results do not definitively indicate what mixtures will give rise to what properties, formulation and processing is largely a matter of experience.

Table 3

Vinyl Chloride Polymer and Copolymer Resin Producers

Company	Location	Nameplate Capacity (MM lbs.)
Air Products & Chemicals, Inc.[1,2,3]	Calvert City, Ky.	150
	Pensacola, Fla.	50
American Chemical Corporation[1,3]	Long Beach, Calif.	150
Atlantic Tubing & Rubber Company[3]	Cranston, R.I.	Unk.
B.A.S.F. Wyandote Corporation[3]	South Kearney, N.J.	Unk.
B. F. Goodrich Chemical Company[1,3,4]	Avon Lake, Ohio	140
	Henry, Ill.	140
	Long Beach, Calif.	140
	Louisville, Ky.	340
	Pedricktown, N.J.	170
Borden, Inc.[1,3,4]	Illiopolis, Ill.	140
	Leominster, Mass.	180
Continental Oil Company[1]	Aberdeen, Miss.	285
	Oklahoma City, Okla.	240
Diamond Shamrock Corporation[1]	Delaware City, Del.	100
	Deer Park, Texas	270
Dow Chemical[3]	Midland, Michigan	Unk.
Ethyl Corporation[1]	Baton Rouge, La.	180
Firestone Tire & Rubber Company[1,3]	Perryville, Md.	230
	Pottstown, Pa.	270
General Tire & Rubber Company[1]	Ashtabula, Ohio	125
	Point Pleasant, W. Va.	50
Goodyear Tire & Rubber Company[1]	Niagara Falls, N.Y.	100
	Plaquemine, La.	100
Great American Chemical Corp.[1]	Fitchburg, Mass.	40
Hooker Chemical Corporation[1,3]	Burlington, N.J.	180
	Hicksville, N.Y.	15
Keysor Century Corporation[1,3]	Saugus, Calif.	35
Monsanto Company[1]	Springfield, Mass.	70
Morton-Norwich Products, Inc.[3]	Ringwood, Ill.	Unk.
National Starch & Chemical Corp.[1,3,4]	Meredosia, Ill.	10
Olin Corporation[1,3]	Assonet, Mass	150
Pantasote Company[1,3]	Passaic, N.J.	60

Table 3 (cont'd)

Vinyl Chloride Polymer and Copolymer Resin Producers

Company	Location	Nameplate Capacity (MM lbs.)
Robintech, Inc.[1]	Painsville, Ohio	250
S.C.M. Corporation[3]	Huron, Ohio	Unk.
Stauffer Chemical Company[1]	Delaware City, Del.	175
Tenneco Chemicals, Inc.[1,4]	Burlington, N.J.	165
	Flemington, N.J.	70
Union Carbide Corporation[1,4]	South Charleston, W. Va.	160
	Texas City, Texas	240
Uniroyal, Inc.[1]	Painsville, Ohio	140
W. R. Grace and Company[3]	Owensboro, Ky.	Unk.
	South Acton, Mass.	Unk.

1/ Homopolymer.
2/ Vinyl chloride - propylene.
3/ Vinyl chloride - vinyl acetate copolymer.
4/ Vinyl chloride - vinylidene chloride copolymer.
Sources: See bibliography references 2, 12, 13, 14.

Four basic processes are employed in polymerization or copolymerization: bulk, suspension, emulsion, and solution. The bulk process is a dry process requiring no water, suspending agents, or emulsifiers. The other three processes require water, solvents, or other liquids, but they are similar enough to use the same equipment, although each plant usually limits itself to only one process. Polymerization of monomers is initiated by free radicals produced by thermal decomposition from peroxides, azo compounds, and persulfates. The rate of polymerization and the molecular weight distribution of the resin are largely determined by the temperature of the reaction and the concentration of initiators. General schematics for the bulk, suspension and emulsion processes are shown in Figures 4 and 5.

(1) Process Descriptions[1,12,13,15]

In the United States, approximately 78 percent of PVC resins is produced by suspension polymerization, 13 percent by emulsion polymerization, 6 percent by bulk polymerization, and 3 percent by the solution method. The bulk polymerization process is relatively new and has been used for an increasing proportion of the production of PVC resins in recent years.

FIGURE 4. MANUFACTURING OF PVC BY BULK POLYMERIZATION

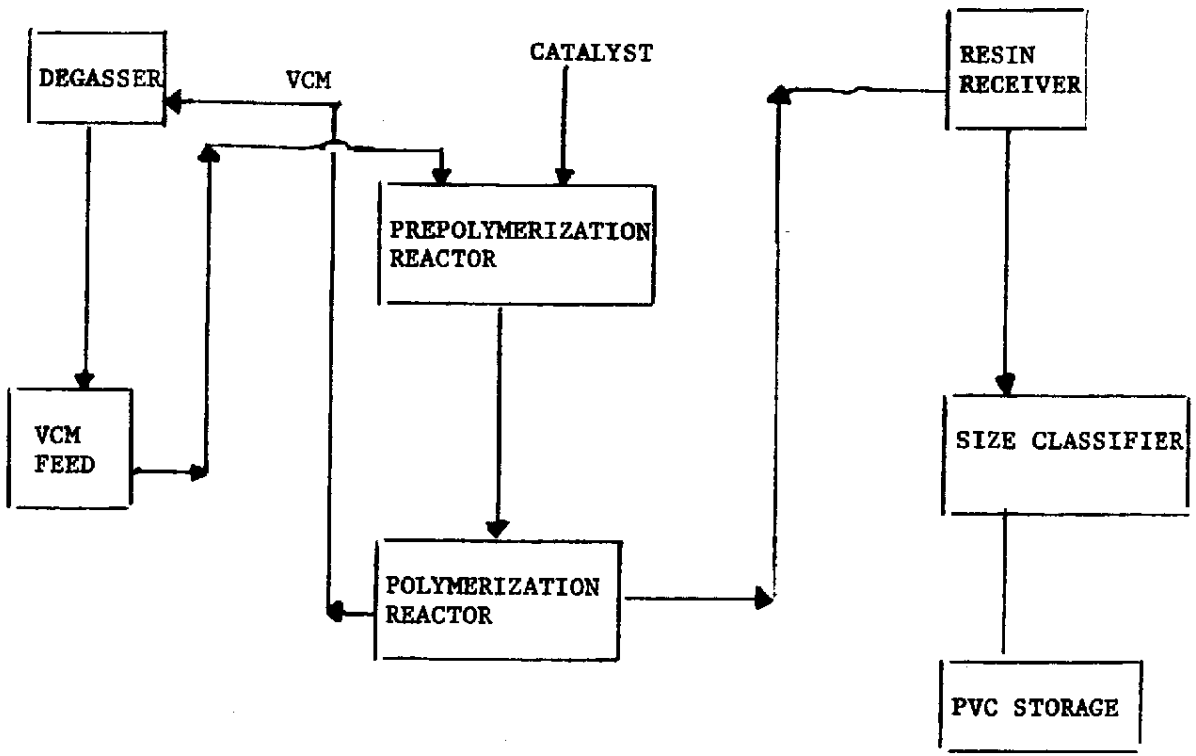
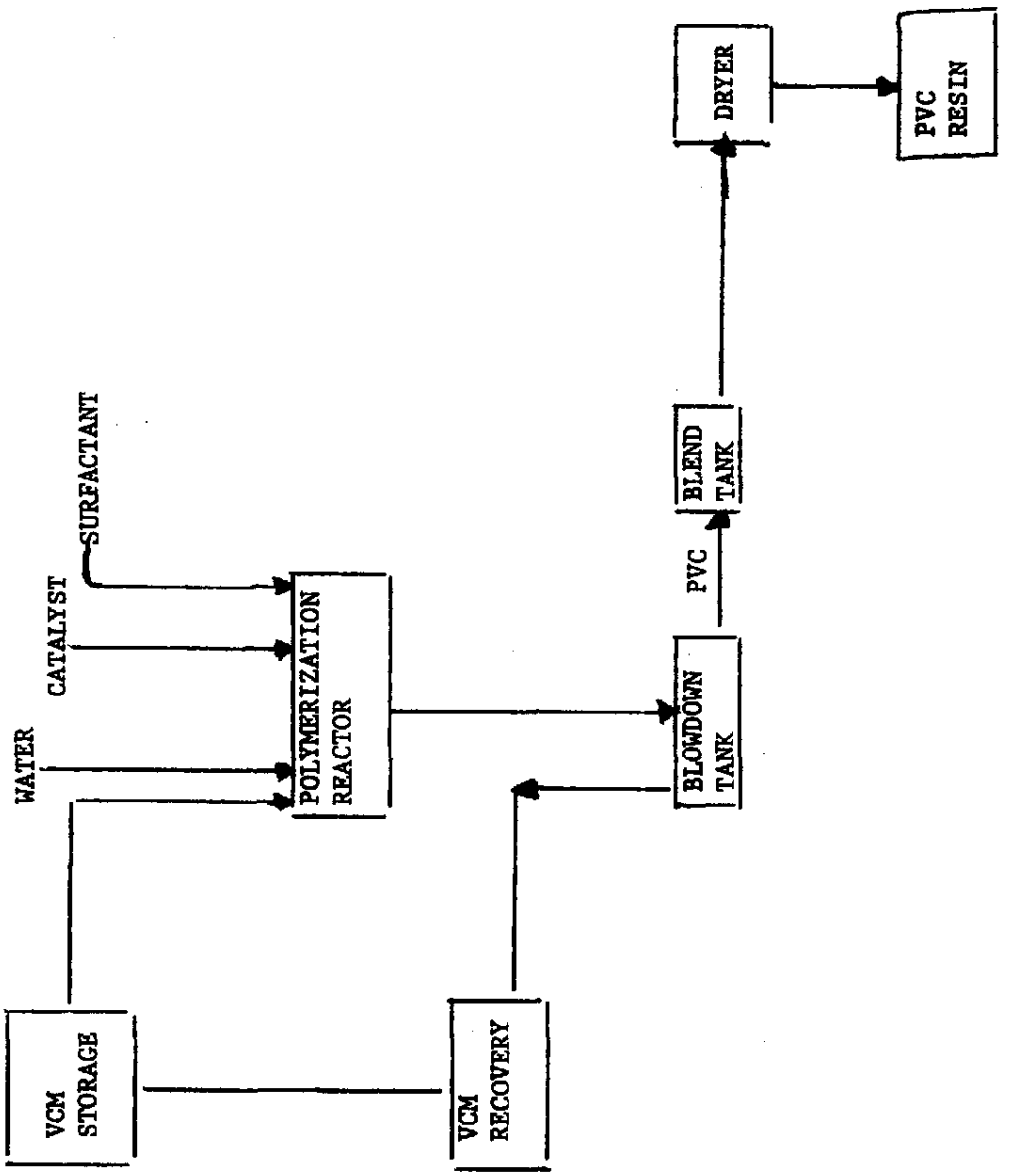


FIGURE 5. MANUFACTURING OF PVC BY SUSPENSION AND EMULSION POLYMERIZATION



Suspension Polymerization - This process is essentially a batch process generally carried out in glass-lined reactors having a capacity of 2,000 to 6,000 U.S. gallons. Monomer soluble initiators, such as lauroyl, decanoyl, and benzoyl peroxides, are dissolved in liquid monomer dispersed in water to form a suspension. The reactor is first charged with the required amount of deionized water. Then the dispersant, a buffer, and the initiator are added. Oxygen is evacuated from the reactor, and the vinyl chloride and any comonomer are fed in. Agitation (to increase the degree of dispersion) is begun, and the contents of the reactor are brought up to the polymerization temperature (45-60°C). After the ten to sixteen hours of the polymerization process, the contents of the reactor (the PVC slurry), are dumped into a large vessel and excess vinyl chloride is recovered for distillation and reuse. The slurry is then blended with other batches in another vessel to reduce small variations and dehydrated by a continuous solid bowl centrifuge to yield a polymer cake containing about 20 percent moisture. The polymer is finally dried in a flash dryer; the resulting particles are sorted out by passage through a cyclone separator. The product is then screened and sent to storage.

Emulsion Polymerization - This process is very similar to the suspension process, and is primarily used to produce exceptionally fine particles. There are two primary differences: (1) The suspension process uses mechanical mixing, while the emulsion process uses surfactants and agitation to convert the monomer to a stable emulsion containing very small monomer particles and; (2) In the emulsion process, the polymer is separated from the water by spray drying, which the nature of the polymer necessitates. While this process is more costly, it is important to users who need PVC in liquid form. In addition, this type of polymer has the ability to form a paste when combined with a plasticizer. In some cases, the slurry is not dried, but instead is produced in a latex form.

Bulk Polymerization - In this process, vinyl chloride is polymerized without the addition of other liquids and in the presence of a free-radical initiator. A portion of a day's supply of monomer is initially pumped into a prepolymerizer.

The mixture from the prepolymerizer, together with an equal amount of fresh monomer, is transferred into an autoclave equipped with slowly rotating agitator blades where the reaction is induced by high pressures. The reaction is autocatalytic and accelerates with increasing conversion of the monomer. After the monomer has been converted, unreacted monomer is removed by a vacuum and recovered in a recycle condenser. The resin is transferred to a

resin receiver. Fines are collected in a dust separator and removed through a manhole. The output of bulk processing plants is said to be more than twice that of good suspension plants of comparable size.[12] This factor will probably lead to a greater use of bulk polymerization during the coming years.

Solution Polymerization - This process is used exclusively for the production of copolymers of vinyl chloride and vinyl acetate. The mixed monomers are dissolved in an organic solvent inside a stirred autoclave heated to 40°C. The reaction in the autoclave has the same autocatalytic characteristic as that occurring in bulk polymerization. In this case, however, the phase separation, arising from the formation of a concentrated polymer base, leads to a decrease in the rate of polymerization. The contents of the autoclave are passed through a filter press to retain the polymer, and the filtrate is recycled. The filtered polymer (in the filter press) is then washed, during which a certain amount of unpolymerized vinyl chloride is recovered by fractional distillation.

(2) Worker Exposure [8,9,16]

It has been estimated that the total number of workers engaged in all aspects of the production of PVC resins is about 5,000. The validity of this figure is suspect, however, since an industrial hygiene survey conducted in 1969 examined over 5,000 PVC-related workers at a time when production was approximately half the current level. Only a small proportion of these workers

were engaged in operations outside the actual resin production. The productivity of these workers has probably increased since 1969 in view of some significant technological changes such as the introduction of the bulk polymerization process, but, on balance, the total number of workers has probably increased beyond 5,000, although less than 10,000. Some of the job classifications of workers involved in resin production with potential exposure to VC are shown in Table 4. No evaluation of the total industry exposure to vinyl chloride can be made at present, because no estimates of the personnel distribution in these categories are available for the entire industry, and because exposure varies according to job category.

The information available does tend to indicate that exposure to VC is greater in resin producing plants than in those synthesizing the monomer. The areas of greatest exposure in a PVC plant are judged to be the following:

- Unloading of incoming vinyl chloride;
- Reactor cleaning;
- Entry of vinyl chloride containing vessels for maintenance and repair work;
- Entry of PVC storage silos;
- Shipping or packaging of PVC; and
- Leaks of vinyl chloride in the process area.

Levels of VC exposure in these plants have been decreasing rapidly since January, 1974. For the entire industry, the average TWA is probably well below 25 ppm. Exposures differ