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REPORT ON MR. JOHN GRASSO

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I. THE HISTORY OF EXPOSURE TO VC/PVC

The potential sources of Mr. Grasso's exposure to VC/PVC over the period from 1964 to 1976 are a complex of the occupational and residential.

1. Occupational*

The Du Pont Chamber Works handled VC from 1964 to 1973, during which time Mr. Grasso was continuously employed there; he worked as a chemical process operator in the Ponsol Colors Area, which primarily handled textile dyes, from 1960 to 1974, and in the Monastral Colors Area, which primarily handled non-textile dye applications, from 1974 to 1976. Du Pont used VC for two processes in separate locations in the approximately 100 buildings comprising its 600 acre plant.

a. The Freon Area. VC was used in the formulation of Freon-propellant mixtures in this area. The VC was obtained from Dow Chemical, in amounts ranging from 27,000 pounds in 1964 to 600,000 pounds in 1973. The total annual VC emissions in 1973 were about 8,000 pounds, representing about 1.3% losses, which apparently occurred largely during tank car unloadings. The Freon area was about 1,000 yards (0.7 miles or 1.1 km) from Mr. Grasso's work site.

b. The Jackson Lab Area. VC was used here in amounts under 2,500 pounds from 1970 to 1972 for R & D on copolymers. This area was about 850 yards from Mr. Grasso's work site. Based on Du Pont data, emissions appear to have been minimal.

c. Estimated VC Exposure. From 1970 to 1973, it is estimated that Mr. Grasso could have been exposed at his workplace to VC emitted from the Freon area at levels of 0.25 to 2.5 ppm for about 976 hours under favorable wind conditions, and up to 100 ppm for about 98 hours under stable atmospheric conditions (Peskin, 1980). Additionally, based on other modelling data, annual average workplace exposures from B.F. Goodrich emissions have been estimated to be about 0.26 ppb (Dames & Moore, 1980).

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*It should be noted that there is no occupational or other history of exposure to arsenic or thorium oxide (thorotrast), the only known causes of angiosarcoma of the liver besides VC/PVC.

2. Residential

Mr. Grasso moved to Pedricktown in 1965. His home there was located about 6 miles from the Du Pont Chambers Works, and about 1.8 miles (3 km) south-east of the B. F. Goodrich plant which opened in 1970. He was thus potentially exposed to VC emissions from the Du Pont plant from 1965 to 1973 and, to a much greater extent, to VC/PVC emissions from the B. F. Goodrich plant from 1970 until July 1976, when his angiosarcoma of the liver was diagnosed.

Goodrich is a major PVC manufacturing facility, purchasing VC from other companies including PPG, Diamond Shamrock, Air Products and Connoco. The VC was shipped in railroad tank cars or tank car trucks, and unloaded directed into pressurized storage tanks. PVC production ranged from 22.5 million pounds in 1970, to 130 million pounds in 1973, peaking at 131 million pounds in 1974. Based on Goodrich data, total VC/PVC emissions in 1973 were about 6.9 million pounds, 3.6 million pounds of which were VC; this is equivalent to 72,000 lbs/weekly, 12,000 lbs/daily or 500 lbs/hourly. VC losses in 1973 were in the order of 4.5%. These emissions had three major origins: continuous point sources; continuous fugitive sources; and episodic point sources.

Some 60 episodic releases of VC from the Goodrich plant are recorded from June, 1973 to December, 1976, many of which "---involve large amounts of VC released to the atmosphere" (Dames & Moore, 1980). For instance, on October 6, 1973, about 13,000 lbs (6,083 kg) of VC were released in a 5 minute period; this is equivalent to 156,000 lbs/hour, some 300-fold in excess of the plant's average hourly 500 lbs emissions in 1973.

From 1970 to 1976, based on an 8 hour working day shift of 5 days/week, Mr. Grasso spent about 14 hours daily during the week and 24 hours daily during the weekend, comprising about 120 hours weekly, in and around his home. Much of this time was spent out-of-doors, including periods when he exercised his hunting dogs and bicycled, particularly after his cardiac surgery in 1973, in

locations closer to the Goodrich plant.

The failure of Goodrich to have monitored community atmospheric VC levels from 1970 onwards (particularly in view of the plant's known substantial VC losses,and also the substantial information available to Goodrich on the carcinogenicity of VC, especially prior to 1974), perforce necessitates reliance on modelling data in attempts to estimate Grasso's residential exposure levels. The limitations in such data are, however, well recognized (Dames & Moore, 1980).

> "....during any specific short-term period significant differences can be expected between the model estimates and actual ambient values. It was not possible to determine from the model evaluation results whether the model produced values with any consistent bias (either high or low) as compared to actual VC concentrations. This is particularly the case concerning any possible bias in the estimation of VC exposures of Mr. Grasso, because numerous differences in details of the calculations exist between the exposure estimates and the model evaluation estimates. These differences include major changes in the source parameters, source-receptor relationships, and averaging times."

There are two sets of estimates on Mr. Grasso's residential exposure to VC. The first is largely derived from modelling based on the limiting assumption that the "suspected effects on health of VC are associated with long-term exposures---, therefore the expected annual average concentration pattern was regarded to be of interest" (Dames & Moore, 1980). On the basis of such data, annual average residential levels were estimated to range from 6.1 to 8.8 ppb, and annual average exposures from 4.4 to 6.2 ppb. Maximum 24 hours exposure from 1974 to 1975 was estimated as 231 ppb, with levels in excess of 10 ppb occurring only in less than 10% of the days in this period. While no estimates were made of residential exposure levels during episodic releases, monitoring on June 29, 1977 (after EPA emission controls were promulgated), detected perimeter levels of 3.36 ppm (Dames & Moore, 1980). The possibility

must be considered that such perimeter levels may underestimate residential exposures, particularly during episodic releases, due to possible "umbrella" effects. The size of these effects is likely to have reflected stack or release heights; for the "mass" building this was 77 feet (Dames & Moore, 1980). While there are also earlier perimeter monitoring data, these have not yet been made available.--"A limited amount of perimeter monitoring was done prior to 1976, but the quality of the data produced is unknown" (Dames & Moore, 1980).

Other modelling estimates, based more selectively on daily meteorological data, conclude that from 1970 to 1976, VC levels from 3.9 to 39 ppm occurred over 1680 hours under favorable wind conditions, and up to 100 ppm over 146 hours during stabl atmospheric conditions (Peskin, 1980).

Residential exposures to Goodrich emissions include PVC particulates, in addition to VC gases. Based on Goodrich data submitted to EPA, PVC and VC emissions in 1973 were 3.3 and 3.6 million lbs, respectively (Davidson, 1980). Goodrich acknowledges VC levels up to 1% in unstripped PVC suspension resins manufactured prior to 1976; following stripping, levels up to 400, 2000, and 3000 ppm were recognized in suspension, dispersion and bulk resins, respectively. Significant amounts of PVC em from Pedricktown were in the 0.1-30 μ range, most being less than 10 μ (Goodrich letter to EPA, 9/3/74). Of interest, are observations that cars parked overnight i the Grasso neighborhood were often covered with light white dust in the mornings.*

3. EPA Experience

The above estimates of Grasso's exposure should be considered in relation to EPA experience, particularly prior to October, 1976, when VC was regulated as a hazardous air pollutant with emissions restricted to 10 ppm.

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*The toxic effect of PVC particulates may reflect the elution of entrapped residual monomer or desorption of adsorbed VC. In spite of a paucity of data, there is suggestive evidence of the carcinogenicity of PVC dust. Intrapleural injection of dust induced "sarcomas" of the liver in 5 of 9 rats dying within a subsequent 18 months (Wagner, 1980). In a case-control study in the B.F. Goodrich, Louisville K plant, exposure to PVC dust was shown to be statistically associated with excess l cancer mortality, specifically with large cell undifferentiated cancer (Waxweiler,

a. EPA Monitoring Data. In preliminary field studies, based on extensive samplings of VC/PVC plants in 1974, average community exposures were 17 ppb in 90% of samplings within 5 miles of plants (EPA, 1975). Based on 24 hour continuous monitoring, 2.5% of community samples had levels in excess of 0.5 ppm, and 1% had levels in excess of 1 ppm. A 10 minute average sample at 3 miles from a plant was 3.4 ppm. Less than 10% of grab samples had levels in excess of 1 ppm. The maximum VC level found was 33 ppm at a distance of 0.3 miles from a PVC plant. The grab sampling data were considered to underestimate real values because of methodological problems (EPA, 1975). Of additional interest is the monitoring of an elementary school in Saugus, California, located near a PVC manufacturing plant (Keysor Century Corporation), where VC levels as high as 2.8 ppm were recorded (EPA 1977); the levels were found to be closely related to tank car unloadings at night.

b. EPA Modelling Estimates. Based on an accidental venting of about 5,000 lb in 10 minutes (such incidents have occurred about 20 times in most PVC plant in 1975), maximum hourly concentrations of 20 ppm at 0.25 miles were derived; peak concentrations were considered to be about 5 to 10 times higher as VC pollutant clouds passed over residential areas (EPA, 1975). It was concluded that populations most effected by spills and non-spills resided within about 1.2 mile of plant, and that impacts of a spill "would be minimal" beyond 3 miles.

4. Comparison of Residential and Occupational Exposures

In spite of the apparently wide divergencies in the two estimates of occupation and residential exposures, ranging from ppm hourly estimates (Peskin, 1980) to the ppb annual averages (Dames & Moore, 1980), both are in substantial agreement that th residential exposures were one order of magnitude greater than the occupational, even though the latter were more prolonged. Additionally, the residential exposures appear to have been punctuated by frequent and sometimes substantial episodic emissions.

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## II. EARLY LITERATURE ON THE TOXICOLOGY AND CARCINOGENICITY OF VC/PVC

This section reviews data on the toxicology and carcinogenicity of VC/PVC prior to January 22, 1974, when B.F. Goodrich first publicly admitted that there had been three deaths from angiosarcoma of the liver since 1971 in its Louisville, Ky. plant. Prior to the former data, there was no open recognition by the chemical industry of the carcinogenicity of VC.

### 1. Animal Studies

The acute toxic effects of VC in experimental animals, particularly rodents, have been recognized since 1930 (Patty et al., 1930). Several publications over the ensuing 20 years established that inhalation of VC in concentrations in excess of 50,000 ppm (5 percent) induced progressive narcosis, cardiac arrythmias, and pulmonary edema. Subsequently, chronic studies in rodents demonstrated the induction of centrilobular degeneration of the liver, and interstitial and tubular renal changes at VC concentrations as low as 500 ppm, then the U.S. occupational standard (Torkelson et al., 1961). These findings were later confirmed and extended with the demonstration of angiofibrosis, cutaneous hyperkeratosis, and periosteal proliferation of bone at higher VC levels (Lester et al., 1963). Studies from 1966-1969 demonstrated the occurrence of chronic fibrotic lesions in the lungs of guinea pigs dying following chronic exposure to VC over a period of three months (Prodan et al., 1966, 1975).

A series of studies from 1961 onwards, demonstrated the persorption of PVC particles, in a size range from 10-40 microns, from the gut of rodents and other animals; the particles were rapidly disseminated in the blood stream, with subsequent embolisation in liver and other organs (Volkheimer, 1961 & 1972). Individual PVC particles were identified in tissue sections for prolonged subsequent periods. Transplacental passage of PVC particles was also demonstrated.

In May, 1970, an Italian toxicologist, Pier Luigi Viola (employed by Solvay Manufacturing Corporation), reported at an international cancer congress in Houston, Texas, that long-term intermittent exposure of a small group of rats to 30,000 ppm of VC in air resulted in the production of cancers in a wide range of organs (Viola, 1970; Viola et al., 1971).

This first report on the carcinogenicity of VC created little impact. This wa because Viola had claimed that the type of tumors induced were peculiar to rats and without human significance, and also because of the very high levels of VC to which animals were exposed. Actually, Viola had induced tumors at much lower concentrations, extending down to less than 5,000 ppm. Thes facts were discussed in detail at a meeting of the Manufacturing Chemists Association (MCA), the major trade association of the U.S. Chemical Industry, in November 1971, when it was concluded that they should not be published, as this would otherwise "lead to serious problems with regard to the vinyl chloride monomer and resin industry...and force an industrial upheaval via new laws or strict interpretation of pollution and occupational health laws" (Wheeler, 1971). Union Carbide further expressed concerns that in view of the large stake it had in "areas most likely to be affected, such as food, food packaging, fiber and aerosols (it) would be seriously hurt by arbitrary or panic-induced government restrictions."

A consortium of European chemical industries, led by Italy's semi-governmental Montedison, and with contributions from British, Belgian, and French firms, then financed a major study initiated in July, 1971, by Cesare Maltoni of the Bologna Cancer Institute (Maltoni & Lefemine, 1975). An extensive series of tests were conducted in which adult, infant, and pregnant mice, rats, and hamsters were exposed to VC in inhalation chambers at concentrations ranging from the relatively low 50 ppm level to the toxic 100,000 ppm level. By August, 1972, Maltoni had confirmed and extended Viola's results. VC was

shown to be a potent carcinogen, inducing the rare angiosarcomas of the liver, as well as the more common hepatomas, and cancers of other organs, including kidney, brain, and lung. The cancers were subsequently found even at the lowest level then tested, 50 ppm. The overall tumor incidence was concentration-dependent, with higher doses increasing the incidence and rate of development of the cancers (Maltoni, 1977).

In October, 1972, the MCA entered into an agreement with the European consortium to share their information, but not to disclose it without prior consent (Edsall, 1975; Turshen, 1976). In January, 1973, the U.S. industry representatives visited Maltoni and were given full details of his experimental studies. The MCA (and Maltoni) subsequently failed to disclose this information, in spite of the fact that NIOSH, in the same month, had publicly requested all available data on the toxic effects of VC. In March, 1973, the MCA recommended to NIOSH a precautionary label for VC that made no reference to toxic or carcinogenic effects on animals or humans.

Four months later, however, representatives of the MCA met in secret with the Director of NIOSH and a small group of his senior staff who were informed that Maltoni had induced tumors in rats exposed to VC levels of 250 ppm. At one stage of the meeting, a Dow Chemical representative adjourned to a separate office for a private meeting with the Director of NIOSH, and subsequently commented that "this private discussion of the carcinogen problem was worth the whole effort" (Wheeler, 1973). Finally, industry concluded that as a result of a meeting "the chances of precipitous action by NIOSH on VC was materially lessened. NIOSH did not appear to want to alienate a cooperative industry nor they did not want to know too much unpublished data."

In March, 1973, following complaints of an unpleasant taste, Schenley Distillers found 10-20 ppm levels of VC in their liquors sold in PVC bottles. On the basis of these findings, and still knowing nothing about the carcinogenicity data, FDA then banned the use of these liquor bottles. In December,

1973, the Society of Plastics Industry, the plastics industry trade association, provided the FDA with data on migration of VC from PVC containers to food, but made no reference to problems of carcinogenicity.

According to a recent special committee report of the American Association for the Advancement of Science, the MCA "appears to have deliberately deceived NIOSH regarding the true facts...Because of the suppression of these data, tens of thousands of workers were exposed without warning, for perhaps some two years, to toxic concentrations of vinyl chloride" (Edsall, 1975).

2. Human Studies

Chronic toxic effects of VC/PVC have been recognized in workers for almost three decades. Chronic hepatitis, gastritis, upper respiratory tract irritation, and skin lesions were noted in a group of 73 workers in a Russian plastic factory (Tribukh et al., 1949). Toxic angioneuropathy was subsequently noted in workers exposed to VC below the then Russian standard of 390 ppm (Filatova et al., 1957). Raynauds-like acroosteolytic disease was also recognized in the same year in VC/PVC workers (Kubota, 1957). The best earliest description of the characteristic spectrum of non-neoplastic VC-induced disease was by a Rumanian group of workers, who recognized chronic hepatitis, splenomegaly, contact allergic dermatitis, pseudoscleroderma, Raynauds-like disease, and gastrointestinal and central nervous system disorders (Suciu et al., 1963). By 1966, acroosteolysis, often accompanied by Raynauds disease, was recognized in VC polymerization workers (Cordier et al., 1966). These findings were confirmed in several subsequent investigations. Further studies over the period of 1962-1970 confirmed the occurrence of VC-induced occupational disease, and demonstrated a dose-response relationship over a range from 36 to 825 ppm, with a highly significant incidence of VC disease at concentrations as low as 40 ppm (Suciu et al., 1972, 1975).

Several reports have drawn attention to the development of chronic

pulmonary disability in VC/PVC workers (Vertkin and Mamontov, 1970; Szende et al., 1970). However, a common factor characterizing these and later reports is chronic exposure to PVC dust. The pulmonary changes range from asymptomatic decrease in pulmonary function tests and radiological abnormalities to clinical bronchitis and emphysema, and to pneumoconiosis.

At least eight fatal cases of primary carcinoma of the liver, subsequently diagnosed as angiosarcoma, have been recognized in VC/PVC workers prior to 1970 (Heath et al., 1975); seven occurred in the USA, including three cases at a B.F. Goodrich plant in Louisville, Ky. (Heath et al., 1975). The eighth case occurred in a Swedish worker in 1969 (Byren et al., 1975).

Studies by Maltoni as early as 1969, but not disclosed until 1975, revealed a high incidence of malignant cells, of a large cell adenocarcinomatous type not generally seen in smokers, in the sputum of VC/PVC workers, suggestive of early lung cancer (Maltoni, 1976).

On January 22, 1974, B. F. Goodrich announced that since 1971 three PVC workers in their Louisville, Kentucky, plant had died of angiosarcoma of the liver. On that same day, the MCA revealed the unpublished Maltoni data to NIOSH. Based on these data, OSHA announced a temporary emergency standard of 50 ppm on April, 1974; this was replaced by the present 1 ppm permanent standard on April 1, 1975.

3. Comments

It is clear that a significant body of animal and human data had established the carcinogenicity of VC prior to January, 1974, and at least as early as 1970. It is also clear that much of these data had not been published or otherwise released by the chemical industry prior to 1974. The control of continuous fugitive and point source, and episodic emissions by Goodrich in 1970 (instead of waiting until so required by the 1976 EPA regulations), together with the development of community monitoring systems, could have effectively

curtailed Mr. Grasso's residential exposure to VC/PVC. In all probability, this would have substantially reduced the chances of his developing angiosarcoma of the liver.

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III. THE CARCINOGENICITY OF VC

VC is a highly potent multi-system carcinogen which is known to induce a wide range of cancers in a wide range of experimental animals, and in humans.

1. Animal Studies

VC induces angiosarcomas of the liver and other organs, and a wide range of other malignant neoplasms in a wide range of experimental animals, rats, mice and hamsters, following chronic inhalation, oral or parenteral exposure. VC also induces hepatocellular carcinomas, carcinoma of the kidney, lung and Zymbal gland, nephroblastomas, brain neuroblastomas, and miscellaneous other malignant neoplasms, including mammary adenocarcinomas, sebaceous gland carcinomas, lymphomas and osteochondromas (Viola et al., 1971; Maltoni & Lefemine, 1975; Keplinger et al., 1975; Maltoni, 1977).

In extensive experiments from 1971 to 1978, the carcinogenic effects of VC were tested in rats, mice and hamsters by inhalation, over a dose range from 1 to 10,000 ppm administered intermittently over periods ranging from 5 weeks to 1 year, and also by other routes (Maltoni, 1977, 1980); inhalation by rats over a dose range from 1 to 2,500 ppm (for 4 hours daily, for 5 days weekly, for 1 year) induced carcinogenic effects down to the lowest doses tested, including breast cancers at 1-5 ppm and liver angiosarcomas at 10 ppm. Angiosarcomas were also induced in rats and mice by 50 ppm VC administered intermittently for 17 and 30 weeks, respectively. Additionally, carcinogenic effects were induced in hamsters by 50 ppm doses over 30 weeks.

In other experiments, angiosarcomas and other neoplasms were induced in mice at the lowest dose tested, 50 ppm, over a 36 week period (Keplinger, 1975), and over a year (Holmberg, 1976; Lee, 1977). Carcinogenic effects have also been reported in rats and mice exposed to 1 ppm levels for 32 weeks (Kaloyanova, 1976).

In extensive experiments contracted by the Consumer Product Safety Commission, the carcinogenic effects of VC in mice were demonstrated after a single exposure to 5,000 ppm for 1 hour only (CPSC, 1979); borderline carcinogenic effects were, however, also noted following 1 hour's exposure to 500 ppm. It was concluded "that even single exposure of sufficient magnitude may be carcinogenic." The study warns that "a one-time exposure occurring, for example, as a result of an accidental spillage---could threaten---nearby residents."

2. Occupational Exposure During Manufacture of VC/PVC

One of the earliest reported occupational epidemiological studies, based on 257 workers exposed to VC for at least 5 years with initial exposure having occurred more than 10 years past, found a 2.3-fold excess in deaths from cancer of all sites combined; three of the cancer deaths were due to angiosarcoma of the liver (Nicholson et al., 1974). In the same year, hepatic angiosarcomas and an excess of cancers of multiple organs, including mouth, pharynx, digestive system, lung and lymphomas, were reported among VC/PVC workers (Tabershaw & Gaffey, 1974). A proportionate mortality analysis of 161 deceased workers in two plants producing and polymerizing VC found an 11-fold excess risk of liver and biliary tract cancers, and a 4-fold excess of brain cancers (Monson et al., 1974).

In subsequent studies, an excess of cancers of four organ systems, liver, brain, lung and lympho-hematopoietic systems, were found among VC polymerization workers (Waxweiler et al., 1976); of fourteen histologically confirmed liver cancers, eleven were hepatic angiosarcomas, a sixteen-fold increased risk of liver cancer mortality.

A statistically significant excess of liver and pancreatic cancer deaths was found among 271 Swedish workers employed in a VC/PVC production plant

(Byren et al., 1976); this excess appeared within the first five years after first exposure to VC.* In a study on cancer mortality among 7,021 males employed in VC production and polymerization, an excess of cancer mortality for multiple organs, liver (12 observed vs. 0.6 expected), stomach (18 observed vs. 9.6 expected), and the lymphatic and hematopoietic systems (15 observed vs. 5.2 expected), was found in comparison with the West German male population (Von Reinl et al., 1977). In a similar study on 7,561 males who at some time between 1940 and 1974 were employed at one of four plants producing PVC, an excess liver cancer mortality was shown for each group of workers irrespective whether exposure to VC was "high, medium, or low" (Fox & Collier, 1977); although the study provided no evidence of excess mortality from cancers other than of the liver, it was emphazied the period of follow-up was too short to permit valid negative inferences.

A NIOSH industrial hygiene survey, conducted in thirteen VC/PVC plants during 1974-1975, found that VC exposures, as determined by personal sampling, ranged from 0.01 to 84.77 ppm (n=119) for VC monomer plants, and from non-detectable to 245.0 ppm (n=449) for VC polymerization plants (Jones, 1978).

3. Occupational Exposure During PVC Fabrication

Levels of exposure to VC are much lower in PVC fabricating plants than in plan manufacturing VC or polymerizing it to PVC. A 1976 NIOSH industrial hygiene survey of PVC fabricating plants found that VC exposures ranged from the non-detectable to 2.44 ppm (Jones, 1978); PVC dust levels ranged from 1.7 to 13.3 $mg/m^3$.

Two confirmed cases of hepatic angiosarcoma have been reported in Connecticut among workers employed in industries using PVC (Christine et al., 1974); one was a 47 year old man who had worked for the previous ten years as an accountant in a factory producing vinyl sheets and processing PVC resins, and the second was a 61 year old man who had spent twenty-five years in an electrical plant operating a machine that applied PVC-containing plastic to wires. A review of fourteen cases

*Other epidemiological studies have confirmed such short latencies for excess risks of cancer following exposure to VC/PVC.

of hepatic angiosarcoma diagnosed in Great Britain during 1963-1973, found one case who had worked in a plant which used PVC as a raw material (Baxter et al., 1977).

A proportionate mortality study of 707 male PVC fabricators and other plastic workers, dying in Great Britain in 1970-1972, found an excess of stomach cancer mortality, 924 observed vs. 16.4 expected, $p<0.05$ (Baxter & Fox, 1976).

A cross-sectional mortality study of 3,845 deaths during 1964-1973 among current and former white male employees of seventeen PVC fabrication facilities found an excess of deaths from digestive tract cancer (210 observed vs. 162.373 expected, PMR=129), from respiratory tract cancer (205 observed vs. 176.899 expected, PMR=116), and from lymphatic cancer (42 observed vs. 32.435 expected, PMR=129) (Chiazze et al., 1977). For white females, there were excesses of deaths from digestive tract cancer (53 observed vs. 34.929 expected, PMR=152), from breast cancer (44 observed vs. 31.907 expected, PMR=138), and from urinary tract cancer (11 observed vs. 4.487 expected, PMR=245).

4. Cancers in Communities Near VC/PVC Plants

A wide range of studies have demonstrated excess cancer risks among residents of communities located in proximity to VC/PVC manufacturing facilities.

Following the findings of excess brain tumors in VC-exposed workers, a significant excess of these tumors, 38 observed vs. 24 expected, $p<0.01$, was found in several Ohio communities where PVC manufacturing facilities are located (Infante, 1976). Similar findings have been reported in a Canadian community where a PVC manufacturing plant had operated for some 30 years (Iturra, 1976).

Two community cases of hepatic angiosarcoma have been reported in Connecticut in individuals with probable residential exposure to VC (Christine et al., 1974); neither had any history of occupational exposure to VC or arsenic, or diagnostic exposure to thorium oxide (the only 3 agents known to induce

hepatic angiosarcoma). One case lived within two miles of a plant producing PVC coated wire, while the second lived within 0.5 miles of a plant producing vinyl sheet; both plants also had cases of hepatic angiosarcoma among their workers.

Another case of liver angiosarcoma was reported in Great Britain in a resident who had lived for six years within half a mile of VC/PVC manufacturing plant (Baxter et al., 1977). On the basis of these observations, a study was undertaken in New York State of 26 confirmed cases of hepatic angiosarcoma (Brady et al., 1975); the controls, comprised of individuals who had an internal malignant tumor other than primary liver cancer, were matched with index cases on the basis of age at diagnosis, race, sex, place of residence and vital status. A statistically significant association was found between angiosarcoma of the liver and direct occupational or therapeutic exposure to arsenic (2 cases), vinyl chloride (3 cases), and thorium dioxide (2 cases). The study further demonstrated that of ten female cases of liver angiosarcoma, without any occupational or therapeutic exposure to VC arsenic or thorium dioxide, one lived within 1,700 feet (0.34 miles) of a VC polymerization plant, and four lived from 500 to 4,500 feet (0.85 miles) of a PVC fabrication plant. In contrast, none of their matched controls lived within one mile of any facility polymerizing VC or fabricating PVC.

5. Comments

VC is a very potent carcinogen inducing angiosarcomas and a wide range of other malignant tumors in rodents and humans. In experimental animals, malignant tumors have been induced by 1 ppm doses administered intermittently over one year, by 50 ppm doses administered from 17 to 36 weeks, and by 5,000 ppm doses (with marginal effects at 500 ppm), following 1 hour exposure only. Angiosarcomas of the liver and other malignant tumors are well recognized in workers in plants manufacturing VC and PVC, where levels of VC exposure are

relatively high. Additionally, an excess of these tumors is recognized among workers involved in PVC fabricating plants, where exposure levels are well under 10 ppm, and probably closer to 1 ppm.* Excess risks of angiosarcoma of the liver and of brain tumors are also recognized among residents of communities located in proximity to VC/PVC manufacturing facilities. However, the chemical industry has not developed systematic monitoring data on ambient levels of VC in communities located in proximity to VC/PVC manufacturing facilities in relation to either continuous or episodic emissions.

Over and above these consideration, as overwhelmingly recognized by the informed independent scientific community, there is no evidence for the existence of safe levels or thresholds for the irreversible processes involved in chemical or physical carcinogenesis.

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* It may be noted that 1 ppm is approximately equivalent to 2,600 ug/$m^3$; assuming inhaltion by an adult of 1 $m^3$/hr, this is equivalent to a dose of 26,000 ug or 26 mg over a 10 hour period.

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## IV. CONCLUSIONS

On the basis of review of available documentation, there is a very substantial probability that Mr. Grasso's fatal angiosarcoma of the liver resulted from exposure to VC. Based on available documentation, there is also a substantial probability that the major site of his exposure was residential, originating from the Pedricktown facility of B.F. Goodrich, although a contributory role for occupational exposure at the Du Pont Chamber Works appears likely. These conclusions reflect the following considerations:

1. Mr. Grasso was exposed residentially to VC/PVC emissions from the Pedricktown plant, a major PVC manufacturing facility, from 1970 to 1976. These included emissions from continuous point and fugitive sources, and episodic plant sources; 6 episodic emissions, some of which resulting in major VC losses, were recorded in the Pedricktown plant from 1973 to 1976.

2. Mr. Grasso was additionally exposed to lower levels of VC emissions in his workplace from 1964 to 1973.

3. VC is a potent carcinogen, inducing angiosarcoma of the liver and malignant neoplasms of other organs in experimental animals following prolonged intermittent exposure to 1 ppm levels, and following 1 hour exposure to 500-5000 ppm.

5. VC has induced angiosarcoma of the liver and other malignant neoplasms in PVC fabrication workers exposed to VC levels, generally below 2.44 ppm.

6. VC has induced angiosarcomas of the liver in residents of communities located near major VC/PVC manufacturing facilities.

Finally, it should be noted that the industry failed, for several years, to openly recognize information available to them on the carcinogenic hazards posed by VC, and to act on such information for the protection of surrounding communities and exposed workers. The institution of appropriate corrective action, in 1970, by industries including B.F. Goodrich and Dow Chemical would have substantially reduced Mr. Grasso's exposure to VC and his subsequent risks of developing angiosarcoma of the liver.