OSCAR AUERBACH, M.D.
158 Long Hill Drive
Short Hills, New Jersey 07078

February 24, 1986

Demond J. Dwyer, Jr.
Dwyer, Connell & Lisbona
427 Bloomfield Avenue
P.O. Box 1557
Montclair, New Jersey 07042

Dear Mr. Dwyer:

At your request I have examined the case of Joseph Memice.

In the dependency claim, it is alleged that while working as a chemical operator at a chemical manufacturing plant, Mr. Memice was exposed to polyvinyl-chloride which caused angiosarcoma of the liver leading to subsequent death.

In your letter to me dated February 4, 1986 you state that Mr. Memice worked for Pantasote, Incorporated from October 7, 1981 until he left work in October, 1982.

I am in possession of partial hospital records as well as medical reports on Mr. Memice.

There is a number of roentgenographic reports dating back to September 5, 1976. The reports are from the Passaic Radiology Associates and are to the Pantasote Company. The first of these reports is dated December 5, 1974 and is as follows:

Radiographic examination of the chest in a single PA projection shows the heart to be normal, lung fields well areated. No abnormalities are seen within the examined area.

The subsequent reports in the years that followed were similar to that reported in 1974.

The roentgenographic report of May 12, 1983 by Dr. Lewis Immerman to Dr. Tauber, Medical Director of the Pantasote Company, is as follows:

Examination of the chest shows the heart shadow to be normal. The lung fields are mildly hyperaerated but show no other significant abnormalities.

Impression: Essentially negative chest.

Mr. Memice was admitted to the Beth Israel Hospital, Passaic, New Jersey on March 13, 1984.

Chief Complaint and Present Illness: This 65 year old white man was admitted because of increasing weakness, loss of weight and anorexia since November of last year. The patient claims there has been increasing fatiguability and off and on loss of appetite and some change in bowel habits during the last few weeks. There is no diarrhea or melena, just vague abdominal pain and discomfort, some nauseousness with no actual vomiting. He was seen in the office approximately 2 to 3 weeks ago at which time he was noted to be pale, weak with cyanosis of the upper and lower extremities and somewhat dyspneic.

He also lost a great deal of weight, although, he claims that he has not lost more than 10-15 pounds.

Initial study of this patient includes an SMA-12 which demonstrated a great deal of abnormality of the liver function test noticeably marked increase in alkaline phosphatase and because of the enlarged liver that was palpable, firm and nontender Liver scan was requested on an outpatient basis and was reported as multiple defects of the right lobe of the liver. The patient is being admitted now to delineate liver pathology whether there is an existing metastatic or primary liver disease and to treat the patient accordingly.

Symptom Review:

Head, Ears, Eyes, Nose and Throat: No complaints.

Cardio-pulmonary System: No chest pain. There has been increasing shortness of breath on effort, this may be secondary to body weakness. There is no chronic cough. The patient claims that he can still

hike a distance without getting tired easily. The patient was noted to be dyspneic on examination.

Gastrointestinal Tract: The patient has been having increasing anorexia and nausea, vague abdominal pain, no vomiting, no diarrhea, no melena. There has been some constipation.

The liver was noted to be enlarged.

Genital-Urinary System: There is no dysuria, frequency, nocturia, no hematuria.

Endocrine System: No diabetes mellitus or other endocrinopathy.

Neurological System: No localizing signs.

Past Medical History: The patient has never been confined to a hospital for any chronic or acute medical problems. He had in the past right inguinal herniorrhaphy, repair of traumatic injury to the right hand.

The patient has had no abdominal surgery.

He is not allergic to any medications or drugs.

Social History: The patient quit smoking more than 27 years ago, he denies any excessive alcohol intake.

Physical Examination:

Head: Normocephalic. No evidence of trauma.

Eyes: Pupils equal, reactive to light. Questionable scleral icterus. Retinal background unremarkable. Discs are clear, no hemorrhages or exudates are seen.

Ears, Nose and Throat: No abnormalities. Tongue is in the midline.

Neck: Supple. Thyroid gland is not palpable, no cervical adenopathy.

Heart: Regular sinus rhythm, no murmur, gallop or, precordial rub.

Lungs: Clear to auscultation and percussion. There

are a few scattered rhonchi heard but no rales are ellicited.

Abdomen: The liver is 3-4 fingerbreadths below the right costal margin, nodular, firm, nontender. A questionable firm mass, probably the spleen, is in the left subcostal area.

On March 15, 1984, a colonoscopy was performed on Mr. Memice. I cannot read the physicians name. He found the rectum within normal limits. The sigmoid colon was also found to be within normal limits.

He indicated that the colonoscopy was inadequate but was essentially normal.

There is a consultation dated March 15, 1984, the name of which I cannot read. It states that the patient is a 65 year old man admitted for increasing weakness, weight loss of 15 pounds and anorexia of 6 months.

SMA-12 showed liver function tests as an outpatient to be increased. A liver scan showed the presence of metastases. The final statement was to rule out colo-rectal carcinoma and a colonoscopy was to be done. Apparently, this is the consulation prior to the colonoscopy.

Dr. S. Goel was consulted on March 19, 1984. He stated as follows:

This 65 year old man was admitted on March 13, 1984, with complaints of increasing weakness, loss of weight and anorexia.

On examination, he was found to have an enlarged liver and multiple defects in liver function.

Following admission, the patient underwent a gastrointestinal series which showed a duodenal deformity, because of an ulcer, in the posterior wall of the bulb.

He was also scheduled to have a barium enema which could not be successfully completed, and after that he had a gastrointestinal consultation with Dr. Ruben who did a colonoscopy which showed no abnormality within the colon.

The patient underwent a CT scan of the abdomen which showed multiple lesions of the liver with a large mass in the center. The liver had multiple other masses consistent with metastatic disease. Laboratory work showed a highly elevated alkaline phosphatase and elvation of LDH with a bilirubin of 2.2.

The patient was seen by Dr. Uhm for oncology consultation, and the possibility of angiosarcoma because of the exposure to chemicals has been considered. Because of the multiple lesions of the liver, and no primary lymph node, he was scheduled for a laporatomy and liver biopsy.

Physical Examination: The patient is a well built healthy man.

Neck: no masses:

Abdomen: Soft, nontender. Liver is enlarged.

Extremities: No varicosities.

Working Diagnoses: Multiple defects in the liver, possible metastatic disease.

The plan was to perform an exploratory laparotomy and liver biopsy.

Dr. Goel operated on Mr. Memice on March 21, 1984.

Dr. Goel found the liver to be massively enlarged, purple-red in color. There were multiple lobulations which were not discrete from the other liver tissue but was merging with the other liver tissue.

Liver sutures were applied on the edge left lobe of the liver and a wedge of the liver was excised and sutured. The specimen was submitted for frozen section and on recent discussion with the pathologist, it was found to have a marked inflammatory reaction with a large amount of giant cells. There was no evidence of any carcinoma cells. It was reported to be some sort of hepatitis and part of a generalized liver disease. Another wedge of the liver was removed after applying liver sutures and sent as a routine specimen to the Pathology Department. There was some oozing from the vascular liver from which the biposy was taken and some Avitene was applied.

Specimens were submitted to the Pathology Department. I do not have the gross or microscopic description. I am, however, in possession of a consultation of two slides which were labeled 84S-918 and submited to Dr. Kenneth Kline of the Univeristy of Medicine and Dentistry of New Jersey, University Hospital. His report is as follows:

Clinical Data: Rule out angiosarcoma of the liver.

Nature of Specimen: Liver biopsies: Slides for consultation (84s918 A&B)

Gross Decription: Received are two slides for consultation from Beth Israel Hospital, Passaic, New Jersey with two blank slides for each.

Diagnosis:

A. Angiosarcoma of liver with moderate chronic inflammation, and focal ground glass hepatocytic change and glycogen nuclei. clinically from wedge biopsy.

B. Reactive changes with fatty change. focal hepatocytic and Kupffer cell dysplasia. focal sinusoidal dilation and hepatocytic ground glass change and glycogen nuclei in the liver. Consistent with vinyl-chloride exposure. Clinically from wedge biopsy.

Dr. Kline noted:

The pathological lesions noted in B are typical for those reported in individuals exposed to vinyl-chloride except for the fatty change and glycogen nuclei. these latter changes could represent the effect of the recent starvation and/or diabetes mellitus. One aspect of vinyl-chloride-induced liver injury not seen in this section, however, is the presence of portal fibrosis and portal vein sclerosis which is usually found in more than 50% of the reported cases and has been responsible for a pre-sinusoidal type of hypertension associated with pronounced splenomegaly.

To eliminate the possibility that the ground glass or induction type change of the hepatocytes was due to an

undiagnosed chronic Hepatitis B virus infection, a Shikata aldehyde fuchsin stain was performed which was negative.

Dr. Uhm, Oncology consultant, saw Mr. Memice on March 17, 1984 and stated as follows:

This 65 year old white man presented with increasing general weakness, loss of appetite and weight since November, 1983. Also he had easy fatiguability, but there was no definite evidence of bowel habit change. The patient denied any history of melena or hematemesis. By the time he was referred to Dr Gonzales, he had lost about 15 pounds over the last few months duration. An SMA-12 showed a very abnormal liver function test and a liver scan as an outpatient showed multiple filling defect in the liver compatible with metastatic disease.

On this admission, he underwent multiple studies including colonoscopy which showed no abnormal lesion, an upper gastrointestinal series showed a deformed duodenal bulb compatible with peptic ulcer disease, but there was no evidence of primary cancer in the stomach or gastrointestinal tract. A CT scan of the abdomen showed no other mass except for a filling defect in the liver. Kidney and pancreas were within normal limits.

Past Medical History: Unremarkable except for right inguinal hernia.

The patient used to work in a factory where they produced polyvinyl-chloride (PVC) and actually he was exposed to PVC for 15 years. He retired in 1983. The patient smoked in the past, he stopped about 27 years ago. He smoked about 2 packs of cigarettes a week.

The patient does not drink excessively.

The essestial physical findings were limited to the abdomen which showed a hepatomegaly with a total span in the right midclavicular line of 15 cm and 9 cm palpable below the right costal margin, 7 cm palpable from his xyphoid process.

Impression: There is a very high chance of angio-sarcoma of the liver since the patient

has a long standing exposure to PVC.

Suggestion: Consider biopsy of the liver.

Hospital Course: The patient was seen by Dr. Uhm for evaluation and he concurred with the possibility of angiosacoma of the liver, as the patient has a long-standing history of PVC exposure.

A liver biopsy was performed by Dr. Goel and this was read as an angiosarcoma of the liver with chronic inflammation as confirmed by the University Hospital, Newark, N.J.

The patient's course was unremarkable. He had a low grade fever. his appetite was fair with no nausea or vomiting. He was in no significant discomfort or pain. The nature of the illness was explained to the patient thoroughly by Dr. Uhm. He agreed to undertake chemotherapy prior to his discharge. the patient was to be followed by Dr. Uhm in his office for further chemotherapy. Mr. Memice left the hospital on March 31, 1984.

There is a short stay record of Mr. Memice at the Beth Israel Hospital on June 6, 1984. The report is written by Dr. Uhm. The final diagnosis:

Angiosarcoma of the liver.

History: This 65 year old man with the above diagnosis is readmitted for chemotherapy. Ever since he was diagnosed in March, 1984, the patient has been treated with Adriamycin which was escalated slowly so that his total bilirubin was decreasing gradually. The patient feels less anorexic and less weakness, but over the past three weeks duration, the patient noted an increasing size of his abdomen.

Physical Examinaiton: General: A well developed but chronically ill appearing emaciated man, not in acute distress. Fully alert.

Skin: Dry and dehydrated. He had papillary disruption in the right forearm as described before. No change in the size or number. The largest measures 2.5 x 2.5 cm.

Head, Ears, Eyes, Nose and Throat: Sclerae are not

icteric. Conjunctivae are pale. The fundoscopic examination did reveal papilloedema or hemorrhage.

The tongue is papillated and shows no mucusitis in the oral cavity.

Neck: Supple, no palpable lymph nodes.

Heart: Regular sinus rhythm. Normal S1, S2. No murmurs or gallops heard.

Lungs: Clear to percussion and auscultation.

Abdomen: Markedly distended. The abdominal circumference around the umbilicus is 119 cm. Because of the ascites, Dr. Uhm could not appreciate the size of the liver, but he stated that it is 7 cm below the costal margin.

Extremities: No peripheral edema. No bony tenderness.

Neurological Examination: All within normal limits.

Progress and Summary: complete blood count was obtained which was at the acceptable level for the continuation for his chemotherapy. There were no significant changes in the electrocardiogram. Dr. Uhm incresed the Adriamycin dose up to 75 mg per meter-square.

For his ascites, Dr. Uhm gave him Aldactone.

Dr. Uhm obtained a CT scan of the abdomen. This was interpreted as showing tumors in the liver much decreased in size. The patient, however, developed ascites which was not present in the past. He also had a collection of fluid in the right pleural space. There was a mild degree of atelectasis in the right lower lobe of the lung.

The patient was to be followed as an outpatient in Dr. Uhm's office.

Mr. Memice died on June 29, 1984. The death certificate was signed by Dr. K. Uhm. His diagnoses was:

Cardiopulmonary arrest, secondary to angiosarcoma of

the liver.

There is a statement that an autopsy was not performed on Mr. Memice.

Although I have not had the opportunity to examine the glass slides of the liver biopsy performed by Dr. Goel, I did have the opportunity of reviewing the many micropscopic pictures of the liver when Dr. Kline recently showed the case to the Liver Conference.

I am in agreement with Dr. Kline that Mr. Memice had an angiosarcoma of the liver.

Discussion: angiosarcoma of the liver is generally an extremely rare tumor. In Great Britain, over a ten year period, there were only four cases reported in the medical literature.

In 1974, the center for Disease Control reported on an increase in risk of developing angiosarcoma for the first time among workers exposed to polyvinyl-chloride in the plastics industry. Popper and Thomas, in an article published in the Annals of the New York Academy of Sciences in 1979, described capsular and subcapsular fibrosis as a characteristic of exposure of polyvinyl-chloride.

The gross appearance of angiosarcoma is that of multiple, blood filled cystic lesions which replace the greater portions of the liver.

The microscopic appearance is that which varies from malignant appearing sinusoidal lining which form irregular spaces, to fibrous tissue enclosing blood filled cysts lined by sheets of anoplastic endothelial cells.

It should be pointed out that other substances such as chronic arsenic poisining and thorium dioxide have been associated with the development of angiosarcoma.

There are two features of the pathologic processes in the liver which speak for the association of polyvinyl-chloride exposure and the development of a pathologic process in the liver. First is the development of the angiosarcoma The second are the reactive changes in the form of fatty change, Kupffer cell dysplasia, hepatocyte dysplsia and dilitation of

the sinusoids and also the ground glass appearance of the nuclei.

The important question to be answered is whether the one year exposure to the polyvinyl-chloride from October 7, 1981 to October, 1982 played any role in the development or exacerbation of his angiosarcoma which led to his death. In my own studies of the carcinogenesis of tumors, I found that the changes from normal to abnormal to malignancy occurs over a long period of time.

Mr. Memice was employed by Pantasote for many years. From the letter to Ms. Tilten by Dr. Uhm on August 27, 1984, I have garnered the information that Mr. Memice was employed by the Pantasote Company for more than 15 years. Dr. Uhm points out that it is a well known fact in medicine that chronic exposure to polyvinyl-chloride is strongly related to the develoment of an angiosarcoma of the liver. It is my opinion based upon my own work on the develoment of malignant tumors that the changes leading to invasive malignancy take place over a long period of time. Unlike carcinoma, which develops in the lung as a result of cigarette smoking, if the individual stops smoking before invasion takes place there is regression.

Such regression is not possible in angiosarcoma.

In your letter to me, Mr. Memice was transfered to another department where he was no longer exposed to polyvinyl-chloride. Mr. Memice had an exposure of only ten months in which your carrier was involved. If Mr. Memice had an exposure to polyvinyl-chloride from October 7, 1981 to August 16, 1982, it is my opinion that he would not have developed angiosarcoma of the liver. It is also my opinion that if Mr. Memice had stopped working on October 7, 1981, he would not, in all probability, not have developed an angiosarcoma of the liver.

Conclusions: Based upon all of the evidence available to me in the case of Mr. Joseph Memice, it is my considered medical opinion that he died of an angiosarcoma of the liver.

It is my considered medical opinion that the angiosarcoma in all probability was related to his,

long exposure to polyvinyl-chloride.

It is my considered medical opinion that his occupation from October 7, 1981 to August 16, 1982 where it is alleged he was exposed to polyvinyl-chloride, was not a factor in the development or exacerbation of his angiosarcoma.

It is my considered medical opinion that his angiosarcoma was a process which occurred over a long period of time and would have occurred even without his exposure from October 7, 1981 to October, 1982.

Sincerely,

OSCAR AUERBACH, M.D.