SIGNATURE INJURY AND CAUSATION

A Westlaw search reveals the following definitions for the concept “signature disease”:

- A so-called “signature disease” is one which is caused only by the product at issue.
- A signature disease is one which is “extremely rare in the general population but far more prevalent among those exposed to a particular substance; the disease in a sense bears the signature of the substance.” Daniel A. Farber, Toxic Causation, 71 Minn. L.Rev. 1219, 1251-52 (1987).
- Signature diseases are those that are uniquely related to exposure to a certain substance and are rarely observed in individuals that are not exposed. Hurtado v. Purdue Pharma Co., 6 Misc.3d 1015, 800 N.Y.S.2d 347 (N.Y.Sup.,2005).

Another court has stated: “A signature disease is one so associated with a particular cause that the presence of the disease presumes that cause. For example, malignant mesothelioma is a signature disease for asbestos causation. In re Joint Eastern & Southern Asbestos Litigation, 52 F.3d at 1130.” Hall v. Baxter Healthcare Corp., 947 F.Supp. 1387, 1402 (D.Or.1996). In contrast, a disease like colon cancer has many risk factors: diet, obesity, exposure to environmental hazards, and genetics. An expert witness who claims that a plaintiff's colon cancer was caused by exposure to a specific toxin must undertake a thorough differential diagnosis, performed by a qualified expert, to rule out other potential causes. In Eastern & Southern District Asbestos Litigation, 827 F.Supp. 1014, 1048-49, (S.D.N.Y.,1993), the court dismissed a claim for colon cancer for failure to perform an adequate differential diagnosis. That plaintiff was only 40 at his death, had no family history of cancer, suffered from no special disease or syndrome, and did not face an abnormal risk from his

With that general understanding of what courts and commentators consider to be a Signature Disease, the ABA Tort and Insurance Practice Section has asked whether benzene has a signature disease. The answer is most certainly that there is no signature disease for benzene.

**AML.** The disease most often alleged by plaintiffs to be linked to exposure to benzene is Acute Myelogenous Leukemia, or AML. Approximately 12,000 new cases of AML are reported in the United States every year. J.L. Jandl, *Blood: textbook of hematology*. (Boston: Little, Brown & Company 1997). It is estimated that between 10% and 20% of these cases occur secondary to chemotherapy (particularly alkylating agents) that is being used to aggressively treat other malignancies. *Id.* AML can be either secondary or de novo (primary), with researchers in the United States estimating that approximately 80% to 90% of all AML cases would be considered to be de novo. The primary, or de novo, AML arises spontaneously without a recognizable etiology, whereas secondary leukemias have a readily identifiable cause, including prior treatment with alkylating chemotherapy or exposure to ionizing radiation or benzene. D. Pyatt, *Benzene and Hematopoietic Malignancies*, Clin Occup Environ Med 4 (2004) 529–555. The Centers for Disease Control states that: “There is currently no known way to prevent most types of leukemia.”

The Leukemia & Lymphoma Society states that people can get leukemia at any age. In 2008, AML was most common in people over age 60. According to the American Cancer Society, for most types of leukemia, the risk factors and possible causes are not known. Most people who have specific leukemia risk factors do not get leukemia - and most people with leukemia do not have these
risk factors. Risk factors for AML as reported by the Leukemia and Lymphoma Society and the American Cancer Society are:

- Certain chemotherapies used for lymphoma or other types of cancer;
- Down syndrome and some other genetic diseases;
- Chronic exposure to benzene (such as in the workplace) that exceeds federally approved safety limits;
- Radiation therapy used to treat other types of cancer; and
- Tobacco smoke.

Current litigation involving claims of benzene-caused AML demonstrate that exposure to benzene occurs virtually everywhere in trace amounts, including cigarette smoke and background air, as well as in use of gasoline and thousands of petroleum based cleaners, lubricants and solvents. A leading expert witness who typically testifies for litigants who have contracted blood cancers recently testified that 80 percent of the causes of AML cases are unknown, and the vast majority of remaining AML cases are caused by smoking.

**Lymphomas.** Current benzene litigation in the U.S. has also focused on non-Hodgkin’s lymphoma (NHL) and myelodysplastic syndrome (MDS). In the United States, NHL is the fifth most common cancer among males and females. The age-adjusted incidence of NHL rose by nearly 79 percent from 1975-2005. Age-specific incidence rates of NHL are 2.9/100,000 at ages 20-24 for males and 1.9/100,000 for females. By ages 60-64, they are 53.9/100,000 for males and 39.2/100,000 for females. The incidence of Hodgkin lymphoma among people under 20 years of age was 0.9 per 100,000 people in 2005. About 74,340 Americans will be diagnosed with lymphoma in 2008. This figure includes approximately 8,220 new cases of Hodgkin lymphoma (4,400 males and 3,820
females), and 66,120 new cases of NHL (35,450 males and 30,670 females).

However, again referring to the American Cancer Society and the Leukemia and Lymphoma Society, known risk factors explain only a small proportion of lymphoma cases. Most patients with NHL have no known risk factors. Scientists have found few risk factors that may make a person more likely to get this cancer. The Centers for Disease Control say that “The main causes of lymphoma are unknown.” The National Cancer Institute (NCI) identifies immune disorders, infections, age and herbicide exposure as NHL risk factors. NCI also links obesity with NHL causation. In specific geographic regions, infection with the Epstein-Barr virus is strongly associated with African Burkitt lymphoma in Africa. Epstein-Barr virus infection may play a role in the increased risk of NHL in persons with immune suppression as a result of organ transplantation and its therapy. Further, most cases of lymphoma occur in people who do not have any identifiable risk factors and most people with presumptive risk factors do not get the disease. Even more significant from a signature disease perspective, NHL is really a family of diseases, encompassing more than 25 separate conditions.

**MDS.** MDS may be primary (also called "de novo") or secondary. The vast majority of patients with MDS have primary MDS. This type usually has no clear-cut cause. It is estimated that there were more than 11,000 new cases of MDS diagnosed in the United States in 2008. The overall incidence rate is estimated at close to four cases per 100,000 population. MDS most commonly strikes males ages 70 and above. For the five-year period 2001-2005, there were approximately 50,484 cases of MDS throughout the United States, averaging 10,097 cases per year (a total of 27,629 in males, averaging 5,526 per year; and a total of 22,856 in females, averaging 4,571 per year). This results in an incidence rate of 3.8 cases per 100,000 population for both genders - 5.1/100,000 population in males, and a much lower 2.9/100,000 population in females. Most people
who are exposed to chemotherapy, radiation therapy and/or benzene do not develop MDS. People who do develop secondary MDS may have inherited genes that limit their ability to detoxify the causative agents, whatever they may be. The only suspected lifestyle-related risk factor for myelodysplastic syndromes (MDS) is smoking, according to the American Cancer Society.

**Causation issues.** In contrast to the history of asbestos litigation, benzene claims arise from what the courts refer to as an “immature tort.” Scientific, legal, and factual issues related to “immature torts” are novel and unsettled, and courts move cautiously in such cases “until enough trials have occurred so that the contours of various types of claims within the ... litigation are known . . . [C]ourts should proceed with extreme caution” in such cases. *In re Bristol-Myers Squibb Co.*, 975 S.W.2d 601, 603 (Tex.1998); *Janssen Pharmaceutica, Inc. v. Armond*, 866 So.2d 1092, 1099 (Miss. 2004). Each of the diseases most often alleged to be associated with benzene exposure in current litigation—AML, lymphomas and MDS—have a significant, if not overwhelming, percentage of cases caused by no known factor. Furthermore, each such disease is known to be caused by factors and exposures other than benzene. As such, there are no Signature Diseases for benzene. Thus, causation standards for tort claims arising from alleged benzene exposure will have to be satisfied by the applicable causation standard for each forum in which the claims are filed.