The Next Wave of Toxic Tort Litigation?
The Great Formaldehyde Cancer Debate

Formaldehyde is a colorless chemical used to manufacture a wide variety of products, from plywood and adhesives to embalming fluid and hair straighteners. Moreover, myriad occupations (e.g., textile workers, painters, electricians, butchers) may expose workers to formaldehyde. Given formaldehyde's ubiquity in industry, a June 10, 2011 *New York Times* article on a report from the National Toxicology Program on the carcinogenicity of formaldehyde may signal the beginning of a wave of litigation alleging damages – including fear of cancer – from formaldehyde exposure.

The extent to which formaldehyde is carcinogenic is already hotly contested in scientific and governmental communities. The National Toxicology Program ("NTP"), which is part of the Department of Health and Human Services ("DHS"), issued its 12th Report on Carcinogens (the "RoC") in June 2011. Previous reports classified formaldehyde as a substance "reasonably anticipated to be a human carcinogen."[1] The NTP now classifies formaldehyde as a substance "known to be a human carcinogen."[2] In particular, the NTP found "sufficient evidence" that formaldehyde exposure causes (1) nasopharyngeal cancer, (2) sinonasal cancer, and (3) "lymphohematopoietic cancer, specifically myeloid leukemia."[3] The primary evidence upon which NTP relied were epidemiological studies; it relied secondarily, on animal studies and on "mechanistic" data that showed *how* an "adverse health outcome occurs."[4]

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[1] *See* National Toxicology Program's Report on Carcinogens — Formaldehyde, Twelfth Edition (2011), p. 195.

[2] *See id.*

[3] *See* Addendum to the 12th Report on Carcinogens, p. 2.

[4] *See id.,* pp. 2-3.

The scientific community is in general agreement with the NTP's position that formaldehyde exposure can cause nasopharyngeal cancer and sinonasal cancer, both of which are relatively rare. Nasopharyngeal cancer, which occurs in the uppermost region of the throat, is contracted by approximately 1 out of every 100,000 people in the United States each year. Sinonasal cancer, which occurs in and around the nose, is contracted by approximately 1 out of every 500,000 people in the United States each year.

One reason for this general agreement is that formaldehyde, which is a gas at room temperature and thus enters the body via inhalation, is absorbed primarily at its first "points of contact" — the nose and upper throat. Accordingly, to the extent formaldehyde is a carcinogen, it is reasonable to conclude that the most likely sites for formaldehyde-related cancer would be the nose and upper throat. In part because this connection between the "points of contact" and sites of cancer is inapplicable to acute myeloid leukemia and other lymphohematopoietic cancers, the opinion that there are causal links between such cancers and formaldehyde exposure is being and will be challenged.

For instance, one year before the NTP Report declared that formaldehyde causes acute myeloid leukemia ("ALM"), the Environmental Protection Agency ("EPA") issued a draft Toxicological Review of Formaldehyde – Inhalation Assessment ("EPA Report") on the carcinogenicity of formaldehyde.[5] The EPA Report stated that "[h]uman epidemiological evidence is sufficient to conclude" that formaldehyde exposure causes, not just nasopharyngeal and sinonasal

[5] *See* Toxicological Review of Formaldehyde — Inhalation Assessment (In Support of Summary Information on the Integrated Risk Information System), Volume III of IV.

cancers, but also "**all leukemias, myeloid leukemia and lymphohematopoietic cancers as a group.**"[6]

On its own, AML, which occurs annually in approximately 3.77 of every 100,000 adults in the United States, has a substantially higher incidence rate than either nasopharyngeal or sinonasal cancer. Viewed as a single unit, lymphohematopoietic cancers, which includes acute myeloid leukemia and other cancers such as non-Hodgkins lymphoma, are one of the most common cancer units in the United States. Indeed, according to the Centers for Disease Control, non-Hodgkins lymphoma and "leukemias" have the sixth and ninth highest incidence rates, respectively, among males in the United States. If EPA's assessment of the risk posed by formaldehyde is accurate, this ubiquitous substance would cause one of the country's most common cancers. The EPA Report has, however, been subject to substantial criticism.

EPA submitted the EPA Report to review by the National Academy of Sciences ("NAS"). EPA asked NAS to evaluate, among other things, the carcinogenic potential of formaldehyde. In April 2011, NAS issued its Review of the Environmental Protection Agency's Draft Assessment of Formaldehyde (the "NAS Report").[7] While NAS agreed with EPA that there is "sufficient evidence" of a "causal association between formaldehyde and the cancers of the nose, naval cavity, and nasopharynx," it disagreed with EPA's conclusion that formaldehyde causes lymphohematopoietic

[6] *See id.,* p. 6-25 (emphasis added).

[7] *See* National Research Council's Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde ("NAS Report").

cancers.[8] In the opinion of NAS, the evidence cited by EPA did not establish a causal link between formaldehyde and any lymphohematopoietic cancer, including AML.

Thus, within the last year, two governmental agencies (NTP and EPA) and one esteemed scientific organization (NAS) have examined the extent to which formaldehyde is carcinogenic. In some respects, the conclusions of these entities converge, but in other critical respects, their opinions conflict, as shown below:

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What cancers are caused by formaldehyde exposure?

	nose and upper throat cancer	AML	all lymphohematopoietic cancers
1) EPA Report	✓	✓	✓
2) NTP Report	✓	✓	X
3) NAS Report	✓	X	X

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The NTP, EPA, and NAS all relied on the same type of information, *i.e.,* epidemiological studies, animal studies, and mechanistic data, but the three reports draw conflicting conclusions drawn from this information. The conflict stems from differing views on (1) the persuasive power of the epidemiological findings and (2) whether those findings trump admitted uncertainty of the mechanism by which formaldehyde purportedly causes lymphohematopoietic cancers like AML.

The nature of this conflict can be explained, in part, by reference to the subject on which NTP, EPA, and NAS agree — that formaldehyde exposure can cause nasopharyngeal and sinonasal

[8] *See id.,* pp. 7-8.

cancer. To support this statement, NTP referred to epidemiological studies that consistently found an increased risk of these types of cancers in formaldehyde-exposed persons. It also relied on "mechanistic" studies, which showed that formaldehyde causes "genetic damage to the nasal tissue of both experimental animals and humans exposed by inhalation."[9] NAS, which reviewed the exact same material as EPA, agreed with EPA that the "combined weight of epidemiological findings, results of animal studies, and mechanistic data" established a causal relationship between formaldehyde and cancers of the nose, naval cavity, and nasopharynx.[10] NAS disagreed, however, that the "combined weight" of the such evidence establishes a causal link between formaldehyde and any other type of cancer.[11]

NAS advanced several criticisms of the conclusions drawn in the EPA Report. First, NAS argued that EPA inaccurately treated lymphohematopoietic cancers as a group instead of as individual malignancies. The hematopoietic system is a bodily system of organs and tissues, which includes bone marrow and lymph nodes, involved in the production of blood. According to NAS, because lymphohematopoietic cancers that arise from this system "are often derived from cells of different origin, can demonstrate unique abnormalities, and may arise in different tissues," the causes of lymphohematopoietic cancers may be distinct.[12] NAS contended that, because lymphohematopoietic cancers may have different causes, EPA erred in applying its causation finding to all such cancers as a group instead of to specific types of lymphohematopoietic cancers.

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[9] *See* National Toxicology Program's Report on Carcinogens — Formaldehyde, Twelfth Edition (2011).

[10] *See* NAS Report, p. 7.

[11] *See id.,* pp. 7-8.

[12] *See id.,* p. 80.

Next, NAS asserted that the EPA Report, which relied on epidemiological studies to support the theory that formaldehyde can cause lymphohematopoietic cancers, did not set forth a framework for deciding how much weight to give to the particular studies. That is, the EPA Report did not contain a criteria on which to judge the quality of the exposure assessment, the control of confounding variables, and the statistical power of the various studies. NAS wrote that, without such a criteria, the ultimate conclusion on the persuasiveness of the epidemiological studies would be based on a "subjective view of the overall data."[13] Because there were, in NAS's view, "inconsistencies in the epidemiologic data," and given the problem with treating lymphohematopoietic cancers as a group, NAS recommended that EPA re-assess the epidemiological data using a framework for weighing evidence and assessing causality of specific types of cancer.[14]

Lastly, NAS found that evidence as to *how* formaldehyde can cause lymphohematopoietic cancers is "generally lacking."[15] Because formaldehyde is "absorbed primarily at the site of first contact" — the nose and upper throat, it is unlikely to appear in the blood or bone marrow as an "intact molecule" except at "overwhelming" levels of exposure.[16] Without evidence showing how formaldehyde is delivered to the blood or bone morrow, the claim that formaldehyde has carcinogenic effects on the blood and bone marrow is undermined.

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[13] *See id.,* p. 83.

[14] *See id.*

[15] *See id.,* p. 4.

[16] *See id*.

According to NAS, EPA has hypothesized that "hematopoietic stem cells" can become exposed to formaldehyde when they migrate to the nasopharynx as part of daily circulation.[17] NAS noted, though, that the experimental evidence necessary to support the hypothesis is absent. Thus, along with its view of the ambiguity of epidemiological data, the uncertainty over the mechanism by which formaldehyde can cause cancer beyond the nose and upper throat led NAS to dispute EPA's conclusion that formaldehyde can cause lymphohematopoietic cancers.

NTP issued the RoC after the EPA Report and the NAS Report. NTP acknowledged the "current lack of understanding of the biological mechanism(s) by which formaldehyde causes cancer at distal sites," *i.e.,* sites beyond the nose and upper throat.[18] But it wrote that proof of such a mechanism is not necessary to list a substance as a known carcinogen. NTP concluded that the epidemiological studies sufficed to establish a causal relationship between formaldehyde and myeloid leukemia. As emphasized by NTP, though, this conclusion did not apply to lymphohematopoietic cancers as a group. The reason for this distinction is that, among the studies that examined the connection between formaldehyde and different types of lymphohematopoietic cancers, the "strongest associations were observed for myeloid leukemia."[19]

The NTP Report, EPA Report, and NAS Report, taken together, provide a guide as to how future litigation over the carcinogenic effects of formaldehyde MAY proceed. First, while there will be debate over the levels of formaldehyde exposure necessary to cause nasopharyngeal or sinonasal cancer, or whether formaldehyde actually caused such cancers in a particular person, the three reports

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[17] *See id.,* pp. 81-82.

[18] *See* Addendum to the 12th Report on Carcinogens, p. 5.

[19] *See* NTP Report.

arguably establish, as a threshold matter, THAT formaldehyde *can cause* nasopharyngeal and sinonasal cancer. For lymphohematopoietic cancers, this threshold issue will be vigorously disputed.

Defendants familiar with benzene litigation recognize that plaintiff experts will often use the established fact that benzene can cause AML to argue that benzene can cause other kinds of lymphohematopoietic cancers. If NTP's conclusion about the connection between formaldehyde and AML is accepted, then it is highly likely that the same argument will be employed to link formaldehyde with all types of lymphohematopoietic cancers.

At this point, it appears that the principle defense to the threshold claim that formaldehyde can cause AML and other lymphohematopoietic cancers would be NAS' observation about the absence of evidence of a "mode of action," *i.e.,* evidence showing *how* such cancers could be caused by formaldehyde. Indeed, even though NTP concluded that formaldehyde can cause AML, it acknowledged uncertainty over the mode of action. A secondary defense could focus on the "highly variable epidemiologic literature."[20] Notably, though, NAS never challenged the basic assertion that several epidemiological studies have shown an increased risk of AML in formaldehyde-exposed persons. It criticized, instead, EPA's failure to set forth an objective criteria under which the persuasiveness of the studies could be examined.

Finally, to the extent that a defendant relies on the NAS report to challenge a claim that formaldehyde exposure caused a plaintiff to develop AML, plaintiff MAY attempt to disparage the report as the result of a request from a conservative senator hostile to EPA and the plaintiffs' bar. NAS has, however, been recognized by courts as the one of most prestigious scientific organizations in the country. Hence, it is not the credibility of NAS, but its conclusions about the carcinogenicity

[20] *See* NAS Report, p. 83.

of formaldehyde, that will likely be the center of a coming dispute over the connection, if any, between formaldehyde and some of the most common cancers in the United States.