Toward a Defense of Mesothelioma Cases on Causation: Low Dose and Genetics

(Session: "Asbestos and Lead Litigation—A National Update on Trends, Developments, and Defenses")

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Today's defendants in asbestos litigation often face plaintiffs' claims that they have contracted mesothelioma from exposure to low or even doubtful doses of asbestos. If the mesothelioma looks to be spontaneous (idiopathic) or the result of an exposure so low that it will not cause the disease or the mesothelioma, genetics may provide the alternate explanation to satisfy the jury about why plaintiff or decedent has mesothelioma.

First Step: Dose

Defense counsel must first determine the dose of exposure to asbestos alleged to be the result of the specific defendant's products, actions, or inactions. Low dose exposures should not be admitted as causative. Plaintiff's counsel uses two prongs to claim as a basis that low doses of asbestos, in fact, vanishingly small doses will cause mesothelioma. Neither is a valid scientific argument. One basis is the "low dose" epidemiology by authors such as Iwatsubo, Rodelsperger, and Lacourt. The second basis is the linear no threshold model of carcinogenesis (LNT) followed by regulatory and other agencies such as WHO and IARC.

"Low Dose" Epidemiology

These studies lack of reliability in their findings. Due to bias inherent to the methods of these studies, their results present risks that are higher than actuality and reach conclusions that are inconsistent from one study to the next. The bias in such studies includes:

- Diagnostic bias: the doctor is more likely to diagnose mesothelioma if he knows that the patient was exposed to asbestos.

- Information (recall) bias: a person knowing that he has mesothelioma and that it is caused by asbestos exposure is more likely to remember exposures that in fact do not exist.

- Exposure assessment (measurement) bias: industrial hygienists estimating exposures 20-40 years ago may not understand the degree to which such exposures were higher than those observed in more recent times.

In addition, the fiber type or mix of fiber types to which the subjects and controls were exposed is not known. As a result, "the dose-response relation derived in a given study would be strictly generalizable only to another population that experienced a mix of fiber types similar to the source population." Siemiatycki, J. et al. "Invited Commentary: Is It Possible to Investigate the Quantitative Relation between Asbestos and Mesothelioma in a Community-based Study?" *American Journal of Epidemiology*. Vol. 148(2) (1998) at 143.

LNT

Although not always defined in the same terms, the Linear No Threshold model of carcinogenesis always involves the following several concepts: carcinogens can and do cause damage to DNA; the damage is irreparable and irreversible; the damage is cumulative, i.e. higher or additional doses constantly add to the risk regardless of time frame; the risk of cancer increases in a linear relationship to cumulative dose; and the risk increases at any exposure exceeding zero, i.e. there is no threshold or safe dose.

LNT was originally conceived in the late 1920s before science understood much of what is known today about genetics, DNA, and carcinogenesis. Edward Calabrese, Professor of Environmental Toxicology at the University of Massachusetts-Amherst, gives this conclusion about LNT:

> "The LNT single-hit dose-response model for cancer risk assessment was conceived, formulated, and applied in a manner which is now known to have been scientifically invalid. . . [T]he concept of LNT . . . is shown to have multiple flaws that reveal its lack of scientific validity. . . [T]he basis for cancer risk assessment, as . . . accepted by virtually all regulatory agencies, is demonstrably incorrect."

Calabrese, E.J. "The linear No Threshold dose response model: A comprehensive assessment of its historical and scientific foundations." *Chemico-Biological Interactions*. Vol. 301 (2019) at 6, 21.

The well-known Bruce Ames presents a similar conclusion. His Ames test is an expeditious and inexpensive method to determine mutagenicity and thereby carcinogenicity of substances. Despite his attention to issues of cancer, he is extraordinarily cautious about overstatement of the dangers of carcinogens: "cancer estimates for toxin control programs are worst-case, hypothetical estimates, and the true risks at low dose are often likely to be zero." Ames, B. et al. "Environmental Pollution, Pesticides, and the Prevention of Cancer: Misconceptions." *The FASEB Journal*. Vol 11 (November 1997) at 1042, 1050. What a regulatory agency sets as its permissible level does not inform anyone, particularly a jury, that a specific dose is in fact causative of disease.

Given all of these thoughts on the effects of low dose exposure to asbestos, the jury may still wonder what then caused the disease. Genetics may provide the answer.

Genetic Predisposition: Inherited Cancer Syndromes as a Cause of Mesothelioma Independent of Asbestos

Looking to Restatement (Second) of Torts, Section 432(2) (1965), causation is not proven and in fact rebutted "if the harm would have been sustained even if the actor had not been negligent." Five to ten percent of tumors occur as a result of monogenic predispositions while another 30-50% occurs due to polygenic predispositions. Lubinski J. et al. "Molecular Basis of Inherited Predisposition for Tumors." *Acta Biochimica Polonica*. Vol. 49(3) (2001) at 571. Mesothelioma, caused by one of a number of genetic predispositions, is not any different.

TP53/Li-Fraumeni

In 1969, Frederick Li and Joseph Fraumeni first described the most clearly established, hereditary, tumor predisposition. It is an autosomal dominant pattern of various tumors including soft tissue sarcoma, breast cancer, brain tumors, adrenocortical carcinoma, leukemia, lymphoma, and melanoma as well as lung, prostate, pancreatic, and ovarian, kidney, testicular, laryngeal, head and neck cancers. Li F. et al. "A Cancer Family Syndrome in Twenty-four Kindred." *Cancer Research*. Vol. 48 (1988) at 5358. The Li-Fraumeni Syndrome, as it is now known, is a germline mutation in the TP53 gene which controls cell growth and division and "encodes" or produces the tumor suppressor protein p53. Fifty percent of individuals with the TP53 mutation developed some sort of cancer by age 30. The risk over a lifetime in men is 70% while almost 100% in women. Li-Fraumeni Syndrome is now accepted as leading to malignant mesothelioma, particularly peritoneal mesothelioma. Celeen W. "Malignant Peritoneal Mesothelioma in a Patient with Li-Fraumeni Syndrome." *Journal of Clinical Oncology*. Vol. 29(17) (2011) at 503

BAP1

In 2010 Carbone et al identified BAP1 as a germline mutation creating an autosomal dominant cancer syndrome. Carbone M. et al. "BAP1 Cancer Syndrome: Malignant Mesothelioma, Uveal and Cutaneous Melanoma and MBAITs." *Journal of Transitional Medicine*. Vol. 10 (2010) at 10.1186/1479-5876-10-179. BRCA1 the associated protein 1 (BAP1) constitutes a tumor suppressor gene located on chromosome 3p21. Its mutation was found to be associated with increased risk of malignant mesothelioma and other neoplasms. The prevalence of cancer among a BAP1-mutated cohort is seven times greater than among the non-mutated cohort, 63% compared to 9% respectively. Other cancers in this syndrome include melanoma (uveal and cutaneous), lung, breast, renal and MBAIT.

The question arises whether BAP1 is an independent factor in the cause of mesothelioma or whether asbestos is a necessary addition to cause the disease.

Science has directed efforts to answer such questions. A group reviewed pathology from 52 mesothelioma patients exhibiting the BAP1 mutation and compared it to indicia of exposure to asbestos. They found no statistically significant association between the BAP1 mutation and asbestos exposure. Azrt L. et al. "BAP1 Protein is a Progression Factor in Malignant Pleural Mesothelioma." *Pathology and Oncology Research*. Vol. 20 (2014) at 145, 148, 149. In addition Carbone found that twenty-one percent of persons with the BAP1 mutation contracted mesothelioma while no one in the non-mutated group had contracted the disease.

More than one researcher has found the BAP1 mutations in persons with mesothelioma, but without asbestos exposure. Wiesner T. "Toward an Improved Definition of the Tumor Spectrum Associated with BAP1 Germline Mutations." *Journal of Clinical Oncology*. ico.ascopubs.org/content/30/32/e337.full; Taylor S. "Malignant Peritoneal Mesothelioma in an Adolescent Male with BAP1 Deletion." *Journal of Pediatric Hematology and Oncology*. Vol 37 (5) (2015) at 323.

NF2/Neurofibromatosis Type 2

Neurofibromatosis Type 2 is a dominantly inherited tumor predisposition syndrome. NF2 refers to the tumor suppressor gene on chromosome 22q12. It provides the capability to produce an amino acid protein "595" also known as "Merlin. Yokoyama, T. et al. "YAP1 Is Involved in Mesothelioma Development and Negatively Regulated by Merlin Through Phosphorylation." *Carcinogenesis*. Vol. 59(11) (2008) at 2139. Significantly, this gene has suffered mutation in approximately 40-50% of mesotheliomas and is important to its tumorigenesis. Monteiro de Assis, L.V. at al. "The Role of Key Genes and Pathways Involved in the Tumorigenesis of Malignant Mesothelioma." *Biochimica et Biophysica Acta*. Vol. 1845 (2014) at 232, 236-237. Bianchi et al opined that "[o]ur findings clearly implicate NF2 in malignant mesothelioma tumorigenesis. . ." Bianchi A. et al. "High Frequency of Inactivating Mutations in the Neurofibromatosis Type 2 Gene (NF2) in Primary Malignant Mesothelioma." *Proceedings of the National Academy of Sciences USA*. Vol. 92 (1995) at 10856.

The NF2 mutation predisposes to a number of tumor types including bilateral vestibular Schwannomas of the eighth cranial nerve and other brain tumors (meningiomas and ependymomas) as well as melanoma and carcinoma of the breast and colon. No literature links these tumors with asbestos exposure except for possibly colon cancer for which such evidence is vanishingly close to non-existent. As a result it is easily conceivable that the pathways to induct these

other tumors not related to asbestos exposure should be similar to the pathways that would induct mesothelioma without any substantial asbestos exposure.

Lynch Syndrome

Lynch syndrome refers to a germline mutation of the MMR genes which provide for DNA mismatch repair. Blood samples may be used to obtain DNA for germline analysis of the five MMR genes (MLH1, MSH2, MSH6, PMS2, EPCAM). For oncological purposes, this deficiency is identified in the tumor with MSI-H/MMR-D as a bio-marker. Lynch Syndrome has been recognized for more than a decade as creating a predisposition to the occurrence of various tumors. Realizing the value of a bio-marker for Lynch Syndrome, scientists employed by or associated with various pharmaceutical companies undertook to explore the value of the bio-maker for Lynch Syndrome. They looked a 15,045 tumors in more than 50 cancer types. Among the cancer types that were predisposed by Lynch Syndrome was mesothelioma. The authors noted that germline MMR mutations, implicated in Lynch Syndrome, were not previously, but were now identified in mesothelioma. Latham, A. et al. "Microsatellite Instability Is Associated with the Presence of Lynch Syndrome Pan-Cancer." *Journal of Clinical Oncology*. Vol. 37 (2018) at 286-295.

Bloom Syndrome

Bloom Syndrome is a rare BLM gene mutation. The genetic mutation is not the result of carcinogens but rather germline in nature. Bononi et al looked at 155 cases of mesothelioma and found 9 cases with the BLM mutation. Although 5 had claimed exposure to asbestos, 4 cases had no such identifiable exposure, raising a reasonable conclusion that Bloom Syndrome could predispose to mesothelioma. To determine whether Bloom Syndrome could increase susceptibility of mesothelioma from asbestos exposure, the authors injected mice in the peritoneum with crocidolite asbestos. More of the mice with the BLM mutation contracted mesothelioma than mice without the mutation (21 of 25 versus 13 of 23). Bononi, A. et al. "Heterozygous Germline BLM mutations Increase Susceptibility to Asbestos and Mesothelioma." *PNAS*. Vol. 117 (December 29. 2020) at 33466-33473. No one should conclude from animal experiments at what total dose of exposure humans with BLM mutations will contract mesothelioma.

Genetic Susceptibility—A Red Herring

Plaintiffs attempt to perpetrate a myth that mesothelioma is somehow unique among tumors. When presenting a low dose case and confronting defendant's argument of a lack of causation, plaintiff's counsel seeks refuge in a simple, but

specious argument: plaintiff or decedent contracted mesothelioma because he was especially susceptible to contracting the disease from small doses of inhaled asbestos. This argument appeals to the time-honored tort principle of the plaintiff with the "egg shell" skull, meaning that a defendant takes his plaintiff as he finds him. *Colonial Inn Motor Lodge, Inc. v. Gay*, 288 Ill.App.3d 32, 45, 680 N.E.2d 407, 416 (1997); *Heppner v. Atchison, Topeka, and Santa Fe Ry. Co.*, 297 S.W.2d 497, 504 (Mo. 1956). The real issue is not just susceptibility, but susceptibility to what dose. Plaintiff should prove that (1) some genetic abnormality causes susceptibility to mesothelioma from a low dose, not just any dose of asbestos exposure and (2) plaintiff or decedent in fact has this genetic characteristic. *In re Hanford Nuclear Reservation Litigation*, No. CY-91-3015-AAM, 1998 WL 775340, at 64-65.

Less than 10% of Selikoff's insulator cohort contracted mesothelioma. Genetic predisposition may be the explanation, but these men were all exposed at high cumulative doses, in fact, doses sufficiently high to cause asbestosis in almost all of them. Science supports this view that genetic make-up will cause some people to contract mesothelioma without asbestos exposure or independent of low dose exposure to asbestos while genetic susceptibility explains why some people but not others with significant occupational exposure to asbestos contract mesothelioma. Matullo G. et al. "Genetic Variants Associated with Increased Risk of Malignant Pleural Mesothelioma: A Genome-Wide Association Study." *PlosOne*. http://dx.doi.org/10.1371 /journal.pone.00861253 (April 13, 2013). They discovered that genetic alterations made "an independent contribution" to the causation of malignant pleural mesothelioma, in some instances, more than doubling the risk of the disease. They also found that it was only occupational exposure in association with these genetic alterations that substantially increased the risk of mesothelioma. The authors concluded "genetic risk factors" should be taken into account in the "risk profile of people with a high exposure to asbestos."

Most of the talk about a special susceptibility to mesothelioma from low dose exposure comes from experiments on mice with the dominant BAP1 mutation. Of course, what is found in animals may not apply to humans, particularly when the mice are exposed through direct injection into the peritoneum while human exposure almost invariably comes from inhalation. Most tellingly, finding an increased number of cases of peritoneal mesothelioma in mice from low doses is inconsistent with human experience. Prolonged and heavy exposure, not a low dose exposure, is necessary to cause peritoneal mesothelioma in humans.

Bringing It Altogether: Industrial Hygiene, Family History and Genetic/Molecular Testing

Methods of genetic testing include biochemical testing, molecular or direct and cytogenic testing. Obtaining the necessary blood or tissue for genetic testing will normally require a court order. Although drawing blood is of course minimally invasive, plaintiff may argue otherwise. It is also possible that normal tissue is available from an autopsy, extra-pleural pneumonectomy, or other procedure.

These are steps in preparation of the defense.

- An industrial hygienist must calculate the dose.
- A medical expert should testify that the dose calculated by the hygienist is not sufficient to increase materially the risk of mesothelioma and in fact did not cause the mesothelioma.
- Experts must establish any family history of cancer among blood relatives as well as any prior or concurrent cancer suffered by plaintiff.
- Defendant should perform genetic testing on plaintiff's tissues.
- Defendant must be prepared to present a genetics expert to opine that a genetic predisposition is the cause of plaintiff's mesothelioma.

US EPA's TSCA Risk Assessment Approach: A Case Study of Asbestos in Automotive Brakes

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The amended Toxic Substances Control Act (TSCA) addresses the production, importation, use, and disposal of specific chemicals and certain substances. Under TSCA, the United States Environmental Protection Agency (US EPA) is required "to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk of injury to health or the environment, under the conditions of use, without consideration of costs or other non-risk factors, including an unreasonable risk to potentially exposed or susceptible subpopulations identified as relevant to the Risk Evaluation" (US EPA, 2020a).

In December 2020, US EPA released a "Risk Evaluation for Asbestos, Part 1: Chrysotile Asbestos" (referred to as the Risk Evaluation herein) under the amended TSCA (US EPA, 2020a). As noted by US EPA (2020a), asbestos has not been mined or otherwise produced in the US since 2002, and the only form of asbestos currently known to be imported, processed, or distributed for use in the US is chrysotile. Among the asbestos-containing products US EPA identified as being imported and used currently are aftermarket automotive brakes and clutches. US EPA evaluated specific conditions of use (COUs) for these products, including importing, processing, and distribution in commerce; occupational and consumer uses; and disposal. The risk evaluation focused on inhalation exposures to workers and occupational non-users (ONUs) in occupational settings, and inhalation exposures to both do-it-yourselfers (DIYers) and bystanders in consumer settings. In addition to considering exposure to asbestos in aftermarket automotive friction products, US EPA considered exposure to asbestos in original manufacturer automotive friction products, primarily in older and vintage vehicles.

US EPA (2020a) derived an inhalation unit risk (IUR) for chrysotile asbestos by applying a linear no-threshold (LNT) model from the point of departure (1% benchmark risk) from two occupational epidemiology studies of one chrysotile asbestos cohort (*i.e.*, Elliott *et al*., 2012; Loomis *et al*., 2019) and exposure-response models with the best fit. US EPA used an absolute risk model for mesothelioma and a relative risk model for lung cancer. The latter assumes a background risk and the former does not (*i.e.*, background risk is assumed to be zero). The final IUR is 0.16 per fibers per cubic centimeter (f/cc) and it addresses both lung cancer and mesothelioma (US EPA, 2020a).

For all the evaluated COUs, US EPA derived exposure concentration estimates from data available in the scientific literature that reflect a variety of activities and practices (*i.e.*, use of compressed air or newer methods to clean out brake dust, arc grinding, brake filing, and unpacking and repacking of asbestos-containing brake pads and linings/shoes). Based on excess lifetime cancer risk (ELCR) benchmarks of 1×10^{-4} for occupational exposures and 1×10^{-6} for consumer exposures, US EPA concluded that occupational uses of aftermarket or original manufacturer automotive asbestos-containing brakes resulted in unreasonable risks (*i.e.*, $>1 \times 10^{-4}$) in all scenarios, and that consumer uses in all indoor garage scenarios and the high-end outdoor driveway scenario also resulted in unreasonable risks (*i.e.*, $>1 \times 10^{-6}$).

In our view, US EPA greatly overestimated cancer risks to professional automobile mechanics and DIYers from exposure to chrysotile asbestos in brakes. Although US EPA acknowledged that many of the assumptions in the Risk Evaluation are likely to be conservative, the extent to which its risk estimates are disconnected from reality is, in our opinion, not fully considered.

IUR Derivation

US EPA based the chrysotile IUR derived for its Risk Evaluation on the results of two studies conducted at asbestos textile plants in the US – one in North Carolina for mesothelioma (Loomis *et al*., 2019) and one in South Carolina for lung cancer (Elliott *et al*., 2012). Workers in this cohort were exposed to long, unbound chrysotile fibers (Dement *et al*., 2009). This is in contrast to the short chrysotile fibers found in automotive brake dust (Hatch, 1970; Rohl *et al*., 1976; Johnson *et al*., 1979; Roberts and Zumwalde, 1982; Sheehy *et al*., 1989). Longer fibers are more potent than shorter fibers for the induction of mesothelioma and lung cancer (Lippmann, 2014), and this contributes to the IUR for chrysotile overestimating risks for auto mechanics.

As acknowledged by US EPA (2020a), some workers in these studies were also likely exposed to amphibole fibers in addition to chrysotile at these plants. More importantly, some members of the study population had potential historical exposures to amphibole fibers used to make amosite or crocidolite products (Yarborough, 2006; Loomis *et al*., 2009). Thus, neither of the studies US EPA selected for the derivation of its chrysotile IUR can be considered studies of chrysotile only, or even commercial chrysotile only. This is an important limitation given the general consensus within the scientific community that amphiboles are far more potent than chrysotile at inducing asbestos-related diseases (*e.g.*, Hodgson and Darnton, 2000; Lippmann, 2014; Bernstein, 2014; Pierce *et al*., 2016; Moolgavkar *et al*., 2017).

Furthermore, the LNT model, which US EPA used to derive the chrysotile IUR, likely considerably overestimates the cancer potency of chrysotile asbestos. An LNT model is not biologically plausible for substances that do not directly interact

with DNA. Although the specific mechanism of chrysotile asbestos-induced carcinogenesis is not established, the evidence is generally supportive of a mode of action involving chronic inflammation and cellular toxicity and repair that leads to the generation of reactive oxygen species and DNA damage, rather than direct interaction with DNA (Huang *et al*., 2011). This threshold mechanism can only occur at exposure concentrations high enough to overwhelm cellular defense mechanisms.

Pierce *et al*. (2016) derived "best estimate" chrysotile no observable adverse effect levels (NOAELs) of 208-415 f/cc-years for mesothelioma and 89-168 f/cc-years for lung cancer that can be applied as thresholds in chrysotile cancer risk assessments. In addition, Glynn *et al*. (2018) reported that the incidence rates of female pleural mesothelioma in urban areas of the US are not significantly higher than in rural areas of the US, even though ambient asbestos concentrations are higher in the former. This is contrary to what would be expected if the LNT model for chrysotile asbestos is accurate. Further, Camus *et al*. (2002) used a linear model for mesothelioma risk developed by US EPA in the 1980s to predict the number of mesothelioma cases in a population with high, non-occupational chrysotile asbestos exposures. They found that the linear model substantially overpredicted the number of cases (*e.g*., the model predicted 150 mesothelioma cases in females in a mining town in which only one female mesothelioma case was observed). US EPA did not discuss any of these studies or acknowledge a possible threshold mode of action for chrysotile.

Exposure

In order for automobile mechanics and DIYers to be exposed to asbestos in the COUs that US EPA evaluated, asbestos-containing used brakes and/or new aftermarket brakes must be sufficiently available and in demand. US EPA stated that older vehicles still in operation may have various asbestos-containing parts, that older stockpiles of previously manufactured asbestos-containing products may still exist, and that foreign-made aftermarket asbestos-containing automotive parts can be purchased from online retailers (US EPA, 2020a). US EPA assumed that automobile mechanics could be exposed to asbestos from asbestos-containing brakes continuously during a working lifetime of 40 years. This assumption is unlikely to be met, given that the supply of asbestos-containing brakes is limited. Even if a reliable supply of asbestos-containing brakes is and will continue to be available to automobile mechanics, continuous occupational use for 40 years is an unlikely amount of time for any mechanic to work on brakes exclusively.

US EPA assumed daily concomitant exposures to re-entrained asbestos is the greatest source of exposure overestimation for the consumer use scenarios. The exposure estimates from this exposure source account for 99.1 and 99.9% of the total consumer ELCRs for the 1 hour working in a garage per day and 8 hours working in a garage per day scenarios, respectively. Thus, only 0.9 and 0.1% of the total consumer ELCRs for the 1 hour per day and 8 hours per day scenarios,

respectively, are assumed to come from exposures during active brake work. These exposure assumptions are not supported by the available science.

Epidemiology and Toxicology Studies

The epidemiology literature addressing motor vehicle mechanics encompasses several different study designs and research groups, and different populations around the world, spanning decades. Despite these different circumstances, the results of these studies were consistent, with no appreciable heterogeneity (Garabrant *et al*., 2016). These findings should have provided US EPA with a reality check on the findings of its Risk Evaluation, which uses data from studies that are far less relevant to the exposure scenarios at issue than those US EPA dismissed. The more relevant motor vehicle mechanic epidemiology studies, along with several brake work exposure monitoring studies, show that generally low, but measurable, airborne concentrations of short chrysotile fibers found in the vicinity of active brake work does not increase the risk of mesothelioma or lung cancer among brake workers.

Mechanistic and toxicology evidence indicate that an association between chrysotile-containing brake dust and cancer is not biologically plausible (*e.g*., see Garabrant *et al*., 2016; Bernstein *et al*., 2020a,b). For example, consistent with earlier studies, Bernstein *et al*. (2020a,b) reported that the lungs of rats exposed to chrysotile-containing brake dust for 90 days at doses orders of magnitude higher than human exposures exhibited little to no accumulation of fibers and no pathological response, while the lungs of rats exposed to asbestiform amphiboles showed extensive fiber accumulation and persistent inflammation, microgranulomas, and fibrosis. Consistent with this, other studies have shown that free chrysotile fibers that are present in brake dust do not persist in the lung (Boyles *et al*., 2019), and that contrary to amphibole fibers, chrysotile fibers do not cause an inflammatory response in the lungs of mice (Ferro *et al*., 2014).

Thus, the mechanistic and toxicology evidence is supportive of the findings of the motor vehicle mechanic epidemiology studies that chrysotile asbestos in brake dust is not associated with increased cancer risk. This indicates that it was inappropriate to extrapolate findings from studies with much higher concentrations of chrysotile fibers of different dimensions and with amphibole co-exposures when there are data available for more relevant exposures that indicate no increased risks.

Conclusions and Future Directions

US EPA's risk estimates were calculated using unrealistic and inappropriate estimates of exposure to, and the toxicity of, chrysotile-containing brakes and brake dust. In some cases, the exposure estimates are based on obsolete brake maintenance techniques; frequencies and durations of exposure that are implausible given the effectively decades-long discontinued use of asbestos-containing automotive parts and the scarcity of such parts; and assumed re-entrainment of

asbestos that is not supported even under highly implausible dust-disturbance activities. The cancer potency of chrysotile was calculated by applying an IUR that was derived using an LNT model and studies of textile manufacturing workers, who not only had much higher exposures to chrysotile asbestos than brake mechanics, but were also exposed to long, unbound fibers, unlike those found in brakes, and likely to amphibole asbestos as well. Epidemiology studies of motor vehicle mechanics do not support there being increased cancer risks, nor do toxicity studies of chrysotile or chrysotile-containing brake dust. All of these studies are directly relevant to US EPA's Risk Evaluation and provide strong evidence that US EPA overestimated risks, but were not given due consideration by US EPA.

US EPA has started planning Part 2 of the asbestos risk evaluation, which will include legacy asbestos uses and associated disposals of asbestos (*i.e.*, COUs for which manufacture [including importation], processing, and distribution in commerce no longer occur, but for which use and disposal are still known, intended, or reasonably foreseen to occur).

However, the National Academies of Sciences, Engineering, and Medicine (NASEM, 2021) recently reviewed the risk assessment approach used in TSCA evaluations. NASEM concluded that US EPA's "approach to systematic review does not adequately meet the state of the practice" and that US EPA's review of evidence from different scientific disciplines was "particularly unsuccessful" (NASEM, 2021). NASEM also noted that the TSCA approach to systematic review was not "comprehensive, workable, objective, and transparent," and that it should incorporate components of methods from other existing systematic review methods, such as those used by the National Toxicology Program's Office of Health Assessment and Translation, the Integrated Risk Information System (IRIS) program developed by the Agency's Office of Research and Development, and the Navigation Guide (NASEM, 2021; NTP, 2019; Woodruff and Sutton, 2011).

In response, in February 2021, US EPA indicated it would no longer use the "structured and systematic review approach" for identifying quality data to support TSCA risk evaluations (US EPA, 2021a). US EPA is currently refining its risk assessment approach for TSCA evaluations based on NASEM's recommendations and plans to incorporate the approach used in the IRIS program (US EPA, 2021a). However, there are also many issues with IRIS's approach (*e.g.*, study quality and relevance evaluations, consideration of mechanistic data, evidence integration; ACC, 2021; Cox *et al.*, 2021), and if these are implemented in TSCA risk evaluations, it could result in risk estimates that are not scientifically supported.

The Agency also stated that it will review the last 10 TSCA risk evaluations it conducted, including the chrysotile assessment, to ensure that they satisfy the requirements of TSCA, and that they are "guided by the best available science, ensure the integrity of Federal decision-making [based on the evaluations' results], and protect human health and the environment" (US EPA, 2021b). However, it is not clear how US EPA will review this chrysotile risk assessment or what risk

management actions it will take. Actions could include requirements for how chrysotile asbestos is used, or limits or prohibitions on the manufacture, processing, distribution in commerce, use, or disposal of chrysotile asbestos. Once finalized, any modifications or adjustments to these risk management actions will become challenging.

Overall, while regulatory agencies need to be conservative to protect public health, unrealistic estimates such as those in this chrysotile asbestos Risk Evaluation can lead to policies and regulations that are not based in reality.

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Lead in Drinking Water and the "Any Exposure" Theory of Causation – Debunking Key Misconceptions

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Introduction

The public's sensitivity to the potential for lead in drinking water has increased dramatically since Flint, Michigan's lead exceedance grabbed national attention in 2016. This heightened awareness has manifested itself in policy debates, proposed regulatory revisions at the state and federal levels, and of course – litigation.

Seasoned toxic tort litigators following these developments likely recognize the much criticized "any exposure" (or "cumulative exposure") theory of causation taking root in this arena. *See e.g., Newark Education Workers Caucus, et al. v. City of Newark, et al.,* 2:18-cv-11025-KSH-CLW (D.N.J. complaint filed 2018) (seeking preliminary injunction to abate alleged harms from lead in drinking water based on theory that there is "no safe level of lead" exposure.). The "any exposure" theory has been successfully challenged in recent years, most notably in the asbestos context, with defense arguments primarily focusing on the theory's failure to identify a dose sufficient to cause the injury alleged. *See generally Bostic v. Georgia-Pacific Corp.*, 439 S.W.3d 332 (Tex. 2014); *Ford Motor Co. v. Boomer*, 736 S.E.2d 724 (Va. 2013); *Betz v. Pneumo-Abex*, 44 A.3d 27, 49 n.25 (Pa. 2012); *Borg-Warner Corp. v. Flores*, 232 S.W.3d 765 (Tex. 2007).

In addition to challenging dose, defendants facing lead in drinking water suits should be aware that plaintiffs' allegations of exposure and injury are additionally vulnerable because they often rely on flawed understandings of how lead in drinking water is regulated and water corrosion science. These misconceptions have intuitive appeal – particularly when accompanied by allegations of high water lead levels in the home or elevated blood lead. Counsel should begin educating the judge on these issues early and often to set the stage for successful dispositive and *in limine* motions.

Misconception #1: The regulatory "action level" for lead in drinking water is a health-based standard.

Much of the public's concern about harm from lead in drinking water is based on a widely-held misunderstanding that U.S. EPA's Lead and Copper Rule (LCR) "action level" of 0.015 mg/L (15 ppb) for lead in drinking water is a threshold level for adverse health effects. It unquestionably is not; the LCR's action level

has no health or risk basis. *See generally* Lead and Copper Rule, 56 Federal Register 26460 (1991). Rather, the 15 ppb action level is based on a technological assessment of what lead levels could feasibly be achieved at household taps with effective corrosion control treatment. *Id*.

Unlike an exceedance of a maximum contaminant level (MCL) – and despite the representations of some plaintiffs' experts – when lead in drinking water is "elevated" that does not per se mean that a risk or harm threshold has been met. Indeed, because the action level is based on the 90th percentile level of tap water samples, the LCR itself contemplates that as many as 10 percent of samples may be above the 15 ppb action level.

Currently, there is no generally accepted health-based water lead hazard level. Predictive models such as the Integrated Exposure Uptake Biokinetic (IEUBK) model are utilized by EPA and other health organizations to estimate blood lead levels based on environmental exposures, but drinking water inputs generally assume constant water lead concentrations that do not reflect real-world variability.

Misconception #2: A system-wide exceedance of the lead action level for drinking water is evidence of exposure.

Suits alleging injuries from lead in drinking water are typically initiated when a water system's sampling results exceed the 15 ppb action level at the 90th percentile. Plaintiffs will often treat this "system-wide" regulatory exceedance as definitive proof that lead is elevated at the tap in all homes in the relevant service area, including at plaintiff's tap.

This is incorrect for several reasons. First, regulatory samples are collected from a relatively small pool of homes (a maximum of 100 in large water systems that may serve millions of water users), and are sampling methods intended to capture "worst-case" conditions. The samples are not representative of conditions at other homes. Second, lead in drinking water is notoriously geographically variable. Neighboring homes with comparable plumbing and water quality can, and often do, have radically different testing results. This is due to a complex set of variables affecting lead scales on the interior of pipes. It should never be accepted as a given that lead is present at a plaintiff's tap on the basis of a regulatory action level exceedance.

Misconception #3: A household water lead test above the lead action level for drinking water is evidence of exposure.

In some cases a plaintiff will obtain a water lead test at the home and proffer the results as proof of exposure. A positive water lead test result is evidence of a lead plumbing source on the premise (*e.g.*, a lead service line), but in and of itself is not evidence of a plaintiff's exposure. With a few rare exceptions, water lead tests

are collected after a period of stagnation time (*i.e.*, no water use in the home) because water must be in prolonged contact with lead plumbing for leaching to occur.

This type of stagnation testing does not replicate actual consumption. Water is rarely sitting stagnant while the home is occupied – the flushing of toilets and the use of tap water for bathing, washing, and cooking keeps water moving through plumbing and there is generally insufficient contact time for lead to dissolve and water lead concentrations to rise. Non-dissolved particulate lead can enter drinking water, but this is essentially a random occurrence. As a result of these factors, water lead levels in a home have significant temporal variability and actual consumed levels will be significantly lower (in many cases at non-detect levels) than in a stagnated water lead sample.

Misconception #4: An elevated blood lead level is evidence of exposure to lead in drinking water.

Lead is ubiquitous in the environment. Blood lead concentrations can reflect a wide range of potential sources (*e.g.*, soil, paint, and dust, in addition to water). The contribution of water lead to blood lead is complex and varies across age groups based on the duration of exposure, behaviors (*e.g.*, dietary), and the presence of lead sources.

Notably, a robust set of epidemiological data from periods of elevated water lead in Washington, DC, Flint, Michigan, and Newark, New Jersey suggests that water lead may not be a significant contributor to blood lead exposures. Between 2001 and 2004, water lead in Washington, DC, rose substantially after the city water service changed its method of water disinfection, causing previously stable lead in lead service lines to leach into water. However, multiple studies observed no significant correlations between water lead levels and blood lead levels in children living in the city during this time. *See* Guidotti, TL; Calhoun, T; Davies-Cole, JO; Knuckles, ME; Stokes, L; Glymph, C; Lum, G; Moses, MS; Goldsmith, DF; Ragain, L.; *Elevated lead in drinking water in Washington, DC, 2003-2004*, (2007). Further, the District of Columbia Department of Heath tested 98 homes with significantly elevated water lead levels (above 300 ppm) and none of the child residents had elevated blood lead results (defined at the time as 10 μg/dL). Studies of blood lead levels of children in Flint have been extensively analyzed and, while there was an slight increase in blood lead levels during the 2014-2015 period of elevated water lead, it was not statistically significant and it was of the same magnitude of increases during periods of no known water lead elevations. Gomez, HF; Borgialli, DA; Sharman, M; Shah, KK; Scolpino, AJ; Oleske, JM; Bogden, JD, *Blood lead levels of children in Flint, Michigan: 2006-2016.* J. Pediatr. 197:158-164 (2018). Finally, recent data on blood lead levels of Newark children showed no impact from elevated water lead during 2017 and 2018.

Conclusion

The fact of exposure to lead in drinking water should not be assumed or lightly inferred. Defendants facing toxic tort claims based on exposure to lead in drinking water should examine the allegations of the complaint closely to determine if these misconceptions form the basis of the exposure claim. If so, counsel should work closely with qualified experts at the outset to develop robust and science-based arguments to challenge plaintiff's claims of exposure.