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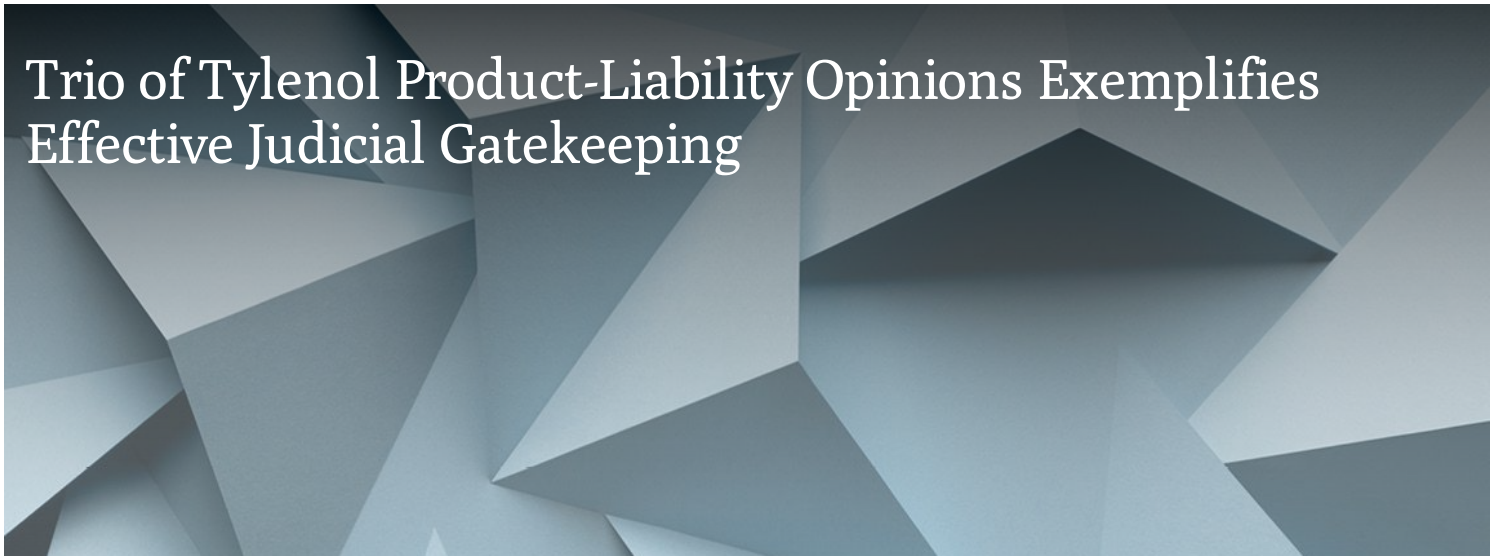
BLOG

Trio of Tylenol Product-Liability Opinions Exemplifies Effective Judicial Gatekeeping



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A series of recent opinions by Judge Denise Cote of the U.S. District Court for the Southern District of New York exemplifies the effective judicial gatekeeping contemplated by Federal Rule of Evidence 702 and *Daubert v. Merrel Dow Pharmaceuticals*.[1] In *In re Acetaminophen – ASD-ADHD Products Liability Litigation*, Judge Cote repeatedly excluded the plaintiffs' general causation experts even though each was "eminently qualified" because they did not reliably apply their methodologies.[2]

BACKGROUND

The *Acetaminophen* litigation involved claims by more than 600 plaintiffs who alleged that in utero exposure to acetaminophen-based products caused children to develop autism spectrum disorder (ASD) or attention deficit-hyperactivity disorder (ADHD).[3] Acetaminophen is the active ingredient in Tylenol and other over-the-counter pain relievers.[4] Plaintiffs sued the manufacturer of Tylenol and retailers of store-branded acetaminophen products alleging violations of state-law duties to warn for failure to disclose the alleged risk of developing ASD or ADHD.[5]

The Judicial Panel on Multidistrict Litigation consolidated the cases before Judge Denise Cote of the Southern District of New York.[6] Judge Cote and the parties agreed to bifurcate discovery, proceeding first with discovery on general causation—or whether the drugs were capable of causing ASD or ADHD.[7] If the plaintiffs' general causation experts survived Rule 702 motions, the remainder of discovery would follow.[8] Ultimately, the second phase of discovery was not necessary. In a series of opinions beginning in December 2023, Judge Cote excluded each of the plaintiffs' general causation experts and granted summary judgment for defendants.

First, in her December 18, 2023 opinion, Judge Cote excluded all five of the plaintiffs' initial general causation experts under Rule 702 and *Daubert*.[9] The plaintiffs had disclosed experts in the fields of epidemiology, toxicology, teratology and genetics, pharmacology, and psychiatry.[10] Although Judge Cote recognized that "[e]ach of the plaintiffs' experts is well qualified to render an opinion in the areas addressed by their reports," she explained that "the state of the scientific evidence on prenatal use of acetaminophen presents a challenge for any expert witness offering the opinion that such use causes ADHD and ASD" because "[t]he epidemiological evidence is highly heterogenous, and major medical organizations and regulators have cautioned against drawing causal

inferences from the existing body of scientific literature."[11] Moreover, she explained that "[n]one of the plaintiffs' experts … has published research that expresses the ultimate opinions they offer here."[12] Instead, the experts presented analyses that "obfuscate the weakness of the evidence on which they purport to rely and the contradictions in the research" by cherry-picking data, ignoring inconsistent results, and dismissing limitations recognized by the study authors rather than "enlighten" the issues.[13]

Judge Cote recognized that "[t]he issues explored by this litigation have great public health significance," and that "[i]t matters to get this right."[14] Because "there is no generally accepted scientific conclusion that in utero exposure to acetaminophen causes either ASD or ADHD," and "the plaintiffs' experts have not reliably opined so either," Judge Cote excluded all their opinions and granted summary judgment for the defendants.[15]

Second, in July 2024, Judge Cote excluded a new general causation expert proffered by plaintiffs in more recently filed suits.[16] The second time around, the plaintiffs focused only on ADHD and put forward an epidemiologist (Dr. Ness) who opined that prenatal exposure to acetaminophen causes ADHD.[17] Like several of the plaintiffs' initial experts, Dr. Ness conducted a Bradford Hill analysis—an analysis of criteria used by some epidemiologists to evaluate the strength of evidence for a causal relationship between two variables.[18] Although Dr. Ness's Bradford Hill analysis "more seriously consider[ed] the issue of confounding" in comparison to the plaintiffs' first set of experts, Judge Cote concluded that Dr. Ness's analysis was "not an objective or rigorous application of scientific methodology" and was instead "result driven" and failed "to confront carefully and fairly the profoundly important issue of confounding by genetics," and excluded it as unreliable under Rule 702 and *Daubert*.[19]

Third, in August 2024, Judge Cote rejected the plaintiffs' last-ditch effort to survive summary judgment. Judge Cote issued a show-cause order requiring the plaintiffs to explain why all remaining cases should not be dismissed in light of the exclusion of all their general causation experts.[20] In response, the plaintiffs argued they could meet their burden on general causation by relying on statements made by one of the *defendants'* experts in "two brief excerpts" from his deposition, "statements in peer-reviewed scientific literature or other formal documents," and "prior unsworn statements, principally LinkedIn posts."[21] Judge Cote disagreed. She held that the plaintiffs had "seize[d] on fragments from … extensive writings and prior statements and misleadingly portray[ed] those fragments" and that their "proposal—that a series of disparate scientific observations is adequate for a jury to find general causation—is not viable."[22] "The issue of general causation in this litigation is complex and serious," she wrote, and "[j]uries are entitled to a thoughtful, reliable analysis by a qualified expert."[23]

Judge Cote's *Acetaminophen* opinions reflect a careful and thoughtful application of the requirements of Rule 702 and *Daubert* and an appreciation of the court's role as a gatekeeper. Several aspects of her opinions are illustrative.

"TRANSDIAGNOSTIC" OR SHARED BRADFORD HILL ANALYSES ARE NOT RELIABLE

Several of the plaintiffs' initial experts conducted Bradford Hill analyses to support their general causation opinions. Each "reviewed the body of scientific literature regarding in utero exposure to acetaminophen and its possible impact on neurodevelopment."[24] Rather than "use[] that literature to render discrete opinions regarding that exposure and the risk of ASD and the risk of ADHD," however, the experts "applied a 'transdiagnostic' analysis that sweeps into their analyses (and conclusions) ASD, ADHD and other neurodevelopmental disorders."[25]

Not only did that approach "raise[] a question of relevance" since the "litigation is brought to obtain recovery on behalf of those who have been diagnosed with ASD or ADHD, not," for example, "anyone with … a deficit in communication or self-regulation," but it raised serious questions of reliability.[26] Indeed, Judge Cote held that the transdiagnostic analyses were inadmissible because they "obscured limitations in the scientific literature," combined studies for which "the diagnostic criteria … are undeniably distinct," and had not "been subjected to peer review and publication either generally or as applied to ASD or ADHD."[27]

GENERAL CAUSATION EXPERTS MUST MEANINGFULLY ENGAGE WITH KNOWN CONFOUNDERS

Confounding is a major source of error in epidemiological studies and "occurs when another causal factor (the confounder) confuses the relationship between the agent of interest and outcome of interest."[28] One of the major sources of confounding relevant to the litigation was confounding by genetics, or the existence of "genetic factors that make pregnant people more likely to take acetaminophen during pregnancy, and also make it more likely that

their offspring will have ADHD or ASD."[29] For instance, a gene might both increase the susceptibility of pregnant women to second-trimester fever and increase the risk of ASD in their children.[30] Although confounding by genetics was a well-known limitation in the acetaminophen literature, one of the plaintiffs' initial experts gave "short shrift to the issue" with a discussion that was "incomplete, unbalanced, and at times misleading."[31] Judge Cote held that the expert failed "to assess with sufficient rigor the relevant evidence of confounding by genetics."[32] Both the Food and Drug Administration ("FDA") and many of the studies relied upon by the plaintiffs' expert recognized confounding by genetics was a limitation.[33] Yet the expert "repeatedly ignore[d] authors' cautions that familial or genetic confounding may explain, at least in part, the observed association" and "downplay[ed] those studies that undercut his causation thesis and emphasize[d] those that align with his thesis."[34] Such a "result-driven analysis," Judge Cote held, "does not reflect a reliable application of scientific methods" under Rule 702 and *Daubert* and "[b]y itself … require[d] the exclusion of his opinion."[35] Nor was Judge Cote persuaded by the plaintiffs' second attempt to address confounding by genetics. In her second *Daubert* opinion, Judge Cote recognized that Dr. Ness "spen[t] more time on the issue of genetic confounding than the plaintiffs' prior experts," but largely wrote off "a sophisticated large-scale study funded by the NIH" that found "that the apparent association between exposure to acetaminophen and ADHD disappears altogether when genetic confounding is accounted for."[36] She held that Dr. Ness's "failure to confront carefully and fairly the profoundly important issue" rendered her entire causation opinion unreliable.[37]

Judge Cote also rejected the plaintiffs' argument that the "Court is certainly not free to interpret a study result for itself, unconstrained by the actual record and adversarial process."[38] She explained that the parties had submitted the study to the court "and have relied upon the Court to examine all of the submitted evidence in light of their arguments," and that it is "the plaintiffs' burden to demonstrate that Dr. Ness's proffered testimony is reliable."[39] She therefore refused to "ignore this study" that had "profound" implications for Dr. Ness's analysis and "decline[d] to blinker [her] assessment of the reliability of Dr. Ness's testimony simply because plaintiffs prefer that the Court not consider the study."[40]

CHERRY-PICKING STUDIES OR FINDINGS CAN RENDER AN ANALYSIS UNRELIABLE

Judge Cote recognized that the plaintiffs' experts repeatedly cherry-picked positive findings and studies and ignored negative ones. In her first *Daubert* opinion, for example, Judge Cote held that "an expert must not cherry-pick from the scientific landscape and present the Court with what he believes the final picture looks like," and that "exclusion of … testimony is warranted where the expert fails to address evidence that is highly relevant to his or her conclusion."[41] In one especially egregious example, she faulted a plaintiffs' expert for presenting a single positive finding from a study when only one of sixteen findings supported his theory and he made "no mention of the fifteen findings of no effect."[42]

Similarly, in her second *Daubert* opinion, Judge Cote wrote that "[t]he only way to find as Dr. Ness did, that the 'great majority' of studies identified the second and/or third trimester as most sensitive to [acetaminophen] exposure is to ignore statistical significance, cherry-pick data, and ignore contrary findings."[43] That was not, she held, "a reliable application of scientific methodology."[44] Nor was the plaintiffs' reliance on a "smattering of … past statements and isolated pieces of [a defense expert's] deposition" sufficient to establish general causation when that expert had repeatedly opined that existing data and studies did not supply a reliable basis to find acetaminophen can cause ADHD.[45]

PRESSING CONCLUSIONS STUDY AUTHORS WERE UNWILLING TO MAKE CREATES AN "ANALYTICAL GAP" BETWEEN THE DATA AND THE OPINION OFFERED

In her first *Daubert* opinion, Judge Cote took issue with the plaintiffs' experts' willingness to "press conclusions that study authors are not willing to make" and to "ignore[] authors' cautions" about limitations in their studies.[46] Those practices "create[d] an 'analytical gap' between the conclusions reached by the authors and the conclusions [the plaintiffs' expert] draws from their work" that crossed the line to impermissible *ipse dixit*.[47]

IGNORING REGULATORS' AND MEDICAL ORGANIZATIONS' CONCLUSIONS CAN RENDER AN ANALYSIS UNRELIABLE

Both of Judge Cote's *Daubert* opinions emphasize the importance of conclusions on causation from regulators like FDA and medical organizations. FDA had conducted periodic reviews of the published literature since 2014 and repeatedly concluded that the evidence was insufficient to establish a causal relationship between in utero acetaminophen exposure and neurodevelopmental outcomes.[48] Medical organizations had come to similar conclusions.[49]

Yet the plaintiffs' lead expert did "not address the FDA's repeated conclusion that the epidemiological evidence does not support his opinions, other than to note his disagreement," and did not "grapple with the contrary conclusions of the American College of Obstetricians and Gynecologists, the Society of Obstetricians and Gynaecologists of Canada, or the European Network of Teratology Information Services."[50] Judge Cote characterized his "rejection of a conclusion that could not be more relevant to his opinions" as "alarming" and evidence of the unreliability of his Bradford Hill analysis.[51]

Judge Cote's *Acetaminophen* opinions provide a roadmap for effective judicial gatekeeping of the type contemplated by Rule 702 and *Daubert*. The opinions reflect careful analyses of the bases for expert opinions and the reliability of the application of experts' methodologies to ensure that opinions that obfuscate rather than enlighten the issues, ignore or conflict with limitations recognized by the authors of the scientific studies, and diverge from the conclusions of relevant regulators and medical organizations do not go to the jury.

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[1] 509 U.S. 579 (1993).

[2] *In re Acetaminophen – ASD-ADHD Prods. Liab. Litig.*, 707 F. Supp. 3d 309, 317 (S.D.N.Y. Dec. 18, 2023) [hereinafter *Acetaminophen I*].

[3] *Id.*

[4] *Id.* at 319.

[5] *Id.* at 317.

[6] *Id.*

[7] *Id.* at 318.

[8] *Id.*

[9] *Id.* at 317.

[10] *Id.* at 319.

[11] *Id.* at 333.

[12] *Id.* at 333.

[13] *Id.* at 334, 357.

[14] *Id.* at 334.

[15] *Id.*

[16] *In re Acetaminophen – ASD-ADHD Prods. Liab. Litig.*, 2024 WL 3357608, at *1 (S.D.N.Y. July 10, 2024) [hereinafter *Acetaminophen II*].

[17] *Id.* at *1.

[18] *Id.* at *17.

[19] *Id.* at *27.

[20] *In re Acetaminophen – ASD-ADHD Prods. Liab. Litig.*, 2024 WL 3874183, at *1, *3 (S.D.N.Y. Aug. 20, 2024) [hereinafter *Acetaminophen III*].

[21] *Id.* at *6.

[22] *Id.* at *6, 7.

[23] *Id.*

[24] *Acetaminophen I* at 334.

[25] *Id.*

[26] *Id.* at 339.

[27] *Id.* at 339–40, 364.

[28] *Acetaminophen I* at 323 (citing Reference Manual on Scientific Evidence (3d ed. 2011) at 591).

[29] *Id.*

[30] *See id.* at 328.

[31] *Id*. at 323.

[32] *Id.* at 351.

[33] *See id.* at 351–52 (detailing studies that observed need to adjust for confounders, including genetic factors, or studies that were specifically designed to measure confounding effect of genetics).

[34] *Id.* at 353, 354.

[35] *Id.* at 351, 364.

[36] *Acetaminophen II* at *21.

[37] *Id.* at *27.

[38] *Id.* at *21 (internal quotation marks omitted).

[39] *Id.*

[40] *Id.*

[41] *Acetaminophen I* at 336.

[42] *Id.* at 360.

[43] *Acetaminophen II* at *22.

[44] *Id.*

[45] *Acetaminophen III* at *2, 6.

[46] *Acetaminophen I* at 353–54.

[47] *Id.* at 353.

[48] *Id.* at 334 (“The FDA has been following this research closely for almost a decade. Internationally, medical associations have weighed in.... [T]here is no generally accepted scientific conclusion that in utero exposure to

acetaminophen causes either ASD or ADHD.”).

[49] *Id.*

[50] *Id.* at 355.

[51] *Id.* at *34-35; *see also Acetaminophen II* at *23 n.37 (“Indeed, Dr. Ness does not adequately address the FDA’s repeated conclusion that the epidemiological evidence does not support her opinions.”).

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