**UNITED STATES DISTRICT COURT**
**SOUTHERN DISTRICT OF NEW YORK**

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| **IN RE: Acetaminophen – ASD-ADHD Products Liability Litigation** | **22md3043 (DLC)** |

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**MEMORANDUM OF LAW IN SUPPORT OF PLAINTIFFS' RULE 702 MOTION TO EXCLUDE DR. ALEXANDER KOLEVZON**

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Plaintiffs submit this Memorandum of Law in support of their motion to exclude the expert testimony and reports of Dr. Alexander Kolevzon, pursuant to Rule 702 of the Federal Rules of Evidence.

## INTRODUCTION

To put it charitably, Dr. Alexander Kolevzon takes a rather transactional approach to the paid opinions he is offering in this litigation. For months before Defendants retained him, Dr. Kolevzon participated in calls and exchanged emails with Stephen Tillery, a plaintiffs' attorney who was investigating "APAP and neurodevelopment." Ex. 3, Kolevzon Dep. Ex. 506 at 3. Following those communications, in September 2022, Dr. Kolevzon agreed to consult for Mr. Tillery for "$600/hr for record review, depo, and trial testimony[.]" *Id.* at 66. But Defendants offered a sweeter deal. So, on December 14, Dr. Kolevzon informed Mr. Tillery that he had "to bow out" of his commitment to plaintiffs. *Id.* at 100. The very next day, on December 15, he invoiced Defendants for work at his new and improved rate: $650 per hour. *Id.* at 102.[1]

Prior to this litigation, in 2022, Dr. Kolevzon was listed as a co-author of a chapter titled "Prenatal, Perinatal and Parental Risk Factors" that appeared in an autism spectrum disorder ("ASD") textbook that was edited by plaintiffs' expert, Dr. Hollander. *See generally* Ex. 4, Kolevzon Dep. Ex. 494. In that "essential" work, the authors conclude that "several prenatal exposures . . . emerge as potential risk factors for ASD," including "[m]ost notably . . . prenatal use of acetaminophen . . . ." *Id.* at 198. It is little wonder Mr. Tillery considered Dr. Kolevzon's services. After bowing out to switch sides, Dr. Kolevzon disavows the textbook chapter that bears his name. He also somehow failed to include this work on his list of publications, as required by

[1] Notably, the other scientists who worked with Dr. Kolevzon and Mr. Tillery, Dr. Shanna Swan and Dr. Ann Bauer, Ex. 3, Kolevzon Dep. Ex. 506 at 28, were the targets of Defendants' third-party subpoenas that Defendants failed to provide prior notice to Plaintiffs' counsel, in contravention of Federal Rule of Civil Procedure 45(a)(4). *See* Dkt. 681 at 2 n.2; Dkt. 689.

the Federal Rules of Civil Procedure. Ex. 5, Kolevzon Dep. Ex. 405 at 18–19. He claims that oversight occurred because he was a named author as a "courtesy," not as an actual writer who approved any of the chapter's substantive content. Ex. 2, Kolevzon Dep. Tr. at 45:23–46:5; 51:11–25; 53:24–54:2. And though he learned of the lone omission in his publications list from "defense attorneys" "about a month [or] three weeks" before his deposition, Dr. Kolevzon did not update his Rule 26(a)(2) disclosures to include the publication. *Id.* at 63:7–9.

Dr. Kolevzon, the prelitigation author, is as right as the Dr. Kolevzon, who had to "bow out" of his commitment to plaintiffs, is wrong: prenatal exposure to acetaminophen is the most notable potential risk factor for ASD in offspring. To disavow a textbook conclusion that bears his name, it is no surprise that Dr. Kolevzon is forced to blinker reality, claiming that a "causality analysis . . . is not warranted" because there is no *association* between acetaminophen exposure and ASD. Ex. 1, Kolevzon Report ¶ 87. Not even the Defendants who upped Dr. Kolevzon's hourly rate deny an *association,* instead training their arguments on the inference of causality. JJCI Mot. Dismiss at 35, Dkt. 426; Ex. 6, Jeffcoat Dep. Tr. at 173:19–174:8 [redacted]; *see also* Ex. 8, D'Alton Dep. Tr. at 29:2–13 (testifying that it has been "reported" there is "an association" between acetaminophen and ASD and ADHD, but she does not believe it is causal). Dr. Kolevzon's opinion here is so divorced from the reality he previously recognized that it cannot satisfy *Daubert*'s reliability prong. It should be excluded.

**BACKGROUND**

Dr. Kolevzon is a professor of psychiatry and pediatrics at the Icahn School of Medicine at Mount Sinai who specializes in the diagnosis and treatment of ASD. Ex. 1, Kolevzon Report

¶ 1. Before Defendants retained him in this litigation, Dr. Kolevzon had not published any research on acetaminophen. Ex. 2, Kolevzon Dep. Tr. At 85:24–86:10.

To reach his opinions in this case, Dr. Kolevzon states that he "reviewed the observational epidemiological studies evaluating whether maternal use of acetaminophen during pregnancy is associated with ASD in offspring." Ex. 1, Kolevzon Report ¶ 86. He does not disclose the databases or search terms he used to identify the relevant studies. He does not explain any criteria for inclusion in his analysis, other than to note that he excluded studies that "did not use a clinical diagnosis of ASD and instead relied upon screening tools and questionnaires." *Id.* ¶ 88. But his reason for including only studies using clinical diagnoses is based on a faulty premise. Dr. Kolevzon identifies only four studies that fulfill his criterion: Liew (2016), Ji (2018), Saunders (2019), and Ji (2020). *Id.* ¶ 91. He claims these studies provide "no reliable evidence of an association between prenatal exposure to acetaminophen and ASD in offspring." *Id.* Yet, as his own Table 2 captures, the studies report *five* statistically significant results of a positive association between acetaminophen exposure and ASD diagnosis:

| Study | ASD Diagnosis | Risk Ratios | Significant Association Detected? |
|---|---|---|---|
| Liew 2016 | Yes | **ASD**<br>aHR: 1.19, 95% CI 1.04-1.35 | Yes |
| | | **ASD+Hyperkinesis**<br>aHR: 1.51, 95% CI 1.19-1.92 | Yes |
| Ji 2020 | Yes | **Cord Acetaminophen Burden**<br>Third tertile OR: 3.62, 95% CI 1.62-8.60 | Yes |
| | | **Cord Acetaminophen Glucuronide**<br>Any detection OR: 2.29, 95% CI 1.06-4.85 | Yes |
| | | **Cord Unchanged Acetaminophen**<br>Third tertile OR: 3.72, 95% CI 1.70-8.55 | Yes |

Adapted from Ex. 1, Kolevzon Report ¶ 91, Table 2.

Dr. Kolevzon testified that he "used [the] Bradford Hill framework," but also that his "review of the literature in this particular case did not indicate the need for Bradford Hill." Ex. 2, Kolevzon Dep. Tr. at 414:10–17. His report is similarly ambiguous, stating that the "Braford [*sic*] Hill framework is frequently used" and "traditionally required evaluation of" nine factors, without any indication that this is the methodology *he* applied. Ex. 1, Kolevzon Report ¶ 85. Regardless of his descriptions, the fact is that Dr. Kolevzon did not perform a Bradford Hill analysis. He apparently (his report does not say) excluded the *five* statistically significant results from his hand-picked studies that show an association between acetaminophen and ASD and concluded that "[i]n the absence of a statistically significant association . . . a causality analysis using traditional methods, such as the Bradford Hill criteria, is not warranted." *Id.* at ¶ 87. He does not consider any of the Bradford Hill criteria or engage in any weighing of the evidence. He simply concludes, contrary to JJCI's own in-house experts, *see* Ex. 6, Jeffcoat Dep. Tr. at 173:19–174:8, and Defendants' own expert, *see* Ex. 8, D'Alton Dep. Tr. at 29:2–13, that there is zero association between acetaminophen and ASD.

## LEGAL STANDARD

Plaintiffs refer the Court to the Rule 702 legal standard set forth in Plaintiffs' Memorandum in Support of their Rule 702 Motion to Exclude Dr. Wendy Chung, Dkt. 1138 at 3–5.

## ARGUMENT

### I. Dr. Kolevzon's Opinions Are Unreliable Because He Fails to Employ a Methodology.

Dr. Kolevzon fails to provide *any* "explanation as to how [he] came to [his] conclusion" and does not identify *any* "methodologies or evidence [to] substantiate that conclusion." *Riegel v. Medtronic, Inc.*, 451 F.3d 104, 127 (2d Cir. 2006). Dr. Kolevzon's opinion is unreliable from the outset because he failed to disclose any search terms or identify the databases he used to locate

relevant literature. "This elementary lapse makes it impossible for a court or adversary to test—or a jury to assess—[Dr. Kolevzon's] methodology, as applied here, for veracity and reliability." *LVL XIII Brands, Inc. v. Louis Vuitton Malletier S.A.*, 209 F. Supp. 3d 612, 645 (S.D.N.Y. 2016). "For this reason alone, exclusion of [Dr. Kolevzon's] conclusions is mandatory under *Daubert*." *Id.*; *see Daniels-Feasel v. Forest Pharms., Inc.*, No. 17 CV 4188-LTS-JLC, 2021 WL 4037820, at *21 (S.D.N.Y. Sept. 3, 2021) ("*Daubert* requires experts to disclose a method subject to replication and testing, for it is the testing of hypotheses to 'see if they can be falsified' that 'distinguishes science from other fields of human inquiry.'" (citing *Daubert v. Merrell Dow Pharms.*, 509 U.S. 579, 593 (1993))), *aff'd* 2023 WL 4837521 (2d Cir. July 28, 2023).

Dr. Kolevzon's opinion is further unreliable because his conclusion that a Bradford Hill analysis "is not warranted" is demonstrably false given his own identification of *five* statistically significant results showing an association. *See* Ex. 1, Kolevzon Report ¶ 91 tbl.2. The only prerequisite for applying the Bradford Hill framework is a controlled observation of a positive association. *See In re Fosamax Prods. Liab. Litig.*, 645 F. Supp. 2d 164, 188 (S.D.N.Y. 2009) (requiring an association from a controlled study before undertaking a Bradford Hill analysis is proper); *In re Mirena Ius Levonorgestrel-Related Prods. Liab. Litig. (No. II)*, 341 F. Supp. 3d 213, 242 (S.D.N.Y. 2018) (hereinafter *Mirena II*) (noting that Bradford Hill criteria "start with an association"); *Dunn v. Sandoz Pharms. Corp.*, 275 F. Supp. 2d 672, 679 (M.D.N.C. 2003) ("The first step in the causation analysis pursuant to Bradford Hill is an epidemiological study that has identified an association between two variables."). A single study with a positive association is sufficient to call for a Bradford Hill analysis. *See* Fed. Jud. Ctr., *Reference Manual on Scientific Evidence* 593 (3d ed. 2011) (hereinafter Ref. Manual); *see generally In re Lipitor (Atorvastatin Calcium) Mktg., Sales Pracs. & Prods. Liab. Litig.*, 174 F. Supp. 3d 911, 916 (D.S.C. 2016)

(collecting cases). Five statistically significant results is more than enough to conclude that a Bradford Hill analysis is warranted. Dr. Kolevzon may have ultimately concluded the association was due to bias, chance, or confounding, but his refusal to even acknowledge the association flies in the face of a basic epidemiological principle. *See* Ref. Manual at 598–99; Ex. 9, Bradford Hill (1965) at 295. And his conclusion is contrary to those of other scientists in the field who Dr. Kolevzon admits are "thoughtful," Ex. 2, Kolevzon Dep. Tr. at 70:17–18, "respected," *id.* at 71:18–19, and "well-intentioned," *id.* at 126:17–18, scientists who "have a real commitment to trying to understand environmental cause of autism." *Id.* at 71:23–72:1.

It is patently unreliable that Dr. Kolevzon ignored—without any explanation—results from his hand-picked evidentiary universe in order to avoid any causality analysis. *See Daniels-Feasel*, 2021 WL 4037820, at *8 (finding an opinion unreliable where the expert "dismisses inconsistent findings without explanation"). This flaw is "large enough that [Dr. Kolevzon] lacks 'good grounds' for his . . . conclusions." *Amorgianos v. Nat'l R.R. Passenger Corp*., 303 F.3d 256, 267 (2d Cir. 2002). His testimony should be excluded.

## II. Dr. Kolevzon's Opinions Are Unreliable Because He Fails to Weigh All of the Relevant Evidence.

Dr. Kolevzon's decision to limit his review of epidemiological studies to those that utilized clinical diagnoses of ASD is based on flawed reasoning and improperly excluded "highly relevant" evidence from his analysis. *Mirena II*, 341 F. Supp. 3d at 242. "Where an expert ignores evidence that is highly relevant to his conclusion . . . exclusion of the expert's testimony is warranted." *Id.*

The only criterion Dr. Kolevzon applied to his collection of scientific literature is that the studies must have used clinical diagnoses of ASD, rather than validated questionnaires, to measure ASD outcomes. *See* Ex. 1, Kolevzon Report ¶ 88. He claimed screening tools and questionnaires "are intentionally overinclusive" and "cannot inform the causal analysis." *Id*. Dr. Kolevzon does

not explain *why* he thinks over-inclusivity is a problem that is so severe it precludes using questionnaire-based studies in a causal analysis. Plaintiffs assume he believes outcome measures that are "overinclusive" would bias the results away from the null, making any association appear stronger than it actually is.

This type of bias is called differential misclassification, meaning there is "systematic error in determining . . . disease status in unexposed cohorts relative to exposed cohorts." Ref. Manual at 589. But there is no way to determine whether a study's results are biased due to differential misclassification without analyzing both exposure and outcome measures of each relevant study. That is precisely the type of study-by-study analysis that Dr. Kolevzon did not do. If he had, he may have concluded it was more likely that the studies he excluded instead suffer from nondifferential misclassification, meaning there was "a great deal of random error" in determining both exposure and outcome. *Id.* And contrary to his assumption that misclassification bias would bias results away from the null, "nondifferential misclassification bias leads to a shift in the odds ratio *toward* one, or, in other words, toward a finding of no effect." *Id.* (emphasis added). Thus, the single disclosed criterion Dr. Kolevzon used to identify relevant studies improperly considered only part of the story.

If Dr. Kolevzon had not artificially limited the universe of scientific evidence on acetaminophen and ASD, he would have discovered even more evidence of a statistically significant association between prenatal acetaminophen exposure and ASD. This evidence is "highly relevant" to his conclusion that there is no association between acetaminophen and ASD. His failure to consider it means that his testimony must be excluded.

## III. Dr. Kolevzon's Opinions Do Not Reflect the Same Level of Intellectual Rigor as His Work Outside of This Litigation.

Dr. Kolevzon's failure to analyze all of the available scientific data and apply any methodology renders his opinions unreliable under *Daubert*. But it also highlights that Dr. Kolevzon did not "employ[] . . . the same level of intellectual rigor that characterizes" his work outside of this litigation, as required under *Daubert*. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). His opinions and flawed methodological assumptions are at odds with his work as a professional scientist.

First, the only acetaminophen-related publication bearing Dr. Kolevzon's name is a chapter in the March 2022 edition of the *Textbook of Autism Spectrum Disorders*, which notes that acetaminophen "has recently been demonstrated to be associated with ASD and ADHD . . . ." Ex. 4, Kolevzon Dep. Ex. 494 at 191. This is directly contrary to Dr. Kolevzon's unsupported opinion that there is no association between acetaminophen and ASD. Further, the chapter cites a systematic review[2] that Dr. Kolevzon rejected in his expert report because "four studies did not use clinical diagnoses of ASD . . . ." Ex. 1, Kolvezon Report ¶ 102. Dr. Kolevzon's own textbook chapter spoke favorably about the quality of data showing an association between acetaminophen and ASD: "In analyses that adjusted for confounding variables, these factors [including prenatal use of acetaminophen] mostly remained considerably robust and statistically significant." Ex. 4, Kolevzon Dep. Ex. 494 at 198. Dr. Kolevzon has never published *anything* that supports his opinions in this case. The conflict between his opinions here and his only publication regarding acetaminophen reveals a lack of rigor that renders his opinions unreliable.

[2] Reem Masarwa et al., *Prenatal Exposure to Acetaminophen and Risk for Attention-Deficit Hyperactivity Disorder and Autism Spectrum Disorder: A Systematic Review, Meta-Analysis, and Meta-Regression Analysis of Cohort Studies*, 187 Am. J. Epidemiology 1817 (2018).

Second, Dr. Kolevzon's report describes ASD as "primarily a genetic disorder." Ex. 1, Kolevzon Report ¶ 49. His limited discussion of environmental factors focuses largely on those with "false positive associations" with ASD. *Id.* ¶ 57. However, in his own research, Dr. Kolevzon is much less guarded about the association between environmental factors and ASD and other neurodevelopment disorders. *See, e.g.*, Kolevzon Dep. Tr. at 368:11–17 (discussing a 2021 paper by Dr. Kolevzon describing "[t]he etiology of ASD" as "multifactorial" including "genetic and environmental factors, as well as their interaction"); *id.* at 520:1–9 (agreeing that "environmental factors . . . can affect . . . the developing fetus"). For example, in one of Dr. Kolevzon's studies, he noted: "Genetic and environmental factors are implicated in ID [intellectual disability] and include . . . factors that affect fetal development, such as . . . congenital exposures to infectious agents or toxic agents." Ex. 10, Viktorin et al. (2017) at 2. In his deposition, Dr. Kolevzon admitted that this is still true. Ex. 2, Kolevzon Dep. Tr. at 359:1–7; *see also id.* at 454:2–11 (discussing another expert report by Dr. Kolevzon that noted "[e]nvironmental factors . . . are major contributors of intellectual disability which is commonly associated with [ASD]"). Similarly, in a 2018 blog post about ASD, Dr. Kolevzon wrote that environmental factors such as "exposure to several toxins during pregnancy" can "act on genetic vulnerability to increase the risk of ASD." Ex. 11, Kolevzon (2018) at 3.[3] If, as Dr. Kolevzon testified, in 70 to 80% of ASD cases there is "no specific gene identified," Ex. 2, Kolevzon Dep. Tr. at 256:9–257:11, it must be that there is an interaction between genes and environmental risk factors like acetaminophen exposure.

[3] It has been a consistent theme among Defendants' experts to state in their own writings and teachings that environmental factors play a causal role with genetics to cause ASD but then do an about-face for their opinions in this litigation and adopt a "genetics-only" causal opinion. *See, e.g.* Pls. Memo. in Support of Mot. to Exclude Dr. Wendy Chung, Dkt. 1138 at 15–20; Pls. Memo. in Support of Mot. to Exclude Dr. Stephen Faraone Dkt. 1146 at 6–8; Pls. Memo. in Support of Mot. to Exclude Dr. Jennifer Pinto-Martin, Dkt. 1143 at 25–28.

His failure to deeply consider acetaminophen as a possible genetic disruptor, despite clear statements on this subject outside of the courtroom, renders his opinions in this case unreliable.

## CONCLUSION

For the reasons stated, the Court should exclude the expert report and testimony of Dr. Alexander Kolevzon.

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Respectfully submitted,

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