

**SUPERIOR COURT OF CALIFORNIA, COUNTY OF LOS ANGELES**  
**Civil Division**

Central District, Spring Street Courthouse, Department 7

**21STCV22822**

**NC vs HAIN CELESTIAL GROUP, INC., et al.**

May 24, 2022

3:04 PM

Judge: Honorable Amy D. Hogue  
Judicial Assistant: Alfredo Morales  
Courtroom Assistant: Crystal Vargas

CSR: None  
ERM: None  
Deputy Sheriff: None

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**APPEARANCES:**

For Plaintiff(s): No Appearances

For Defendant(s): No Appearances

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**NATURE OF PROCEEDINGS: Ruling on Submitted Matter**

The Court, having taken the matter under submission on 04/04/2022 for Evidentiary Hearing 402 EC /Motions in Limine, now rules as follows:

The Motion re: Notice of Motion and Motion to Exclude Expert Testimony filed by Beech-Nut Nutrition Company, Plum, PBC, Sprout Foods, Inc., Walmart, Inc., Nurture, Inc., Gerber Products Company, Hain Celestial Group, Inc., Ralphs Grocery Company on 01/07/2022 is Denied.

The Order Denying Defendants' Motion in Limine to Exclude Plaintiff's Expert Testimony on General Causation is signed and filed this date.

On the Court's own motion, the Hearing on Motion for Trial Preference scheduled for 07/13/2022 is advanced to this date and continued to 08/03/2022 at 02:00 PM in Department 7 at Spring Street Courthouse.

The clerk is to give notice.

Clerk's Certificate of Service By Electronic Service is attached.

<b>SUPERIOR COURT OF CALIFORNIA COUNTY OF LOS ANGELES</b>		Reserved for Clerk's File Stamp
COURTHOUSE ADDRESS: Spring Street Courthouse 312 North Spring Street, Los Angeles, CA 90012		<b>FILED</b> Superior Court of California County of Los Angeles <b>05/24/2022</b>
PLAINTIFF: NC		Sherri R. Carter, Executive Officer / Clerk of Court By: <u>          A. Morales          </u> Deputy
DEFENDANT: Hain Celestial Group, Inc. et al		
<b>CERTIFICATE OF ELECTRONIC SERVICE CODE OF CIVIL PROCEDURE 1010.6</b>		CASE NUMBER: <b>21STCV22822</b>

I, the below named Executive Officer/Clerk of Court of the above-entitled court, do hereby certify that I am not a party to the cause herein, and that on this date I served one copy of the Minute Order and Order entered herein, on 05/24/2022, upon each party or counsel of record in the above entitled action, by electronically serving the document(s) on Case Anywhere at secure.caseanywhere.com on 05/24/2022 from my place of business, Spring Street Courthouse 312 North Spring Street, Los Angeles, CA 90012 in accordance with standard court practices.

Sherri R. Carter, Executive Officer / Clerk of Court

Dated: 05/24/2022

By: A. Morales

Deputy Clerk

**MAY 24 2022**

Sherri R. Carter, Clerk  
Alfredo Morales deputy  
ALFREDO MORALES

SUPERIOR COURT OF THE STATE OF CALIFORNIA  
FOR THE COUNTY OF LOS ANGELES

NC, a minor,

Plaintiff,

v.

HAIN CELESTIAL GROUP, INC; BEECH-  
NUT NUTRITION COMPANY; NURTURE,  
INC.; PLUM, PBC, dba PLUM ORGANICS;  
GERBER PRODUCTS COMPANY;  
WALMART, INC.; SPROUT FOODS, INC.;  
RALPHS GROCERY COMPANY; AND  
DOES 1 THROUGH 100, INCLUSIVE,

Defendants.

) Case No.: 21STCV22822

) ORDER DENYING DEFENDANTS'  
) MOTION IN LIMINE TO EXCLUDE  
) PLAINTIFF'S EXPERT TESTIMONY  
) ON GENERAL CAUSATION

) Hearing Dates:

) January 31, February 1-4 (Plaintiff's experts);  
) March 14 (Defendants' expert);  
) April 4, 2022 (closing arguments)

) Dept.: 7

This is a complex litigation matter requiring exceptional judicial case management in accordance with California Rules of Court, rule 3.400 et seq. The minor plaintiff in this action has been diagnosed with autism-spectrum disorder (ASD) and attention-deficit hyperactivity disorder (ADHD). He alleges that his consumption of heavy metals (lead, arsenic, and/or mercury) contained in baby foods manufactured by the Defendants caused his disorders. Defendants deny that their food products contain harmful levels of heavy metals or caused Plaintiff to suffer any harm. From their point of view, consumption of baby food could not have caused Plaintiff's ASD

1 because ASD is a genetic disorder that develops prior to birth or in the weeks immediately  
2 following birth.

3 To prevail at his jury trial, Plaintiff must present expert testimony establishing general and  
4 specific causation. Under *Sargon Enterprises, Inc. v. University of Southern California* (2012) 55  
5 Cal.4th 747, 771-772 (*Sargon*), the Court has a “substantial gatekeeping responsibility” to ensure  
6 that the expert causation opinions presented to the jury are not “based on a leap of logic or  
7 conjecture.” At the Court’s suggestion and before the parties embarked on the expensive process  
8 of discovery, the parties agreed to seek an early ruling on the question whether Plaintiff’s experts’  
9 opinions that heavy metals are capable of causing ASD and/or ADHD are admissible under  
10 *Sargon*. To that end, Plaintiff retained four experts who presented written opinions, answered  
11 questions in deposition, and testified in Evidence Code section 402 hearings: Drs. Beate Ritz and  
12 Hannah Gardener, both epidemiologists; Dr. Michael Aschner, a neurotoxicologist; and Dr. Kevin  
13 Shapiro, a pediatric neurologist.<sup>1</sup> Defendants likewise retained an expert epidemiologist, Dr. Eric  
14 Fombonne, who submitted a report, submitted to deposition, and testified in a section 402 hearing.

15 Defendants now move, in limine, to exclude Plaintiff’s expert-witness testimony, citing  
16 four analytical gaps identified by their expert, Dr. Fombonne. Based on the briefing, argument,  
17 and evidence, the Court concludes that Plaintiff’s expert opinions that lead, arsenic and/or mercury  
18 are capable of being a substantial factor in causing ASD and ADHD are not inadmissible under  
19 *Sargon*.

20  
21 I. Allegations

22 Now seven years old, Plaintiff NC ate baby food contaminated with lead, mercury, and  
23 arsenic (hereafter, “heavy metals”), causing him to develop ASD — diagnosed in 2016, when he  
24 was age two years, nine months — and ADHD, diagnosed in 2020, when he was six. (First  
25  
26

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27  
28 <sup>1</sup> Evidence Code section 402, subdivision (b) permits the court to “hear and determine the question of the  
admissibility of evidence out of the presence of the jury....”

1 Amended Complaint (Sept. 7, 2021) ¶¶ 1, 55-78.)<sup>2</sup> On various theories of strict liability and  
2 negligence, he brings eight claims against Defendants as the manufacturers, distributors, and  
3 retailers of the baby food. (*Id.* at ¶¶ 82-206.)

4  
5 **II. Standards**

6  
7 **A. Legal Standard: Admissibility of Expert Testimony**

8 If “the complexity of the causation issue is beyond common experience, expert testimony  
9 is required to establish causation.” (*Webster v. Claremont Yoga* (2018) 26 Cal.App.5th 284, 290.)  
10 There are two aspects to proof of causation of harm. Plaintiffs must establish “general causation”  
11 by presenting expert scientific opinion that the allegedly toxic substances are capable of causing  
12 the harm that the plaintiff suffered. Plaintiffs must also prove “specific causation” by presenting  
13 expert testimony that, to reasonable degree of medical certainty, the plaintiff’s harm was caused  
14 by his or her exposure. (*Cottle v. Superior Court* (1992) 3 Cal.App.4th 1367, 1385; *Hendrickson*  
15 *v. ConocoPhillips Co.* (2009) 605 F. Supp. 2d 1142, 1155.) In this case, the issues of general  
16 causation — whether heavy metals can contribute to ASD and ADHD — and specific causation  
17 — whether heavy metals were a “substantial factor” in causing Plaintiff’s ASD and ADHD — are  
18 issues beyond common experience. (See *Johnson & Johnson Talcum Power Cases* (2019) 37  
19 Cal.App.5th 292, 302 (*Johnson & Johnson*.) Expert testimony is required.<sup>3</sup>

20 A court has an obligation to “keep unfounded [expert] opinions from the jury.” (*People v.*  
21 *Azcona* (2020) 58 Cal.App.5th 504, 513.) “[U]nder Evidence Code sections 801, subdivision (b),  
22 and 802, the trial court acts as a gatekeeper to exclude expert opinion testimony that is (1) based  
23

24  
25 <sup>2</sup> Plaintiff also alleges the baby food exposed him to cadmium, but his experts’ opinions do not address this  
26 metal. (FAC, ¶ 1.)

27 <sup>3</sup> This Order only addresses Plaintiff’s experts on general causation, that is, the issue of whether heavy metals  
28 can cause ASD and ADHD. As the term implies, general causation is mostly abstracted from specific causation and  
the specific allegations of this case. This Order does not consider, for example, the dosages of heavy metals to which  
Plaintiff was allegedly exposed, the time frame when he was allegedly exposed, or whether heavy metals were a  
substantial factor in causing his disorders.

1 on matter of a type on which an expert may not reasonably rely, (2) based on reasons unsupported  
2 by the material on which the expert relies, or (3) speculative.” (*Sargon, supra*, 55 Cal.4th at pp.  
3 771-772, page number omitted.) “This means that a court may inquire into, not only the type of  
4 material on which an expert relies, but also whether that material actually supports the expert’s  
5 reasoning. ‘A court may conclude that there is simply too great an analytical gap between the data  
6 and the opinion proffered.’” (*Id.* at p. 771.)

7         However, a court excludes expert opinion cautiously, keeping from the jury only “clearly  
8 invalid and unreliable” opinion that “fails to meet the minimum qualifications for admission.”  
9 (*Sargon, supra*, 55 Cal.4th at p. 772; *Davis v. Honeywell Internat. Inc.* (2016) 245 Cal.App.4th  
10 477, 492 (*Davis*)). A court does not “choose[] between competing expert opinions ... weigh an  
11 opinion’s probative value ... [or] resolve scientific controversies.” (*Sargon*, at p. 772.) It instead  
12 “conducts a ‘circumscribed inquiry’ to ‘determine whether, as a matter of logic, the studies and  
13 other information cited by experts adequately support the conclusion that the expert’s general  
14 theory or technique is valid’” — ensuring, in short, “that an expert, whether basing testimony upon  
15 professional studies or personal experience, employs in the courtroom the same level of intellectual  
16 rigor that characterizes the practice of an expert in the relevant field.” (*Ibid.*) “If the opinion is  
17 based on materials on which the expert may reasonably rely in forming the opinion, and flows in  
18 a reasoned chain of logic from those materials rather than from speculation or conjecture, the  
19 opinion may pass, even though the trial court or other experts disagree with its conclusion or the  
20 methods and materials used to reach it.” (*Davis*, at p. 429 [citing *Sargon*, at pp. 771-772].)

21  
22         B.         Scientific Standard: Inferring Causation from Epidemiological Data

23         Epidemiology is the study of the “incidence, distribution, and etiology” of human disease.  
24 (Green et al., Reference Manual on Scientific Evidence (3d ed.) Reference Guide on  
25 Epidemiology, p. 551 (“Reference Manual”).)<sup>4</sup> Based on the assumption that disease is not  
26

27  
28         <sup>4</sup> California courts use the Reference Manual to evaluate scientific evidence. (See *Duran v. U.S. Bank National Assn.* (2014) 59 Cal.4th 1, 38; *Johnson & Johnson, supra*, 37 Cal.App.5th 292 at p. 303, fn. 4.)

1 distributed randomly in a population, an epidemiological study “identifies agents that are  
2 associated with an increased risk of disease in groups of individuals, quantifies the amount of  
3 excess disease that is associated with an agent, and provides a profile of the type of individual who  
4 is likely to contract a disease after being exposed to an agent.” (*Id.* at pp. 551-552.) Just because  
5 an agent and a disease are associated, however, does not necessarily mean the agent causes the  
6 disease. (*Ibid.*) To assess whether an association is causal, a scientist must understand the  
7 strengths and weaknesses of a study’s design and implementation, and judge how the study’s  
8 findings fit with other scientific knowledge. (*Id.* at p. 553.) “[E]pidemiology cannot prove  
9 causation; rather causation is a judgment for epidemiologists and others interpreting the  
10 epidemiologic data.” (*Id.* at p. 598.)

11 The two main types of human epidemiologic studies are experimental and observational.  
12 An experimental study divides test subjects into one of two groups, exposes one group to an agent,  
13 and observes the results compared to the other, unexposed group. (Reference Manual, p. 555.)  
14 Because experimental human studies allowing exposure to potentially toxic agents are unethical,  
15 epidemiologists typically rely on observational studies. Observational studies typically observe  
16 the outcomes in people who were exposed to an agent compared to the outcomes in people who  
17 were not exposed to the agent. (*Id.* at pp. 555-556.) Observational studies can be of several  
18 different designs, but the two main designs are a) cohort studies and b) case-control studies. (*Id.*  
19 at p. 556.) If a study observes a disease is associated with an agent, researchers first consider  
20 alternative explanations for the association, particularly a) the possibility it was observed by  
21 chance or b) it resulted from bias in the study’s methodology, or c) it was observed not because  
22 the agent caused the disease, but because both the disease and the agent were jointly caused by a  
23 third, confounding factor. (*Id.* at pp. 572, 598.)

24 After considering alternative explanations for the agent-disease association,  
25 epidemiologists assess whether the association is causal using the nine Bradford Hill factors:

- 26 (1) Temporal relationship: Exposure to an agent must occur before a disease develops  
27 — “[w]ithout exposure before the disease, causation cannot exist.”  
28

- 1 (2) Strength of the association: Relative risk, “one of the cornerstones for causal  
2 inferences,” measures how often a disease is observed in people exposed to an agent  
3 relative to how often the disease is observed in people not exposed to the agent.
- 4 (3) Dose-response relationship: A dose-response relationship exists if the greater the  
5 exposure to an agent, the greater the risk of disease. Higher exposures generally,  
6 but not always, increase the incidence or severity of a disease. A dose-response  
7 relationship is therefore “strong, but not essential” evidence of a causal relationship.
- 8 (4) Replication of the findings: As in many areas of science, a causal relationship is  
9 more likely if a study’s findings can be replicated, especially in different conditions  
10 or populations. “Rarely, if ever, does a single study persuasively demonstrate a  
11 cause-effect relationship.”
- 12 (5) Biological plausibility (coherence with existing knowledge): Given what is known  
13 about the biological “mechanisms by which the disease develops,” can the agent  
14 plausibly cause the disease? If it is biologically plausible that an agent causes a  
15 disease, then it “lends credence to an inference of causality.”
- 16 (6) Consideration of alternative explanations: As discussed above, a researcher should  
17 consider whether an observed association resulted from chance, bias, or  
18 confounding.
- 19 (7) Cessation of exposure: If an agent causes a disease, then risk of the disease should  
20 decrease when exposure to the agent stops. Often data is not available showing the  
21 effects of ending an exposure, but if the data is available and it shows a reduction  
22 in the incidence of disease, then it “strongly” supports a causal relationship.
- 23 (8) Specificity of the association: “An association exhibits specificity if the exposure  
24 is associated only with a single disease or type of disease.” “[E]vidence of  
25 specificity may strengthen the case for causation, [but] lack of specificity does not  
26 necessarily undermine it where there is a good biological explanation for its  
27 absence.”
- 28



1 (9) Consistency with other knowledge: Data showed that as cigarette sales in the  
2 United States increased, for example, so did men's rate of death from lung cancer.  
3 This other knowledge was consistent with a causal relationship between smoking  
4 and lung cancer.

5 (Reference Manual, pp. 597-607.) These factors are not a rigid formula. "One or more factors  
6 may be absent even when a true causal relationship exists. Similarly, the existence of some factors  
7 does not ensure that a causal relationship exists. Drawing causal inferences after finding an  
8 association and considering these factors requires judgment and searching analysis, based on  
9 biology, of why a factor or factors may be absent despite a causal relationship, and vice versa."  
10 (*Id.* at p. 600, footnote omitted.)

11 Both sides in this case and courts agree: a Bradford Hill analysis is an accepted  
12 epidemiological method to infer causation from data that shows an association between an  
13 exposure and a disease. Defendants contend, however, that Plaintiff's experts' Bradford Hill  
14 analysis was flawed under *Sargon*.

### 15 16 III. The Experts

17 Two of Plaintiff's four experts, Drs. Ritz and Gardener, are epidemiologists who conducted  
18 a Bradford Hill analysis. The other two experts are Dr. Aschner, a neurotoxicologist, and Dr.  
19 Shapiro, a pediatric neurologist, both of whom opine on one Bradford Hill factor, biological  
20 plausibility. Defendants proffered their own expert, Dr. Eric Fombonne, who identified four  
21 "analytical gaps" in Plaintiff's experts' methodology.

22 This section summarizes the experts' credentials (which are not at issue on this motion),  
23 their opinions, and methodology.

#### 24 25 A. General Causation Experts

##### 26 27 I. Dr. Ritz, Epidemiologist

28

1 Dr. Beate Ritz is Professor of Epidemiology at the UCLA Fielding School of Public Health  
2 and holds co-appointments in the Environmental Health Sciences and Neurology at the UCLA  
3 School of Medicine. (Declaration of Pedram Esfandiary in Opposition (“Esfandiary Decl.”), ¶ 23,  
4 Exh. 22, p. 3 (“Ritz Report”).) She holds an M.D. (1984) and a doctoral degree in Medical  
5 Sociology (1986) from the University of Hamburg, and a doctoral degree in Epidemiology (1995)  
6 from UCLA. (*Ibid.*) She primarily researches the health effects of occupational and environmental  
7 exposures, focusing on the effects of pesticides and air pollution on chronic diseases including  
8 neurodevelopmental disorders and diseases. (*Ibid.*)

9 She opines that exposure to mercury, arsenic, and lead during sensitive developmental  
10 periods in early childhood can cause ASD, and lead exposure can cause ASD at relatively low  
11 concentrations; and exposure to lead during sensitive developmental periods in early childhood  
12 can cause ADHD, even at low levels of exposure. (Ritz Report, pp. 4-5.)<sup>5</sup> Her opinion is based  
13 on peer-reviewed studies on the relationship between exposure to heavy metals and ASD, and lead  
14 and ADHD. To reach her opinion, she applied the Bradford Hill factors to the studies’ findings.  
15 (*Id.* at pp. 12-15, 22-49.)

16  
17 2. Dr. Gardener, Epidemiologist

18 Dr. Hannah Gardener has been an epidemiologist at the University of Miami Miller School  
19 of Medicine for over 14 years. (Esfandiary Decl., Exh. 20, p. 3 (“Gardener Report”).) She holds  
20 a Doctorate in Epidemiology and a minor in Biostatistics (2007) from the Harvard School of Public  
21 Health. (*Ibid.*) Her research focuses on diet and other environmental causes of neurological  
22 diseases; she has published over 100 peer-reviewed manuscripts. (*Ibid.*) She has studied heavy  
23 metals in consumer products since 2015, and is currently studying heavy metals in prenatal  
24 vitamins, CBD, and pet food. (*Ibid.*) Her areas of expertise include risk factors for neurological  
25  
26

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27  
28 <sup>5</sup> All of Plaintiff’s experts state their opinions “to a reasonable degree of scientific certainty,” but since this  
statement is a legal conclusion, the Court omits it from the summary.

1 outcomes, environmental health, and epidemiological methods. (*Id.* at pp. 3-4.) She currently co-  
2 teaches a course on epidemiological methods and biostatistics. (*Ibid.*)

3 She opines that lead, arsenic, and methylmercury accumulation in the body can cause the  
4 development of ASD, and lead accumulation in the body can also cause the development of  
5 ADHD. (Gardener Report, 4-5.) Like Dr. Ritz, she based her opinion on peer-reviewed studies,  
6 and reached her opinion by applying the Bradford Hill factors to the studies' findings. (*Ibid.*)

7  
8 **B. Biological Plausibility Experts**

9  
10 **1. Dr. Aschner, Neurotoxicologist**

11 Dr. Michael Aschner holds multiple titles at the Albert Einstein College of Medicine in  
12 The Bronx, New York, including Professor of Molecular Pharmacology, Professor of  
13 Neuroscience, Professor of Pediatrics, Investigator at the Rose F. Kennedy Intellectual and  
14 Developmental Disabilities Research Center, and Member of the Nathan Shock Center of  
15 Excellence in the Basic Biology of Aging. (Esfandiary Decl., Exh. 5, p. 4 ("Aschner Report").)  
16 He holds a Ph.D. in Anatomy and Neurobiology (1985) from the University of Rochester, School  
17 of Medicine and Dentistry in Rochester, New York, where he researched the potential neurotoxic  
18 effects of methylmercury. (*Ibid.*) Among his many credentials, he is a European Registered  
19 Toxicologist, a Fellow of the American Academy for the Advancement of Science, Chair of the  
20 External Advisory Board of the National Center for Toxicological Research (a center of the United  
21 States FDA), and past president of both the International Neurotoxicology Association and the  
22 International Society for Trace Element Research in Humans. (*Id.* at p. 5-7.) He has authored  
23 over 800 peer-reviewed articles, 100 book chapters, and hundreds of abstracts, and estimates his  
24 work has been cited nearly 49,000 times. (*Id.* at pp. 7-8.) As a neurotoxicologist, he specializes  
25 in assessing the adverse effect of pharmaceuticals, non-therapeutic chemicals, and other potential  
26 toxins on humans with an emphasis on neurological outcomes, and his research interest is the  
27 interaction between genetic and environmental triggers of brain diseases. (*Id.* at p. 5.) He has  
28

1 experience interpreting epidemiological studies and modeling in vivo and in vitro blood-brain  
2 barrier and mechanisms of neurodegeneration. (*Ibid.*)

3 He opines there are “well-established” mechanisms by which lead, arsenic, and mercury  
4 can pass through the blood-brain barrier and cause “significant and permanent” disruption to the  
5 brain’s neuropathways. (Aschner Report, p. 9.) He further opines that lead, arsenic, and mercury  
6 exposure can cause ASD in children, and lead exposure can cause ADHD in children, via  
7 “biologically plausible” mechanisms. (*Ibid.*) Lastly, exposure to mixtures of lead, arsenic, and  
8 mercury “will lead to the additive and synergistic effects of the[] metals, given that they share  
9 common toxicological modes-of-action.” (*Ibid.*) His conclusions are “supported by a wealth of  
10 epidemiological data” and the metals’ toxicological profiles. (*Ibid.*)

11 Dr. Aschner did not conduct a Bradford Hill analysis, as he is not an epidemiologist.  
12 (Aschner Report, p. 12.) Instead, based on his 35-plus years of professional experience studying  
13 the neurotoxicity of heavy metals, he reviewed the scientific literature on the risk of contracting a  
14 disease at any given dose and considered whether the toxicological evidence supports finding  
15 biological plausibility. (*Id.* at p. 12-13.)

## 16 17 2. Dr. Shapiro, Pediatric Neurologist

18 Dr. Kevin Shapiro is Medical Director and Clinical Executive for Research and  
19 Therapeutic Technologies at Cortica Healthcare, an organization that provides “comprehensive  
20 assessment and therapeutic services for children with autism and other neurodevelopmental  
21 disorders.” (Esfandiary Decl., Exh. 1, p. 3 (“Shapiro Report”).) He is also on the neurology staff  
22 at Children’s Hospital Los Angeles and is an affiliate staff member at Rady Children’s Hospital in  
23 San Diego. (*Ibid.*) He holds an M.D. from Harvard Medical School (2008) and a Ph.D. in  
24 psychology from Harvard University (2008). (*Ibid.*) He divides his work at Cortica Healthcare  
25 between clinical care — evaluating, treating, and following-up with children who have  
26 neurodevelopmental conditions including ASD and ADHD — and research into the “efficacy of  
27 novel treatment paradigms” for symptoms of ASD and ADHD. (*Id.* at p. 4.)

1 While ASD has a genetic component, he opines that genetic factors alone cannot explain  
2 the varied presentation and severity of ASD behaviors. (Shapiro Report, p. 5.) “Epigenetic  
3 mechanisms, environmental risk factors, and gene-environment interactions also contribute to the  
4 emergence of [ASD] symptoms.” (*Ibid.*) Known environmental risk factors for ASD include  
5 “exogenous agents that affect brain function” by altering cellular signaling and neurotransmitter  
6 release and by increasing oxidative stress and inflammation, all of which can occur following  
7 exposure to heavy metals in utero or within the first two years of life. (*Ibid.*) The mechanisms by  
8 which heavy metals affect neuronal function and development in vivo and in vitro overlap “to a  
9 significant degree” with the biological pathways that are implicated in ASD pathogenesis. (*Id.* at  
10 p. 6.)

11 He reached his opinions “using the methods, procedures, and techniques typically used by  
12 experts” in his field, relying on his ten-plus years of clinical experience diagnosing and treating  
13 ASD, his clinical research into the biological pathogenesis of ASD, and his clinical and research  
14 experience on how neurological injuries might produce core ASD symptoms. (Shapiro Report, p.  
15 6.) He also reviewed the “extensive” literature on ASD — its etiology, biological mechanisms,  
16 and risk factors — focusing on whether the neurological effect of exposure to lead, mercury, and  
17 arsenic is clinically relevant to the pathogenesis of ASD. (*Ibid.*)

### 18 19 C. Defendants’ Expert

20 Dr. Eric Fombonne is a Professor in the Department of Psychology and the Director of the  
21 Autism Research Institute on Development and Disability and the Child Development and  
22 Rehabilitation Center at Oregon Health and Safety University. (Declaration of Ali Mojibi in  
23 Support (“Mojibi Decl.”), ¶ 6, Exh. 5, p. 3 (“Fombonne Report”).) As a researcher, he has  
24 conducted epidemiological surveys; as a clinician, diagnosed and treated children with ASD and  
25 ADHD; and as a teacher, lectured and trained clinicians on the treatment, diagnosis, and causes of  
26 ASD, and trained researchers on how to conduct epidemiological studies on autism. (*Id.* at pp. 3-  
27 6.) He belongs to several professional associations, including the International Society for Autism  
28 Research and the Scientific Committee of the Association for Research on Autism and Infantile

1 Psychosis; has published over 350 peer-reviewed articles; and regularly reviews research articles  
2 on autism for publication. (*Ibid.*)

3 He testified Plaintiffs' experts' opinions contain the following four "analytical gaps" or  
4 leaps of logic. They:

- 5 (1) speculated that the temporality factor was satisfied by studies that could "not  
6 establish[]" temporality;
- 7 (2) relied on studies that compared heavy-metal concentrations to scores on behavioral  
8 questionnaires, rather than clinical ASD diagnoses,
- 9 (3) reached their conclusions "in the face of a body of evidence that finds no consistent  
10 association between heavy metal exposure and ASD," and
- 11 (4) failed to consider "what is known about ASD."

12 As Dr. Fombonne put it, "Plaintiff's expert[s] did not follow a methodology [that] is rigorous  
13 enough and would be accepted in admitting the standards of the epidemiological community."  
14 (Defendants' Closing Arguments, *Sargon* Hearing (Apr. 4, 2022) Slide No. 5 [citing Hearing  
15 Transcript (Mar. 14, 2022) at p. 15], Slide No. 8.)

16  
17 IV. Analysis

18 The first part of the Court's analysis addresses the four analytical gaps identified by  
19 Defendants' expert and the second part addresses arguments presented in Defendants' moving  
20 papers.

21  
22 A. Dr. Fombonne's "Analytical Gaps"

23 The Court first considers the four "analytical gaps" Dr. Fombonne identified in Plaintiffs'  
24 experts' methodology: (1) speculative conclusions resting on studies that lack temporality, (2)  
25 improper reliance on behavioral questionnaires, (3) lack of consistent association, and (4) failure  
26 to account for what is known about ASD.

27  
28 1. Temporality

1 According to Dr. Fombonne, few of the peer-reviewed studies underlying Dr. Ritz’s and  
2 Gardener’s opinions are “capable of establishing temporality,” the Bradford Hill factor that  
3 considers whether there is evidence that the exposure preceded the disease. (Reference Manual,  
4 p. 601.) “Although temporal relationship is often listed as one of the many factors in assessing  
5 whether an inference of causation is justified, this aspect of a temporal relationship is a necessary  
6 factor: Without exposure before the disease, causation cannot exist.” (*Ibid.*)

7 Drs. Ritz and Gardener relied on several studies that measured the amounts of heavy metals  
8 present in human “biomarkers” such as blood, urine, hair, and nails. The problem, according to  
9 Dr. Fombonne, is that most of these studies relied on exposures that occurred too late in time.  
10 Because, in his opinion, ASD is a genetic disorder that develops before birth possibly extending  
11 to shortly after birth, the relevant period of exposure is pre-natal. To illustrate his point, Dr.  
12 Fombonne cited approvingly the Doherty et al. (2020) study, which measured concentrations of  
13 metals in maternal and infant toenails. (Mojibi Decl., Exh. 17, p. 2 [peer-reviewed, published as  
14 *Periconceptional and prenatal exposure to metal mixtures in relation to behavioral development*  
15 *at 3 years of age* (2020) *Environmental Epidemiology*, pp. 1-8].) The researchers in that study  
16 collected maternal toenails at 27 weeks of gestation and 4 weeks postpartum, and collected infant  
17 toenails at 6 weeks after birth.<sup>6</sup> According to the study’s authors, maternal toenail metal  
18 concentrations “reflect exposures approximately 6-12 months before toenail collection,” whereas  
19 infant toenails grow faster — though they admitted the literature on this issue is “sparse,” infant  
20 toenails “collected at 6 weeks after birth likely represent exposures that occurred in late pregnancy  
21 and early neonatal life.” (*Ibid.*) The study’s measured effect was a child behavioral assessment  
22 called the Social Responsiveness Scale, 2nd edition, completed by the mothers when their children  
23 were three years old. (*Ibid.*) The Doherty study researchers therefore measured metal exposure  
24 before they measured the potential effect, which in Dr. Fombonne’s opinion means the Doherty  
25 study “is capable of establishing” temporality, that is, capable of establishing the exposure  
26

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27  
28 <sup>6</sup> These are median values. (Mojibi Decl., Exh. 17, p. 2.)

1 preceded the disease. (Defendants' Direct Examination of Dr. Fombonne Slides (Mar. 14, 2022)  
2 Slide No. 19.)

3 On the other hand, Dr. Fombonne criticized the Filon et al. (2020) study which collected  
4 hair samples from two groups of children aged 2 to 8 years, one "case" group of children who had  
5 been diagnosed with ASD and a second "control" group of neurotypical children, that is, children  
6 who had not been diagnosed with a neurological disorder. (Esfandiary Decl., Exh. 36, p. 2 [peer-  
7 reviewed, published as *Analysis of lead, arsenic and calcium content in the hair of children with*  
8 *autism spectrum disorder* (2020) BMC Public Health, pp. 1-8].) The researchers then compared  
9 the metal concentrations in the two groups' hair samples and found a statistically significant  
10 association between lead and ASD. (*Id.* at p. 1.) The problem, from Dr. Fombonne's point of  
11 view, is that the researchers collected the biomarkers after the outcome (the diagnosis of ASD)  
12 without analyzing or addressing how long ago the exposures to lead had actually occurred or could  
13 have occurred given the growth and replacement cycle of human hair. This procedure not only  
14 violated the cause-and-effect temporality requirement, it introduced the possibility of reverse  
15 causation, i.e., that the ASD may have caused the children's exposure to lead, and not vice versa.  
16 As an illustration, Dr. Fombonne suggested an explanation for the potential reverse causation:  
17 children afflicted with ASD can suffer PICA, a pathological craving for things that are not food,  
18 including things that contain lead.

19 Plaintiffs argue that their expert testimony has no "leaps of logic" and is not inadmissible  
20 under *Sargon* because Drs. Ritz and Gardener logically explained their analysis of the temporality  
21 factor. Dr. Ritz wrote that temporality is a "necessary element for inferring causality," and Dr.  
22 Gardener gave "careful consideration to the possibilities of reverse causality." (Ritz Report, p. 13;  
23 Gardener Report, p. 12.) Both acknowledged that establishing temporality can be a problem in  
24 case-control and cross-sectional studies. A "primary weakness" of these studies is "the timing of  
25 the assessment of exposure to heavy metals," wrote Dr. Gardener. (Gardener Report, p. 14.)  
26 Ideally "we would assess heavy metal exposure in very early life when there were no clear signs  
27 of ASD/ADHD" and then "follow children up until the time of diagnosis with repeated heavy  
28 metal assessments," but these studies, if they could be conducted accurately, would be "extremely



1 expensive[,] time-consuming[,] and would require very large samples due to the rarity” of ASD  
2 and ADHD. (*Id.* at pp. 14-15.) She explained, however, that the “important” issues of temporality  
3 and reverse-causation can be addressed by considering prospective human data and experimental  
4 animal data (exposing an animal to an agent and observing the outcome). (Gardener Report, p.  
5 15.) If the prospective data is consistent with the retrospective and cross-sectional study data, she  
6 wrote, then reverse causation is an “unlikely explanation” for the observed associations. (*Ibid.*)  
7 Some of the biomarkers, in her opinion, can show long-term heavy metal exposure, contrary to Dr.  
8 Fombonne’s opinion that biomarkers can only show exposures in the few months preceding  
9 measurement. (*Ibid.*) And to her, PICA did “not appear” to explain the causal association between  
10 lead exposure and ASD or ADHD, citing one study that “observed no significant difference in hair  
11 lead and mercury levels between children with and without PICA, while children with PICA were  
12 observed to in fact have lower arsenic levels.” (*Id.* at p. 15-16.)

13 Dr. Ritz also recognized the importance of temporality in reducing or eliminating the  
14 “potential of reverse causation i.e., it might be possible that the disease caused the exposure and  
15 not vice versa ... [the] disease [may have] caused certain behaviors or psychological states that  
16 increased exposure levels among the cases” when the samples were collected. (Ritz Report, p.  
17 12.) Echoing Dr. Gardener, she wrote that prospective data from studies of prenatal and early-life  
18 exposures can “refute the likelihood of reverse causation.” (Ritz Report, p. 12.) For lead and  
19 ASD, for example, she cited, as capable of establishing temporality, the Kim et al. (2016), Arora  
20 et al. (2017), and Abdullah et al. (2012) studies, which assessed exposures early in a child’s infancy  
21 by measuring lead levels in shed baby teeth; the Long et al. (2019) study, which measured lead  
22 levels in stored amniotic fluid; the Doherty (2020) study, which measured lead in maternal and  
23 infant toenails; and the Skogheim et. al. (2021) study, which measured lead in maternal blood at  
24 gestation week 17 — all peer-reviewed, published studies. (*Id.* at p. 23, 24, 26, 30.)

25 The Court concludes that even on Dr. Fombonne’s terms, Drs. Ritz’s and Gardener’s  
26 opinions on temporality are sufficiently logical and non-speculative to pass through the *Sargon*  
27 gate. As illustrated below, Dr. Fombonne grouped the various studies by whether they can satisfy  
28 temporality or not — that is, whether the study documented evidence of heavy-metal exposure that

1 occurred prior to any diagnosis of ASD or the observation of ASD-proxy behaviors. Plaintiff's  
2 experts' agreed with Fombonne's grouping of studies that satisfied temporality, pointing out that  
3 some of them observed a positive association between heavy metals and ASD or ASD-proxy  
4 behaviors; some returned mixed results; others found a null association; and some a negative  
5 association. Based on these studies, Dr. Ritz and Dr. Gardener's opinions are logical. And the  
6 extent to which causation can be inferred from these studies, in the Court's view, falls within the  
7 range of acceptable scientific disagreement.

8 As mentioned, Dr. Fombonne's temporality argument is largely an issue of study design.  
9 Prospective cohort studies, he explained, "verif[y]" temporality "by their very design."  
10 (Fombonne Report, ¶ 153.) Case-control or cross-sectional studies, however, generally assess  
11 exposure when participants are included in the study, that is, "when participants were already  
12 diagnosed with autism..." (*Ibid.*)<sup>7</sup> He therefore divides case-control studies into two categories.  
13 First are studies that measure past exposure and "allow the temporality criterion to be met." (*Id.*  
14 at ¶ 154.) Examples are studies that measured metal concentrations in deciduous teeth, cord blood  
15 or archived blood spots, or amniotic fluid samples — all of which can be used to "estimate (past)  
16 exposure levels." (*Ibid.*) The second category of case-control studies evaluate exposures  
17 retroactively using, for example, "food frequency questionnaires" that "evaluate material diet  
18 during pregnancy" to "reconstruct metal exposure..." (*Ibid.*) Both categories of case-control  
19 studies, in Dr. Fombonne's opinion, can satisfy temporality "since exposure has necessarily  
20 preceded the disorder." (*Ibid.*) He calls them "Informative case-control studies." (*Ibid.*)

21 On the other hand, case-control studies that assess exposure "contemporaneously with  
22 study recruitment do not meet the temporality criterion" and are "inapt to evaluate causality."  
23 (Fombonne Report, ¶ 156.) These studies measured the concentrations of heavy metals in certain  
24 human biomarkers such as hair, blood, and urine, to approximate past exposures to the metals. But

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25  
26 <sup>7</sup> For lead, arsenic, and mercury, both parties referenced charts that arrange the cited studies by their results.  
27 The five groups are: (1) statistically significant association; (2) positive but not statistically significant association;  
28 (3) null association; (4) negative but not statistically significant association; and (5) a negative and statistically  
significant association. (Defendants' Direct Examination of Dr. Fombonne Slides (Mar. 14, 2022) Slides Nos. 10-  
18.)

1 Dr. Fombonne rejects this method as “futile” because biomarkers only reflect exposures in the  
 2 near-past — urine and blood, for example, reflect metal exposures in only the past few hours or  
 3 days; hair, at most the past few months. (*Ibid.*) If researchers sampled the blood of a five-year-  
 4 old child with ASD, the heavy metal concentrations would only reflect exposures in the past few  
 5 months at most, likely after the child was diagnosed. (*Ibid.*) In his opinion, these studies are  
 6 “uninformative case-control studies.” (*Ibid.*)

7 In his Report, Dr. Fombonne grouped by type the studies that support Drs. Ritz and  
 8 Gardener’s opinions: (a) cohort studies and informative case-control studies that can, in his  
 9 opinion, establish temporality; (b) uninformative case-control and cross-section studies, which, in  
 10 his opinion, cannot; and lastly (c) cross-sectional and ecological studies and meta-analyses and  
 11 systemic reviews. For each of the three heavy metals, the following tables list only (a) the studies  
 12 that Dr. Fombonne opines can satisfy temporality; their design, biomarkers measured, and  
 13 findings; and excerpts from his comments about their methodology and findings. For comparison,  
 14 the bottom of each table recounts Dr. Ritz’s and Dr. Gardener’s opinions on temporality.

15

16 **LEAD & ASD:**  
 17 **Studies that, according to Dr. Fombonne, can satisfy temporality**

18 <b>Study</b> Fombonne Report citation	19 <b>Design</b> <sup>8</sup>	20 <b>Biomarker</b> (time of measurement)	21 <b>Findings</b> <sup>9</sup> (Dr. Fombonne’s description)	22 <b>Dr. Fombonne’s Comments on Study</b> <b>Methodology and/or Findings</b>
23 Abdullah (2012) ¶¶ 197-200	24 Case- control	Primary teeth, shed ages 6- 12	Null (“no difference”)	[Quoting study authors:] “No significant differences ... [findings] do not support an association...”
Adams (2007) ¶ 201	Case- control	Baby teeth	Positive, not SS	“Substantial methodological shortcomings ... results [therefore] not relevant for evaluating prenatal or early post-natal exposures.”
Alampi (2021)	Cohort	Maternal blood and	Mixed: null, positive at	“Suggestive findings about more appropriate methods to model the relationship between [heavy

25 <sup>8</sup> All cited cohort studies are prospective.

26 <sup>9</sup> Findings are taken from Plaintiff’s Sargon Hearing Exhibits Nos. 139, 142, and 143, which both sides  
 27 referenced, including Dr. Fombonne. (Defendants’ Direct Examination of Dr. Fombonne Slides (Mar. 14, 2022)  
 28 Slides Nos. 10-18.) For studies that were not included on Plaintiff’s Exhibits (see *id.* at Slides Nos. 12, 15, 18), the  
 Findings are based on how the studies’ authors described their results. Descriptions of findings (in parentheses) are  
 Dr. Fombonne’s. His comments on methodology are from his Report, citations to which appear in the first column.

1	¶¶ 193-196		urine, 1 <sup>st</sup> trimester	higher SRS scores, but not SS	metal] concentrations and child outcomes ... findings for lead ... inconsistent..."
2					
3	Arora (2017) ¶¶ 202-205	Case-control	Teeth; fetal and early postnatal	Positive, SS ("[L]ead levels generally higher ... significant differences...")	"Severe limitations..."
4					
5					
6	Doherty (2020) ¶¶ 180-183	Cohort	Maternal and infant toenails, 3x (27th gestation; 4th week postpartum; 6th week life)	Null ("no significant main effect")	"[S]tudy is of generally high quality." Results are "negative."
7					
8					
9					
10	Frye (2020) ¶¶ 206-209	Case-control	Tooth matrix	Mixed: Null, positive but not SS ("correlations ... not significant")	"[V]ery low quality ... results should be disregarded altogether."
11					
12					
13	Kim (2016) ¶¶ 189-191	Cohort	Child's blood, 3x (ages 7-8, 9-10, 11-12)	Positive, SS	"Significant methodological weaknesses ... basic design failure to address central question of links between lead exposure and [ASD]" ... exposures measured after ASD development window... findings thus "noncontributory"
14					
15					
16	Long (2019) ¶¶ 210-212	Case-control	Amniotic fluid (conserved samples)	Mixed: positive, not SS; null	"No evidence for an increased risk of ASD in relation to mid-pregnancy exposures to lead..."
17					
18					
19	Skogheim (2021) ¶¶ 184-188	Cohort	Maternal blood, 17 <sup>th</sup> week gestation	Mixed: positive, non-linear ("V-shaped relationship ... protective effect for lead levels in the middle of the distribution...")	"This study has several strengths."
20					
21					
22					
23					

**Dr. Ritz on temporality:** "That disease occurred after exposure and that there is an expected delay between the cause and effect has also been reported, i.e., exposures were assessed and recorded for early infancy in baby teeth [Arora?] and the Korean child cohort study [Kim (2016)] and the Norwegian MoBa cohort [Skogheim (2021)]." (Ritz Report, p. 30.)

**Dr. Gardener on temporality:** "In the nested case control study (MoBa) [Skogheim (2021)] and the cohort study (New Hampshire) [Doherty (2020)] disease occurred after exposure i.e. there is a delay between the cause and effect supporting causal inference." (Gardener Report, p. 35.)

**MERCURY & ASD:**

Studies that, according to Dr. Fombonne, can satisfy temporality

<b>Study</b> Fombonne Report citation	<b>Design</b>	<b>Biomarker</b> (Time of measurement)	<b>Findings</b> (Dr. Fombonne's description)	<b>Dr. Fombonne's Comments on Study</b> <b>Methodology and/or Findings</b>
Abdullah (2012) ¶¶ 323-325	Case- control	Baby teeth (shed ages 6- 12)	Negative, not SS ("no difference")	[Quoting study authors:] "No significant differences ... [findings] do not support an association..."
Adams (2007) ¶ 326	Case- control	Baby teeth	Positive, SS ("Mercury levels ... were significantly raised in children with autism...")	"[R]esults of this study are unreliable."
Alampi (2021) ¶¶ 320-322	Cohort	Maternal blood and urine (1st trimester)	Mixed: inverted-U distribution, not SS ("unremarkable ... no association with elevated SRS scores...")	"[S]tudy had limitations that make it not contributory."
Faroe Islands Study – Grandjean (1997, 1999, 2014) ¶¶ 292-294	Cohort	Cord blood, maternal hair (prenatal); child hair, 2x (1, 7 years); child blood (7 years)	Positive, SS (1999 findings); Positive (2014 findings)	Cohort was "intensively scrutinized, tested and clinically examined. The absence of reporting of autism diagnoses or of increases in such a diagnosis is of interest. Furthermore, it should be noted that an epidemiological survey of autism in the population of the Faroe Islands was performed in 2002 in the local population of children aged 8 to 17. There was no evidence that the prevalence of autism was higher in this mercury exposed population compared to other populations (Ellefsen et al., 2007)."
Geier (2009) ¶¶ 371-373	Cross- sectiona l	Maternal dental amalgams, number self- reported and unverified	Positive, SS	"The authors found a significant association between risk of autism and having 6 or more dental amalgams opposed to having 5 or fewer ... [but] [t]his study is flawed in key aspects" and "cannot be relied upon for any information."
Golding (2018) ¶¶ 311-315	Cohort	Maternal blood (gestation weeks 9-13); proxy measurement (questionnaire and dental	Null	Some strengths (successful recruitment, measurement early in pregnancy, cofounder adjustment); some limitations (no later measurements, few formal diagnoses). Findings "provide no support for an association between mercury exposure and autism."

		records during pregnancy)			
1					
2	Long (2019) ¶¶ 331-333	Case-control	Amniotic fluid (conserved samples)	Null — mercury not detected in samples	“No evidence for an increased risk of ASD in relation to mid-pregnancy exposures to mercury...”
3					
4	McKean (2015) ¶¶ 327-330	Case-control	Complex modeling of newborn blood spots combined with food-frequency questionnaires	Null: “After adjusting for potential confounding, we found no association between cumulative MeHg exposure and the risk of autism ... or developmental delay”	“This is a well-designed and executed study that provides no support for the hypothesis of an association between mercury exposure and autism risk.”
5					
6					
7					
8					
9	Ryu (2017) ¶¶ 316-319	Cohort	Maternal blood, 2x (early gestation, late pregnancy); child blood, 2x (birth, ages 2-3)	Positive, SS	“[S]ignificant increase in SRS scores for every doubling of the total mercury blood level ... [and] a significant increase ... in the probability of scoring high on the SRS” ... study’s “longitudinal prospective design” is a strength, though it also has “several limitations ... [and] does not provide evidence of an association between mercury exposure and autism.”
10					
11					
12					
13					
14	Skogheim (2021) ¶¶ 307-310	Cohort	Maternal blood (17th week gestation)	Null (“no significant association”)	“This study has several strengths.”
15					
16	van Wijngaarden (2013) ¶¶ 295-300)	Cohort	Maternal hair (at child’s birth)	Null: “No consistent association...”	“No significant association ... strengths of this study lie in its prospective design, its population-based sampling, and its large sample size.”
17					
18					
19	Yau (2014) ¶¶ 301-209	Case-control nested in cohort	Maternal serum (mid pregnancy); neonatal blood (1-2 days post-birth)	Mixed — positive, SS; null when adjusted	“[W]ell-designed” ... identifies several confounders “that ought to be controlled for in all investigations” ... findings show autism risk is not raised by “exposure levels that slightly exceed [EPA’s] recommended thresholds for mercury”
20					
21					

**Dr. Ritz on temporality:** “This criterion is met by the Korean child cohort study [Kim (2016)] and also the Faroese study [Grandjean (1997, 1999, 2014)] but the later assessed general psychomotor development.” (Ritz Report, p. 42.)

**Dr. Gardener on temporality:** “Prospective data confirmed an association between mercury exposure and ASD risk, lending support to a temporal relationship consistent with causality. Further, the likelihood of reverse causality is implausible.” (Gardener Report, p. 45.)

**ARSENIC & ASD:**

**Studies that, according to Dr. Fombonne, can satisfy temporality**

<u>Study</u> Fombonne Report citation	<u>Design</u>	<u>Biomarker</u> (Time of measurement)	<u>Findings</u> (Dr. Fombonne's description)	<u>Dr. Fombonne's Comments on Study Methodology and/or Findings</u>
Alampi (2021) ¶¶ 407-409	Cohort	Maternal blood and urine (1st trimester)	Mixed: somewhat linear relationship, from negative to positive, not SS	"[S]tudy had limitations that make it not contributory."
Doherty (2020) ¶¶ 399-402	Cohort	Maternal and infant toenails. 3x (27th week gestation; 4th week postpartum; 6th week life)	Positive, SS	"[S]tudy is of generally high quality" ... Positive associations observed, but were "attenuated" after "imputation of missing covariate data..." "[N]o support for an increase in the risk of autism following arsenic exposure...."
Long (2019) ¶¶ 410-412	Case- control	Amniotic fluid (conserved samples)	Positive, not SS	"No evidence for an increased risk of ASD in relation to mid-pregnancy exposures" to arsenic
Skogheim (2021) ¶¶ 403-406	Cohort	Maternal blood (gestation week 17)	Mixed: positive, SS in 2 <sup>nd</sup> quartile	"This study has several strengths ... [but] provides no evidence that arsenic exposure increases the risk of ASD."

**Dr. Ritz on temporality:** "In the nested case control study (MoBa) [Skogheim (2021)] and the cohort study (New Hampshire) [Doherty (2020)] disease occurred after exposure i.e. there is a delay between the cause and effect supporting causal inference." (Ritz Report, p. 35.)

**Dr. Gardener on temporality:** "An association observed between maternal arsenic levels during pregnancy and an increased risk of ASD demonstrate that arsenic levels early in life, prior to an ASD diagnosis, are in fact etiologically relevant. These findings lend support to a temporal relationship consistent with causality." (Gardener Report, p. 34.)

These tables illustrate a few points. First, the room for professional judgment and scientific disagreement increases from left to right. On the left are hard facts: the year a study was published (column one), its design (column two), and the biomarker it measured (column three). Study results (column four), too, are published as data, but here some professional judgment is introduced. Data can be presented in different ways, and statistical assessments of the data require judgment. Two measurements of statistical significance are the p-value — the probability of observing an association as large as the association actually observed, assuming there is, in fact, no association between the toxin and the disease — and the confidence interval, a range of results that would be observed x% of the time if the study was repeated multiple times drawing

1 samples from the same population. (Reference Manual, pp. 574-583.) Some courts have  
2 established baselines for these measures by referring to baselines conventionally used in science,<sup>10</sup>  
3 and excluded testimony based on studies that do not meet the baseline. Among epidemiologists  
4 and biostatisticians, however, “[t]here is some controversy ... about the appropriate role of  
5 significance testing.” (*Id.* at pp. 578-579.) Some scientists reject as inadequate studies whose p-  
6 value is not less than a chosen level while others criticize this approach. (*Ibid.*)<sup>11</sup>

7 The tables’ rightmost columns afford the most room for professional judgment and, by  
8 extension, disagreement. For example, based on limitations in the design of some studies, Dr.  
9 Fombonne discounted them as “not contributory” or “unreliable” even though the studies observed  
10 a positive association. From the Court’s point of view, the extent to which a study is “unreliable”  
11 is a matter properly reserved for cross-examination at trial. As noted in the Reference Manual,  
12 “[i]t is important to emphasize that all studies have ‘flaws’ in the sense of limitations that add  
13 uncertainty about the property interpretations of the results.” (Reference Manual, p. 553; *Cooper*  
14 *v. Takeda Pharmaceuticals America, Inc.* (2015) 239 Cal.App.4th 555, 589 (*Cooper*)). “Some  
15 flaws are inevitable given the limits of technology, resources, the ability and willingness of persons  
16 to participate in a study, and ethical constraints. In evaluating epidemiologic evidence, the key  
17 questions, then, are the extent to which a study’s limitations compromise its findings and permit  
18 inferences about causation.” (Reference Manual, p. 553.)

19 Second and most importantly, even if Plaintiffs’ experts relied only on the studies Dr.  
20 Fombonne identifies as satisfying temporality, their conclusions on the temporality factor would  
21

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22  
23 <sup>10</sup> Conventional p-values are <0.05, meaning there is less than a 5% chance of observing the same association  
24 assuming there is, in fact, no true association, and a 95% confidence interval, that is, a range of values that  
encompasses the results that would be expected 95% of time in samples drawn repeatedly from the same population.  
(Reference Manual, pp. 577-578.)

25 <sup>11</sup> Bradford Hill was himself skeptical of statistical baselines as necessary conditions for causation. “No  
26 formal tests of significance can answer” the question of causation; “[s]uch tests can, and should, remind us of the  
27 effects that the play of chance can create, and they will instruct us in the likely magnitude of those effects. Beyond  
28 that they contribute nothing to the ‘proof’ of our hypothesis.” (Bradford Hill Article, p. 299.) “[T]oo often I suspect  
we waste a deal of time, we grasp the shadow and lose the substance, we weaken our capacity to interpret data and to  
take reasonable decisions whatever the value of P. And far too often we deduce ‘no difference’ from ‘no significant’  
difference.” (*Id.* pp. 299-300.)



1 not be “clearly invalid and unreliable” under *Sargon*. (*Sargon, supra*, 55 Cal.4th at p. 772.) By  
2 way of contrast, an expert’s opinion is “unreliable” when it gives “significant weight” to the  
3 strength-of-association Bradford Hill factor based on data revealing a risk factor “somewhere  
4 around 1.2.” (*In re Viagra (Sildenafil Citrate) and Cialis (Tadalafil) Products Liability Litigation*  
5 (N.D. Cal. 2020) 424 F.Supp.3d 781, 796 (*Viagra*)). “Although a risk factor in that range would  
6 not necessarily preclude a conclusion that causation exists, it is undeniably not a strong  
7 association” — given that no association is calculated as a risk factor of 1.0. (*Ibid.*) It was  
8 particularly unreliable where the expert was also “unwilling to identify what she perceived the  
9 strength of association to be, instead testifying that she found it in the ‘totality’ of the evidence.”  
10 (*Ibid.*)

11 Here, the studies Dr. Fombonne identified as “capable of satisfying temporality” returned  
12 mixed results overall. Where researchers found a positive, even statistically significant association  
13 using a study with a compromised design, Dr. Fombonne gave the findings little or no weight.  
14 Where researchers using better-designed studies found a null association, he gave the findings  
15 more weight. In his opinion, the studies that both satisfy temporality and observed a positive  
16 association provide overall weak evidence of causation.

17 Drs. Ritz and Gardener, in contrast, view these studies’ findings as stronger evidence of  
18 causation, despite the design limitations. Their disagreement with Dr. Fombonne does not make  
19 their opinions “clearly invalid and unreliable.” (*Sargon, supra*, 55 Cal.4th at p. 772.) Under  
20 California law, the interpretation of epidemiological data — especially data reported in peer-  
21 reviewed, published articles — is generally a matter of professional judgment outside the trial  
22 court’s purview, including the interpretation of the strengths and weaknesses of a study’s design.  
23 If the validity of studies, their strengths and weaknesses, are subject to “considerable scientific  
24 interpretation and debate,” a court abuses its discretion by “stepping in and resolving the debate  
25 over the validity of the studies.” (*Cooper, supra*, 239 Cal.App.4th at p. 589.) Nor can a court  
26 disregard “piecemeal ... individual studies” because it finds their methodology, “fully explained  
27 to the scientific community in peer-reviewed journals, to be misleading” — “it is essential that ...  
28 the body of studies be considered as a whole.” (*Id.* at pp. 590, 593.) Flaws in study methodology

1 should instead be “explored in detail through cross-examination and with the defense expert  
2 witnesses” and affect “the weight[,] not the admissibility” of an expert’s opinions. (*Id.* at p. 593,  
3 page number omitted.)

4 As a final point, there is a distinction between studies that, on the one hand and in Dr.  
5 Fombonne’s opinion, cannot as a matter of design establish temporality and, on the other hand,  
6 studies that conclusively prove temporality is not met — a study that measures an exposure in  
7 diagnosed subjects who definitively were not exposed before their diagnoses. Dr. Fombonne’s  
8 opinion is logical — temporality is not established by a study that measures an exposure at the  
9 same time as or long after a disease is diagnosed. Such a study does not, however, prove that the  
10 exposure came after diagnosis of the disease. Dr. Fombonne’s argument ultimately goes to the  
11 weight of Dr. Ritz’s and Dr. Gardener’s opinions rather than admissibility under *Sargon*.

12  
13 2. Questionnaire Scores

14 Dr. Fombonne criticizes Plaintiff’s experts’ reliance on studies that, as a proxy for  
15 diagnosed ASD, compared metal concentrations to scores on behavioral assessments such as the  
16 Social Responsiveness Scale, 2nd edition (SRS-2), the Behavior Assessment System for Children,  
17 2nd edition (BASC-2), and the Autism Spectrum Screening Questionnaire (ASSQ). He testified  
18 that an SRS score is not a reliable substitute for an ASD diagnosis because the SRS questionnaire  
19 has a 90% error rate in identifying “true” ASD, meaning 90% of the children who screen positive  
20 for ASD on the SRS do not actually have ASD, or at least do not meet the standard for a clinical  
21 ASD diagnosis. (Defendants’ Direct Examination of Dr. Fombonne Slides (Mar. 14, 2022) Slide  
22 No. 26.)

23 To support Dr. Fombonne’s opinion, Defendants point out that Dr. Ritz agreed with Dr.  
24 Fombonne that ASD is a neurodevelopmental disorder characterized by impairments in language  
25 development, social interaction, communication, behaviors, and reaction to environmental  
26 changes, the severity of which can be “quite variable making the autism phenotype look clinically  
27 distinct.” (Ritz Report, pp. 15-16.) Defendants similarly criticize Dr. Ritz’s reliance on the  
28 Doherty et al. (2020) study, which found a statistically significant association between the levels

1 of arsenic in infant toenails and scores on the BASC-2 Behavioral Symptoms Index, one of four  
2 BASC-2 composite scores, rather than a diagnosis of ASD. (Mojibi Decl., Exh. 17, pp. 2-3, 6.)  
3 Defendants point out that even though none of the three other composite scores or the SRS-2 total  
4 score showed a statistically significant association with a 95% confidence interval, Plaintiff cited  
5 Doherty (2020) as evidence of a positive, statistically significant association between arsenic  
6 exposure and ASD. (*Id.* at p. 6; Defendants’ Direct Examination of Dr. Fombonne Slides (Mar.  
7 14, 2022) Slide No. 16.)

8 Plaintiff responds that ASD is a spectrum of disorders and that the presence of disorders,  
9 registered on a questionnaire, can at least approximate diagnosed ASD. As Dr. Shapiro testified,  
10 ASD is a “complex constellation of symptoms” diagnosed “based on the presence of certain  
11 behavioral symptoms.” (Mojibi Decl., Exh. 47, 177:15-25, 212:17-19 (“Shapiro Depo.”).)  
12 “[F]rom a clinical perspective, particularly it’s the symptoms that are interesting and not the label.”  
13 (*Id.* at 177:23-25.)

14 Although Dr. Ritz and Gardener’s use of questionnaire scores as a proxy for ASD relies on  
15 an inference, the Court finds it is not “too great an analytical gap” under *Sargon*. (*Sargon, supra*,  
16 55 Cal.4th at p. 771 [citing *General Electric Co. v. Joiner* (1997) 522 U.S. 136, 146 (*Joiner*)].)  
17 With all of the experts agreeing that ASD is a spectrum of behavioral disorders, it is not  
18 unreasonable to measure the presence and severity of ASD’s characteristic behavioral disorders to  
19 approximate diagnosed ASD. Where on the spectrum the presence and severity of various  
20 behaviors become diagnosable as ASD is a matter of degree, and reasonable clinicians can disagree  
21 about where on the spectrum an ASD diagnosis is appropriate. The Court accordingly finds that Dr.  
22 Fombonne’s opinion the SRS poorly approximates an ASD diagnosis goes to the weight of  
23 Plaintiff’s experts’ testimony, not its admissibility.

24 Moreover, it would be one thing if Drs. Ritz and Gardener based their opinions solely on  
25 the results of unpublished studies or on studies that they themselves designed or were the only  
26 epidemiologists using behavioral questionnaires as proxies for diagnosed ASD. But they instead  
27 base their opinions on peer-reviewed, published studies by other epidemiologists and researchers  
28 who likewise accepted these proxies as a measurement of ASD. Citing other scientific authorities,

1 the Kim et al. (2015) study’s authors, for example, wrote that the SRS “evaluates autistic behaviors  
2 as a continuum, rather than ‘all or none,’ and gives an index of deficiency in reciprocal social  
3 interactions.” (Mojibi Decl., Exh. 20, p. 195 [peer-reviewed, published as *Low-level lead exposure*  
4 *and autistic behaviors in school-age children* (2016) 53 *NeuroToxicology*, pp. 193-200].) It “is a  
5 widely used instrument to screen ASD in the public health setting, among children and adolescents  
6 aged between 4 and 18 years (Constantino and Gruber, 2007),” the Ryu et al. (2017) study’s  
7 authors wrote, “comparable to other assessing instruments such as the Autism Diagnostic  
8 Interview (ADI-R), the Autism Diagnostic Observation Scale (ADOS), and the Social  
9 Communication Questionnaire (SCQ) in terms of validity and reliability (Bölte et al., 2008;  
10 Charman et al., 2007; Murray et al., 2001).” (Mojibi Decl., Exh. 19, p. 253 [peer-reviewed,  
11 published as *Associations of prenatal and early childhood mercury exposure with autistic*  
12 *behaviors at 5 years of age: The Mothers and Children’s Environmental Health (MOCEH) study*  
13 (2017) *Science of the Total Environment*, pp. 251-257].) In short, *other* professional scientists, in  
14 articles reviewed by *their* peers, have assumed that autistic behaviors can approximate diagnosed  
15 ASD. The Court therefore declines to exclude the testimony of Drs. Ritz and Gardener on this  
16 ground under *Sargon*, even though other professionals such as Dr. Fombonne reject the same  
17 assumption. (*Davis, supra*, 245 Cal.App.4th at p. 492; *Sargon, supra*, 55 Cal.4th at p. 772 [citing  
18 *Kumho Tire Co. v. Carmichael* (1999) 526 U.S. 137, 152].)<sup>12</sup>

19 Defendants cite an interesting case from Maryland’s highest court. In that case, Dr. Hall-  
20 Carrington testified to general and specific causation — that lead exposure can generally cause  
21 “attention problems[] or ADHD” and specifically caused the plaintiff’s ADHD. (*Rochkind v.*  
22 *Stevenson* (2017) 454 Md. 277, 283 (*Rochkind*)). The court had not yet “decide[d] the extent to  
23 which epidemiological studies can support expert testimony on causation,” so it looked to *Joiner*,  
24 *supra*, 522 U.S. at p. 136, the second case in the Supreme Court’s *Daubert* trilogy. (*Rochkind*, at  
25 p. 289.) *Joiner* “held that the studies could not support the expert testimony because none of them

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26  
27 <sup>12</sup> The potential unreliability of the SRS-2 as a proxy for ASD is mitigated by the other behavioral scores the  
28 studies used. And as the Kim et al. (2015) study’s authors note, a measurement of behaviors on a numerical scale is  
more sensitive to potential associations than a binary yes-ASD-diagnosis versus no-ASD-diagnosis.

1 had found a causal link between PCB's and cancer," and although one study found higher-than-  
2 expected lung cancer deaths among former employees of an electric plant, the study could not  
3 support an expert's causation opinion because the study's authors "were unwilling to say that PCB  
4 exposure had caused cancer among the workers they examined...." (*Ibid.* [citing *Joiner*, at p.  
5 145].)

6 Following *Joiner*, the Maryland court excluded Dr. Hall-Carrington's testimony, which  
7 was based on an Integrated Science Assessment by Environmental Protection Agency (EPA-ISA)  
8 study noting that "'multiple, high-quality epidemiologic studies' have revealed 'a causal  
9 relationship between [lead] exposure and attention decrements, impulsivity, and hyperactivity in  
10 children.'" (*Rochkind, supra*, 454 Md. at p. 288.) According to the court, the expert "did not  
11 provide a sufficient factual foundation" because she failed to explain "why she thought the EPA-  
12 ISA supported her conclusion that lead exposure can cause ADHD [and] [t]he studies described in  
13 the EPA-ISA finding a causal relationship between lead exposure and attention deficits and  
14 hyperactivity do not go that far." (*Id.* at p. 290.) The Maryland court also concluded "the jump  
15 from attention deficits and hyperactivity to a clinical ADHD diagnosis may seem reasonable, but  
16 we have explained that 'just because a conclusion is reasonable does not mean that a court must  
17 permit an expert to make it.'" (*Id.* at p. 291 [citing *Ross v. Housing Authority of Baltimore City*  
18 (2013) 430 Md. 648, 664].)

19 There are at least two problems with the *Rochkind* court's reasoning for purposes of  
20 proving general causation under California law. First, epidemiological studies generally do not  
21 make conclusions on causation; they report findings as data. Other experts then review the studies  
22 and the data, apply the Bradford Hill criteria (among other methods), and make a judgment on  
23 causation. "[E]pidemiology cannot prove causation; rather causation is a judgment for  
24 epidemiologists and others interpreting the epidemiologic data." (Reference Manual, p. 598; Ritz  
25 Depo., 223:10 ["No data establish causality."].) The Maryland court did not seem to understand  
26 the distinction between studies documenting statistical associations between an agent and an effect  
27 and expert testimony applying the Bradford Hill factors to opine that the documented associations  
28 were "causal." The court said that "[w]ithout epidemiological studies — or other reliable evidence

1 — demonstrating a *causal link* between lead exposure and ADHD ... Dr. Hall-Carrington’s  
2 testimony ‘amounted to no more than mere speculation and conjecture.’” (*Rochkind, supra*, 454  
3 Md. at p. 294; emphasis added.) This statement overlooks the fact that the expert’s testimony on  
4 causation *was* the “other ... evidence ... [of] a causal link.” (*Ibid.*)

5 Second, citing Maryland precedent, the court excluded the expert’s opinion because it  
6 involved an inferential “jump” — the use of “attention deficits” as a proxy for diagnosed ADHD  
7 — even though, to the court, the inference “seem[ed] reasonable.” (*Rochkind, supra*, 454 Md. at  
8 p. 291.) California law allows such inferences: “If the opinion is based on materials on which the  
9 expert may reasonably rely in forming the opinion, and flows in a reasoned chain of logic from  
10 those materials rather than from speculation or conjecture, the opinion may pass, even though the  
11 trial court or other experts disagree with its conclusion or the methods and materials used to reach  
12 it.” (*Davis, supra*, 245 Cal.App.4th at p. 492 [citing *Sargon*, at pp. 771-772].)

13  
14 3. No Consistent Association

15 Combining gaps (1) and (2), Dr. Fombonne testified there is no consistent positive  
16 association between heavy metals and ASD among the studies that satisfy the temporality factor  
17 and assess a clinical ASD diagnosis as the outcome as opposed to a behavioral assessment.  
18 (Defendants’ Direct Examination of Dr. Fombonne Slides (Mar. 14, 2022) Slide No. 30.) The  
19 Court finds that this argument goes to the weight of Plaintiffs’ expert testimony, not its  
20 admissibility. Bradford Hill called his nine points “viewpoints.” (Bradford Hill Article, p. 299.)  
21 Dr. Fombonne applied the “viewpoints” more like criteria — he excluded studies from his analysis  
22 that, in his opinion, did not a) satisfy temporality or b) measure clinically diagnosed ASD, and  
23 then considered only the studies that remained.

24 The fact that Plaintiff’s experts did not follow the same procedure in their Bradford Hill  
25 analysis does not render their opinions impermissibly illogical. Drs. Ritz and Gardener applied  
26 each Bradford Hill “viewpoint” separately to the entire body of underlying studies, regardless of  
27 whether any particular study failed to satisfy other viewpoints. Neither their nor Dr. Fombonne’s  
28

1 approach is “clearly invalid and unreliable” even though the approaches resulted in different  
2 conclusions. (*Sargon, supra*, 55 Cal.4th at p. 772; *Davis, supra*, 245 Cal.App.4th at p. 492.)

3  
4 4. Failure to Account for What Is Known About ASD

5 Dr. Fombonne’s final challenge to Plaintiff’s experts’ methodology is the failure to  
6 consider the role of genetics as a cause of ASD. They did not rely on any articles, according to  
7 Dr. Fombonne, examining whether “genetics combined with an exposure to lead, arsenic, or  
8 mercury cause autism.” (Defendants’ Closing Argument Slides (Apr. 4, 2022) Slide No. 38 [citing  
9 Dr. Fombonne’s Mar. 14, 2022 testimony at p. 65].) As Defendants’ counsel aptly summarized  
10 Dr. Fombonne’s argument, “[I]f you’re going to try to figure out whether there’s a causal  
11 relationship between an exposure and an outcome and you’re looking at two groups of kids, one  
12 who have autism and one who don’t, you want to know if there’s genetic differences. And there’s  
13 no such study.” (*Sargon Closing Arguments Transcript* (Apr. 4, 2022) 57:23-25, 58:1-4.)

14 Like the null hypothesis, Dr. Fombonne’s is a hypothesis that, when assumed to be true,  
15 can expose weaknesses in a study’s design and the probability its findings are due to random  
16 chance. Two common errors in a study’s design and execution are confounding and bias.  
17 “Confounding occurs when another causal factor (the confounder) confuses the relationship  
18 between the agent of interest and the outcome of interest.” (Reference Manual, p. 24.) Genes in  
19 this case are a potential confounding variable: they might both cause ASD and inhibit the body’s  
20 ability to shed heavy metals, thereby confounding an observed association between ASD and  
21 bodily heavy-metal concentrations.

22 As for bias, a gene-related example of bias would be a case-control study on the effects of  
23 smoking (exposure) and heart disease (outcome) that solicits volunteer subjects for study.  
24 (Reference Manual, p. 583-584.) If subjects volunteer because they smoke cigarettes and have a  
25 family history of heart disease, then the study will suffer from selection bias, its observed  
26 association “biased upward because of the additional disease among the exposed smokers caused  
27 by genetics.” (*Id.* at p. 584.) “[C]ases and controls in case-control studies should be selected  
28 independently of their exposure status, so the exposed and unexposed participants in cohort studies

1 should be selected independently of their exposure status.” (*Ibid.*) Similarly, “the exposed and  
2 unexposed participants in cohort studies should be selected independently of their disease risk.  
3 For example, if women with hysterectomies are overrepresented among exposed women in a  
4 cohort study of cervical cancer, this could overstate the association between the exposure and the  
5 disease.” (*Ibid.*)

6 Dr. Fombonne’s argument highlights potential biases in Plaintiff’s cited studies. In the  
7 case-control studies, the “cases” — children with ASD or ASD-like behaviors — may have been  
8 genetically predisposed to ASD. If so, any observed association between their disorders and  
9 heavy-metal concentrations is explained either by chance or confounding. The studied cohorts  
10 may also over-represent children who are genetically predisposed to ASD. If so, the observed  
11 results would overstate any association between heavy metals and ASD.

12 For *Sargon* purposes, however, Dr. Fombonne’s points about possible confounding and  
13 bias do not require the Court to find that Plaintiff’s experts’ methodology is impermissibly  
14 illogical. It is certainly plausible that at least some of the studied individuals’ ASD or ASD-  
15 behaviors were caused not by their exposures to heavy metals, but by genetic factors. “It is  
16 important to emphasize that all studies have ‘flaws’ in the sense of limitations that add uncertainty  
17 about the property interpretations of the results.” (Reference Manual, p. 553.) The authors of the  
18 studies that support Plaintiff’s experts’ opinions, and Plaintiff’s experts themselves, acknowledged  
19 the evidence that genetic factors play a role in ASD etiology. (See, e.g., Mojibi Decl., Exh. 25, p.  
20 2, footnotes omitted [Long et al. (2019), peer-reviewed and published as *Autism spectrum*  
21 *disorders, endocrine disrupting compounds, and heavy metals in amniotic fluid: a case-control*  
22 *study*, *Molecular Autism* (2019) pp. 1-19].) Plaintiff’s expert Dr. Shapiro, for example, agreed  
23 there are “genetic syndromes that are highly associated with the emergence of [ASD] symptoms,”  
24 and Dr. Aschner wrote that brain development during the pre- and post-natal months “is largely  
25 subject to genetic control....” (Shapiro Depo., 117:6-11; Aschner Report, p. 48.)

26 As a matter of logic, however, Dr. Fombonne’s hypothesis — ASD is primarily caused by  
27 genes — and Plaintiff’s experts’ hypothesis — environmental factors are capable of causing ASD  
28 — are not mutually exclusive theories. Genes and environmental factors could logically both be



1 substantial factors in causing ASD behaviors. As Dr. Shapiro testified, “Fragile X” is a “well-  
2 recognized genetic [factor] associate[ed] with autism,” but “not nearly a hundred percent of kids  
3 with Fragile X go on to have the diagnosis of autism. The figure is something like 30 to 50 percent.  
4 So even if .... in a child [diagnosed] with autism, Fragile X is a reason for the autism or a  
5 contributor, it can’t be the only contributor. There must be other things that have contributed to  
6 that particular constellation of behavioral symptoms in th[e] child.” (Shapiro Depo., 117:6-25  
7 [citing Dr. Fombonne’s Report], 118:1-2; Dr. Aschner Report, p. 48 [“clearly the environment can  
8 play a role; for example, lack of nutrition ... and the presence of toxins...”].) “Genetics is an  
9 important risk factor for ASD, but it cannot explain ASD entirely [citation],” wrote the authors of  
10 the Alampi et al. (2021) study. (Mojibi Decl., Exh. 16, p. 1803 [Alampi et al. (2021), peer-  
11 reviewed and published as *Association Between Gestational Exposure to Toxicants and Autistic*  
12 *Behaviors Using Bayseian Quantile Regression* (Mar. 29, 2021) American Journal of  
13 Epidemiology, vol. 190, no. 9].) “A growing body of research shows that environmental factors,  
14 especially those that affect the developing fetus, play an important role in ASD [citation].” (*Ibid.*)  
15 “We must ... keep in mind that diseases may have more than one cause,” wrote Bradford Hill.  
16 (Bradford Hill Article, p. 297.) “Indeed[,] I believe that multi-causation is generally more likely  
17 than single causation....” (*Ibid.*)<sup>13</sup>

18 \*\*\*\*\*

19 Dr. Fombonne’s four points together form a cohesive hypothesis: of the studies that both  
20 establish temporality and measured clinically-diagnosed ASD, the results are mixed, and none of  
21

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22  
23 <sup>13</sup> Relatedly, Dr. Fombonne opined that Drs. Ritz and Gardener only considered studies that analyzed ADHD  
24 comorbid with ASD, rather than analyzing heavy metals and ADHD alone. In his opinion, ADHD manifests  
25 differently by itself than it does when comorbid with ASD. (Defendants’ Direct Examination of Dr. Fombonne Slides  
26 (Mar. 14, 2022) Slide No. 46.) His argument is essentially that the experts did not consider studies that isolated  
27 ADHD’s causal factor, instead linking it to ASD. But as he testified, ADHD is “substantially” more prevalent in  
28 people with ASD than in people without ASD, and though he opines this fact is also explained by genetics, it also  
makes Plaintiff’s experts’ use of studies that measured ASD and ADHD together not illogical. (*Ibid.*) In other words,  
if heavy metals are associated ASD, and ADHD is associated with ASD, then it is not illogical to opine heavy metals  
are associated with and can contribute to both disorders. Whether this “reasoned chain of logic” is ultimately  
unpersuasive against Dr. Fombonne’s genetics argument is not at issue here. (*Davis, supra*, 245 Cal.App.4th at p.  
492.)

1 the studies considered that ASD is primarily caused by genes. His hypothesis is, however,  
2 ultimately an opinion on general causation that competes with the opinions proffered by Plaintiff's  
3 experts. It is not the Court's role to resolve scientific controversies. (*Cooper, supra*, 239  
4 Cal.App.4th at p. 592.) Dr. Fombonne's critiques go to the weight of Plaintiff's evidence, not its  
5 admissibility.

6  
7 **B. Points Raised in Defendants' Moving Papers**

8 In their moving papers, Defendants raise several arguments regarding each of Plaintiff's  
9 experts, (1) Dr. Ritz, (2) Dr. Gardener, (3) Dr. Aschner, and (4) Dr. Shapiro, based on their  
10 respective deposition testimony.

11  
12 **1. Dr. Ritz**

13 Defendants argue Dr. Ritz's testimony should be excluded because she (a) "repeatedly  
14 disagreed" with the conclusions of the studies on which she relied; (b) "disregarded or attempted  
15 to rewrite basic epidemiological concepts" so she could conform the studies to her "preferred  
16 outcome"; and (c) applied her "unreliable methodology" to reach a "pre-determined conclusion on  
17 causation, all under the guise of a Bradford Hill analysis." (Motion Brief, 34:17-23.)

18  
19 **a. Basis for Opinion**

20 Defendants argue Dr. Ritz's deposition testimony shows she is at odds with the studies that  
21 support her opinion. "She repeatedly rejected the study authors' explanations of the relevant  
22 literature, disagreed with their cautionary statements about the limitations of their own studies, and  
23 dismissed every author's reference to the need for further research before reaching conclusions on  
24 causation." (Motion Brief, 35:10-12.)

25 Defendants first cite her responses to questions about statements in the studies'  
26 introductions. The Skogheim et al. (2021) study, for example, says, "Altogether, there is still  
27 limited knowledge on prenatal exposure to metal or variations of maternal levels of essential  
28 elements and clinician-based ASD and ADHD diagnoses in childhood. In addition, there are

1 inconsistencies regarding study designs and findings.” (Mojibi Decl., Exh. 22, p. 2.)<sup>14</sup> When  
2 asked if she agreed with this statement, Dr. Ritz said it was “not [her] opinion. That’s what these  
3 authors say. And I can tell you that I write this in my introduction so that reviewers will consider  
4 my paper novel. That’s an old trick ... they are stating what they have to state to get their paper  
5 published, and one of the statements that you do in the end of your introductory paragraph is say,  
6 oh, this is novel because there’s not enough knowledge, we are — we are here to fill this gap,  
7 because otherwise this is not new and journals don’t publish something just because you’re for the  
8 tenth time showing that something actually exists.” (Mojibi Decl., Exh. 4, 138:25, 139:1-18 (“Ritz  
9 Depo.”).)

10 Dr. Ritz’s statements do not put her at odds with the studies’ authors. She explained that  
11 researchers often introduce their studies with a “general statement” that does not necessarily reflect  
12 a “systemic review or evaluation” of previous studies, but instead “paraphras[es] what’s out there  
13 in the literature” while “emphasizing something that is still unexplained in order to make it novel,  
14 and in order to make the audience and the editors interested in publishing your results.” (Ritz  
15 Depo., 197:9-19.) An author’s statement in a study introduction, in other words, is not necessarily  
16 a definitive statement supported by systemic review of the literature.

17 Defendants next cite Dr. Ritz’s testimony about limitations the study authors placed on  
18 their findings. The authors of the Arora et al. (2017) study, for example, wrote that it “has multiple  
19 strengths, such as the inclusion of an informative twin sample recruited from population-based  
20 cohorts, a rigorous diagnostic assessment, and the use of direct fetal biomarkers,” whereas  
21 limitations were “a relatively small non-random sample, although the sample size was adequate to  
22 uncover significant associations after stringent statistical adjustments, and our twin sample  
23

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24  
25 <sup>14</sup> Other examples of statements from study introductions: “[D]ue to lack of consistency among the various  
26 study findings, the effects of iAs [inorganic arsenic] and Pb [lead] on ASD have not been established” (Mojibi Decl.,  
27 Exh. 34, p. 1905 [Wang et al. (2019)]); “Studies of toxic metals and nutritional elements in ASD have yielded mixed  
28 results” (Mojibi Decl., Exh. 26, p. 2 [Arora et al. (2017)]); and “[P]revious studies evaluating the association between  
lead exposure and ASD have reported inconclusive results, with evidence for positive [citations], null [citations], and  
negative associations [citations]” (Mojibi Decl., Exh. 20, p. 194 [Kim et al. (2016)]).

1 represented a significant subsample (11.3%) of the total population of twins discordant for ASD  
2 in Sweden in the examined age range.” (Mojibi Decl., Exh. 26, p. 8 [peer-reviewed, published as  
3 *Fetal and postnatal metal dysregulation in autism* (June 1, 2017) Nature Communications].) Dr.  
4 Ritz logically explained, however, that she disagreed with the statement that the Arora sample was  
5 “non-random” because “[t]wins are never a random sample — never” and the author thus  
6 “misuse[d] the term ‘nonrandom.’” (Ritz Depo., 208:17-25, 209:1-25, 210:1-3.) Defendants also  
7 cite her response to a question about one limitation stated by the authors of the Kim et al. (2016)  
8 study — “Is that a limitation of the study?” “I don’t see it as a limitation, no.” — but omit her  
9 extensive answer that “all of these are limitations because they are introducing measurement error.  
10 I totally agree with the authors ... [t]he more error you — you introduce into a study, the less  
11 signal you get. It’s a signal to noise ratio. You raise the noise, you don’t see the signal, you drown  
12 it out. And that’s, of course, a limitation. We wish that wouldn’t be the case.” (*Id.* at 223:11-16,  
13 243:7-25, 244:1-5.)

14 Lastly, Defendants argue Dr. Ritz dismissed the authors’ cautionary statements about the  
15 need for more research. The authors of the Arora et al. (2017) study, for example, wrote that  
16 “caution should be exercised when generalizing our findings, and additional studies are needed in  
17 different populations, particularly larger non-twin ASD samples to corroborate our findings, and  
18 differentiate genetic and non-genetic contributions in understanding the relation between metals  
19 and ASD.” (Mojibi Decl., Exh. 26, p. 8.) Dr. Ritz “dismissed out of hand” this statement,  
20 Defendants argue, as “merely reflect[ing] the authors’ ulterior financial motives,” citing her  
21 testimony that “You always ask for more research ... And guess what, Manish [Arora] wanted  
22 more money for more studies and this is one of the arguments you make.” (Motion Brief, 36:19-  
23 28; Ritz Depo., 222:15-18.) But her complete testimony is more nuanced. “Well, that’s what we  
24 always teach our students to say, right? You never conclude anything from just one study. You  
25 always ask for more research, and you ask for more studies and nontwins. And guess what, Manish  
26 wanted more money for more studies and this is one of the arguments you make.” (Ritz Depo.,  
27 222:13-18.) She generally agreed with Arora — she “hope[d]” that “larger nontwin ASD samples”  
28 could be identified and studied “to differentiate between genetic and nongenetic contributions,”

1 but she did not believe such a study would be feasible financially. Given “the sample size of those  
2 kind of studies ... [it] would be great if we got hundreds of millions of dollars to do th[em]. I’m  
3 all for it.” (*Id.* at 222:1-6.) Her statement is logical.

4 In sum, Dr. Ritz has reasonable critiques of statements by the authors of the studies that  
5 support her opinion. But this does not demonstrate that her opinion is “unsupported by the material  
6 on which [she] relies....” (*Sargon, supra*, 55 Cal.4th at pp. 771-772.)

7  
8 b. Methodological Deviation from Epidemiological Principles

9 Defendants argue Dr. Ritz deviated from or distorted “bedrock epidemiological  
10 principles.” (Motion Brief, 37:14-15.)

11 Defendants first argue that Dr. Ritz discounted or ignored the importance of the temporality  
12 factor. They asked her, for example, if “as a general matter” she agreed that an advantage of a  
13 cohort study is the “temporal relationship between exposure and disease can be established more  
14 readily than in [a] case-control study.” (Ritz Depo., 46:21-25.) The statement, she replied, is “too  
15 general” because “there are nested case-control studies within cohorts that do exactly the same  
16 thing.” (*Id.* at 46:10-12, 47:9.)<sup>15</sup> Disagreeing with Dr. Fombonne, she further explained that  
17 certain biomarkers “store” toxins so the exposure can be tracked “quite far back” in time:

18 It can go quite far back because lead is stored in the bone and there’s a constant replacement  
19 of lead in the blood from the bone. So if a child, for example, was very highly exposed in  
20 its first life year through drinking leaded — from leaded pipes water, then that gets stored  
21 in the child’s bone and it constantly replaces what you see in the blood. It never has to be  
22 exposed again, it can tell you about this first year of life.

22 (*Id.* at 38:14-23.) She also said a study can examine blood samples collected at birth “so there is  
23 sampling from an earlier time period.” (*Id.* at 37:14-21.)

24 As discussed above, the interpretation of the effect of study design on study results is  
25 primarily a matter of professional judgment. The evidence does not show that Dr. Ritz and Dr.  
26 Fombonne disagree on the fundamentals of temporality. If anything, they differ in how they apply

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27  
28 <sup>15</sup> For example, Dr. Ritz cited in her Report a case-control study nested with the Historic Birth Cohort at  
Statens Serum Institute in Denmark. (Ritz Report, 23-24.)

1 the fundamentals. Dr. Fombonne appears more hesitant to conclude that evidence establishes  
2 temporality than Dr. Ritz; he discussed at length how by design a study's findings can fail to  
3 provide evidence of temporality, whereas she discussed how by design a study's findings can  
4 provide evidence of temporality. Their different approaches to applying their professional  
5 judgment are within the bounds of reasonable scientific disagreement.

6 Defendants also argue Dr. Ritz "brushed aside" the requirement that an epidemiologist,  
7 before she can apply the Bradford Hill factors, must have evidence of an association between an  
8 agent and a disease. They asked her, "Didn't Dr. Bradford-Hill, in his article where he announced  
9 the Bradford-Hill criteria, say that you first have to have an unconfounded association before you  
10 apply the Bradford-Hill factors?" "If he had said that," she replied, "we couldn't apply his factors  
11 ever." (Ritz Depo., 86:20-25, 87:1.) Arguing that her answer is wrong and outside the scientific  
12 mainstream, Defendants cite a portion of Bradford Hill's 1965 article. "[W]e have this situation.  
13 Our observations reveal an association between two variables, *perfectly clear-cut and beyond what*  
14 *we would care to attribute to the play of chance.* What aspects of that association should we  
15 especially consider before deciding that the most likely interpretation of it is causation?" (Mojibi  
16 Decl., Exh. 15, p. 295, emphasis added ["Bradford Hill Article"].)

17 Yet Bradford Hill never said that causation can only be inferred from a "perfectly clear-  
18 cut" positive association. The statement Defendants cite comes early in his article where it appears  
19 he referred to a "perfectly clear-cut" association as an idealized, hypothetical "situation" to  
20 expound his factors. (Bradford Hill Article, p. 295 ["we have this situation..."].) He went on to  
21 write, "We must not be too ready to dismiss a cause-and-effect hypothesis merely on the grounds  
22 that the observed association appears to be slight. There are many occasions in medicine when  
23 this is in truth so. Relatively few persons harbouring the meningococcus fall sick of  
24 meningococcal meningitis. Relatively few persons occupationally exposed to rat's urine contract  
25 Weil's disease." (*Id.* at p. 296.) He was also skeptical of rigid statistical tests — "[T]oo far often  
26 we deduce 'no difference' from 'no significant difference'." (*Id.* at p. 300.) Therefore, the  
27 observed association, "perfectly clear-cut" or otherwise, should be considered not as an isolated  
28 prerequisite to a Bradford Hill analysis, but as part of the analysis itself. "First upon my list [of

1 factors] I would put the *strength* of the association”; second, “the *consistency* of the observed  
2 association”; and third, the “*specificity* of the association.” (*Id.* at pp. 295-297.)

3 Dr. Ritz agreed. “Bradford Hill is there because you are evaluating studies according to  
4 validity criteria, and confounding is one of the validity criteria you’re assessing. You’re not stating  
5 beforehand that there is no problem with validity and then you assess it, [instead] you’re actually  
6 doing the assessment.” (Ritz Depo., 326:16-22.) She logically said that to require a “pure,  
7 unconfounded” association was “tautologic[al]” because the observed association — its statistical  
8 strength, potential confounding variables, and so forth — are considered as part of the Bradford  
9 Hill analysis. Ultimately, while the Bradford Hill factors are “employed only *after* a study finds  
10 an association,” Reference Manual, pp. 598-599, there is no requirement the association first be  
11 “perfectly clear-cut” or “unconfounded.”

12 Defendants also argue Dr. Ritz “reshape[d]” the Bradford Hill analysis, citing her  
13 description of the “consistency” factor. (Motion Brief, 39:13-14.) In her analysis, they argue, she  
14 considered the “consistency” factor “met” if a study’s results were “consistent with what *she*  
15 believe[d] the answer should be,” but her testimony does not support their argument. (Motion  
16 Brief, 39:21-23.) “[C]onsistency,” she said, “means given the hypothesis you have and given what  
17 you already know[,] is the study consistent with that kind of reading.” (Ritz Depo., 273:18-20.)  
18 Asked to explain how she “reached a conclusion that the consistency Bradford-Hill factor was  
19 met” given “all th[e] null studies that we just discussed,” she said “it’s not consistency of study  
20 results. It’s consistency of what you would expect from certain studies and what you wouldn’t  
21 expect from them, and how you put them into context. So you have different studies that have  
22 different criteria — that have different methods of analyzing their results. This Saghazadeh [and  
23 Rezaei (2017) study] did a ton of different comparisons, but, you know, overall results are only so  
24 much. You also want to look at the individual studies, and you want to consider individual studies,  
25 not just — because they pick and choose — these meta-analysts pick and choose which studies to  
26 include and which studies to exclude. And when you look at the studies overall, there is a  
27 consistent signal.” (Ritz Depo., 258:8-25, 259:1-2; Mojibi Decl., Exh. 42 [Saghazadeh & Rezaei,  
28 *Systematic review and meta-analysis links autism and toxic metals and highlights the impact of*

1 country development status: Higher blood and erythrocyte levels for mercury and lead, and higher  
2 hair antimony, cadmium, lead, and mercury (July 14, 2017) Progress in  
3 Neuropsychopharmacology & Biological Psychiatry, vol. 79, pp. 340-368].) Her description is  
4 consistent with the Reference Manual’s description of the “consistent with existing knowledge”  
5 factor — whether the association is consistent with “other relevant knowledge,” such as the  
6 association between smoking and lung cancer being consistent with data that shows increased  
7 cigarette sales are positively associated with an increase in lung cancer death rates. (Reference  
8 Manual, pp. 604-605.)<sup>16</sup>

9 Dr. Ritz’s description of her methodological principles does not support a finding that her  
10 methods were illogical or impermissibly speculative.

11  
12 c. Methodology: Bradford-Hill Factors

13 Lastly, Defendants argue Dr. Ritz’s Bradford Hill analysis was “highly subjective” and  
14 “results-driven.” (Motion Brief, 40:8-9.) Specifically, they argue she could not describe the  
15 weight she gave to the specific factors and she formulated them to support her pre-determined  
16 opinion.

17 Defendants first argue that Dr. Ritz could not describe how much weight she gave to any  
18 individual Bradford Hill factor in her overall analysis citing, as an example, her reasoning that for  
19 arsenic and ASD, the strength of association factor is “partially met” because “the overall meta-  
20 analytical (point) effect estimates reported reflecting a weak to moderate size differences and the  
21 dose response relation-ship [*sic*] was non-linear at low levels of exposure in the MoBa study.”  
22 (Ritz Report, p. 35.) She entered on a spreadsheet the weight each meta-analysis she read gave to  
23 the underlying studies, though she admits this was not possible to do for some of the meta-analyses  
24 she reviewed. (Ritz Depo., 102:6-12.) She also admitted she did not have the spreadsheet and  
25 “probably deleted” it. (*Id.* at 103:7-8.) She also failed, as Defendants point out, to list “dose-  
26

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27 <sup>16</sup> Bradford Hill called this factor “coherence,” but described it substantially the same as “consistency” —  
28 “the cause-and-effect interpretation of our data should not seriously conflict with the generally known facts of the  
natural history and biology of the disease...” (Bradford Hill Article, p. 298.)



1 response” as one of the nine Bradford Hill factors — she lists only eight — though she did discuss  
2 dose-response as a statistical and methodological term in her “Methodology” section. (Ritz  
3 Report, p. 11, 13-14.) She also did not separately analyze the “strength of association” and “dose-  
4 response” factors but combined them under one “strength” factor. (*Id.* at p. 35.)

5 What matters under *Sargon* is whether the studies supporting Dr. Ritz’ opinions “can  
6 provide a reasonable basis” for her opinion irrespective of whether Defendants disagree with her  
7 conclusion. (*Cooper, supra*, 239 Cal.App.4th at p. 590.) To take Defendants’ example, her  
8 conclusion the “strength” factor was “partially met” for arsenic and ASD is not an impermissible  
9 leap of logic. Dr. Ritz cited several studies that observed at least some positive association between  
10 arsenic exposure and ASD. She ascribed “high validity” to the Norwegian case-control study, for  
11 example, because the autism diagnoses used for the “case” group were “retrieved from national  
12 disease registers” and Norwegians have universal access to health care. (Ritz Report, p. 34  
13 [Skogheim et al. (2021)].) And the study’s findings — an “increased risk of ASD and ADHD [are]  
14 associated with prenatal arsenic exposure” — were “important,” in her view, because the study  
15 measured a large sample size and, in Dr. Fombonne’s words, satisfied temporality, the arsenic in  
16 the study population having “originated mainly from fish and seafood consumption of the  
17 participating pregnant women.” (Ritz Report, p. 34; Mojibi Decl., Exh. 34, p. 9.) She also  
18 considered the Wang (2019) meta-analysis of 14 studies on arsenic exposure, the results of which  
19 she interpreted as “consistent evidence supporting a positive association between early life  
20 [inorganic arsenic] exposure and diagnosis of ASD, and a meta-analysis by Saghazadeh and Rezaei  
21 (2017) of 15 studies whose results were generally mixed — “no difference in blood, urine, or hair  
22 arsenic concentrations between ASD and control subjects overall” — but “[f]or arsenic  
23 measurements of hair, the summary effect of 4 studies from developing countries with a total of  
24 158 cases and 167 controls was marginally statistically significant.” (Ritz Report, p. 33.) Based  
25 on these peer-reviewed studies and others, it was not a leap of logic for Dr. Ritz to conclude the  
26 strength-of-association factor is “partially met.”

27 Defendants’ argument Dr. Ritz admitted her Bradford Hill analysis was “somewhat  
28 arbitrary” omits her complete testimony. Aside from the temporality factor — “we do want

1 temporality” — she refused to rank the factors she considers “most important” because “[e]ach  
2 one of them, I have to consider. If I don’t have data on one, then, you know, I have to live with  
3 that and still make my consideration.” (Ritz Depo., 274:6-11.) She applies the factors to  
4 “everything I know about these studies, and then I — I mean, it’s arbitrary in a way that you have  
5 to say, okay, this study meets this, this, or this. That study meets this, this, and something else.”  
6 (*Id.* at 275:12-16.) Defendants omit what she went on to say: “It seems arbitrary, *but it’s not* [,]  
7 because it’s a big puzzle piece. And some studies may not help me with consistency and some  
8 studies may not help me with specificity or strengths, but each one of them tells a piece of this  
9 puzzle that in the end is the Bradford Hill and makes up the picture. [¶] So it’s not like I rank  
10 them. It is really the integration of the knowledge, the studies, what I know about the subject  
11 matter and how it fits together. Whether a picture emerges or doesn’t emerge, that tells me that  
12 the Bradford-Hill is actually applicable in the way that we described it.” (*Id.* at 275:17-25, 276:1-  
13 3, italics added.)

14 Her answer largely tracks the Reference Manual.

15 There is no formula or algorithm that can be used to assess whether a causal inference is  
16 appropriate based on these guidelines. One or more factors may be absent even when a  
17 true causal relationship exists. Similarly, the existence of some factors does not ensure that  
18 a causal relationship exists. Drawing causal inferences after finding an association and  
19 considering these factors requires judgment and searching analysis, based on biology, of  
20 why a factor or factors may be absent despite a causal relationship, and vice versa.  
Although the drawing of causal inferences is informed by scientific expertise, it is not a  
determination that is made by using an objective or algorithmic methodology.

21 It also tracks Bradford Hill’s own description of the factors.

22 What I do not believe — and this has been suggested — is that we can usefully lay down  
23 some hard-and-fast rules of evidence that must be obeyed before we accept cause and  
24 effect. None of my nine viewpoints can bring indisputable evidence for or against the  
25 cause-and-effect hypothesis and none can be required as a *sine qua non*. What they can  
26 do, with greater or less strength, is to help us make up our minds on the fundamental  
question — is there any other way of explaining the set of facts before us, is there any other  
answer equally, or more, likely than cause and effect?

27 (Reference Manual, p. 600, footnotes omitted; Bradford Hill Article, p. 299.)  
28

1 Defendants' argument Dr. Ritz defined the Bradford Hill factors to suit her preferred  
2 outcome — she allegedly “reconfigure[ed]” the “consistency” factor, for example, to “construe  
3 virtually any study outcome as supporting her position” — also omits relevant portions of her  
4 testimony. Defendants cite her description of this factor as “consistent with the expectation with  
5 respect to what I think the answer should be.” (Motion Brief, 42:9-11 [citing Ritz Depo., 134:5-  
6 7].) But her complete answer is more illuminating. “You say [whether a study’s findings are]  
7 consistent with the expectation with respect to what I think the answer should be ...

8 if the study had been done correctly or if the study had been done unbiased or what I know  
9 from mechanisms, what I know about this population, what I know about the exposure  
10 level, what I know about co-exposures, and what I would expect to be able to see given the  
11 size of the cohort, the size of the study. And that is consistency in a scientific way.

12 It’s not consistency check mark one study yes, one study no, one study null. That is  
13 simplistic and that’s not science.

14 ...

15 That it is consistent with the expectation of what science has to say about the data and what  
16 the measures that each of the studies are using are actually telling me as a scientist, and  
17 I’m not — you know, otherwise I could do a computer analysis. I could say, okay,  
18 computer count one, count two, count three, and then we look on average. That’s not how  
19 I do my analysis and nobody has recommended that.

20 (Ritz Depo., 133-10:25, 134:1-25, 135:1-16.) Her complete answer is reasonable: the Bradford  
21 Hill consistency factor considers whether a study’s findings are consistent with other, relevant  
22 scientific knowledge. (Reference Manual, p. 606.)

23 The Court likewise cannot exclude Dr. Ritz’s conclusion on consistency as illogical. The  
24 Skogheim et al. (2021) study, for example, found a negative association between mercury and  
25 ASD. (Mojibi Decl., Exh. 22.) This finding, Dr. Ritz explained, was “consistent” with other  
26 knowledge and her opinion because, as the study’s authors wrote, the participants, all Norwegian,  
27 were likely exposed to mercury from eating fish and shellfish, and “if mercury is from certain  
28 types of fish that also contain other omega-3 fatty acids, then the adverse effect of mercury is  
counteracted, most likely by these beneficial effects in fish-eating ... So this is very consistent  
with everything we know about mercury and fish.” (*Id.* at p. 2; Ritz Depo., 151:15-25, 152:7-8.)

1 As another example, Defendants asked her if a statistically significant negative association  
2 between a compound and an outcome suggests the compound has a “protective effect.” (Ritz  
3 Depo., 116:21-24.) The answer, she explained, depends on the context, but if a study shows a  
4 negative association and protective effect between a known neurotoxin and a disease — lead, for  
5 example, and ASD — then she would, given her scientific knowledge, “scratch my head and say,  
6 ‘What’s wrong with my study?’ And that’s when I search for factors that could have caused this  
7 ... factors [that] are usually considered bias.” (*Id.* at 117:2-16.) Dr. Ritz explains she reached her  
8 consistency opinion logically.

9 Defendants argue Dr. Ritz refused to admit that the dose-response factor would not be met  
10 by a hypothetical study that found a negative association between lead and ASD. (Motion, 42-  
11 43.) The testimony Defendants cite, however, addressed a single graph, Figure 2, in the Skogheim  
12 et al. (2021) study, which ultimately found a positive albeit non-linear association between lead  
13 exposure and ASD. (Ritz Depo., 136:4-5 [introducing Skogheim study], 137:8-9 [“Let’s look at  
14 that study”], 147:7-18, 155:20-22.) The study’s authors wrote,

15 We identified a non-linear (U-shaped) association with prenatal lead exposure and ASD,  
16 while there were no such findings for ADHD diagnosis in children. The non-linear/U-  
17 shape observed in this study, indicate that both low-level and higher prenatal exposures to  
18 lead are associated with increased risk of ASD in children. Non-linear dose-response  
relationships have been shown in several studies of lead exposure in childhood and  
neurodevelopmental outcomes, such as IQ [citation].

19 (Exh. 22, p. 10 [§ 4.1.4].) From Figure 2 alone, Dr. Ritz did find support for or a rejection of a  
20 dose-response relationship between lead and ASD. But Figure 3, which shows a spline regression,  
21 was a more sophisticated way, in her opinion, to present the data to show a dose-response  
22 relationship, if one existed. (Ritz Depo., 145:9-23, 147:13-18.) She considered both Figures 2  
23 and 3 and Figure 2 had limitations; it showed only data for the 17th week of gestation, for example,  
24 and not the 27th week, where lead exposure could have a larger effect. (*Id.* at 144:9-21, 145:20-  
25 23, 147:19-21.) Her analysis is not unduly speculative.

26 As for the temporality factor, Defendants argue Dr. Ritz suggested “an epidemiologist  
27 might be able to find causation in the *absence* of clear evidence of temporality, provided that there  
28

1 is no conclusive evidence in either direction.” (Motion Brief, 43:7-9.) While she admitted  
2 temporality is “the most important” Bradford Hill factor and if the evidence shows temporality is  
3 *not* met, then a causal inference cannot generally be inferred, she further explained she evaluated  
4 temporality “study by study, piece of evidence by piece of evidence,” and even if temporality was  
5 not clearly established because “there’s not enough data,” she might nevertheless use other  
6 Bradford Hill factors to infer causation, such as the consistency factor (consistent with “other data  
7 ... from animal studies”) and biological plausibility (“mechanism”). (Ritz Depo., 88:19-20, 89:3-  
8 4, 90:5-10, 24-25, 91:1-4.) Her testimony echoes Bradford Hill’s statement that temporality  
9 “certainly needs to be remembered” but none of his nine “viewpoints” are “required as a *sine qua*  
10 *non*” of causal inference. (Bradford Hill Article, p. 299.)

11 Lastly, Defendants argue Dr. Ritz admitted she essentially began her analysis on the  
12 assumption that heavy metals can cause ASD and then looked for studies that disproved her  
13 assumption. Their argument, however, is based on her testimony discussing the results of  
14 individual studies in isolation. They asked her, for example, whether the Doherty et al. (2020)  
15 study “support[ed] her opinion,” a study that compared lead concentration in maternal and infant  
16 toenails to a behavioral assessment of the child at age three. (Ritz Depo., 129:24-25, 130:1-2;  
17 Mojibi Decl., Exh. 17, p. 2.) The authors observed “inconsistent associations” between lead levels  
18 and behavioral problems, which they concluded was “unexpected” and “not supported by the prior  
19 literature,” but possibly attributable to “residual confounding by, for example, unmeasured  
20 lifestyle factors” or “chance, as we did not correct for multiple testing owing to dependence among  
21 outcomes (and potentially exposures) and because this was an exploratory analysis.” (Mojibi  
22 Decl., Exh. 17, p. 2 pp. 4, 6.)

23 Though its findings made Doherty a “null study,” Dr. Ritz did not exclude it from her  
24 analysis. She had considered it “carefully ... what they measured, how they measured it,” and  
25 said, “It supports my opinion like every other piece of evidence ... I do not exclude null studies  
26 from what I look at ... null studies are [a] piece of the puzzle, and I try to understand why they are  
27 null. [¶] I’m not saying they are wrong, they’re not wrong, they are what they are. They are data.  
28 I do not exclude data and every piece of data that I see informs me. So yes, they did inform my

1 opinion.” (Ritz Depo., 129:16-17, 130:9-14, 131:11-19.) Her explanation turns on the word  
2 “support” — because one null study does not logically support a causal inference, the Doherty  
3 study *by itself* did not “support” her opinion, but it did “support” her opinion as *one of many* studies  
4 she read and considered. She also logically explained how it figured into her overall analysis. “It  
5 was a relatively small study for the level of lead ... measured in [infants’] toenails. You probably  
6 need a much larger study to see differences at these levels.” (*Id.* at 130:15-18.)

7 As additional evidence Dr. Ritz began her analysis with speculative assumptions,  
8 Defendants cite her testimony the findings of the Skogheim et al. (2021) study were “not enough  
9 data to convince [her] otherwise.” (Ritz Depo., 143:21-23.) But she said this in response to a  
10 question whether the Skogheim study’s findings *alone* were “consistent with [her] opinions,” and  
11 she answered it did not “convince [her] otherwise” considering the findings of the *many studies*  
12 she had read. Defendants’ counsel acknowledged this difference: “Well, surely one — one study’s  
13 not going to convince you of anything, correct, you need more than one study?” “Correct.” (*Id.*  
14 at p. 143:24-25, 144:1-2.) And she again gave a reasoned explanation of how she interpreted the  
15 Skogheim study’s results:

16 I really don’t know what you mean by “support.” But I’m looking at this, I’m saying, well,  
17 this is 17th week, maybe they’re correct. Maybe in the 17th week, there’s no effect. Maybe  
18 in the 27th week, there’s a big effect. They haven’t given me data for the 27th week. They  
19 haven’t given me data for the 7th week after birth or for the seven[th] year after birth. They  
20 are just showing 17th week estimates. 17th week estimates are what they are, in this case  
21 suggesting a null association, but that doesn’t convince me that lead is not a neurotoxicant  
at the levels that they actually have lead in the blood of these women, which is relatively  
low.

22 (Ritz Depo., 144:7-21.) Dr. Ritz’s comments on individual studies, in other words, do not  
23 demonstrate her preferred outcome drove her Bradford Hill analysis.

24 \*\*\*\*\*

25 “It bears repeating that applying the Bradford Hill criteria involves a certain amount of  
26 subjectivity, and experts will often disagree when doing so.” (*In re Roundup Products Liability*  
27 *Litigation* (N.D. Cal. 2018) 390 F.Supp.3d 1102, 1134.) The evidence does not show that Dr.  
28 Ritz’s opinion is “(1) based on matter of a type on which an expert may not reasonably rely, (2)

1 based on reasons unsupported by the material on which the expert relies, or (3) speculative.”  
2 (*Sargon, supra*, 55 Cal.4th at p. 771-772, page number omitted.)

3  
4 2. Dr. Gardener

5 Defendants argue Dr. Gardener should not be allowed to testify (a) because she did not  
6 reliably apply the Bradford Hill factors and because of (b) her previous statements and (c) issues  
7 with how she prepared her Report.  
8

9 a. Methodology: Bradford Hill Analysis

10 Dr. Gardener described a reliable Bradford Hill analysis. Pressed to name the quantity of  
11 positive studies needed to infer causation, she said she would not infer causation from one study  
12 alone, but beyond that there was “no [set] number” of positive studies.

13 My methodology would be the same if I had 20 studies all showing the exact same thing  
14 or 20 studies with only one study showing a statistically significant [association]. I look at  
15 the literature in totality. I look at the strengths, the weaknesses, the methodological  
16 differences. I look at whether the studies are all the same or whether they’re different.

17 “Different” is great because then what it does is it tests your assumption in all sorts of  
18 different scenarios. I look at issues related to validity, accuracy ... Accuracy relates to  
19 validity, and I look at the literature in totality and determine how likely an association  
20 might be biased to the degree that what we’re observing would not be the real association.  
The process is the same no matter how many studies there are and no matter how varied  
the results are.

21 You go through all of the different studies and you think about what are their strengths,  
22 what are their limitations, what does the totality of the literature show. You think about  
23 things like sample size and different study populations and different statistical techniques  
and you go through the Bradford Hill criteria and then you use your judgment.

24 (*Mojibi Decl.*, Exh. 8, 175:13-25, 176:1-8; 181:15-23 (“Gardener Depo.”).)

25 Defendants argue Dr. Gardener admitted she applied the Bradford Hill factors without  
26 evidence of a positive association between heavy metals and ASD. She never said this. She said  
27 that “in the world of biostatistics,” “everything is associated. There’s always an association ... an  
28

1 association is equivalent to a relationship.” (Gardener Depo., 143:12-22; 145:17-18.) “[A] 1.0  
2 means ... the relative risks are the same. That is the association. That is the relationship.” (*Id.* at  
3 145:23-25; 146:1.) For a study that observed a relative risk of 1.0, she would still “refer” to the  
4 Bradford Hill factors to consider “how valid that 1.0 is, whether it was ... biased toward the null  
5 ... [a]nd that’s where the Hill criteria come into play because one of the Hill criteria is the strength  
6 of the association, so that would be, that would represent the strength of the association, would be  
7 a relative risk of 1.0.” (*Id.* at 146:8-20.) She considered a study’s findings, in other words, as part  
8 of her Bradford Hill analysis — a logical method, as discussed above regarding Dr. Ritz.

9 Defendants argue Dr. Gardener “summarily categorize[d]” the associations between lead,  
10 arsenic, and mercury and ASD as “strong” without explaining why and “rejected the  
11 meaningfulness of statistical significance....” (Motion Brief, 46:18-24.) The evidence does not  
12 support this argument. Dr. Gardener explained at length how she evaluates a study’s findings.  
13 Like Dr. Ritz, she cited a study’s design and sample size as affecting “the validity of the estimate  
14 as well as the reliability ... how big, how wide the confidence bounds are.” (Gardener Depo.,  
15 198:4-14.) Another “important” factor, in her opinion, is the unit of measurement of the heavy  
16 metal — for example, the blood-lead concentration expressed in micrograms of lead per deciliter  
17 — and whether it is significant in real-world terms. (*Id.* at 198:20-23.) “Are you talking about a  
18 ten-microgram [of lead]-per-deciliter [of blood] increase? Are you talking about greater than ten  
19 versus less than two micrograms per deciliter? Are you talking about greater than ten versus less  
20 than five? So the contrast is the first thing that you want to keep in mind when evaluating the  
21 magnitude because a really small magnitude associated with a .001-microgram-per-deciliter  
22 difference could be actually really huge. It’s that the unit of measurement is really small, and  
23 that’s something that we, as epidemiologists, always sort of strive to put into context for our  
24 readers, is understanding sort of real-world understanding of the magnitude of effect.” (*Id.* at  
25 197:7-25; 198:1-3.) Variations in the effect magnitude also explained why she did not simply  
26 calculate the numerical average of the studies’ findings to measure the strength-of-association  
27 factor.



1 [I]f you were comparing kids with greater than 20 micrograms per deciliter of blood versus  
2 kids with less than one, that would be a huge, huge contrast ... [but for each of the studies,]  
3 each of the comparisons are different. So, for example, if you look at Kim 2013, their  
4 contrast was kids with greater than two micrograms per deciliter versus less than two ...  
5 So the comparison is different for each of [the studies]. If all of them, if each study had  
6 compared greater than or equal to two versus less than two, then it would be really easy to  
7 create a summary effect.

8 (Gardener Depo., 167:10-25.)

9 Defendants' argument that Dr. Gardener did not "apply *any* statistical testing or 'numerical  
10 thresholds' to her consideration of the epidemiological evidence" misstates her testimony. She  
11 said that epidemiologists do not rate a positive association "strong" simply because it exceeds a  
12 certain risk ratio, even though courts sometimes do.<sup>17</sup> (Gardener Depo., 204:1-10.) She explained  
13 other factors that epidemiologists use to evaluate risk ratios include the baseline risk and the  
14 consequences of the increased risk. "If something increased your risk of a cold by tenfold, that's  
15 not as much of a public health problem as if something increased your risk of ALS or childhood  
16 cancer tenfold. The disability, the years ... lost are very different." (*Id.* at 201:23-25, 202:1-3.)  
17 And there is no evidence Dr. Gardener ignored statistical significance.

18 I factored [statistical significance] in in terms of like if an association — if I see an effect  
19 estimate that's really strong but the confidence bound goes right below one so the P-value  
20 is .06, you know, there are methodological reasons why the confidence bounds could be  
21 wide, especially if it's a small study or if they over-adjusted or, you know, then I might  
22 say, like I'm not so worried about it being a P-value of .06. Like I have enough clinical  
23 experience to say, you know, that's not really meaningfully different than if the P-value,  
24 than if the confidence bounds went right above one. But I'm an epidemiologist. I am part  
25 of this sort of world of medicine where we conventionally use this .05. That is the P-value  
26 that we pretty much use in my studies, and so it is certainly something I keep — it's  
27 impossible not to sort of keep that in mind, but it's not the full picture. I would never  
28 discount an association that didn't reach that threshold. I try to say like why, like look at  
the confidence interval and say let's think about that confidence interval, why is it so wide,  
why is it so narrow?

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<sup>17</sup> "[O]nly [epidemiological] studies showing relative risk estimates greater than 2.0 are useful to the jury and may properly be used to 'extrapolate from generic population-based studies to conclusions'" on specific causation, that is, "what caused a specific person's disease." (*Johnson & Johnson, supra*, 37 Cal.App.5th at p. 325 [citing *Cooper, supra*, 239 Cal.App.4th at p. 593].)

1 (Gardener Depo., 208:13-25, 209:1-17.)

2 Defendants next argue Dr. Gardener reformulated the Bradford Hill consistency factor into  
3 a subjective test of whether the study results were “consistent with her preexisting opinions.”  
4 (Motion Brief, 47:3.) This was not her testimony, however. She declined to set a number or  
5 percentage of studies that must have positive findings in order to be “consistent” — there are  
6 many other factors that affect how a study’s findings should be interpreted, and she thus explained  
7 that epidemiologists weigh consistency based on their “judgment and expertise.” (Gardener Depo.,  
8 251:9-18.)

9 There is no definition of ‘consistency.’ In any literature, you won’t find perfect  
10 consistency. If you look through all my literature, you will see that I once published a  
11 study showing no association between maternal smoking during pregnancy and birth  
12 weight. We know maternal smoking affects birth weight. My study was sort of particularly  
13 methodologically strong using a sibling design. We know that smoking during pregnancy  
14 affects it even within families. So when we have known associations, you’re never going  
15 to see perfect consistency, so there’s no perfect number. It’s not like 50/50 or 60/40.

14 ...

15 [I]n my training, there is no number, you know, oh, consistent association is 50 percent of  
16 observed studies. You have to really think about what consistency you’re looking for. Are  
17 you looking for always statistically significant, statistical significance in every single  
18 study? Are you looking for effect estimates that are similar in magnitude across studies?  
19 You have to think about a lot of things when you’re thinking about consistency.

18 ...

19 So what I thought about is when studies showed different associations, why? Like, you  
20 know, was the magnitude of effect different because the cutpoints are really different  
21 because the time periods were really different?

22 Like these days you wouldn’t, you might not look at a contrast of greater than 20  
23 micrograms per deciliter of blood lead because that’s so rare right now. When we were all  
24 children, that blood lead level was far more common, so you want to think about  
25 consistency in relation to why studies might be different. Are the study populations  
26 different? Is the frequency of exposure or the types of exposure? It’s like you were saying  
27 before, most of these studies didn’t assess where the lead, arsenic or mercury was coming  
28 from. That will vary between populations, and can explain differences that you see in  
different populations.

27 (Gardener Depo., 250:10-25, 251:10-20, 251:23-25, 252:1-19.)

1 Defendants asked her, for example, if an “even division” between positive and null studies  
2 would “weigh against a causal inference,” comparing the number of positive studies to the number  
3 of times a coin-flip returns heads versus tails. (*Id.* at 278:5-13, 23-25; 279:1.) But the consistency  
4 factor does not simply compare the number of positive studies to the number of null studies — it  
5 involves a more nuanced inquiry.

6 There’s no definition of what percentage would be consistent. You have to think about the  
7 strengths and weaknesses of the designs. You have to think about consistency in terms of  
8 what, whether they are finding an association or not, the strength of the association,  
9 whether the association is more in some populations than the other. And you have to think  
10 about why the studies are inconsistent, what are the reasons for the inconsistencies. Is it  
11 that every study that included both males and females showed something and then all  
12 studies that just included males showed something else, and then you could think, all right,  
the association between your exposure and your outcome would be stronger in females, so  
things like that. You want to think about whether there are reasons to explain any  
inconsistencies that you do see.

13 (*Id.* at 277:10-25; 278:1-4.) The Court is not persuaded that Dr. Gardener reformulated the  
14 consistency factor.

15 Defendants argue she ignored the principle that exposures might be causally associated  
16 with an outcome at a high, but not low level of exposure — essentially the “dose-response”  
17 Bradford Hill factor. They also argue her analysis was results-driven because she started on the  
18 assumption that lead causes ASD and then looked for studies that disproved her assumption. But  
19 once again, her testimony was more nuanced. She admitted she could not “off the top of [her]  
20 head” recall any specific epidemiological studies that established a dose-response relationship  
21 between heavy metals and ASD, and when asked if she believed “any amount of exposure to lead  
22 is causally associated with autism,” she replied she did not see a level of lead exposure “that is  
23 reliably not associated” with lead. (Gardener Depo., 185:19-22, 347:6-348:8.) There is no  
24 “amount of lead exposure” at which a “causal association emerges with autism” — “[i]t does not  
25 exist. Like if you said what number of cigarettes does an association with lung cancer exist, you  
26 would never see that because it doesn’t exist ... it’s not a realistic epidemiological question. It’s  
27 not like people say, oh, at 20 cigarettes you get lung cancer.” (*Id.* at 153:22-25, 154:1-6.) Her  
28

1 answer is logical: there is possibly some level of lead exposure, perhaps an infinitesimal amount,  
2 below which no association with ASD is observed, but no study has pinpointed the threshold, if it  
3 exists.

4 Lastly, Defendants argue Dr. Gardener “buck[ed] the scientific consensus” by “ignor[ing]”  
5 the “specificity of association” Bradford Hill factor. (Motion Brief, 48:6-10.) Contrary to  
6 Defendants’ argument, she did not ignore the factor, but instead gave a logical explanation of how  
7 it played into her overall analysis:

8 [T]he specificity criteria refers to whether the exposure of interest only impacts the disease  
9 of interest which is almost never applicable even in the situation of causality. Like smoking  
10 causes lung cancer. The fact that smoking also causes heart disease, oral cancers, head and  
11 neck cancers doesn’t detract from the fact that smoking causes lung cancer, so it’s a criteria  
12 that rarely applies to human exposures that are causal ... It’s part of the Hill criteria ...  
13 [but] [i]t’s really totally irrelevant. If it were the Hannah Gardener criteria, specificity  
14 would not be included. That’s sort of a widely-held belief among epidemiologists that of  
all of the criteria especially, it is most often very — I can’t even think of an example,  
actually, where off the top of my head it does apply in a situation where you have a causal  
association.

15 (Gardener Depo., 339:21-25; 340:1-6, 11, 22-5; 341:1-6.) At first glance, her opinion the  
16 specificity factor is “almost never applicable” is somewhat at odds with the Reference Manual,  
17 which says “[t]he vast majority of agents do not cause a wide variety of effects.” (Reference  
18 Manual, pp. 605-606.) But the Manual gives the example of asbestos exposure — no evidence  
19 shows asbestos causes cancers besides mesothelioma, lung cancer, and perhaps “one or two other  
20 cancers” — arguably proving Dr. Gardener’s point that *one* agent is rarely associated with only  
21 *one* disease. (*Id.* at p. 606.) The Manual also echoes her smoking example but explains “one good  
22 reason” why tobacco’s health consequences “do not require specificity”: tobacco and cigarette  
23 smoke are not single agents but consist of “numerous harmful agents.” (*Ibid.*) “Thus, whereas  
24 evidence of specificity may strengthen the case for causation, lack of specificity does not  
25 necessarily undermine it where there is a good biological explanation for its absence.” (*Ibid.*)  
26 Ultimately, Dr. Gardener’s statement on specificity as applied to her opinion in this case, however,  
27 is not illogical and does not render unreliable her overall Bradford Hill analysis.

1           b.     Previous Statements

2           Defendants contend that Dr. Gardener has previously written that ASD commonly  
3 develops during gestation or shortly after birth, but contradicted herself in her deposition, “steering  
4 so wildly in the other direction as to assert that full grown adults aged 30 or more can, for the first  
5 time, develop the brain abnormalities that give rise to ASD....” (Motion Brief, 49:11-14.)  
6 Defendants argue this evidence shows she has not employed the same rigor in this case as she  
7 employs in her profession.

8           In 2014, for example, Dr. Gardener co-wrote a paper entitled “Perinatal and Neonatal  
9 Complications in Autism Etiology.” (Mojibi Decl., Exh. 44, p. 1.) It begins: “The perinatal time  
10 period, which encompasses the 5 months before to the 1 month after birth, is increasingly  
11 recognized as key in autism’s etiology. Critical phases of brain development occur during fetal  
12 development through early postnatal life, and alterations in brain development are thought to be  
13 involved in autism.” (*Ibid.*) She co-wrote another paper in 2009, “the first quantitative review  
14 and meta-analysis of the association between maternal pregnancy complications and pregnancy-  
15 related factors and risk of autism,” that says, “[a]lthough the distinctive neuropathology [of ASD]  
16 remains elusive, studies have shown macroscopic, microscopic and functional brain abnormalities.  
17 These brain abnormalities suggest that the aetiologically relevant period may be *in utero* because  
18 the pathogenesis may begin during the prenatal period.” (Mojibi Decl., Exh. 45, p. 1.)

19           Dr. Gardener did not contradict her previous writings. The deposition testimony  
20 Defendants cite to support their argument is Dr. Gardener’s response to an irrelevant hypothetical  
21 question: “Do you believe that a 30-year-old who is not autistic can be exposed to a chemical or  
22 substance or heavy metal and because of that develop autism?” (Gardener Depo., 269:20-23.)  
23 Adult ASD was not the subject of either her opinion or the studies upon which she based opinion,  
24 nor is adult-ASD causation or diagnosis at issue in this case. She did say that people are often  
25 diagnosed with ASD as adults, sometimes aged 30 years or older. (*Id.* at 268:12-16.) She also  
26 said “we don’t really sort of define when people develop autism,” but instead define autism by  
27 when people start show behavioral symptoms, which can change over time, appear, disappear, and  
28

1 then reappear. (*Id.* at 269:24-25; 270:1-10.) But she said nothing to contradict her previous  
2 writings about the importance of early life in ASD etiology.

3 Dr. Gardener’s previous writings do not show her opinion in this case is unreliable.  
4

5 c. Issues with Report Preparation

6 Defendants argue Dr. Gardener could not answer basic questions about the studies she cited  
7 in her Report, implying that counsel prepared it for her or she simply copied Dr. Ritz’s Report.  
8 She cited the Kim et al. (2016) study in her Report, for example, as a prospective cohort study that  
9 observed a “strong” association between lead and ASD behaviors, and the Skogheim et al. (2021)  
10 study that found a “non-linear association between maternal blood arsenic during pregnancy and  
11 offspring ASD risk.” (Gardener Report, pp. 29, 32.) During her deposition, however, she had  
12 “no idea what the Kim study is,” the name Skogheim “did not ring a bell,” and she had not read  
13 her Report again after November 12, over a month before her deposition on December 16.  
14 (Gardener Depo., 304:3-7, 309:22-25, 312:10-22.)

15 Plaintiff protests that Defendants did not afford Dr. Gardener an opportunity during her  
16 deposition to read and review the studies when asked about them. Indeed, given the number of  
17 studies that form the basis for her opinion, some of the questions asked of her were quite specific  
18 — for example, “whether or not any measurement of heavy metals in the blood was taken during  
19 infancy or early childhood in the Kim study?” (Gardener Depo., 305:25; 306:1-2.) To answer this  
20 question, Dr. Gardener would have needed to recall the Kim study by name and the biomarkers it  
21 had measured — a difficult task for anyone to perform on the spot. She testified that she had “no  
22 recollection of the details” of the Kim study. (*Id.* at 306:3-7.)

23 On the other hand, Dr. Gardener might reasonably have been expected to recognize the  
24 names of the studies she cites in her Report and, as Defendants pointed out on the record, an expert  
25 witness must generally be “sufficiently familiar with the pending action to submit to a meaningful  
26 oral deposition concerning the specific testimony, including an opinion *and its basis*, that the  
27 expert is expected to give at trial.” (Code Civ. Proc., § 2034.260, subd. (c)(4), italics added.) At  
28 this stage, however, the Court’s “circumscribed inquiry” is limited to whether Dr. Gardener based

1 her opinion on “matter of a type on which an expert may not reasonably rely” and whether the  
2 matter logically supports her opinion. (*Sargon, supra*, 55 Cal.4th at pp. 771-772.) Her failure  
3 during her deposition to recall details of specific studies goes to the weight of her opinion, not its  
4 admissibility.

5  
6 3. Dr. Aschner

7 Defendants argue Dr. Aschner, the toxicologist, should not be allowed to testify for four  
8 reasons: (a) he is not qualified to review epidemiological data, (b) the data does not show an  
9 association between heavy metals and ASD; (c) his opinion is speculative, and (d) he improperly  
10 equates ASD-like symptoms with clinical ASD.

11  
12 a. Qualifications

13 Defendants argue Dr. Aschner’s deposition revealed he “lacks a basic understanding of  
14 epidemiological principles and the rules for using epidemiology” and “ma[de] no pretense of  
15 conducting a Bradford Hill analysis or otherwise engaging in a reproducible method for assessing  
16 causation.” (Motion Brief, 51:14-15, 26-27.)

17 Toxicology is “primarily concerned with identifying and understanding the adverse effects  
18 of external chemical and physical agents on biological systems.” (Reference Manual, Reference  
19 Guide on Toxicology, p. 635.) While Dr. Aschner is a toxicologist, not an epidemiologist, the two  
20 disciplines lean on each other, “often go[ing] hand in hand with assessments of the risks of  
21 chemical exposure, without artificial distinctions being drawn between them.” (Reference  
22 Manual, pp. 657-658.) His opinion partly relies on epidemiological studies. He began by  
23 reviewing the “relevant scientific literature, including animal studies and epidemiological papers,”  
24 and writes that “discussion of a biological mechanism” by which an exposure causes a disease —  
25 the subject of his opinion in this case — must be founded upon “reliable scientific evidence of an  
26 association....” (Aschner Report, pp. 10, 12.)

27 Defendants’ argument is based on Dr. Aschner’s deposition testimony. He gave an unclear  
28 definition of a case-control study, defining it as “mostly case reports ... you look specifically at

1 one individual and potential exposures” and then, moments later, said “a case control is not a case  
2 report. They’re different because case report refers only to one individual.” (Mojibi Decl., Exh.  
3 32, 94:7-13, 95:3-6 (“Aschner Depo.”).) He also said that when reviewing epidemiological  
4 studies, he did “not try to parcel out” the studies by their design, “whether they are case reports,  
5 whether they are cross-sectional or whether they are ecological studies. I did not do that because,  
6 again, it’s not my expertise.” (*Id.* at 95:7-11.) Assuming he meant he did not consider study  
7 design, his statement is a potential concern — a study’s design, as discussed, can have a serious  
8 impact on its findings and whether the findings can reliably support the temporality and strength-  
9 of-association Bradford Hill factors, among others. His testimony would also conflict with his  
10 Report, where he wrote that he “considered the benefits and limitations of observational  
11 epidemiology in general, as well as the strengths and weaknesses of specific epidemiological  
12 studies prior to arriving at my conclusions.” (Aschner Report, p. 12.) And though Plaintiff argues  
13 Dr. Aschner merely “supplement[ed]” his “causation opinions” with epidemiological findings, he  
14 discusses epidemiological studies at length in his Report and expressly bases his opinions on their  
15 findings. (Opposition Brief, 40:23-24.) For lead and ASD, for example, he writes that “[a] large  
16 body of epidemiological data demonstrates the causal association between lead exposure and  
17 ASD” and then spends several pages discussing these studies. (Aschner Report, pp. 29-33.)

18 Defendants’ argument exposes a broader issue: the scope of Dr. Aschner’s opinion is  
19 unclear. One opinion in his Report is that “exposure to arsenic, mercury, and lead can cause ASD  
20 in children,” “supported by a wealth of epidemiological data and the toxicological profile of these  
21 heavy metals.” (Aschner Report, p. 9.) He testified, however, that his opinion was limited to only  
22 one Bradford Hill factor, biological plausibility. “[E]pidemiology is not my expertise. I was asked  
23 to look at biological plausibility.” (Aschner Depo., 98:18-20.)

24 A few factors, however, weigh in favor of admitting Dr. Aschner’s more-limited opinion  
25 on biological plausibility. As an initial matter, it is not clear he meant to say he did not consider  
26 study design. In his Report, he recognized and discussed the importance of study design, noting,  
27 for example, the Doherty et al. (2020) study had “etiological relevance” as a prospective cohort  
28 study that measured arsenic exposure “pre-diagnosis.” (Aschner Report, p. 25.) He has also



1 written about epidemiological studies and their findings in peer-reviewed, published articles,  
2 suggesting by not “parcel[ing] out” studies he simply meant he did not follow Drs. Ritz and  
3 Gardener and categorize by design studies mentioned in his Report. (Esfandiary Decl., Exh. 62  
4 [Goel & Aschner, *The Effect of Lead Exposure on Autism Development* (Feb. 6, 2021) International  
5 Journal of Molecular Sciences]; Exh. 63 [Ijomone et al., *Environmental influence on*  
6 *neurodevelopmental disorders: Potential association of heavy metal exposure and autism* (Aug.  
7 29, 2020) Journal of Trace Elements in Medicine and Biology].)<sup>18</sup>

8 Most importantly, although the findings of epidemiological studies provide a background  
9 for his opinion, its logic is not affected by the studies’ designs. Unlike Drs. Ritz and Gardener, he  
10 does not interpret or analyze the studies’ findings; he instead explains toxicologically *how* an  
11 association could plausibly be causal — *how* heavy metals could plausibly affect biological  
12 mechanisms and result in ASD and ADHD — an opinion that, to be logical and reliable, does not  
13 require an epidemiologist’s knowledge of study design. “‘Biological plausibility’ ... is only a  
14 subsidiary consideration in the larger question of general causation.” (*Viagra, supra*, 424  
15 F.Supp.3d at p. 791.)

16 Dr. Aschner’s biological plausibility opinion is not barred by *Sargon*. He may not,  
17 however, testify as an expert epidemiologist. Dr. Aschner admits he is not an epidemiologist and  
18 did not conduct a Bradford Hill analysis. He therefore may not opine that epidemiological studies,  
19 analyzed using the Bradford Hill factors, provide evidence that heavy metals can generally cause  
20 ASD and ADHD.

21  
22 b. No Association

23 Defendants argue Dr. Aschner should not be allowed to testify because “the human  
24 evidence is insufficient” to support an association. (Motion Brief, 52:8-9.) This is Dr. Fombonne’s  
25 third point and is addressed above.

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26  
27 <sup>18</sup> Plaintiff also notes Dr. Aschner did not solely look at observational epidemiological studies; for example,  
28 he also considered animal studies and in vitro studies. (Aschner Report, pp. 13-16.)

1 Defendants' authority is distinguishable. (*In re Bausch & Lomb, Inc. Contact Lens*  
2 *Solution Products Liability Litigation* (D.C. S. Carolina, 2009) 2009 WL 2750462.) The expert in  
3 that case based her general-causation opinion on in vitro tests, the results of which she then  
4 extrapolated to "real world causation," even though she and the defendant's experts "agree[d] that  
5 in-vitro tests are only the first step, and that animal studies followed by human trials are necessary  
6 to determine applicability of an hypothesis to humans." (*Id.* at \*12.) The in vitro tests  
7 "suggest[ed]" it was biologically plausible that contact-lens solution caused eye infections, but  
8 plausibility alone was "insufficient to demonstrate causation." (*Ibid.*) "While [the expert's]  
9 biological theory may be exactly right, at this point it is merely plausible, not proven, and  
10 biological possibility is not proof of causation...." (*Id.* at \*12 [citing *In re Accutane Products*  
11 *Liability* (M.D. Fl. 2007) 511 F.Supp.2d 1288, 1296].) The expert's testimony was inadmissible  
12 under *Daubert*.

13 Here, in contrast, Dr. Aschner does not opine that because it is biologically plausible, heavy  
14 metals can cause ASD — essentially bootstrapping *heavy metals plausibly cause ASD* into *heavy*  
15 *metals cause ASD*, "mak[ing] the leap," as Defendants put it, "from possible mechanisms to  
16 causation." (Defendants' Closing Argument Slides (Apr. 4, 2022) Slide No. 48, capitalization  
17 omitted.) He instead opines that causation is biologically plausible — "a subsidiary consideration  
18 in the larger question of general causation." (*Viagra, supra*, 424 F.Supp.3d at p. 791.)

19  
20 c. Speculative Opinion

21 The court excludes speculative expert opinions. (*Sargon, supra*, 55 Cal.4th at p. 771-772.)  
22 Plaintiff's general-causation theory is that heavy-metal exposure can cause ASD and ADHD, and  
23 Dr. Aschner opines this theory is biologically plausible.

24 Defendants argue Dr. Aschner's opinion is speculative because the biological mechanisms  
25 he describes in his Report "are not specific to ASD or ADHD ... or even the human brain or  
26 neurological injury." (Opposition Brief, 53:15-16.) They cite his opinion that "arsenic activates  
27 p38 mitogen -activated protein kinase (P38 MAPK) ... leading to neuronal cell death (Karri et al.,  
28 2016)." (Aschner Report, p. 22.) "MAP kinase signaled pathways," he testified, are a "very basic

1 biological function, a signaling pathway ... implicated in many [other] diseases” besides ASD —  
2 Parkinson’s disease, Alzheimer’s disease, various cancers, renal, digestive, and cardiovascular  
3 diseases — akin to “oxidative stress,” another mechanism he identified as a plausible ASD causal  
4 mechanism, which similarly “happens at all ages and ... many things cause it.” (Aschner Depo.,  
5 242:7-10, 274:6-25, 275:1-15, 276:4-6.) Defendants argue these are “catch-all mechanisms that  
6 effectively prove everything and nothing.” (Opposition Brief, 53:27-28.)

7 Defendants’ argument that Dr. Aschner does not identify a biological mechanism “unique  
8 to ASD” is misplaced. (Aschner Depo., 243:24-25, 244:1-2 [“oxidative stress ... It’s not specific  
9 to anything unique to ASD?”].) The Bradford Hill plausibility factor is not limited to whether  
10 heavy metals can biologically cause ASD and ASD only — it is whether a causal relationship is  
11 plausible based upon “existing knowledge about the mechanisms by which the disease develops.”  
12 (Reference Manual, p. 604.) Merely because Dr. Aschner identifies common biological  
13 mechanisms that are linked to other diseases — that heavy metals have many biological effects  
14 (“[t]here’s a lot of other mechanisms that are affected by arsenic,” for example) — does not mean  
15 his opinion as to heavy metals and ASD is illogical or speculative. (Aschner Depo., 248:2-4.)

16  
17 d. Symptoms

18 Defendants’ final argument is essentially Dr. Fombonne’s fourth point — Dr. Aschner  
19 considered whether heavy metals can biologically cause certain symptoms, but these symptoms  
20 are not logically equivalent to an ASD or ADHD diagnosis, and he did not “bother to familiarize  
21 himself” with the DSM-5’s criteria used to clinically diagnose ASD. (Motion Brief, 55:5-6.) As  
22 discussed above, the Court is not persuaded by this argument, and Defendants’ authority *Rochkind*  
23 is distinguishable. And although “lead-caused behaviors do not necessarily indicate that an  
24 individual has ADHD because these behaviors are also symptoms of a variety of other disorders  
25 and learning disabilities,” the Maryland court actually concluded the inferential “jump” from  
26 “attention deficits and hyperactivity” to “a clinical ASHD diagnosis ... seem[ed] reasonable.”  
27 (*Rochkind, supra*, 454 Md. at p. 291.)

1           4.     Dr. Kevin Shapiro

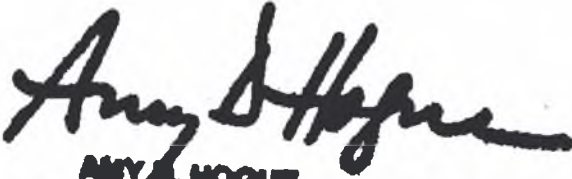
2           Defendants argue Dr. Shapiro’s opinion is speculative because he offers only “an inventory  
3 of theories by which heavy metals *could* interfere with certain biological mechanisms that *may* be  
4 involved in the development of symptoms that overlap with some ASD symptoms.” (Motion  
5 Brief, 56:1-4.) But Defendants misstate his opinion, which he summarized as: “Heavy metals are  
6 toxic to the brain and have a measurable and demonstrable impact on neurodevelopment .... [a]nd  
7 ... the mechanisms by which they affect neurodevelopment are similar and in many cases the same  
8 as the biological mechanisms that have been implicated in Autism Spectrum Disorders.” (Shapiro  
9 Depo., 119:7-16.) His opinion, like Dr. Aschner’s, is limited to one Bradford Hill factor, biological  
10 plausibility, not the broader causation question of whether heavy metals can contribute to ASD  
11 and ADHD.

12           “Mere possibility alone is insufficient to establish [causation],” Defendants argue, citing  
13 *Jones v. Ortho Pharmaceutical Corp.* (1985) 163 Cal.App.3d 396, 402. But *Jones* was the appeal  
14 of a motion for nonsuit following trial, and the court held the experts’ “conjectural and ambiguous  
15 testimony ... that the ingestion of the drug may have had some effect on the development or  
16 progression of the disease” was insufficient evidence to support the verdict for the plaintiff. (*Ibid.*)  
17 “That there is a distinction between a reasonable medical ‘probability’ and a medical ‘possibility’  
18 needs little discussion ... A possible cause only becomes ‘probable’ when, in the absence of other  
19 reasonable causal explanations, it becomes more likely than not that the injury was a result of its  
20 action.” (*Id.* at p. 403.) Unlike the *Jones* experts, who opined on both general and specific  
21 causation, Dr. Shapiro’s opinion is limited a subsidiary issue within general causation — whether  
22 heavy metals can plausibly cause ASD, given what is known “about the mechanisms by which the  
23 disease develops.” (Reference Manual, p. 604.) His opinion is not speculative.

24  
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1 IV. Conclusion

2 The Court finds that, consistent with the Court's gatekeeping role under *Sargon*, Plaintiff's  
3 experts' opinions that heavy metals are capable of being a substantial factor in causing ASD and  
4 ADHD are admissible.

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9 AMY D. HOGUE

Dated: MAY 24 2022

10 AMY D. HOGUE  
11 JUDGE OF THE SUPERIOR COURT  
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