Differential Diagnosis and *Daubert*: Preventing the Misuse of Differential Etiology to Prove Causation in Toxic Tort Cases

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In medicine, a differential diagnosis is a technique physicians sometimes use to identify the cause of a patient's symptoms. As its name indicates, the process is intended to result in a medical diagnosis.

The term "differential diagnosis" has often been used in toxic tort litigation to mean something completely different. A

plaintiff who files a toxic tort case should already have a medical diagnosis. Indeed, it should be the diagnosis which leads the plaintiff to file the lawsuit in the first place. The toxic tort "differential diagnosis" is not a diagnosis at all, but rather a method whereby a plaintiff's expert purports to "rule in" various potential causes for the plaintiff's illness and then to "rule out" alternative causes until only one cause remains. It should come as no surprise to defense attorneys that, when a plaintiff's expert uses the technique, it inevitably points to the defendant.

The more accurate name for the technique as used in litigation is "differential etiology." Yet, courts persist in calling it a differential diagnosis and sometimes confuse the medical standard for diagnosing an illness with the legal standard for determining cause and effect. When that happens, a plaintiff's expert may be allowed to introduce causation opinions that are based on unscientific speculation.

The case law on differential diagnosis is inconsistent and sometimes contradictory. This article is intended as a guide for defense lawyers who are facing claims in which the plaintiff's expert purports to base his or her causation opinion on a differential etiology. It will explore the method as it has been employed in state and federal courts, and provide some practice tips for defending against such opinions. The goal of this article is to place defense counsel in the best position to exclude differential etiology opinions and, if the opinions survive the defense challenge, to cross examine the expert.

I. Differential Diagnosis in Perspective: The *Daubert*/*Frye* Framework and the Plaintiff's Burden

The cases in which courts have admitted speculative differential etiology opinions generally appear to be ones in which the courts have ignored the *Daubert* or *Frye* standard and accepted the expert's characterization that his or her causation opinion is based on clinical experience or professional judgment. To be in the best position to keep such testimony out of evidence, the defense lawyer must plan the expert's deposition in such a way that the expert either agrees with the generally-accepted legal standard for proving causation or admits that he or she did not follow that standard. A *Daubert* or *Frye* motion should follow.

A. *Daubert*: Science, not speculation

The purpose of Federal Rule of Evidence 702 is to ensure that any and all scientific testimony or evidence admitted is not only

relevant, but reliable.[1] The Supreme Court has explained that an expert must employ in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.[2] The "knowledge" requirement of Rule 702 requires "more than subjective belief or unsupported speculation."[3]

When deciding a *Daubert* challenge, the judge's task is to separate real science from speculation masquerading as science. *Daubert* cautioned, however, that the trial court's focus "must be *solely on principles and methodology*, not on the *conclusions* that they generate."[4] Since *Daubert*, appellate courts have sometimes reversed trial courts because the trial courts focused more on the expert's conclusion (with which it disagreed) rather than on the expert's methodology.[5]

One obstacle to mounting a *Daubert* challenge to a differential etiology opinion is that many courts have already accepted the technique as a valid method for determining causation.[6] As set forth below, there should still be room to attack a differential etiology by arguing that the expert applied the technique in an unreliable and unscientific way.

B. *Joiner* and the "analytical gap"

The Supreme Court's decision in *General Electric v. Joiner* dealt with extrapolation from animal studies to human results.[7] The plaintiff's experts had relied on "relevant animal studies which support their opinions" and a handful of human epidemiology studies to conclude that PCBs caused plaintiff's lung cancer.[8] The Supreme Court observed that the

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[1] Daubert v. Merrell Dow Pharm., Inc., 509 U.S. 579, 589 (1993).

[2] Kumho Tire Co. v. Carmichael, 526 U.S. 137, 152 (1999).

[3] *Daubert*, 509 U.S. at 590; *see also* Demaree v. Toyota Motor Corp., 37 F. Supp.2d 959, 961 (W.D. Ky. 1999) (finding that an expert's subjective belief or unsupported speculation is not admissible).

[4] *Daubert,* 509 U.S. at 594-595 (emphasis added); *see also* Chapman v. Proctor & Gamble Distrib., LLC, 766 F.3d 1296, 1305 (11th Cir. 2014); McDowell v. Brown, 392 F.3d 1283, 1298 (11th Cir. 2004).

[5] *See* Milward v. Acuity Specialty Prods. Grp., Inc., 639 F.3d 11, 26 (1st Cir. 2011); Schultz v. Akzo Nobel Paints, LLC, 721 F.3d 426, 434 (7th Cir. 2013).

[6] Clausen v. M/V New Carissa, 339 F.3d 1049, 1057 (9th Cir. 2003); Ervin v. Johnson & Johnson, Inc., 492 F.3d 901, 904 (7th Cir. 2007); McClain v. Metabolife Int'l, Inc., 401 F.3d 1233, 1252 (11th Cir. 2005); Goebel v. Denver & Rio Grande W. R.R. Co., 346 F.3d 987, 999 (10th Cir. 2003); Cooper v. Smith & Nephew, Inc., 259 F.3d 194, 202 (4th Cir. 2001); Turner v. Iowa Fire Equip. Co., 229 F.3d 1202, 1208 (8th Cir. 2000); Baker v. Dalkon Shield Claimants Trust, 156 F.3d 248, 253 (1st Cir. 1998); Ambrosini v. Labarraque, 101 F.3d 129, 140 (D.C. Cir. 1996).

[7] Gen. Elec. Co. v. Joiner, 522 U.S. 136, 144 (1997).

[8] *Id*. at 143.

animal studies were on infant mice who had received direct injections of high doses of PCBs, whereas the plaintiff was an adult male who had been exposed to much lower concentrations. The mice also developed a different form of cancer.

Plaintiff defended his experts' opinions by claiming that, under *Daubert*, the court's focus should be on "principles and methodology" and not on the experts' conclusions. The Supreme Court responded with perhaps the most widely quoted language in all of *Daubert* jurisprudence:

> *But conclusions and methodology are not entirely distinct from one another*. Trained experts commonly extrapolate from existing data. But nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered.[9]

Joiner both clarified and complicated the district court's gatekeeper role. It freed district courts from focusing exclusively on an expert's methodology in determining whether opinions are admissible, but also saddled the court with the sometimes murky responsibility of determining whether the "analytical gap" between an expert's source material and his or her conclusions is "too wide." After *Joiner*, district courts were free to review epidemiological studies, animal studies, *in vitro* studies and other forms of scientific proof in order to evaluate whether the relevant scientific studies supported the experts' conclusions.[10]

Joiner provided no guidance for the lower courts on how to tell when "the gap" was "too great." Ever since, district courts have generally observed that the *Daubert*/*Joiner* analysis is fact specific and case-by-case.[11] While

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[9] *Id.* at 146 (emphasis added).

[10] FEDERAL JUDICIAL CENTER, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 23 (3d ed. 2011).

[11] Loewen v. Wyeth, Inc., No. CV 03-J-2166-S, 2011 WL 6140908, at *1 (N.D. Ala. Nov. 14, 2011) ("the inquiry required by *Daubert* is meant to be a 'flexible one,' and expert testimony which does not meet all or most

some courts merely seek to evaluate the "weight" of the scientific evidence without closely examining that evidence, other courts have rolled up their sleeves and dug into the often-unfamiliar territories of toxicology, epidemiology and animal research at a granular level.[12] The Seventh Circuit recently described the analysis this way: "The district court's primary concern, and ours on appeal, is the failure of the experts to *connect the dots* from the studies to the illnesses endured by the [plaintiffs]." [13] The *Joiner*/ analytical gap assault is another potential strategy for keeping a speculative differential etiology opinion out of evidence. The defense lawyer can argue that the dots do not connect because the gap between the evidence on which the expert purports to rely and the ultimate result is too wide.

C. The *Frye* standard: General acceptance

In jurisdictions that follow the *Frye* standard, the court's focus is on whether the expert's theory is generally accepted in the relevant scientific community. [14] Even in *Frye* jurisdictions, many courts have added a reliability test. That is, the technique the expert applies must give rise to reliable results and the expert must have applied the technique in a reliable manner. The addition of the "reliability" element in *Frye* jurisdictions gives courts wider latitude to exclude expert opinions, and some courts

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of the *Daubert* factors may still be admissible based on the specific facts of a particular case"); Nelson v. Wal-Mart Stores, Inc., No. 2:04-CV-00171-WRW, 2009 WL 330299, at *1 (E.D. Ark. Jan. 13, 2009) ("Because the [*Daubert*] inquiry is 'flexible and fact-specific, a court should use, adapt, or reject *Daubert* factors' as needed based on the facts of a particular case.") (citation omitted); Target Corp. v. Greenberg Farrow Architecture, Inc., No. CIV. 10-4810 RHK/JSM, 2012 WL 1963362, at *10 (D. Minn. May 31, 2012) ("Even a theory that meets certain *Daubert* factors should not be admitted if it does not apply to the specific facts of the case.").

[12] *See In re* Breast Implant Litig., 11 F. Supp.2d 1217, 1231 (D. Colo. 1998) (stating that the court "examined the numerous studies" submitted by the plaintiffs, including 40 epidemiology studies, and determined that the studies "do not reasonably support the conclusions of the Plaintiffs' expert witnesses"); Hamilton v. Breg, Inc., No. 2:09-CV-146, 2011 WL 833614, at *3-8 (S.D. Ohio Jan. 24, 2011) (conducting a review of multiple expert studies); Mercer v. Rockwell Int'l Corp., 24 F. Supp.2d 735, 747-748 (W.D. Ky. 1998) (discussing various epidemiological studies relied upon by expert witness); Baker v. Chevron USA, Inc., 680 F. Supp.2d 865, 880-887 (S.D. Ohio 2010) (conducting an extensive review of various epidemiology studies), *aff'd sub nom.* Baker v. Chevron U.S.A. Inc., 533 Fed. App'x 509 (6th Cir. 2013).

[13] C.W. ex rel. Wood v. Textron, Inc., 807 F.3d 827, 837 (7th Cir. 2015) (emphasis added).

[14] *See*, *e.g.*, Zandi v. Wyeth, No. A08-1455, 2009 WL 2151141, at *5 (Minn. Ct. App. July 21, 2009).

have applied the "*Frye* plus reliability" standard to exclude differential etiology opinions.[15]

II. Differential Diagnosis vs. Differential Etiology

The terms differential diagnosis and differential etiology sound similar, but they describe vastly different processes. The Federal Judicial Center's Manual on Scientific Evidence defines the term "differential diagnosis" as:

> The method by which a physician determines what disease process has caused a patient's symptoms. The physician considers all relevant potential causes of the symptoms and then eliminates alternative causes based on a physical examination, clinical tests and a thorough case history.[16]

Somewhat paradoxically, even courts that have allowed plaintiff's experts to testify to a *differential etiology* have recognized that a *differential diagnosis* is a technique used to identify, *i.e.*, diagnose, the plaintiff's illness, not to determine the *cause* of the plaintiff's illness.[17]

For example, in *Tamraz v. Lincoln Electric Company*, [18] the court criticized the plaintiff's expert for conflating diagnosis and etiology. The plaintiff had been exposed to manganese, but developed Parkinson's, not manganism. Manganism is caused by exposure to manganese, Parkinson's is not. The two conditions share similar symptoms, but arise from damage in different parts of the brain. The plaintiff's expert called the plaintiff's illness "manganese-induced parkinsonism," and attempted to "elide[ ] the distinction between [plaintiff's] disease and what caused it." [19] The Sixth Circuit excluded the opinion, but still held that a differential etiology – when done correctly – is an admissible method for proving causation.

The court noted that, when most physicians think about etiology in a clinical setting, they may think about it in a different way than judges and juries think about it in a courtroom. Getting a diagnosis

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[15] Berry v. CSX Transp., Inc., 709 So.2d 552, 568 (Fla. Dist. Ct. App. 1998); Montgomery Mut. Ins. Co. v. Chesson, 206 Md.App. 569, 594 (Md. App. 2012); Cornell v. 360 W. 51st St. Realty, LLC, 22 N.Y.3d 762, 780-781 (N.Y. 2014); Blackwell v. Wyeth, 408 Md. 575, 584 (Md. 2009).

[16] FEDERAL JUDICIAL CENTER, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 214 (1994).

[17] Brown v. Burlington N. Santa Fe Ry. Co., 765 F.3d 765, 772 (7th Cir. 2014); Higgins v. Koch Dev. Corp., 794 F.3d 697 (7th Cir. 2015) ("'Differential diagnosis' actually refers to a method of *diagnosing* an ailment, not determining its cause.").

[18] 620 F.3d 665 (6th Cir. 2010).

[19] *Id*. at 673.

right matters greatly to a treating physician, as a bungled diagnosis can lead to an unnecessary procedure, or worse. But with etiology, the physician may follow a precautionary approach. If a particular factor *might* cause the disease, the physician may tell the patient to avoid it. In other words, according to the Sixth Circuit, physicians apply a less stringent standard to evaluating etiology than they do to diagnosing an illness. The Sixth Circuit went on to observe that in its own prior opinions,[20] it had used the term "differential diagnosis" to broadly include what might better be called a differential etiology. But the court had never before been forced to distinguish the two concepts. The *Tamraz* court appeared to recognize that using the terms "diagnosis" and "etiology" interchangeably had resulted in admitting opinions into evidence which were not reliably grounded in science.

The court concluded, "This low threshold for making a decision serves well in the clinic but not in the courtroom, where decision requires not just an educated hunch but at least a preponderance of the evidence."[21] Similarly, the Seventh Circuit has recently highlighted the distinction, observing, "'Differential diagnosis' actually refers to a method of *diagnosing* an ailment, not determining its cause. 'Differential etiology,' on the other hand, is a causation-determining methodology. But, to be validly conducted, an expert must systematically 'rule in' and 'rule out' potential causes in arriving at her ultimate conclusion."[22]

Unfortunately, few courts acknowledge the distinction between diagnosis and etiology. A *Daubert* or *Frye* motion attacking a differential diagnosis, therefore, should begin by establishing the appropriate method for reliably proving causation and should demonstrate how the plaintiff's expert's opinion does not satisfy that standard. Fortunately, both inside and outside the context of differential diagnosis, courts have addressed the "right" way to prove causation, and there is a robust body of case law on the subject.

A. General Causation: The substance can cause the disease

It is by now arguably hornbook law in both *Daubert* and *Frye* jurisdictions that proving medical causation in a toxic tort case is a two-step analysis. It requires proof of both "general causation" and

[20] Hardyman v. Norfolk & W. Ry. Co., 243 F.3d 255, 260 n.2 (6th Cir. 2001).
[21] *Tamraz*, 620 F.3d at 673.
[22] *Higgins*, 794 F.3d at 705 (internal citations omitted) (emphasis in original).

"specific causation." [23] General causation is a question of whether the chemical at issue *can* cause the injury alleged by the plaintiff.[24] It is proven by demonstrating, primarily through the medical and scientific literature, that exposure to a substance is capable of causing a particular disease.

Proof of general causation almost always requires the use of epidemiology. [25] Where epidemiology is available, courts have held that it cannot be ignored.[26] This is particularly true if there are negative epidemiological studies which are directly on point (*i.e.*, studies that have looked for the alleged association and not found it). Where there is a large body of epidemiological evidence that contradicts a plaintiff's claim, it is necessary for the plaintiff to at least address it with evidence that is based on medically reliable and scientific methodology.[27]

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[23] Pluck v. BP Oil Pipeline Co., 640 F.3d 671, 676-677 (6th Cir. 2011); *McClain*, 401 F.3d at 1239; Dickson v. Nat'l Maint. & Repair of Ky., Inc., No. 5:08-CV-00008, 2011 WL 12538613, at *2 (W.D. Ky. April 28, 2011); Siharath v. Sandoz Pharms. Corp., 131 F. Supp.2d 1347, 1363 (N.D. Ga. 2001); Adams v. Cooper Indus., Inc., No. CIV.A. 03-476-JBC, 2012 WL 2339741, at *1 (E.D. Ky. June 19, 2012); *Ex parte* Valdez, 636 So.2d 401, 405 (Ala. 1994); *Berry*, 709 So.2d at 567-568; *Chesson*, 206 Md.App. at 606-607; Sean R. *ex rel.* Debra R. v. BMW of N. Am., LLC, 48 N.E.3d 937 (N.Y. 2016); Blum by Blum v. Merrell Dow Pharm., Inc., 705 A.2d 1314, 1316 (Pa. Super. Ct. 1997), *aff'd sub nom.* Blum ex rel. Blum v. Merrell Dow Pharm., Inc., 764 A.2d 1 (Pa. 2000).

[24] *See McClain*, 401 F.3d at 1239.

[25] *See*, *e.g.*, *Dickson*, 2011 WL 12538613 at *5 ("Epidemiology is usually the best evidence of general causation in toxic tort cases"); Norris v. Baxter Healthcare Corp., 397 F.3d 878, 882 (10th Cir. 2005) (citing Linda A. Bailey, et al., *Reference Guide on Epidemiology*, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 126 (1994)); Castellow v. Chevron USA, 97 F. Supp.2d 780, 786 (S.D. Tex. 2000) (citing Allen v. Pa. Eng'g Corp., 102 F.3d 194, 196 (5th Cir. 1996)); *see also* Turpin v. Merrell Dow Pharm., Inc., 959 F.2d 1349, 1351-1356, 1360 (6th Cir. 1992) (affirming grant of summary judgment for defendants because the evidence relied upon by plaintiffs, which did not include epidemiological studies, was an insufficient basis for an opinion on causation), *cert. denied*, 506 U.S. 826 (1992); *see generally In re Breast Implant Litig.*, 11 F. Supp.2d at 1224 (collecting cases standing for the proposition that epidemiological studies are the best evidence of causation). "Courts should normally require more than one epidemiological study showing a positive association to establish general causation, because a study's results must be capable of replication." *Dickson,* 2011 WL 12538613, at *6 (citing King v. Burlington N. Santa Fe Ry. Co., 762 N.W.2d 24, 48 (Neb. 2009)).

[26] *Norris*, 397 F.3d at 882.

[27] *Id.*; Turpin v. Merrell Dow Pharm., Inc., 736 F. Supp. 736, 743 (E.D. Ky. 1990) (determining that, where there were over 30 epidemiological studies, none of which found a statistically significant relationship between defendant's product and plaintiffs' disease, plaintiffs could not meet their burden); Conde v. Velsicol Chem. Corp., 24 F.3d 809, 814-815 (6th Cir. 1994) (finding that plaintiffs failed to account for nineteen contrary studies, and therefore granting summary judgment in favor of defendants was warranted); *see also* Grant v. Pharmavite, LLC, 452 F. Supp.2d 903, 908

Of course, simply identifying one (or even a handful) of positive studies does not end the inquiry. The plaintiff's expert must examine both the positive and negative results using the *Bradford Hill* criteria or some other objective standard in order to prove that the association is truly causal, and not just an anomaly. [28] The plaintiff must establish general causation by reference to published literature and must use some type of transparent, reproducible method for analyzing the available science if the expert is to prove that his or her analysis is "reliable."

The general causation stage is where the *Joiner* "connect the dots" analysis often comes into play. There are only a handful of situations in which courts will assume, without expert evidence, that a substance is capable of causing a particular disease. [29] These include asbestos and asbestosis; silica and silicosis; cigarettes and lung cancer; and alcohol and cirrhosis.[30] For the vast majority of cases, the court will not assume that general causation has been established, and a plaintiff's experts will be required to prove that the studies on which they rely demonstrate a causal relationship between the defendant's product and the plaintiff's disease at some dose level. The court will be asked

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(D. Neb. 2006) ("This is not a case where there is no epidemiology. Instead, it is a case where the body of epidemiology finds no association"); *In re* Bausch & Lomb, Inc. Contact Lens Solution Prods. Liab. Litig., No. CIV A 2:06MN77777DCN, 2009 WL 2750462, at *14 (D. S.C. Aug. 26, 2009) (finding that the failure to address contrary data renders plaintiff's theory inherently unreliable).

[28] *See In re* Joint E. & S. Dist. Asbestos Litig., 52 F.3d 1124, 1128-1130 (2d Cir. 1995); Gannon v. United States, 571 F. Supp.2d 615, 626-627 (E.D. Pa. 2007) (stating preeminent scientists have relied on the *Hill* criteria to determine causation); *Castellow*, 97 F. Supp.2d at 786-787 (stating that expert testified "without contradiction[] that scientists generally rely on the *Bradford-Hill* factors to ascertain valid opinions on medical causation"); Amorgianos v. Nat. R.R. Passenger Corp., 137 F. Supp.2d 147, 167-168 (E.D.N.Y. 2001); Rains v. PPG Indus., Inc., 361 F. Supp.2d 829, 835-836 (S.D. Ill. 2004); *In re* Viagra Prods. Liab. Litig., 572 F. Supp.2d 1071, 1081 (D. Minn. 2008); *In re* Stand 'N Seal Prods. Liab. Litig., 623 F. Supp.2d 1355, 1373 (N.D. Ga. 2009); Rimbert v. Eli Lilly & Co., No. CIV 06-0874 JCH/LFG, 2009 WL 2208570, at *14 (D. N.M. July 21, 2009) (stating that expert testified that the *Hill* criteria are generally accepted); *In re* Trasylol Prods. Liab. Litig., No. 08-MD-01928, 2010 WL 1489734, at *10 (S.D. Fla. Mar. 8, 2010) (finding that experts' method, including the *Hill* criteria, was "scientifically reliable"); Kristensen ex rel. Kristensen v. Spotnitz, No. 3:09-cv-00084, 2011 WL 4566239, at *9 (W.D. Va. Sept. 30, 2011) (stating that the *Hill* criteria are "widely accepted in toxic exposure causation analyses"); *In re* Zoloft (Sertraline Hydrocloride) Prods. Liab. Litig., 26 F. Supp.3d 466, 474-475 (E.D. Pa. 2014); *In re* Actos (Pioglitazone) Prods. Liab. Litig., No. 12-cv-00064, 2014 WL 60324, at *6 (W.D. La. Jan. 7, 2014) (stating that the *Hill* criteria are "both reliable and credible").

[29] *See McClain*, 401 F.3d at 1239.

[30] *Id.*; *see also* Hendrix ex. rel. G.P. v. Evenflo Co., 609 F.3d 1183, 1196 (11th Cir. 2010).

to determine whether "the gap" between the studies' conclusions and the plaintiff's illness is "too wide." When "ruling in" the defendant's product as a potential cause of the plaintiff's illness, therefore, the plaintiff's expert should be required to provide a robust, transparent and reproducible general causation analysis.

B. Specific Causation: The substance did cause the disease

Proof of specific causation means that a plaintiff's actual exposure to the alleged toxin was at a level sufficient to cause the plaintiff's disease.[31] To establish specific causation, a plaintiff must show: (i) proof of exposure to the substance; (ii) that the exposure or dose levels were comparable to or greater than those in epidemiological studies; (iii) that the exposure occurred before the onset of injury; and (iv) that the timing of the onset of injury was consistent with that experienced by those in the study.[32] This is often referred to as a "dose-response relationship."

Toxicologists recognize that substances have threshold doses. Courts generally reject the notion that there is "no safe dose" of toxic substance, even a carcinogen.[33] As

[31] *See*, *e.g.*, *Pluck*, 640 F.3d at 677; Raynor v. Merrell Pharm., Inc., 104 F.3d 1371, 1376 (D.C. Cir. 1997); *Dickson*, 2011 WL 12538613, at *2; Adams v. Cooper Indus., Inc., No. CIVA 03-476 JBC, 2007 WL 2219212, at *2 (E.D. Ky. July 30, 2007); Savage v. Union Pac. R.R. Co., 67 F. Supp.2d 1021, 1031 (E.D. Ark. 1999); Cano v. Everest Minerals Corp., 362 F. Supp.2d 814, 824 (W.D. Tex. 2005); *Sean R. ex rel. Debra R.*, 48 N.E.3d 937; *Ex parte Valdez*, 636 So.2d 401 (*Frye* jurisdiction requiring proof of specific causation).

[32] *Pluck*, 640 F.3d at 677.

[33] *Id.* at 675 (finding an expert witness's testimony unreliable because "he relied upon a 'no safe dose' theory that had been discredited by other courts as a basis for establishing specific causation"); Moore v. Ashland Chem. Inc., 151 F.3d 269, 278 (5th Cir. 1998) (excluding expert witness testimony in part because the expert offered no scientific support for his general theory that "exposure to Toluene solution at any level would cause RADS"); *Cano*, 362 F. Supp.2d at 849 ("Several courts have considered and rejected the use of the linear no-threshold model in the litigation context."); *In re* Denture Cream Prods. Liab. Litig., 795 F. Supp.2d 1345, 1352 (S.D. Fla. 2011) ("for most types of dose-response relationships following chronic (repeated) exposure, thresholds exist, such that there is some dose below which even repeated, long-term exposure would not cause an effect in any individual"); Henricksen v. ConocoPhillips Co., 605 F. Supp.2d 1142, 1166 (E.D. Wash. 2009) ("Sawyer's theory

a result, even in cases in which the plaintiff's experts apply a differential diagnosis approach, some courts have still held that the experts must provide admissible evidence of the dose or exposure level required to cause the plaintiff's illness.[34] While courts do not require plaintiffs to prove exposure or dose with mathematical precision, some degree of relative quantification is required (*i.e.*, how much exposure is *enough* to cause the illness?).[35]

A plaintiff's expert using a differential etiology approach

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that any amount of exposure more than negligible should be considered substantial risk factor for AML flies in the face of the scientific literature reviewed and other expert testimony in this case that there is a threshold or dose below which you do not see a statistically significant risk of developing AML."); *Adams*, 2007 WL 2219212, at *7 ("The court finds that the 'no-safe-dose' theory is not a reliable methodology, and it rejects the plaintiffs' claim that said theory entitled their specific causation experts to pay so little attention to the level of exposure in the bellwether plaintiffs."); Wills v. Amerada Hess Corp., No. 98 CIV. 7126 (RPP), 2002 WL 140542, at *14 (S.D.N.Y. Jan. 31, 2002) ("'To the extent that it has been subjected to peer review and publication, [the no threshold model for carcinogenic effects] has been rejected by the overwhelming majority of the scientific community.'") (quoting Whiting v. Boston Edison Co., 891 F. Supp. 12, 25 (D. Mass. 1995)); Sutera v. Perrier Grp. of Am. Inc., 986 F. Supp. 655, 666 (D. Mass. 1997); Johnston v. United States, 597 F. Supp. 374, 393 (D. Kan. 1984) (noting that the linear no-threshold hypothesis is an assumption and that regulators use this model because it is more prudent to overestimate risk than to underestimate it and "just because scientists use hypotheses to describe something they really don't know for sure does not justify a court of law in using speculative hypotheses to determine that one person has caused harm to another"); Richardson v. Union Pac. R. Co., 386 S.W.3d 77, 79 (Ark. Ct. App. 2011) ("causation requires more than mere proof of exposure to above-ambient levels of the alleged toxin, and instead requires evidence of the levels of exposure that are hazardous to human beings generally, as well as the plaintiff's actual level of exposure to the defendant's toxic substance"); Gregg v. V-J Auto Parts, Co., 943 A.2d 216, 226-227 (Pa. 2007) ("we do not believe that it is a viable solution to indulge in a fiction that each and every exposure to asbestos, no matter how minimal in relation to other exposures, implicates a fact issue concerning substantial-factor causation").

[34] *Pluck,* 640 F.3d at 677-680; *Dickson*, 2011 WL 1258613, at *7-10.

[35] *See* Nelson v. Tenn. Gas Pipeline Co., No. 95-1112, 1998 WL 1297690, at *6 (W.D. Tenn. Aug. 31, 1998) (stating that an appropriate methodology requires evidence from which the trier of fact could conclude that the plaintiff was exposed to levels of toxins sufficient to cause the harm complained of); *McClain*, 401 F.3d at 1242-1243 (11th Cir. 2005) (stating that expert's opinion that "any amount of Metabolife" was too much "clearly contradict[ed] the principles of reliable methodology" as he offered "no opinion about the dose of Metabolife" that purportedly caused the plaintiffs' ailments); *Henricksen*, 605 F. Supp.2d at 1161-1162 (stating that expert opinion failed to quantify plaintiff's level of exposure to benzene and although "proof of . . . exposure through specific quantitative measurement is not a requirement, exposure at some level must be shown before a link between benzene exposure and AML could be drawn").

should be required to satisfy specific causation as a part of "ruling in" the defendant's product. Unless the plaintiff's expert can establish that the plaintiff's exposure was high enough to cause his or her illness, there should be no basis for ruling in the defendant's product as a cause.

A significant handful of courts have held that a differential diagnosis can only be used to establish specific causation and that the method should not even be considered if the plaintiff has not already proven general causation.[36] Other courts have either disagreed or ignored the distinction completely.[37] Still others have held that a differential diagnosis is a substitute for a dose/response.[38] The most sensible rule appears to be that the established standards for proving specific causation apply whether or not the expert is using a differential diagnosis. The defense lawyer should attempt to persuade the court to apply the established standard.

II. Differential Diagnosis in the Courtroom

A. Differential Diagnosis misapplied

As indicated above, a clinical differential diagnosis shares certain surface similarities with a differential etiology causation opinion. Both techniques purport to "rule in" certain causes and to "rule out" others. The critical distinction is that, in the clinical setting, "cause" means diagnosis, while in the legal setting "cause" means a proximate cause. As the Sixth Circuit recognized in *Tamraz,* the standard for assigning a cause in the clinical setting is less stringent than the standard the courts use to find proximate cause. But when the same word and the same rule in/rule out technique apply to two such disparate concepts, it is no wonder that courts have mistakenly allowed experts to apply the less stringent, clinical approach without pausing to recognize the difference between "causation" and "etiology." Courts from around the country have held

[36] Kilpatrick v. Breg, Inc., 613 F.3d 1329, 1343 (10th Cir. 2010) (stating a differential diagnosis "assumes the existence of general causation"); *In re* Meridia Prods. Liab. Litig., 328 F. Supp.2d 791, 799 (N.D. Ohio 2004), *aff'd*, 447 F.3d 861 (6th Cir. 2006); Harvard v. Baxter Int'l. Inc., 2000 U.S. Dist. LEXIS 21316, at *17 (N.D. Ohio July 21, 2000); *Cornell*, 9 N.E.3d at 900; *Norris*, 397 F.3d at 885; Hall v. Baxter Healthcare Corp., 947 F. Supp. 1387, 1413 (D. Or. 1996); Ruggerio v. Warner Lambert Co., 424 F.3d 249, 254 (2d Cir. 2005); *Blackwell*, 408 Md. at 615.

[37] *See*, *e.g.*, *C.W. ex. rel. Wood*, 807 F.3d at 839; *Ruggerio*, 424 F.3d at 254.

[38] Westberry v. Gislaved Gummi AB, 178 F.3d 257 (4th Cir. 1999); *Hardyman*, 243 F.3d at 260-261; Cutlip v. Norfolk S. Co., No. L-02-1051, 2003 WL 1861015 (Ohio App. April 11, 2003).

that a "differential diagnosis" is a standard scientific technique for identifying the *cause* of a medical condition.[39] The Third Circuit has noted that "differential diagnosis generally is a technique that has widespread acceptance in the medical community, has been subject to peer review, and does not frequently lead to incorrect results."[40] The Seventh Circuit has stated that there is "nothing controversial" about using differential diagnosis to establish legal cause. A large number of reported decisions reflect the confusion between diagnosis and legal cause.[41]

In *Best v. Lowe's Home Centers, Inc.*,[42] the Sixth Circuit defined a three-part test for when a differential etiology opinion is reliable and admissible. The expert:

> (1) objectively ascertains, to the extent possible, the nature of the plaintiff's injury . . . ,
> (2) "rules in" one or more causes of the injury using a valid methodology, and
> (3) engages in standard diagnostic techniques by which doctors normally rule out alternative causes to reach a conclusion as to which cause is most likely.[43]

Best applied a clinical standard when it should have applied a legal one. The plaintiff splashed pool chemicals into his face in 2003, but the expert did not diagnose his condition (anosmia – loss of the sense of smell) and conduct his differential diagnosis until 2008. The court admitted that there was

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[39] *Hardyman*, 243 F.3d at 260; *Westberry*, 178 F.3d at 263; *Turner*, 229 F.3d at 1208; *Baker*, 156 F.3d at 253 ("Indeed, 'differential diagnosis' is a standard medical technique."); *In re* Paoli R.R. Yard PCB Litig., 35 F.3d 717, 733 (3d Cir. 1994) ("in the absence of employment of standard techniques of differential diagnosis, and failure to provide any explanation as to why he concluded that PCBs rather than alternative possibilities had caused plaintiffs' illnesses, we conclude that [the expert's] assessment of causation was unreliable"); Perkins v. Origin Medsystems, Inc., 299 F. Supp.2d 45, 57 (D. Conn. 2004) ("differential diagnosis, is a standard scientific technique of identifying the cause of a medical problem"); Castillo v. E.I. DuPont De Nemours & Co., Inc., 854 So.2d 1264, 1271 (Fla. 2003).

[40] *In re Paoli*, 35 F.3d at 758.

[41] *See, e.g.*, *Schultz*, 721 F.3d at 433.

[42] 563 F.3d 171, 179-180 (6th Cir. 2009).

[43] *Id.* at 179.

no published literature associating inhalation of the product with anosmia. The expert, however, "ruled in" the product as a potential cause based "on his own experience" and generic statements on the product's MSDS, and the Sixth Circuit approved. He also ruled out a potential idiopathic cause for the injury based on "his own experience." The Sixth Circuit approved the expert's approach to causation because it was not "arbitrary" but was based on his experience and general knowledge.

It is not difficult to find similar cases. In *McCullock v. H.B. Fuller*,[44] the plaintiff developed throat polyps after being exposed to hot glue fumes. Her treating physician, "an experienced medical doctor" and board-certified otolaryngologist, opined that the glue caused the polyps because the MSDS for the product stated that it could cause throat irritation. Despite defendant's insistence that not a single piece of medical literature said that glue fumes could cause throat polyps, the court admitted the testimony citing in support the physician's "review of the MSDS" and "his training and experience."

Berry v. CSX Transportation, Inc.[45] was a FELA case in which a railroad worker alleged that exposure to solvents had caused him to develop toxic encephalopathy. While the parties disagreed on the issue of general causation, the court held that there was sufficient evidence that solvent exposure could cause toxic encephalopathy, so general causation had been established.

In order to prove specific causation, the plaintiff turned to R. Michael Kelly, M.D.[46] Dr. Kelly did not provide any opinions on how

[44] 61 F.3d 1038 (2d Cir. 1995).

[45] 709 So.2d 552.

[46] In 2008, Dr. Kelly was the focus of an exposé in the Wall Street Journal entitled *Michigan Malpractice*. Review & Outlook, *Michigan Malpractice*, WALL ST. J., Nov. 10, 2008, available at http://www.wsj.com/articles/SB122628156208212443. The subject of the piece was Dr. Kelly's work on an asbestos case in Michigan, Miles v. Sure Seal Prods. Co. Inc., No. 04-434812-NP, 2008 WL 5071712 (Mich. Cir. Ct. Nov. 19, 2008). In *Miles,* the trial court excluded Dr. Kelly's opinions after finding that he had expressed nearly identical conclusions with respect to each of the 75 plaintiffs. The plaintiffs' treating physicians and a panel of hospital radiologists overwhelmingly concluded that the plaintiffs did not have the symptoms identified by Dr. Kelly or the

much exposure is necessary to cause toxic encephalopathy or how much exposure plaintiff had. Instead, he took a medical history from the plaintiff and his wife, obtained a work history from plaintiff and ordered laboratory tests, including an MRI and an EEG. Dr. Kelly's examination and tests appeared to be geared toward confirming plaintiff's medical diagnosis, rather than evaluating the cause of his disease. The court noted that Dr. Kelly provided a "biologically plausible explanation" that the solvents have the ability to dissolve fatty materials, making it more difficult for the body to metabolize them and thereby prolonging the exposure. The prolonged exposure, in Dr. Kelly's view, caused the plaintiffs toxic encephalopathy. The trial court held that Dr. Kelly's opinions were inadmissible under *Frye,* but the appellate court reversed, noting that the differential diagnosis method is "scientifically acceptable."

Even more distressing for defense attorneys is the Ninth Circuit's recent rationale for allowing a differential etiology into evidence: "Given the difficulties in establishing a medical cause and effect relationship, '[c]ausation can be proved even when we don't know precisely *how* the damage occurred, if there is sufficiently compelling proof that the agent must have caused the damage *somehow*.'" [47] This philosophy is completely at odds with the well-developed legal standard for proving general and specific causation.

B. Differential Etiology correctly applied

A second line of cases takes a more stringent look at the elements of a differential diagnosis and analyzes the experts' opinions against the backdrop of *Daubert, Frye, Joiner* and related cases.

The *Tamraz* decision came out of the Sixth Circuit one year after *Best,* but represents a completely different philosophy with respect to differential etiology. *Best* ignored *Daubert* and held that an expert would be allowed to rule in and rule out causes as long as he followed a "valid" methodology. The *Best* court did not define "valid," and the expert's method was deemed acceptable because he said it was based on his experience. Had *Best* applied a standard *Daubert* approach, an expert opinion based

asbestos disease diagnosed by Dr. Kelly. *Id*. For further background on the Dr. Kelly controversy, *see* Mark A. Behrens, *Asbestos Litigation Screening Challenges: An Update*, 26 T.M. COOLEY L. REV. 721, 735-747 (2008).

[47] Messick v. Novartis Pharm. Corp., 747 F.3d 1193, 1198 (9th Cir. 2014) (internal citation omitted) (emphasis in original).

on "experience" likely would not have been admitted.

Tamraz, by contrast, observed that calling something a differential diagnosis does not answer the *Daubert* reliability question, but instead raises three more:[48]

(1) Did the expert make an accurate diagnosis of the nature of the disease?
(2) Did the expert *reliably* rule in the possible causes?
(3) Did the expert *reliably* rule out the rejected causes?[49]

The seemingly subtle distinction between *Best* and *Tamraz* – substituting the word "reliable" in the standard for the word "valid" – had a profound effect. The "reliability" standard comes from *Daubert* and the "*Frye* plus reliability" case law and brings to bear all of the law on how experts are required to prove general and specific causation. Other decisions follow a similar approach.

For example, in *Pluck v. B.P. Oil Pipeline Co.,*[50] the court held that the expert had failed to reliably rule in benzene as a cause of the plaintiff's Non-Hodgkin's Lymphoma because he did not ascertain her level of benzene exposure or determine whether the exposure was in excess of EPA mandated "safe" levels. The expert also did not reliably "rule out" alternative causes. The expert acknowledged other exposures which could have caused or contributed to the plaintiff's illness (*i.e.*, cigarettes) but did not identify his method for discounting them.

In *Chapman v. Proctor & Gamble Distribution, LLC,*[51] the plaintiff attempted to blame her denture adhesive for her myelopathy. The court held that a differential diagnosis cannot overcome the "fundamental failure of laying a scientific groundwork for the general toxicity of the drug and that it can cause the harm a plaintiff suffered."[52] The expert in *Chapman* had identified several potential alternative causes for plaintiff's illness but failed to address them in his opinion. The court held that an expert must provide "reasons for rejecting alternative hypotheses using scientific methods and procedures and the elimination of those hypotheses must be founded on more than subjective beliefs or unsupported speculation."[53]

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[48] *Tamraz*, 620 F.3d at 674 (*citing* Bowers v. Norfolk S. Corp., 537 F. Supp.2d 1343 (M.D. Ga. 2007)).
[49] *Id*. at 665.
[50] 640 F.3d at 679-680.
[51] 766 F.3d 1296.
[52] *Id.* at 1309.
[53] *Id*. at 1310.

Other courts evaluating differential etiology opinions have reached similar results. They have demanded transparent, reliable methods for ruling in a substance as a potential cause of the plaintiff's disease and by so doing have brought to bear the case law which states that epidemiology is the best evidence of general causation. [54] They have also closely examined the studies on which the experts relied in assessing general causation to see if the analytical gap between the science and the opinion is too wide. [55] They have likewise looked at experts' approaches to specific causation to determine whether the expert has reliably extrapolated from the dose/response literature to the plaintiff's individual exposure situation, and they have alluded to the near impossibility of ruling out alternative causes.[56] The objective of a defense attorney should be to steer the court toward an interpretation of differential diagnosis that requires the full *Daubert* or "*Frye* plus reliability" treatment.

III. Practice Tips

The presence of the phrase "differential diagnosis" in an expert's report, by itself, may be an indication that the expert is not prepared to answer the traditional questions about epidemiology and dose response. For that reason, the defense lawyer should take the time to build a careful record of both the work that the expert did to compile the differential diagnosis, but more importantly, the work the expert did not do. At the end of the deposition, the defense attorney should have a transcript that proves that the expert understood the traditional method for proving causation, but intentionally chose not to follow it. Just as importantly,

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[54] *Norris*, 397 F.3d at 882 ("epidemiology is the best evidence of general causation in a toxic tort case"); Rider v. Sandoz Pharm. Corp., 295 F.3d 1194, 1198 (11th Cir. 2002) ("Epidemiology, a field that concerns itself with finding the causal nexus between external factors and disease, is generally considered to be the best evidence of causation in toxic tort actions."); *In re Breast Implant Litig.*, 11 F. Supp.2d at 1224 ("Epidemiology is the best evidence of causation in the mass torts context."); *Baker*, 680 F. Supp.2d at 875 ("Epidemiology is usually the best evidence of general causation in toxic tort cases."); Burst v. Shell Oil Co., No. CIV.A. 14-109, 2015 WL 3755953, at *4 (E.D. La. June 16, 2015) ("Epidemiology provides the best evidence of general causation in toxic tort cases."); *Zandi*, 2009 WL 2151141 at *6 (stating that breast cancer does not lend itself to differential diagnosis because the scientific community has not accepted that breast cancer has a limited number of discrete causes, such that ruling out one cause would implicate another).

[55] C.W. v. Textron, Inc., No. 3:10 CV 87 PPS, 2014 WL 1047940, at *11, 14 (N.D. Ind. Mar. 17, 2014), *aff'd sub nom.*, C.W. ex rel. Wood v. Textron, Inc., 807 F.3d 827 (7th Cir. 2015); *Moore*, 151 F.3d at 279.

[56] *Henricksen*, 605 F.Supp.2d at 1157; *McClain*, 401 F.3d 1233.

the defense lawyer should explore in detail the expert's rationale for "ruling in" potential causes and "ruling out" others.

A. Nail down the diagnosis

The plaintiff's actual diagnosis should be the least controversial part of the differential diagnosis process. If the plaintiff does not have a solid, verifiable diagnosis, his or her experts should not even begin to address causation.

Still, in the same case, the plaintiff's actual diagnosis may be uncertain or non-specific. *Tamraz* is an example. The plaintiff had Parkinson's, but the expert wanted to call it "manganese-induced movement disorder." When the diagnosis is uncertain, the defense lawyer should be prepared to make a detailed record of each possible diagnosis. It should be difficult (or impossible) for an expert to assess general causation or specific causation, or to rule in or rule out potential causes, if the diagnosis is uncertain or open to debate. Disagreement or uncertainty over the plaintiff's diagnosis is a red flag for a *Daubert* challenge.

B. Break apart the "Ruling-In" step

It is arguable that "ruling in" a substance as the cause of an illness collapses both general and specific causation into a single step. How can an expert rule in the defendant's product as a cause of the plaintiff's disease unless the expert can demonstrate that the product *can* cause the disease? [57] Likewise, how can the expert rule in the defendant's product unless plaintiff's exposure or dose level was high enough for the disease to occur? The challenge for the defense lawyer is to identify and separate the multiple components of the "ruling in" step.

1. Get the expert to commit to the legal standard for causation

"General causation" and "specific causation" may be legal terms, but they are also terms that toxicologists and medical experts understand. The defense lawyer should ask the expert to define general causation and specific causation. If the expert balks or claims not to know, the defense lawyer can ask: "Do you agree that in order to establish causation, you

[57] As indicated above, some courts hold that a differential diagnosis only applies to specific causation and that general causation must be established first, before a differential diagnosis becomes relevant.

must first demonstrate that my client's product can cause the plaintiff's illness at some dose level?" and "Do you agree that you also need to show that my client had a high enough exposure to cause the illness?" The case law arguably requires the expert to answer both questions in the affirmative. If the expert says no, he or she is out of sync with the law. If he or she says yes, the expert has opened himself or herself up to detailed questions on general and specific causation.

2. Know the epidemiology

Before the deposition, the expert should have disclosed a written report or disclosure providing the basis for his or her opinions. If that report discloses epidemiological evidence in support of the expert's opinions, the defense lawyer should read each study and be prepared to ask the expert about the distinctions between the studies and the plaintiff's situation. The defense lawyer should also have a working knowledge of any negative epidemiology so that the lawyer can at least ask the expert to admit that there are studies which looked for the connection between the product and the plaintiff's illness, but didn't find it.

At a minimum, the defense lawyer should ask the expert to identify each primary study which the expert believes supports an association between the product and the plaintiff's condition. An expert who is attempting to rely on a differential diagnosis may not be able to identify epidemiology in support of his or her opinion. The absence of epidemiological evidence of an association should be a key feature of a *Daubert* or *Frye* motion.

3. Ask about the *Hill* criteria and similar standards

A properly trained toxicologist or epidemiologist should understand the *Hill* criteria and similar methods for evaluating multiple studies in order to establish causation. The defense attorney should also learn and understand the criteria. The defense lawyer should be prepared to ask the expert to name each of the criteria and to describe in detail how he or she applied them. Most often, the expert's answers will be equivocal or vague.

A related technique is to ask the expert for any work papers or notes which specifically demonstrate how the expert applied the criteria and the weight or importance the expert applied to each study. Ask if the expert created a *Hill* criteria "scorecard" or "matrix." The case law does not appear to require such detail, but the absence of such proof

opens the expert up to criticism that his or her work is not transparent.

4. Ask for the dose/ response evidence

The case law generally indicates that experts need not prove dose/response with mathematical precision, but *some evidence* of dose/response is required. The defense lawyer should be prepared to ask: "How much exposure to my client's product is necessary to cause plaintiff's illness?" If the expert has an answer to that question, the defense lawyer should ask for all the evidence in support of that answer and be able to question the expert's reliance on that evidence. For example, if the answer involves animal research, the defense lawyer should be able to ask for information on how the expert extrapolated from animal evidence to human effects. The goal with this question is to set up a *Joiner*-type challenge.

Likewise, the defense lawyer should ask for all of the information in the expert's possession regarding plaintiff's actual exposure. Most often, the exposure giving rise to the alleged affect happened in the distant past, and exposure data does not exist. The attorney should document the absence of exposure data and then probe any alternative methods the expert used to evaluate exposure. Dose reconstruction years or decades after the fact is usually fraught with speculation and unfounded and unproven assumptions.

5. Be alert to reliance on "judgment"

While it is true that some courts have allowed experts to rely on "professional judgment" or "professional experience" to support a differential diagnosis opinion, those decisions are not in tune with the prevailing case law on proving causation. By its nature, professional judgment is personal to the expert, and arguably non-reproducible.

If an expert attempts to rely on judgment, the defense lawyer should document the points in the process where judgment came into play and what parts of the traditional analysis the expert replaced with judgment. Defense counsel should also ask the expert to admit that a similarly trained expert might arrive at a different judgment when faced with the same facts.

6. Other illnesses are not causes

While building the detailed record of which potential causes the expert purported to rule in, the defense lawyer should pay careful attention to what items the expert places on the list. Experts applying differential diagnoses have a

tendency to pad the "rule in" list with items that clearly do not apply. Often this list includes alternative illnesses which could have caused the plaintiff's symptoms or condition. If it is clear from plaintiff's medical records that he or she did not have the illness under consideration, it does not belong on the list. In a toxic exposure case, the only items that should go on the list are other exposures or conditions that could cause the plaintiff's illness and that the plaintiff clearly did have or could have had.

Idiopathic origin should almost always be on the list. As will be discussed below, ruling out an idiopathic cause is (and should be) much more difficult than ruling one in.

7. A Material Safety Data Sheet (MSDS) is not proof of causation

It is not uncommon for an expert to attempt to rely on an MSDS as proof that the defendant's product "could cause" one or more of the health effects set forth on the MSDS. A detailed review of the reasons for including potential health effects on MSDSs is beyond the scope of this article, but courts have generally ruled that an expert cannot use an MSDS as proof of causation unless the expert understands and can explain the scientific evidence used to compile the MSDS.[58]

[58] Mallozzi v. EcoSMART Techs., Inc., No. 11–CV–2884 (SJF)(ARL), 2013 WL 2415677, at *13 (E.D.N.Y. May 31, 2013); *Moore*, 151 F.3d at 278 (stating that an MSDS has limited scientific value when it is not known what tests were conducted in generating the MSDS); *Turner*, 229 F.3d at 1209 (stating that the product's MSDS indicating that breathing dust may irritate the nose and throat and aggravate respiratory diseases was not a sufficient basis for an expert opinion where the expert did not rely upon the MSDS, and "nothing in the record demonstrate[d] what scientific tests or information [the manufacturer] used to generate its MSDS"); Ingram v. Solkatronic Chem., Inc., No 04-CV-0287, 2005 WL 3544244, at *6 (N.D. Okla. Dec. 28, 2005) (stating that expert's reliance upon an MSDS was not reliable since the expert "knew nothing about the source of the information contained in the MSDS" and "[w]hen an expert purports to offer an opinion based upon his review of

C. Identify common "red flags"

The ruling in stage is a common place for experts to engage in some of the logical fallacies that courts have identified as "red flags."

1. Cherry picking

Negative epidemiology is as important as positive epidemiology. The expert should be able to explain why negative epidemiology (*i.e.*, studies which looked for a connection between the exposure and the illness but did not find it) does not detract from the expert's opinion. Relying on only the positive studies while ignoring the negative ones is "cherry picking" and courts have refused to admit expert evidence employing this technique.[59]

2. Post-hoc reasoning

Some experts claim to rule in substances based on the temporal connection between the exposure and the illness. That is, the expert will claim that he or she knows that the plaintiff was exposed (because the plaintiff said so), and that the exposure was high enough to cause the illness *because* the plaintiff got sick. This type of circular reasoning from effects to cause should not survive *Daubert* scrutiny.[60]

existing literature, it is . . . critical [that] the proposed expert carefully review the methodology utilized by the scientist conducting the study to ensure the quality of the assumptions and data therein"); Yates v. Ford Motor Co., 143 F. Supp.3d 386, 390 (E.D.N.C. 2015) (determining that a court may refrain from treating an MSDS as reliable until it is presented with scientific evidence justifying the statements contained in the MSDS); Johnson v. Arkema, Inc., 685 F.3d 452, 462-465 (5th Cir. 2012) (stating that an MSDS, without an explanation of its scientific basis, is not sufficient support for a causation opinion); Coastal Tankships, U.S.A., Inc. v. Anderson, 87 S.W.3d 591, 610-611 (Tex. App. 2002) (stating that an MSDS is of little value in determining causation if there is no evidence of what tests were conducted to compile the MSDS); Brookshire Bros., Inc. v. Smith, 176 S.W.3d 30, 35-39 (Tex. App. 2004) (stating MSDS is not reliable evidence that plaintiffs' exposure caused his illness).

[59] *Norris*, 397 F.3d at 884; Adams v. Cooper Indus. Inc., No. 03-476-JBC, 2007 WL 1805586, at *7 (E.D. Ky. June 21, 2007); *In re* Bextra & Celebrex Mktg. Sales Practices & Prods. Liab. Litig., 524 F. Supp.2d 1166, 1176 (N.D. Ca. 2007); Newell Rubbermaid, Inc. v. Raymond Corp., 676 F.3d 521, 527 (6th Cir. 2012).

[60] *See Nelson*, 1998 WL 1297690, at *11 (stating that expert's conclusion that plaintiffs' PCB levels were high enough to cause their illness because they had the illness was "circular reasoning without basis" and was improper), *aff'd*, 243 F.3d 244, 254 (6th Cir. 2001) ("The magistrate judge properly rejected the circular reasoning that the plaintiffs must have been exposed to the PCBs because PCBs were present in the environment and plaintiffs showed symptoms."); Young v. Burton, 567 F. Supp.2d 121, 137 (D. D.C. 2008) (finding that expert's methodology in diagnosing "mold illness" was unreliable because among other things, "he used circular

3. Unique genetic susceptibility

An expert trying to establish that a common exposure (*i.e.*, vaccines) causes a relatively rare illness (*i.e.*, autism) needs to state why all or most of the people exposed to the substance do not get the illness. Some experts solve this problem by claiming that the plaintiff must have had a unique genetic susceptibility to the alleged ill effects of the product.[61] The science of genetics has advanced so much in recent years, however, that any expert making such a claim should be required to provide evidence that the plaintiff had or has a specific polymorphism that increases the risk of the disease at issue, and that the defendant's product increases the risk in people with that polymorphism.

The "ruling in" step is the place where the differential diagnosis technique intersects most closely with existing *Daubert* and *Frye* case law. The defense lawyer should take advantage of that intersection to develop as detailed a record as possible on how the expert assessed both general and specific causation. The expert who is seeking to avoid *Daubert* and *Frye* scrutiny may attempt to evade questions by claiming that a differential diagnosis does not involve issues such as epidemiology and dose response. The defense lawyer should understand that a significant number of reported decisions *do require* such an analysis, even in the context of a differential diagnosis. It is important not to let the expert shut down the questioning, but rather to document all of the things the expert did to reach a conclusion and all of the things the expert did not do.

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reasoning to work backwards from diagnosis to proof of exposure"); Mancuso v. Consol. Edison Co. of N.Y., 967 F. Supp. 1437, 1450 (S.D.N.Y. 1997) ("As courts have recognized, it is improper for an expert to presume that the plaintiff "must have somehow been exposed to a high enough dose to exceed the threshold [necessary to cause the illness], thereby justifying his initial diagnosis. This is circular reasoning.") (citing O'Conner v. Commonwealth Edison Co., 807 F. Supp. 1376, 1396 (C.D. Ill. 1992) (stating that expert engaged in circular reasoning by presuming that plaintiff's cataracts "were radiation induced, and then presumed that the plaintiff must have somehow been exposed to a high enough dose to exceed the threshold in order to have caused the cataracts, thereby justifying his initial diagnosis")), *aff'd*, 13 F.3d 1090 (7th Cir. 1994); Durden v. Sec'y of Dep't of Health & Human Servs., No. 05-163V, 2007 WL 4962000, at *13 (Fed. Cl. Sept. 26, 2007) (describing expert's opinion that "because cytokines cause immune mediated disorders, and [the plaintiffs' son] has an immune mediated disorder, therefore, his disease process was triggered by cytokines" as "circular reasoning").

[61] *Blackwell*, 408 Md. at 613.

D. Collect detail on the rationale for "Ruling Out"

The "ruling out" portion of the differential etiology technique has no true analog in the *Daubert* case law. It is a unique aspect of the differential diagnosis approach and therefore poses special problems. Courts have generally held that experts must "reliably" rule out causes other than the defendants' product in order to arrive at an admissible differential diagnosis.[62] The existing case law, however, provides very little guidance as to how an expert should go about this step.

But "ruling out" should logically be much more difficult than "ruling in." Once an expert has ruled in a potential cause by reference to medical or scientific literature, he or she should have a very good reason for ruling it back out again. Further, identifying what may have caused an illness is a complicated, inherently uncertain process. Determining what *did not* cause it should logically be all but impossible.

Therein lies the opportunity for defense counsel to make a useful *Daubert* record. The defense counsel should be prepared to press the expert on why and how the expert knows that each item he or she "ruled in" did not in fact cause the plaintiff's illness. If the expert had a good reason to rule some potential cause in, he or she should have an even better reason to rule it out. The expert's answers to these questions have the potential to be unscientific and circular. This is the place where defense counsel should make the record that the expert's opinion is based on speculation. It is important to be patient and to ask detailed questions about each potential cause and all of the reasons it was ruled out.

A common fallacy relied on by plaintiff's experts at this stage of the differential diagnosis is to rule out diseases or medical conditions that the plaintiff undisputedly did not have. While a clinician using a

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[62] *See Tamraz*, 620 F.3d at 674; *Pluck*, 640 F.3d at 680 (ruling that expert "failed to 'rule out' alternative causes" of plaintiff's non-Hodgkin's lymphoma); Lauzon v. Senco Products, Inc., 270 F.3d 681, 694 (8th Cir. 2001) (stating that expert needed to "be able to explain why other conceivable causes" of plaintiff's illness "are excludable"); *Best*, 563 F.3d at 179 (stating that "the doctor must provide a reasonable explanation as to why 'he or she has concluded that [any alternative cause suggested by the defense] was not the sole cause'" of plaintiff's injury) (citing *In re Paoli*, 35 F.3d at 759 (determining that where a defendant points to a plausible alternative cause and the doctor offers *no* explanation for why he or she has concluded that was not the sole cause, that doctor's methodology is unreliable)); *Hall*, 947 F. Supp. at 1414 ("General causation issues aside, an expert must rule out other potential causes of the patient's condition in order for differential diagnosis testimony to be admissible.").

differential technique to diagnose an illness will rule out diseases or medical conditions, an expert using the technique to assess causation should not be allowed to do that. The defense lawyer should be prepared to press the expert on the question of what exposures or risk factors are known to cause the plaintiff's illness and how the expert determined that the plaintiff's illness was not caused by any of those risk factors or a combination of risk factors.

E. The special problem of unknown etiology

The truth is, in most cases, no one knows what caused a particular person to develop a particular disease. The defense lawyer should be prepared to explore the notion of "unknown etiology," using a few simple questions:

- How many cases of the disease are diagnosed in the U.S. each year?
- In how many of those cases is the cause identified?
- Would you agree that most cases of the disease have an unknown cause?
- Would you agree that the cause of the disease is identified in only a small number of cases?

In *Tamraz,* the court held that, when an idiopathic origin accounts for the vast majority of the cases of the disease, an idiopathic explanation is "impossible to ignore and difficult to rule out." [63] In *McCarty v. Arch Wood Protection, Inc.*, [64] the district court excluded the expert's opinions because they admitted that all prior cases of plaintiff's extremely rare disease had been idiopathic. Because the experts agreed that medical science did not know the cause of plaintiff's illness, their conclusions – reached through a differential etiology technique – that the defendants' product caused the illness, were nothing more than speculation.[65]

Whether failing to rule out an idiopathic origin for an illness will result in the exclusion of the expert's testimony will depend on how often the illness arises idiopathically. That is, if a small percentage of the cases of the disease are idiopathic, the expert's

[63] *Tamraz*, 620 F.3d at 675.
[64] No. CV 11-109-HRW, 2016 WL 1306067 (E.D. Ky. Mar. 31, 2016).
[65] *See also Henrickson*, 605 F. Supp.2d 1142; Soldo v. Sandoz Pharm. Corp., 244 F. Supp.2d 434 (W.D. Pa. 2003); Nelson v. Am. Home Prods., 92 F. Supp.2d 954 (W.D. Mo. 2000); *Anderson*, 87 S.W.3d at 609.

failure to rule out an idiopathic cause will likely not doom the opinion because experts are not generally expected to definitively rule out *all* potential causes.[66] On the other hand, if most cases of the disease are idiopathic, the expert should have a very difficult time explaining how he or she ruled out an idiopathic origin.[67]

V. Conclusion

Both differential diagnosis in clinical practice and differential etiology in the courtroom seek to determine the "cause" of a person's condition, and both use similar steps to do that. The similarities between the two processes, however, can sometimes be used to mask the very important distinctions between a medical cause and a legal cause. Courts have sometimes ignored or misunderstood the distinction and have admitted speculative causation opinions they should have excluded. A defense lawyer, however, should be prepared to explain the differences between medical cause and legal cause to the court and to guide the court to the appropriate standard for ruling on the admissibility of causation opinions based on a "differential diagnosis" or "differential etiology."

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[66] *See* Johnson v. Mead Johnson & Co., LLC, 754 F.3d 557 (8th Cir. 2014) ("experts are not required to rule out all possible causes when performing the differential etiology analysis"); Hammer v. Residential Credit Sols., Inc., No. 13 C 6397, 2015 WL 7776807, at *38 (N.D. Ill. Dec. 3, 2015) (stating that a "reliable expert should consider alternative causes, they do not require an expert to rule out every alternative cause"); Perry v. Novartis Pharm. Corp., 564 F. Supp.2d 452, 469 (E.D. Pa. 2008) (stating that "[a]dmissible expert testimony need not rule out *all* alternative causes" of the plaintiff's disease); Luttrell v. Novartis Pharm. Corp., 894 F. Supp.2d 1324, 1341 (E.D. Wash. 2012) ("The Court acknowledges that . . . it is not necessary to rule out all other possible causes of [plaintiff's injury] injury in order to survive summary judgment."), *aff'd*, 555 Fed. App'x 710 (9th Cir. 2014).

[67] *See Tamraz*, 620 F.3d 665; *McCarty*, 2016 WL 1306067.