IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ALABAMA
MIDDLE DIVISION

JANIE SUTHERLAND, Plaintiff, v. MATRIXX INITIATIVES, INC., et al., Defendants	No. CV-04-AR-0129-M

MEMORANDUM IN SUPPORT
OF DEFENDANTS' MOTION TO EXCLUDE
THE EXPERT REPORT AND TESTIMONY OF BRUCE W. JAFEK, M.D.

Defendants Matrixx Initiatives, Inc. ("Matrixx"), Zicam, L.L.C., Botanical Laboratories, Inc., and McKesson Corp. ("defendants") hereby file this memorandum in support of their motion to exclude the expert report and testimony of Bruce W. Jafek, M.D. because his causation testimony does not qualify as relevant scientific knowledge under Federal Rule of Evidence 702.

SUMMARY OF ARGUMENT

The question presented is whether there is sound scientific basis for this witness's conclusion that the smell loss claimed by plaintiff (but not found by the expert who tested her smell function) was caused by her use of an over-the-counter cold remedy rather than by the cold which prompted her to use the product, or several other conditions or medications which have been associated with smell loss. For the reasons described below, Dr. Jafek's causation testimony does not qualify as relevant scientific knowledge under Rule 702 and must be excluded.

There are over 200 causes of persistent smell loss. The most common cause of chronic smell disorders is upper respiratory infections (URIs) such as the common cold. Zicam® Cold Remedy No-Drip Liquid Nasal Gel ("Zicam") treats the common cold, and individuals who have used Zicam to treat their cold and then experienced smell dysfunction have attributed their condition to Zicam. Dr. Bruce W. Jafek ("Jafek") claims that Zicam, rather than the cold she was treating, caused plaintiff Janie Sutherland ("Sutherland") to suffer anosmia, the total and permanent loss of her sense of smell.

Jafek's opinion testimony runs afoul of Rule 702 in several ways. The common thread is that his methodology and chain of reasoning violate the scientific method, which calls for starting with a hypothesis and forming a scientific conclusion only after rigorously testing the hypothesis through controlled experimentation and careful application of accepted scientific principles to the data. Jafek ignores or dismisses data inconsistent with his conclusion; at first ignored and now distorts and misapplies the fundamental principle of dose-response; fails to consider and compare the background risk of smell disorder; and relies on unwarranted and unexplained extrapolations from collateral evidence, and data that science considers anecdotal or otherwise incapable of proving cause and effect. Several steps in the chain between the underlying data and his conclusions are connected only by impermissible speculation and leaps of faith, leaving intolerable analytical gaps. Consequently, his causation opinions are unreliable and fail to "fit" the case under Federal Rule of Evidence 702, *Daubert v. Merrell Dow Pharms*., 509 U.S. 579 (1993), and *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1238 (11th Cir. 2005). Specifically, his testimony is not based on sufficient facts or data, and is not the product of reliable application of reliable principles and methods of science to the facts of the case, violating Rule 702.

In concluding that Zicam can cause total and permanent smell loss when used as directed (general causation), Jafek has inverted the scientific method: He assumed his conclusion from the outset and then relied on unverified assumptions and distorted cherry picking of data and stray statements in articles, all assembled to *confirm* rather than *test* his personal belief. For example, after prematurely reaching his causality conclusion and having it challenged in litigation, Jafek hypothesized a dose-response curve for Zicam by adopting an extrapolation methodology that has never been validated and has no support in toxicology. Moreover, Jafek's dose-response testimony fails to answer the question posed by this case – how much Zicam must reach the smell tissue to cause *permanent anosmia*? He has ignored the background rate of smell loss and data suggesting that there is no increased risk of smell loss with use of Zicam, relying instead on anecdotal reports premised on temporal sequence. He has adopted assumptions concerning drug distribution, chemical analogy, and nasal anatomy that are not only scientifically unsupported, they are *contradicted* by scientific testing and principles. This is not the way scientists evaluate causal relationships outside the courtroom; under Rule 702, it is not a permissible methodology for doing it inside the courtroom.

Having concluded without adequate scientific foundation that Zicam is a cause of smell loss, Jafek overreaches further in concluding that Zicam actually did cause Sutherland to sustain anosmia. First, he lacks a reliable basis even to conclude that Sutherland has experienced smell loss. He relies on the smell testing performed by his colleague, Miriam Linschoten Ph.D. But Dr. Linschoten (also designated as an expert for Sutherland) testified at deposition that Sutherland's testing revealed her a malingerer, and that the testing failed to reliably demonstrate any credible smell loss. Nevertheless, Jafek concludes that Sutherland has smell loss and it was caused by Zicam. Second, it is only by subjective *choice* that Jafek can rule out established or suspected

causes of smell loss in Sutherland's medical history, such as URI, rhinitis, sinusitis, and gastroesophageal reflux disease (GERD), in favor of Zicam, which only Dr. Jafek believes to be a generally accepted cause of smell loss. This is not the reliable scientific judgment that *Daubert* requires.

Finally, Dr. Jafek selects Zicam as the cause here despite the complete absence of evidence that Sutherland's smell tissue was exposed to enough Zicam to cause permanent anosmia, or at all. Ignoring Sutherland's testimony that she used the product as instructed on the package and his own prior concession that when the product is used in this manner it will *not* reach the smell tissue and *cannot* affect smell function, Jafek opines that a toxic dose of zinc gluconate reached Sutherland's smell tissue, destroying her sense of smell. He offers no reliable evidence of (1) how much zinc gluconate must reach the smell tissue in order to produce permanent anosmia, and (2) that this much or more reached Sutherland's smell tissue, and indeed, that any did so at all. Rule 702 precludes a causation opinion without this dose-response foundation.[1]

Dr. Jafek is not practicing science, but advocacy. Rule 702 exists to prevent juries from hearing opinion testimony like this.

FACTUAL BACKGROUND

A. The Facts and Allegations Surrounding Sutherland's Alleged Loss of Sense of Smell

Sutherland, age 58, alleges that she used Zicam on December 21, 2001 in accordance with the package directions after experiencing two days of worsening cold symptoms; that she

[1] *See, e.g., McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1238 (11th Cir. 2005); *Allen v. Pennsylvania Engineering* Corp., 102 F.3d 194, 199 (5th Cir. 1996).

experienced a slight burning sensation in both nostrils; and that within minutes, she could not smell or taste anything.[2]

Sutherland has a history of upper respiratory infection, sinusitis, rhinitis, tonsillitis, GERD, and other conditions which have been associated with smell loss.[3] She also has an extensive history with numerous medications, some of them associated with smell loss.[4]

B. Jafek's Examination of Sutherland

Prior to forming his conclusion and issuing his report, there wasn't any. Before issuing his report in October 2004, Jafek never met, spoke to, or examined Sutherland and never reviewed any of her films or scans. He had never performed any testing of her sense of smell to determine the level of function.[5]

Just prior to his deposition and supplemental report, Jafek examined Sutherland on June 5, 2006, and his colleague and fellow expert, Miriam Linschoten Ph.D performed smell testing to evaluate her degree of dysfunction.[6] Linschoten subsequently reported and testified that Sutherland scored as a malingerer and did not appear to give honest answers to the test

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[2] Exhibit ("Exh.") A (Sutherland depo) at 172-178, 183-187.

[3] *Id.* at 92, 107-109, 131; Exh. D (Jafek depo) at 107, 320, 331, 333-336, 351-353; Exh. LL (Doctors Med Care of E. Gadsen records) at 3-4, 6, 16, 24, 39; Exh. MM (ENT Associates of Gadsen records) at 43-44, 50; Exh. NN (Dowling & Caldwell, PC) at 107; Exh. W (Jones report) at 6.

[4] Exh. A (Sutherland depo) at 250-251; Exh. OO (Jerry's Pharmacy records) at 72-75; Exh. LL (Doctors Med Care of E. Gadsen records) at 16, 24, 32, 36-37, 39; Exh. MM (ENT Associates of Gadsen records) at 46; Exh. NN (Dowling & Caldwell, PC) at 112.

[5] Exh. D (Jafek depo) at 74, 337-339, 343-346; Exh. B (Jafek report); Exh. C (Jafek supp. report).

[6] Exh. C (Jafek supp. report); Exh. PP (Linschoten supp. report).

questions.[7] Linschoten testified that she could not conclude that Sutherland actually had lost smell function.[8] Jafek relies on Linschoten's testing and ordinarily defers to and agrees with her interpretation of the test data, describing her as a "world class psychophysicist" and "international expert" in smell and taste testing, with greater testing experience than he.[9] Nevertheless, departing from his usual practice, Jafek testified that he disagrees with Linschoten's interpretation, and in his opinion, given the history obtained from Sutherland, she has permanent anosmia caused by Zicam.[10]

Jafek testified that Sutherland's anosmia was caused by Zicam, rather than established causes such as her cold, rhinitis or sinusitis, even though Sutherland testified under oath that she used the product as directed on the package.[11] Jafek has testified elsewhere that use of Zicam as directed does not deliver the gel to the smell tissue and would not produce smell loss.[12]

C. Smell Disorders

Smell dysfunction, including anosmia, is a fairly common condition. At least between 2 and 5 million people in this country, and probably much more than that, have chronic smell

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[7] Exh. PP (Linschoten supp. report) at 2; Exh. M (Linschoten depo) at 49-51, 147-148. Linschoten defines "malingering" as "the intentional production of false or grossly exaggerated physical or psychological symptoms motivated by external incentives such as … obtaining financial compensation." Exh. QQ (Linschoten depo – Hilton) at 16-17.

[8] Exh. PP (Linschoten supp. report) at 2-3; Exh. M (Linschoten depo) at 43, 143-144.

[9] Exh. D (Jafek depo) at 74, 76-79.

[10] *Id.* at 321-328, 342-343.

[11] Exh. A (Sutherland depo) at 183; Exh. D (Jafek depo) at 319-320.

[12] Exh. F (Jafek depo - Lusch) at 237-238.

disorders.[13] About 25% of the population aged 50 or older has impaired sense of smell.[14] It is generally accepted that the most common causes of persistent smell loss are URIs, such as cold and flu (which account for up to 25% of all smell disorders), sino-nasal diseases such as rhinitis and sinusitis, and head trauma, and that a substantial percentage of cases are classified as idiopathic, meaning the cause is unknown to medical science. These etiologies are said to account for between 70% and 85% of all cases of chronic smell disturbance.[15] There are over 200 known causes of chronic smell loss.[16]

The nerves associated with smell function are a small patch of tissue approximately one square centimeter in size tucked away in the remote, superior (upper) and posterior (rearward) portion of the nose in each nostril near the midline of the eyes, known as the "olfactory epithelium" or "neuroepithelium." Jafek wrote in 1983 that the neuroepithelium is "almost anatomically inaccessible."[17] However, when he began to testify in Zicam cases and realized that his causation theory required that Zicam reach the neuroepithelium, Jafek abruptly reversed course, describing the path as a "straight shot" in most people, accessible to Zicam gel.[18] He routinely opines that the plaintiff in question had a straight shot, even where, as here, he has

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[13] Exh. G (Jafek depo - Nelson vol. 1) at 141-142; Exh. J (Jafek depo - Nelson vol. 2) at 499; Exh. W (Jones report) at 4-5.

[14] Exh. T (Jafek depo - Wyatt) at 85-86.

[15] Exh. G (Jafek depo - Nelson vol. 1) 168-169; Exh. W (Jones report) at 4-5.

[16] Exh. C (Jafek supp. report) at 9; Exh. W (Jones report) at 4, 7.

[17] Exh. N (Jafek 1983 paper); Exh. G (Jafek depo - Nelson vol. 1) at 66-70.

[18] Exh. G (Jafek depo - Nelson vol. 1) at 66-70; Exh. K (Jafek depo - Nelson vol. 3) at 638-639, 645-647. *See* Exh. C (Jafek supp. report) at 4-5.

absolutely no basis for characterizing the plaintiff's nasal anatomy as of the time of use, and/or where, as here, existing medical records or testimony indicate septal deviations, enlarged turbinates, or other nasal deformities that impede access to the neuroepithelium.[19]

D. Jafek's Attack on Zicam and Connection to Zicam Litigation

Dr. Jafek's hypothesis generated the litigation against Zicam.[20] In or about March 2003 he and Linschoten submitted a poster to the American Rhinological Society (ARS) for presentation at its meeting in September 2003.[21] It reported the case of a 55 year old man who presented with smell loss after using Zicam to treat a cold. Jafek attributed the smell loss to the Zicam use, despite the several potential causes in the patient's medical history, including his URI and use of Flonase, which warns of potential smell loss.[22] The poster indicated Jafek had seen nine other patients with a similar history, but did not present details of their cases.[23] It theorized that zinc gluconate, the active ingredient in Zicam, caused the smell loss, implicitly ruling out

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[19] *E.g.,* Exh. E (Jafek depo – Hans) at 11-12, 49, 123-128; Exh. C (Jafek supp. report) at 3-5; Exh. D (Jafek depo) at 115, 334-340.

[20] Dr. Jafek has created a cottage industry in testifying that Zicam causes smell loss. He has now been deposed or written reports attributing individuals' smell loss to Zicam in 15 cases. He has never evaluated an individual who used Zicam and later lost sense of smell without reaching the conclusion that Zicam was the cause. Exh. T (Jafek depo - Wyatt) at 29-30.

[21] Exh. J (Jafek depo - Nelson vol. 2) at 370. A poster presentation simply makes the poster available for passive display at a meeting. Unlike a podium presentation, there is no accompanying discussion to the audience.

[22] Exh. O (Jafek 2003 poster); Exh. G (Jafek depo - Nelson vol. 1) at 195-198; Exh. J (Jafek depo - Nelson vol. 2) at 373-376; Exh. X (Kern report re Hans) at 1; Exh. EE (Winstead report re Hurst) at 2-3; Exh. RR (PDR for Flonase) at 11.

[23] Exh. O (Jafek 2003 poster).

other explanations based on patient histories and temporality.[24] It cited unsuccessful polio prevention experiments from the 1930s where high volumes of a different compound, *zinc sulfate*, were applied directly to the neuroepithelium and were sometimes able to produce transient smell loss, and the use of zinc sulfate in behavioral studies in animals to temporarily defeat smell function. It cited no toxicology evidence concerning zinc gluconate. It concluded, based on Jafek's interpretation of the zinc sulfate literature and the temporal, anecdotal experience described by his small group of patient(s), that Zicam rather than their colds or other potential causes produced the smell loss.[25] The ARS later published a paper by Jafek, Linschoten and their colleague based on the same questionable data and analysis.[26]

Neither the poster nor the published paper revealed that Jafek's causation conclusion as to eight of the ten patients was based solely on questionnaires they filled out and submitted over the internet. None of the authors had ever examined these eight "patients", they had no objective testing to verify and characterize their claimed smell loss, and Jafek was and remains unaware of their litigation status and potential litigation biases. No medical records were reviewed, and Jafek's published algorithm for evaluating smell loss in the diagnosis and treatment of patients was violated.[27] The paper stated that other causes of smell loss could be ruled out for all ten patients, but in fact, even with the limited available information, the authors could not rule out

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[24] Exh. T (Jafek depo - Wyatt) at 96.

[25] Exh. O (Jafek 2003 poster).

[26] Exh. P (Jafek 2004 paper).

[27] Exh. J (Jafek depo - Nelson vol. 2) at 270-272; Exh. V (James report) at 14; Exh. W (Jones report) at 8; Exh. Y (Schwob report) at 3-4; Exh. R (Linschoten depo - Lusch) at 164-178; Exh. T (Jafek depo - Wyatt) at 97.

alternative causes for three of the patients, and told them so. Dr. Linschoten has since acknowledged under oath that the paper was "inconsistent" with the data. All of these issues came to light in the litigation that the poster and paper spawned.[28]

Around the same time Jafek submitted his poster to the ARS he was discussing potential Zicam litigation with attorneys.[29] Within a month of his presentation, he became actively involved in assisting plaintiffs' attorneys in planning and pursuing litigation involving Zicam.[30] He has regularly appeared as an expert for plaintiffs ever since, and much of the work cited in his report was developed during, and in the context of, his ongoing work as a testifying expert.[31]

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[28] Exh. R (Linschoten depo - Lusch) at 173-178. Though Jafek's case series was published after peer review, this is not an indication of reliability. First, Jafek effectively undermined the peer review process by failing to disclose his numerous departures from good scientific practice and his deep involvement as a consulting expert for plaintiffs in Zicam litigation. Second, this is not a clinical or epidemiological study with a design protocol, where peer review and publication may actually help to expose flaws in the study's methodology (*Daubert*, 509 U.S. at 593); it is merely a small collection of case reports. Peer review of case reports does not make them more reliable. *See Nelson v. American Home Prods. Corp.*, 92 F.Supp.2d 954, 969 (W.D. Mo. 2000) (though case reports were published and peer reviewed, "such reports evade review because they do not advance testable scientific analysis"); *see also Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1313, 1314, 1316 (11th Cir. 1999) (peer review does not by itself make a theory reliable, nor does the fact that studies the expert relies on have been peer reviewed make them an adequate basis for the expert's opinion); *In re Diet Drugs Prods. Liab. Litig*, 2000 U.S. Dist. LEXIS 9661, at *19, *39 (E.D. Pa.). Peer review was not helpful here; it took subpoena power and cross-examination to expose the questionable methods employed in Jafek's case series.

[29] Exh. S (excerpt from exh. 17 to Linschoten depo - Lusch: Jafek email 4/22/03 to Linschoten).

[30] Exh. I (excerpt from exh. 17 to Jafek depo – Nelson vol. 1; Jafek email Nov. 2003 to Mark Wenzel, Esq.).

[31] In this Circuit, one of the factors raising questions about reliability is that the expert's evidence or conclusion was developed in the course of litigation. *See Allison*, 184 F.3d at 1321.

Jafek's involvement in litigation was not disclosed in his paper, nor revealed to the journal when he submitted the paper for publication.[32]

In support of his opinion that Zicam causes smell loss, and specifically caused Sutherland's anosmia, Jafek reaches six critical conclusions: (1) That when used as directed Zicam navigates the circuitous nasal anatomy to reach the remote neuroepithelium; (2) that effects shown in dissimilar studies concerning zinc sulfate, a compound different from the active ingredient in Zicam, zinc gluconate, can be extrapolated to proper use of Zicam; (3) that intranasal zinc has been shown to cause permanent anosmia; (4) that when used as directed, Zicam reaches the neuroepithelium in a dose sufficient to cause permanent anosmia, and did so when Sutherland used it; (5) that Sutherland has anosmia; and (6) that Zicam, and not the cold which caused Sutherland to use it (or any other condition or medication), is the cause of her smell loss.

Dr. Jafek does not have a reliable scientific foundation for *any* of these conclusions. None of them are based on "sufficient facts or data" under Rule 702 (1). And because they were not derived by adherence to the scientific method, none of them are the product of the reliable application of reliable principles and methods of science to the facts of the case under Rule 702 (2) and (3).

E. Studies Concerning the Safety of Zicam

Prior to Jafek's poster, Zicam was the subject of four studies evaluating efficacy and safety. In these studies, a total of 319 subjects were given multiple doses of Zicam. All subjects

[32] Exh. G (Jafek depo - Nelson vol. 1) at 185-186; Exh. P (Jafek 2004 paper).

were asked to report any adverse effects. There were no reports of any adverse effect on smell or taste function.[33]

Since Jafek's allegations, three studies have been funded by Matrixx and conducted by members of its Scientific Advisory Board to test Jafek's hypothesis that Zicam can reach the neuroepithelium and cause smell loss. These are the only controlled human and animal studies which directly address these key general causation questions. They demonstrate that (1) when used in accordance with the package directions, Zicam does not reach the neuroepithelium,[34] and (2) amounts equivalent to at least four times the human dose of Zicam do not damage the smell tissue, or effect smell function, in mice.[35]

In the two distribution studies, Zicam with blue dye added and the active ingredient omitted was administered according to the directions and the extent of dye deposition was observed and documented. None of the 64 subjects had the gel climb to the vicinity of the neuroepithelium. One of the studies, performed in Spain, has been published in a Spanish language peer-reviewed medical journal.[36]

In the mouse study, Zicam and zinc sulfate were administered to mice in irrigation doses (50 microliters, flooding the nasal cavity), and lesser overdoses (8 and 2 microliters). Transient

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[33] Exh. V (James report) at 13-14.

[34] Exh. TT (University of Pittsburgh study at 1 and 10/15/05 letter from Joseph Dohar M.D. to Tim Clarot)); Exh. Z (Herranz study – English translation at 3, Spanish version at 132); Exh. UU (Schwob depo) at 86-89, 118-120, 130-131; Exh. V (James report) at 15. The studies also investigated the effect of failure to follow the directions, which is not relevant in this case given Sutherland's testimony that she followed the directions.

[35] Exh. KK (Slotnick abstract).

[36] Exh. TT (University of Pittsburgh study and 10/15/05 letter from Joseph Dohar M.D. to Tim Clarot); Exh. Z (Herranz study).

damage and function deficits were sometimes seen at 8 microliters (equivalent to at least 16 times the human dose of Zicam) and no damage or deficit was seen at 2 microliters (at least 4 times the human dose).[37]

Jafek's report never mentions these studies. He had not reviewed the data for the distribution studies until after it was prepared.[38] He has not attempted to replicate the studies, nor perform any human or animal research. He has not studied where and how Zicam travels through the nose when used as directed. He can criticize the studies, but he cannot challenge them, and for this reason relies solely on his anecdotal evidence published in the form of a case series and his untested subjective opinions. This is insufficient to survive a *Daubert* challenge.[39]

DISCUSSION AND APPLICATION OF RULE 702 TO DR. JAFEK'S OPINION TESTIMONY

A. The Law Precludes Opinions Based On Junk Science

Rule 702 and *Daubert* require trial courts to police the foundations of expert causation opinions, principally so that juries are not burdened with junk science as they sort out complex

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[37] Exh. KK (Slotnick abstract); Exh. VV (Slotnick depo) at 84-112, , 120-134 & ex. 9.

[38] Exh. D (Jafek depo) at 13-14, 195, 342.

[39] *See Haggerty v. Upjohn Co.,* 950 F.Supp. 1160, 1164, 1166, 1167 (S.D. Fla. 1996) (offering hypothesis which has not yet been rigorously tested for verification or refutation is not the scientific knowledge envisioned by Rule 702; excluding opinion based on incomplete data, due in part to expert's failure to consider significant studies on the subject); *Finestone v. Florida Power & Light Co.*, 2006 WL 267330, *11 (S.D. Fla. 1/6/06) (finding a significant reliability defect in expert's exposure theory where actual testing by others refuted it, and expert relied on incomplete data); *Conde v. Velsicol Chem. Corp.*, 24 F.3d 809, 814 (6th Cir. 1994) (criticism of the available studies that fail to support causation may suggest the need for further study, but cannot establish causation); *Siharath v. Sandoz Pharm. Corp.,* 131 F.Supp.2d 1347, 1358 (N.D. Ga. 2001) (same), *aff'd*, *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194 (11th Cir. 2002); *In re Diet Drugs Prods. Liab. Litig.*, 2000 U.S. Dist. LEXIS 9661, at *35 (where hypothesis has not been tested, it is merely subjective belief and can provide no assistance to the jury).

scientific issues. "Expert evidence can be both powerful and quite misleading because of the difficulty in evaluating it."[40] Rule 702 provides:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

The burden is on Sutherland to demonstrate that Jafek's opinion testimony is sufficiently reliable and relevant to be admissible under Rule 702.[41]

The Eleventh Circuit recently applied Rule 702 and *Daubert* to general causation in a toxic tort case in *McClain*.[42] The court found the expert's opinions unreliable because: (1) he drew speculative conclusions about the product's toxicity from questionable principles of pharmacology; (2) his general causation opinions neglected to address the dose-response relationship, failed to take into account the background rate of the alleged injury, and relied heavily on the temporal relationship between the alleged ingestion and the alleged response; (3) he drew an unsubstantiated analogy between ephedrine and another drug; and (4) he unjustifiably

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[40] *Daubert*, 509 U.S. at 595. *See also Allison,* , 184 F.3d at 1310-12; *Michigan Millers Mut. Ins. Corp. v. Benfield*, 140 F.3d 915, 920 (11th Cir. 1998) (use of "science" to explain how something occurred may carry great weight with a jury).

[41] *Daubert*, 509 U.S. at 592 n.10; *Allison*, 184 F.3d at 1312.

[42] *McClain*, 401 F.3d at 1238.

relied on consumer complaints to establish medical causation.[43] Dr. Jafek's opinions in this case suffer from very similar flaws, and others.[44]

B. Jafek's General Causation Opinions Are Not Supported By Reliable, Valid, and Relevant Scientific Data, Methods, and Reasoning

Jafek opines that when Zicam is used as directed, its active ingredient, zinc gluconate, can permanently destroy the neuroepithelium and with it the sense of smell.[45]

1. There Is No Reliable Scientific Evidence That Zicam Reaches The Neuroepithelium When Used As Directed.

It is undisputed that in order to damage the neuroepithelium and produce smell loss, Zicam gel must reach the neuroepithelium upon application.[46] Jafek opines that it does when the product is used as directed.[47] There is no reliable basis for this opinion.

When the directions are followed, as here, the nozzle is inserted only 1/8" into the nasal cavity and pointed outward, delivering the gel directly into the lateral wall of the nose – not vertically toward the neuroepithelium. Under these circumstances, there is no scientific basis for

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[43] *Id*. at 1240.

[44] Case law interpreting Rule 702 is discussed below as it applies to Dr. Jafek's testimony. For a more detailed discussion of the general standards of admissibility under Rule 702, *Daubert,* and its progeny (omitted here in the interest of brevity and to avoid unnecessary repetition), see the discussion under this heading in the accompanying Motion to Exclude the Testimony of James O'Donnell, another expert for Sutherland (and one of the experts in question in *McClain*).

[45] Exh. B (Jafek report); Exh. C (Jafek supp. report).

[46] Exh. G (Jafek depo - Nelson vol. 1) at 96-97, 189; Exh. J (Jafek depo - Nelson vol. 2) at 349.

[47] Exh. C (Jafek supp, report) at 4.

concluding that any of the gel reaches the neuroepithelium. Distribution testing funded by Matrixx confirms this,[48] and even Jafek has grudgingly conceded this under oath:

> Q: I want you to assume that a patient interpreted outward in the directions to mean to the side of the nose and not upward or straight up. If the patient so interpreted the direction, where would the Zicam go, in your opinion?
>
> A: I suppose if the patient so interpreted the directions, different from those on the box, that the Zicam would go to the side of the nose.
>
> Q: And under those circumstances, would you expect that it would reach the olfactory epithelium?
>
> A: Under those circumstances, it probably would not reach the olfactory cleft area.[49]

Nevertheless, in his report in this case, Jafek reverses course and opines that when used as directed Zicam reaches the neuroepithelium. His simplistic basis is the short distance to the neuroepithelium and his personal observations that Zicam squirts much further than that in the open air and that most people have a straight path to the neuroepithelium.[50] This foundation fails to satisfy *Daubert*'s reliability requirements, but it also fails for a more basic reason – it is completely beside the point. In *Daubert* terms, it fails to "fit" the facts, because it has no valid

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[48] Exh. Z (Herranz study); Exh. TT (University of Pittsburgh study at 1 and 10/15/05 letter from Joseph Dohar M.D. to Tim Clarot)). *See* Exh. U (Dalby report) at 8-9 & Att. B; Exh. V (James report) at 11-12, 15; Exh. Y (Schwob report) at 1.

[49] Exh. F (Jafek depo - Lusch) at 237-238. Jafek's quibble about the directions on the box stems from his persistent and unfounded view that the directions are difficult to understand – even though they are accompanied by a clear illustration of the intended insertion angle of the bottle. *See* Exh. U (Dalby expert report) at Att. B. *Compare* Exh. AAA (O'Donnell depo) at 155-156 (Sutherland's expert designated to address warnings opines that the directions are clear).

[50] Exh. C (Jafek supp. report) at 4-5; Exh. G (Jafek depo – Nelson vol. 1) at 119-123, 164, 177-178, 189, 196-197; Exh. J (Jafek depo – Nelson vol. 2) at 328.

scientific connection to the conclusion that Zicam reaches the neuroepithelium *when the product is used as directed*, and there is too great an analytical gap between these observations and that conclusion. Sutherland testified that she followed the directions, and thus she pointed the nozzle outward toward the lateral nasal wall, away from the direction of the neuroepithelium.[51] No matter how far Zicam can travel unobstructed, and no matter how short or straight the vertical path to the neuroepithelium, when the gel is applied directly into the lateral nasal wall pursuant to the directions, there is no basis for believing it will reach the neuroepithelium (as Jafek has elsewhere conceded). Jafek has not explained how a straight path can make a difference when that path has not been taken. Under the circumstances, his opinion lacks a valid scientific (and logical) connection to the facts and is inadmissible.[52]

In any event, Jafek's theory of delivery to the neuroepithelium is unreliable. He failed to test his theory before forming his conclusion. Failure to test critical, testable assumptions before reaching a conclusion departs from the scientific method and lacks the intellectual rigor expected

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[51] Exh. A (Sutherland depo) at 183.

[52] *See Daubert*, 509 U.S. at 591; *General Elec. Co. v. Joiner*, 522 U.S. 129, 146 (1997); *Allison*, 184 F.3d at 1312-1315. Long after he had formed and testified to his conclusion that Zicam reaches the neuroepithelium, in preparation for trial testimony, Jafek administered Zicam to a frozen, thawed and sagitally dissected head of a cadaver, with the septum replaced by plexiglass. He claims this experiment supports his opinion that Zicam is capable of reaching the neuroepithelium. Exh. C (Jafek supp. report) at 5; Exh. Q (Jafek cadaver test); Exh. K (Jafek depo - Nelson vol. 3) at 611-629. It does not. *See* Exh. V (James report) at 16-17; Exh. Y (Schwob report) at 2. In addition to the substantial methodological and reliability problems with this experiment and Dr. Jafek's inference from it, this also lacks "fit" in this case. Sutherland is a living human with a physiologically intact nose and she testified she pointed the Zicam nozzle outward as specified in the package directions, not straight up toward the neuroepithelium. *See* Exh. Y (Schwob report) at 2.

from scientists pursuing scientific truth.[53] Moreover, the theory *has* been tested, and refuted, by the distribution studies. Opinions based on bare assumption and unverified personal observation, which have been refuted by existing experimental data, are inconsistent with scientific principles, and have been previously abandoned by the expert under oath, are obviously highly prone to error. The theory that a viscous gel can navigate the interior topography of the nose and reach the roof of the nose is not generally accepted – it is contrary to the available scientific literature and applicable scientific principles, as well as beyond Jafek's expertise.[54] And though Jafek has published a case series theorizing that Zicam causes smell loss, neither that publication nor any other asserts that a viscous gel can be delivered by standard nasal pump to the neuroepithelium when used in the manner called for by the Zicam directions.[55] Jafek not only lacks a *reliable* methodology for coming to this opinion – he lacks *any* methodology. Dr. Jafek's previously abandoned, untested, subjective belief and unsupported speculation that

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[53] *See Daubert*, 509 U.S. at 593. *Compare* Exh. G (Jafek depo – Nelson vol. 1) at 164 (he assumes the zinc gets to the neuroepithelium in some people); *id.* at 189 (he assumed Zicam reached the neuroepithelium in that case because there was burning and smell loss which he attributes to the Zicam); Exh. L (Jafek depo – Hilton) at 73 (same); Exh. J (Jafek depo – Nelson vol. 2) at 335-336 (he had not seen any studies investigating the anatomic distribution pattern of Zicam; his opinion was "validated" solely by patient observations); *id.* at 329 (he had never applied Zicam to the nose of anyone).

[54] Exh. U (Dalby report). Jafek's expertise in this area is limited to his experience in examining noses and spraying Zicam into the open air a few times. Before he formed and testified to his opinion, he had never sprayed a gel into a nose, (Exh. G (Jafek depo – Nelson vol. 1) at 119-121, 123-124; Exh. J (Jafek depo – Nelson vol. 2) at 329), and he had never seen a scientific study investigating the distribution pattern of Zicam (*id.* at 335-336).

[55] *See Nelson v. Tennessee Gas Pipeline Co.*, 243 F.3d 244, 251 (6th Cir. 2001) (peer review factor was unsatisfied because the expert's published studies did not demonstrate the reliability of the specific theory in question); *Allison*, 184 F.3d at 1316 (question is whether the specific premise at issue has been subjected to peer review). *See also* note 28, above.

Zicam reaches the neuroepithelium when used according to the directions fails all applicable *Daubert* reliability factors.[56]

In sum, Dr. Jafek's testimony that Zicam reaches the neuroepithelium when the product is used as directed, a prerequisite to causation, is not based on sufficient relevant and reliable facts and data, and is not the product of a reliable application of reliable scientific principles and methods to the facts. Accordingly, Jafek's causation testimony fails at the threshold.

2. There is No Reliable Scientific Evidence That A Dose Sufficient To Cause Permanent Anosmia Reaches The Neuroepithelium When Zicam Is Used As Directed

Even if there were sufficient scientific basis to believe that *some* Zicam gets to the neuroepithelium, as Dr. Jafek assumes, the courts require more. Causation opinions in toxic exposure cases are inherently speculative, unfounded and unreliable where they lack a reliable predicate in dose-response and actual exposure, that (1) a specified dose of the substance causes the injury in question, and (2) plaintiff was exposed to that dose or more.

> Scientific knowledge of the harmful level of exposure to a chemical, plus knowledge that the plaintiff was exposed to such

[56] *See Allison*, 184 F.3d at 1319 (opinions based more on personal opinion than on scientific knowledge are unreliable); *id.* at 1320-1321 (theory untested, unsupported by scientific literature, and not generally accepted, is unreliable); *id.* at 1321 (opinion developed for litigation unreliable); *id.* at 1312 (expert's reliance on anecdotal evidence indicates lack of reliability) *Finestone*, 2006 WL 267330 at *11-12 (untested theory refuted by testing of others unreliable); *Haggerty*, 950 F.Supp. at 1163-1164 (untested hypothesis with unknown error rate is not scientific knowledge); *McDowell v. Brown*, 392 F.3d 1283, 1300-1301 (11th Cir. 2004) (untested theory with undetermined error rate unreliable; medical causation opinion based primarily on experience, training, general observations and "medical logic" amounted to more a guess than a scientific theory).

> quantities, are minimal facts necessary to sustain plaintiff's burden in a toxic tort case.[57]

Simply put, the causation opinion lacks foundation unless the expert can reliably establish "*how much is too much*" and reliably demonstrate that use of the product as directed causes (and caused) this overdose.[58]

Jafek offers no reliable evidence of either, only speculation. He has not shown that *any* Zicam reaches the neuroepithelium under proper use, and he has ignored the evidence that it does not. He has not conducted any tests or other analysis to determine the dose of Zicam to the neuroepithelium necessary to cause permanent anosmia.[59]

Here again Jafek violates Rule 702 by tardily attempting to answer a *different* question, in an effort to justify his view that Zicam causes smell loss. Long after forming and testifying to his opinion he cobbled together a theory, from indirect evidence and distortion of toxicological principles, of how much Zicam is necessary to cause *some adverse effect on smell function.* But even if that analysis were valid, it would lack fit because it does not answer the question posed by this case – how much Zicam must reach the neuroepithelium to cause *permanent anosmia*. In any event, Jafek's attempt to define the level which (in his view) causes *some adverse effect*

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[57] *McClain*, 401 F.3d at 1241; *see id.* at 1240-1242 & n.6 (11th Cir. 2005) (holding causation testimony inadmissible where expert lacked reliable dose-response foundation, observing that the dose-response relationship is "the basic methodology that scientists use to determine causation" and "a key element of reliability in toxic tort cases"). *See also, e.g., Allen*, 102 F.3d at 199; *Wright v. Willamette Indus., Inc.*, 91 F.3d 1105, 1107 (8th Cir. 1996); *Nelson*, 243 F.3d at 252; *Mitchell v. Gencorp.*, 165 F.3d 778, 781 (10th Cir. 1999) (same).

[58] *McClain*, 401 F.3d at 1240-1241 (emphasis added).

[59] Exh. B (Jafek report); Exh. C (Jafek supp. report); Exh. G (Jafek depo - Nelson vol. 1) at 25, 103-104, 121, 164-166, 210; Exh. J (Jafek depo - Nelson vol. 2) at 335-336, 340-341, 350; Exh. K (Jafek depo - Nelson vol. 3) at 579, 610-611; Exh. L (Jafek depo - Hilton) at 14, 17-19, 73, 99; Exh. V (James report) at 18-19.

departs drastically from generally accepted scientific methods – he can point to no reference work which actually establishes or endorses his method, or can be *reasonably read* to support his analysis.[60] , Indeed, his analysis assumes the physically impossible – that the *entire maximum metered dose* of Zicam gel (140 microliters) reaches the neuroepithelium [61] Because it has never been tested, peer-reviewed or published, is highly prone to error, is not generally accepted, and is based on an assumption not merely unsupported but absurd, it is unreliable and lacks the intellectual rigor demanded by Rule 702.

In sum, without reliable scientific evidence of how much is too much and that use as directed delivers such an overdose, Jafek's opinion that smell loss is caused by exposure to Zicam, or was in any particular case, is speculative and fails to qualify as scientific knowledge. It is not based on sufficient relevant facts or data, and it is not the product of a reliable application of reliable scientific methods and principles to the facts of this case, as required by Rule 702.

3. It Is Not Scientifically Valid To Extrapolate From Experiments Involving Dissimilar Exposures To A Different Substance, Zinc Sulfate, To Reach Causation Conclusions Concerning Use Of Zicam.

Lacking direct data demonstrating that Zicam causes smell loss when used as directed, what we have here is theory that Dr. Jafek pulled together from a combination of indirect evidence, assumptions and extrapolations, and anecdotal data.

Much of Jafek's theory is drawn from his interpretation of unsuccessful polio prevention experiments performed close to 70 years ago with zinc sulfate, a different compound, and using

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[60] *Cabrera v. Cordis*, 134 F.3d 1418, 1422-1423 (9th Cir. 1998) (expert's failure to point to an objective source showing that he has followed the scientific method).

[61] Exh. C (Jafek supp. report) at 6-7.

methods of application and doses that bear no resemblance to the use of Zicam. He also relies on inapposite behavioral studies in animals exposed to zinc sulfate.[62] This violates the scientific method and Rule 702 because there is no scientific basis to extrapolate from these studies, involving a different chemical administered in a different way in different doses, and sometimes a different species, sometimes resulting in temporary smell deficits, to the conclusion that a single dose of Zicam properly applied can cause permanent anosmia. This unwarranted and unsupported extrapolation produces exactly the type of analytical gap that violates Rule 702.[63]

When an expert attempts to extrapolate from studies concerning one substance to draw inferences about the biological effects of another, it is incumbent upon the expert to explain and demonstrate why the extrapolation is scientifically proper. *McClain* held that an expert's reliance on chemical analogy between two drugs in the same family was inherently unsound because "even small differences in chemical structures can sometimes make very large differences in the type of toxic response that is produced" and "even minor deviations … can radically change a particular substance's properties and propensities." Accordingly, it was improper for the expert to assume that the two substances had similar effects.[64]

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[62] Exh. B (Jafek report); Exhibit C (Jafek supp. report).

[63] *See Joiner*, 522 U.S. at 146; *In re Diet Drugs Prods. Liab. Litig.*, 2000 U.S. Dist. LEXIS 9661, at *36 (extrapolation from animal studies is ordinarily unreliable due to differences I n species, dosages, manner of administration, and metabolism); *id.* at *27-30, 36 (finding extrapolations from various human and animal studies unreasonable due to differences in chemicals, doses, and method of administration); *Moore v. Ashland Chem., Inc.*, 151 F.3d 269, 278 (5th Cir. 1998)(expert's reliance on study involving high dose exposure and on study involving a different chemical unreliable). *See also Allison*, 184 F.3d at 1312 (citing improper extrapolation as an indication of reliability defect under Rule 702)

[64] *McClain*, 401 F.3d at 1246-1247. *See also See Rider,* 295 F.3d at 1201-1202 (expert's reliance on analogy to other drugs within the same class lacked both reliability and fit).

Jafek defends his extrapolation by arguing that both compounds contain zinc, and it is the zinc that damages the neuroepithelium.[65] Even if that were true, however, the justification is far too simplistic, as it ignores several critical differences between the two compounds: (1) zinc gluconate contains about three times less zinc than zinc sulfate;[66] (2) Jafek has not shown that the gluconate and sulfate components do not significantly affect the activity of the zinc;[67] (3) zinc sulfate solution dissociates far more readily, quickly, and completely than zinc gluconate gel, thereby releasing more of its zinc faster;[68] and (4) the zinc sulfate is a liquid solution which spreads easily and can atomize, while the viscous, sticky Zicam gel tends to stay where it is deposited until carried to the throat by mucociliary action and natural clearance.[69] Under these circumstances, Dr. Jafek's "zinc is zinc" explanation fails to justify his reliance on zinc sulfate evidence to reach conclusions about the effects of Zicam.

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[65] Exh. C (Jafek supp. report) at 5; Exh. G (Jafek depo – Nelson vol. 1) at 102-103.

[66] A zinc sulfate molecule is about 40% zinc; a molecule of zinc gluconate is larger and consists of only 13-14% zinc. Accordingly, the 1% zinc sulfate solution used in the polio experiments contains about twice the concentration of zinc as the 1.58% zinc gluconate concentration in Zicam. Exh. AA (Kern depo - Nelson) at 110 and exh. 1-6. *See* Exh. V (James report) at 11-12. Animal experiments typically use a 5% zinc sulfate solution, containing 10 times the concentration of zinc. Exh. AA (Kern depo - Nelson) at 36-39, 110; Exh, HH (McBride, Slotnick and Margolis 2003 paper) at 660. Jafek has conceded that the amount of available zinc is the critical factor in his theory of toxicity and that the different concentrations of zinc in Zicam and experimental zinc sulfate solutions is important to consider when comparing study results. Exh. D (Jafek depo) at 223-224.

[67] Exh. G (Jafek depo - Nelson vol. 1) at 102-104, 160, 191-192, 224; Exh. K (Jafek depo - Nelson vol. 3) at 686.

[68] Exh. D (James depo - Nelson) at 52-54; Exh. G (Jafek depo - Nelson vol. 1) at 208-209.

[69] Exh. G (Jafek depo - Nelson vol. 1) at 96, 107; Exh. J (Jafek depo - Nelson vol. 2) at 365; Exh. U (Dalby report) at 7; Exh. V (James report) at 11-12.

Extrapolation from the zinc sulfate literature is also not scientifically valid because of the compelling differences between those experiments and the circumstances and dose of exposure to Zicam. In the polio prevention experiments, experts were intentionally trying not only to *reach* the neuroepithelium, but to *bathe* it with high volume doses of zinc sulfate solution, using special instruments, special administration techniques, special positioning of the subjects (including positioning the subject almost upside down),[70] high doses (both in concentration and volume),[71] and a low viscosity solution. Even when they succeeded in defeating smell function, the losses achieved were only temporary.[72]

These experiments bear no resemblance to the proper use of Zicam. Used as directed, it remains in the lower portion of the nasal cavity.[73]

In sum, the polio experiments intentionally delivered high doses of zinc sulfate solution to the neuroepithelium. Zicam contains much less zinc in a viscous gel and releases less of its

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[70] Exh. FF (Ashley 1939 paper) at 112-113; Exh. GG (Peet 1937 paper); Exh. H (exhs.10A and 11 from Jafek depo - Nelson vol. 1); Exh. G (Jafek depo - Nelson vol. 1) at 95-96, 104-105; Exh. V (James report) at 11-12; Exh. W (Jones report) at 8; Exh. Y (Schwob report) at 3-4.

[71] As noted above, 1% zinc sulfate contains twice the zinc as the 1.58% zinc gluconate gel in Zicam. Moreover, whereas a metered dose of Zicam delivers between 120 and 140 microliters of the gel (or .12-.14 milliliters) to the lower nasal cavity, the polio experiments bathed the neuroepithelium with .5 to 1 cc (500 to 1000 microliters, or .5 to 1 milliliter) of zinc sulfate solution. Exh. AA (Kern depo - Nelson) at 36-39, 110, and exh. 1-6; Exh. G (Jafek depo - Nelson vol. 1) at 107; Exh. K (Jafek depo - Nelson vol. 3) at 559; Exh. L (Jafek depo - Hilton) at 144; Exh. V (James report) at 11-12. Thus, the amount of total zinc *in the nose* was between 7 and 18 times greater than a dose of Zicam (which also dissociates slower and less completely and does not even reach the neuroepithelium).

[72] Exh. G (Jafek depo - Nelson vol. 1) at 96-100, 103-105, 107-110; Exh. J (Jafek depo - Nelson vol. 2) at 526-527; Exh. K (Jafek depo - Nelson vol. 3) at 696; Exh. L (Jafek depo - Hilton) at 116-118; Exh. Y (Schwob report) at 3-4; Exh. V (James report) at 11-12; Exh. W (Jones report) at 8.

[73] Exh. U (Dalby report) at 7-9 & Att. B; Exh. F (Jafek depo - Lusch) at 237-238.

zinc, and used as directed, it delivers none of its zinc to the neuroepithelium. The polio experiments are not a reasonable and reliable predicate for conclusions about the effects of proper Zicam use. There is simply too great an analytical gap between the data and Jafek's conclusion. That high doses of a liquid solution of zinc sulfate intentionally bathing the neuroepithelium occasionally caused transient smell loss hardly *fits* or supports Dr. Jafek's theory that proper administration of a single therapeutic dose of Zicam causes permanent smell loss.[74] Rule 702 precludes testimony which leaps from an accepted premise to an unsupported one.[75]

Dr. Jafek also relies on studies where high doses of high concentration zinc sulfate solution were applied directly to the neuroepithelium in fish and mice to temporarily defeat smell function in behavioral experiments.[76] Much of this research used a 5% zinc sulfate solution containing ten times the concentration of zinc as Zicam.[77] Fish and mice olfactory systems are

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[74] *See Daubert*, 509 U.S. at 591-593; *Allison*, 184 F.3d at 1312-1314. *See also Rider,* 295 F.3d at 1201-1202 (expert's reliance on studies indicating potential minor vasoconstrictive effect in animals from active ingredient did not "fit" plaintiff's theory that drug caused hemorrhagic stroke); *McDowell*, 392 F.3d at 1299-1300 (study showing that 48 hour delay in medical treatment could not support opinion that delay of 24 hours or less exacerbated plaintiff's injuries); *Rink v. Cheminova, Inc.*, 400 F.3d 1286, 1292 (11th Cir. 2005) (expert's facile extrapolation of temperature data from one warehouse to another in same latitude lacked the required intellectual rigor).

[75] *Allison*, 184 F.3d at 1314; *McDowell*, 392 F.3d at 1300, 1302.

[76] Exh. B (Jafek report); Exh. C (Jafek supp. report); Exh. G (Jafek depo - Nelson vol. 1) at 74, 97, 113-115, 132-133,158, 187-188; Exh. J (Jafek depo - Nelson vol. 2) at 302-303, 527; Exh. L (Jafek depo - Hilton) at 124-125, 141; Exh. HH (McBride, Slotnick and Margolis 2003 paper); Exh. II (Cancalon 1982 paper); Exh. V (James report) at 18-19..

[77] Exh. HH (McBride, Slotnick and Margolis 2003 paper); Exh. JJ (Slotnick and Gutman 1977 paper); Exh. KK (Slotnick abstract); Exh. AA (Kern depo - Nelson) at 110 and exh. 1-6.

radically different from human systems.[78] Reliance on such extrapolations is unreasonable and unreliable in the absence of adequate explanation for why extrapolation is appropriate and relevant to human causation despite differences in species, dose, and application, and the evidence fails to fit.[79] Dr. Jafek has offered no reasonable explanation of how these animal experiments with zinc sulfate demonstrate that proper use of Zicam causes permanent anosmia in humans.[80]

Finally, Jafek lacks reliable support even for the underlying premise that zinc *sulfate* causes *permanent* smell loss. First, he cites to statements by early polio researchers that simply fail to support his assertion that the polio experiments produced instances of confirmed permanent anosmia.[81] In any event, stray comments like these cannot be considered reliable scientific proof that zinc sulfate causes permanent anosmia, much less that Zicam does.[82]

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[78] Exh. G (Jafek depo - Nelson vol. 1) at 113-114; Exh. J (Jafek depo - Nelson vol. 2) at 302-303; Exh. L (Jafek depo - Hilton) at 114-115; Exh. D (Jafek depo) at 148-149.

[79] *E.g., Joiner*, 522 U.S. at 144-145; *Rider*, 295 F.3d at 1201-02; *Allison*, 184 F.3d at 1313-1315; *Siharath*, 131 F. Supp.2d at 1366-67 ; *Hall v. Baxter Healthcare Corp.*, 947 F.Supp. 1387, 1410 (D. Or. 1996); *Bell v. Swift Adhesives, Inc.*, 804 F.Supp. 1577, 1579 (S.D. Ga. 1992).

[80] *See* Exhs. B & C (Jafek reports). Indeed, the scientist who performed the mouse study with Zicam and zinc sulfate recently testified that "we have found it relatively easy to produce anosmia using five percent zinc sulfate, and we've essentially failed to produce anosmia using equivalent volumes of Zicam product." Exh. VV (Slotnick depo) at 134.

[81] Jafek cites statements by Schultz and Tisdall in 1938, a 1942 statement attributed to Schultz but appearing in a polio history text, and a hearsay statement that an unnamed individual lost her sense of smell in the polio experiments and never regained it. Schultz 1938 statement was a letter to the editor noting that a few adults had experienced anosmia lasting longer than six months. It neither stated nor implied that the authors were aware of any confirmed instances of permanent anosmia; it merely urged caution due to the suggestion that there *may* be a rare risk of permanent anosmia. Exh WW (Schultz & Gebhardt 1938 letter to the editor of JAMA). *See* Exh. G (Jafek depo – Nelson vol. 1) at 90 (six months of deficit does not constitute a permanent loss). Berg's popular history of polio research does not contain the purported Schultz 1942 statement; this anecdotal account merely observes that Schultz "receiv[ed] complaints from physicians that

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Second, Dr. Jafek, not an animal researcher, relies on animal studies, particularly studies by prominent animal research scientists Burton Slotnick Ph.D, for his opinion that intranasal application of zinc sulfate in rodents produces permanent anosmia.[83] Jafek simply misinterprets the literature. As Dr. Slotnick explained in a recent deposition:

> We have never produced a permanent anosmia, nor has anybody else on record. The effect is not permanent because the turnover of cells in the olfactory epithelium, new cells are born, excuse me, and grow out and replace the cells that have been killed by the zinc salt. And there's a return of function and there's been a return of function in every single study that has looked for return of function, and that return of function generally occurs in eight to ten days, at least the beginning of the return of function. So, no, it is not -- if you were an investigator interested in producing a permanent anosmia, zinc sulfate would not be your method of choice.[84]

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many of the patients had suffered a complete and evidently permanent loss of the sense of the smell." Exh. XX (Berg chapter 5) at 42. Tisdall 1938 reports a small number of subjects had not regained complete smell function after six months. He neither stated nor implied that he was aware of any instances of permanent anosmia. Exh. YY (Tisdall 1938 paper) at 3-4. The unidentified polio research subject Jafek "heard about" is paradigm anecdotal, unverified, unreliable hearsay, obviously not the type of scientific evidence an expert would rely upon, clearly inadmissible under Rule 703. Exh. D (Jafek depo) at 153; Exh. G (Jafek depo – Nelson vol. 1) at 25-26, 53; Exh. L (Jafek depo – Hilton) at 116.

[82] *See McClain*, 401 F.3d at 1245-1248 (improper to draw inferences from studies that study researchers failed to draw).

[83] Exh. C (Jafek supp. report) at 6, 9; Exh. D (Jafek depo) at 348. Dr. Slotnick has been doing experimental research with rodents for 46 years, and his research has involved thousands of rodents. Exh. VV (Slotnick depo) at 240.

[84] Exh. VV (Slotnick depo) at 134.

It is invalid and unreliable to leap from an *accepted* scientific premise to an unsupported one.[85] *A fortiori* Dr. Jafek's leap from his *unsupported* premise that zinc sulfate use in polio experiments caused permanent anosmia to the conclusion that proper use of Zicam causes permanent anosmia is utterly lacking in scientific rigor.

In sum, Dr. Jafek's extrapolation from and reliance upon the zinc sulfate literature violates the scientific method and the requirements of reliability and fit.

4. There Is No Evidence That Those Who Use Zicam To Treat A Cold Experience Smell Loss More Frequently Than Those Who Do Not, And Anecdotal Observations Based Largely On Temporality Are Not A Reliable Substitute.

McClain noted the importance of a controlled comparison between the incidence of the harm associated with exposure and the background risk, an issue of epidemiology.[86] Consideration of background rate is particularly important here, because the very condition Zicam is used to treat, the cold, is itself a common, well-recognized cause of the disease at issue, and because Jafek relies on case reports predicated on temporal associations to support his causal hypothesis.[87]

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[85] *Allison*, 184 F.3d at 1314. *See Leathers v. Pfizer, Inc.*, 233 F.R.D. 687, 691, 694 (N.D. Ga. 2006) (opinion that drug causes permanent and severe muscular effects could not be based on studies showing only temporary effects).

[86] *McClain*, 401 F.3d at 1243-1244; *see also Rider*, 295 F.3d at 1198-1199; Exh. W (Jones report) at 2-3; Exh. V (James report) at 5-6.

[87] Exhs. B & C (Jafek reports); Exh. G (Jafek depo - Nelson vol. 1) at 23-24, 195-197; Exh. J (Jafek depo - Nelson vol. 2) at 360, 432; Exh. L (Jafek depo - Hilton) at 17, 106-109, 129-130; Exh. V (James report) at 5-6, 14, 15, 18-19; Exh. W (Jones report) at 4, 7-8; Exh. Y (Schwob report) at 3-4. *See In re Meridia Prods. Liab. Litig.,* 328 F.Supp.2d 791, 798-799 (N.D. Ohio 2004) (in a similar causation scenario – the drug treated a condition (obesity) which was an established cause of the disease (cardiovascular disease) allegedly caused by the drug – plaintiff's causation evidence, predicated on case reports rather than epidemiology, was unreliable); *Casey v. Ohio*

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It is well-established that uncontrolled observations of cases based primarily on temporality and/or anecdote are not scientifically valid proof of causation.

> [P]roving a temporal relationship between taking Metabolife and the onset of symptoms does not establish a causal relationship. In other words, simply because a person takes drugs and then suffers an injury does not show causation. Drawing such a conclusion from temporal relationships leads to the blunder of the *post hoc ergo propter hoc* fallacy. [¶] The *post hoc ergo propter hoc* fallacy assumes causality from temporal sequence. … It is called a fallacy because it makes an assumption based on the false inference that a temporal relationship proves a causal relationship.[88]

The Eleventh Circuit rejected the expert's reliance on case reports, concluding: "Simply stated, case reports raise questions; they do not answer them."[89]

Given the omnipresent confounding factors (URI, rhinitis, sinusitis), the question is not whether there have been reports of smell loss following Zicam use, because it would be surprising if there weren't; the issue is whether Zicam use increases the rate of anosmia above the background rate for cold sufferers.[90] Particularly under these circumstances, Jafek's reliance

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Medical Products, 877 F.Supp. 1380, 1385 (N.D. Cal. 1995) (case reports "are not reliable scientific evidence of causation, because they simply describe reported phenomena without comparison to the rate at which the phenomena occur in the general population or in a defined control group . . . they do not isolate and exclude potentially alternative causes . . . and do not investigate or explain the mechanism of causation."); *Chambers v. Exxon Corp.*, 81 F.Supp.2d 661, 664 (M.D. La. 2000) (when the disease occurs in the general population without the exposure, epidemiological evidence is necessary to prove the disease is caused by the exposure), *aff'd*, 247 F.3d 240 (5th Cir. 2001).

[88] *McClain*, 401 F.3d at 1243.

[89] *Id.* at 1254; *see also id.* ("Furthermore, 'the temporal connection between exposure to chemicals and an onset of symptoms, standing alone, is entitled to little weight in determining causation.'") (quoting *Moore,* 151 F.3d at 278); *Rider*, 295 F.3d at 1199-1200; *Allison*, 184 F.3d at 1316; Exh. V (James report) at 4-5, 14, 15.

[90] *See McClain*, 401 F.3d at 1243-1244 ("A reliable methodology should take into account the background risk.").

on case reports and temporality to prove causation is inconsistent with the scientific method in violation of Rule 702(2).[91] Jafek has performed no controlled epidemiology analysis, nor does he cite any, and he has ignored the background risk.[92] The epidemiological data that does exist suggests that there is no increased risk of smell loss from the use of Zicam.[93] Jafek at first ignored and now simply rejects this data.[94]

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[91] *See Siharath*, 131 F.Supp.2d at 1359, 1371 (reliance on case reports to prove causation is inconsistent with the scientific method and cannot satisfy *Daubert*). Case reports cannot be used as a substitute for epidemiological analysis. *Id.* at 1363; *McClain*, 401 F.3d at 1253; *Allison*, 184 F.3d at 1316; *Haggerty*, 950 F.Supp. at 1165.

[92] Exh. C (Jafek supp. report); Exh. D (Jafek depo) at 186-195; Exh. J (Jafek depo - Nelson vol. 2) at 340-341; Exh. V (James report) at 19-21. Jafek highlights this departure from the scientific method when he attempts to characterize his case series as an "epidemiology" study and suggests that no statistical analysis (i.e., comparison to control or background rate) is necessary (Exh. C. (Jafek supp. report) at 8-9; Exh. L (Jafek depo – Hilton) at 121, 129), but his case series is just that. *In re Diet Drugs Prods. Liab. Litig.*, 2000 U.S. Dist. LEXIS 9661, at *20-21 ("without utilizing a control group for comparison purposes, a conclusion that a substance caused a particular condition is scientifically unreliable."); Exh. W (Jones report) at 8. Jafek's *ipse dixit* mention that he has an additional, ongoing accumulation of cases and that he understands defendants have received over 500 reports adds nothing of scientific significance. Exh. C (Jafek supp. report) at 8; Exh. D (Jafek depo) at 274. *See Haggerty*, 950 F. Supp. at 1164-1166 (explaining why references to such material is not valid scientific proof of causation); *Leathers*, 233 F.R.D. at 694.

[93] Dr. Judith Jones, an M.D., Ph.D pharmacoepidemiologist and a member of the Matrixx Scientific Advisory Board, analyzed large medical claims databases to estimate the rate of smell loss associated with URIs and compared that to the rate of reports of smell loss following use of Zicam. She found that, under conservative assumptions of use and consumption rates for Zicam, the reported rate of smell loss among Zicam users was well within the background rate for individuals with URIs. Exh. W (Jones report) at 4-7; Exh. ZZ (Jones depo exh.10).

[94] Exh. D (Jafek depo) at 187; Exh. J (Jafek depo – Nelson vol. 2) at 258-262, 293-295; Exh. K (Jafek depo – Nelson vol. 3) at 579-582; Exh E (Jafek depo – Hans) at 8-10, 136-152. There is no mention of Dr. Jones' analysis in Jafek's reports; rather, under the heading "Epidemiology studies support acute zinc gluconate olfactory toxicity as the etiology of loss of smell". Jafek lists his case series, an ongoing data collection effort at his University of Colorado clinic, and testimony that Matrixx had received over 500 reports from individuals. Exh. C (Jafek supp. report) at 8.

Dr. Jafek's opinion, unsupported by any epidemiologic proof, contrary to the only epidemiologic evidence available, and predicated on anecdotal data, should be excluded.[95] Contrary to Rule 702, it is not supported by facts or data of the type relied on by scientists, and it is not based on a reliable application of reliable scientific principles and methods to the facts of this case.

C. Dr. Jafek's Specific Causation Opinions Are Inadmissible Because He Lacks Reliable Evidence That Sutherland Experienced Smell Loss That Was Caused By Zicam Rather Than Other Potential Causes Of Anosmia

Plaintiff also has the burden of proving specific causation, *i.e.*, that Zicam, not something else, caused her permanent anosmia.[96]

The first hurdle is that Jafek does not have a sufficient scientific basis for general causation. Absent reliable evidence that the exposure can cause the harm in question under the exposure circumstances, there is no basis for concluding that it did cause the harm experienced by the plaintiff. [97]

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[95] *See Allen*, 102 F.3d at 197 (causation conclusions reached despite contrary epidemiological evidence are unreliable); *In re Breast Implant Litig.*, 11 F.Supp.2d 1217, 1235 (D. Colo. 1998) (reliance on anecdotal case report inconsistent with epidemiology unreliable); *Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 884, 886 (10th Cir. 2005); *Conde*, 24 F.3d at 814 (criticism of the available epidemiological studies that fail to support causation may suggest the need for further study, but cannot itself establish causation).

[96] *Allison*, 184 F.3d at 1306.

[97] *See*, *e.g.*, *McClain*, 401 F.3d at 1242 ("the toxic substance in question must have been demonstrated to cause the type of illness or disease in question.") (quoting "Scientific Judgment and Toxic Torts – A Primer in Toxicology for Judges and Lawyers" by Dr. David Eaton). To establish specific causation (that a product was the cause-in-fact of plaintiff's injury), an expert must demonstrate that "the individual must have been exposed to a sufficient amount of the substance in question to elicit the health effect in question." *Id.*

The second hurdle is that Jafek lacks a reliable basis to conclude that Sutherland has anosmia. Jafek typically relies on his colleague, Dr. Linschoten, to test the individual's smell function and interpret the data, and planned to do so in this case. Here, however, Dr. Linschoten, designated to testify as an expert for Sutherland, concluded after testing that Sutherland is a "malingerer" who failed to honestly respond to the test questions, and that her testing failed to reliably demonstrate that Sutherland had smell loss. Departing from his usual protocol in service of the desired conclusion, Jafek nevertheless testified that Sutherland has permanent anosmia.[98]

Jafek's selective rejection of Linschoten's interpretation is obviously unreliable and unscientific. It also highlights the overwhelming subjectivity of his analysis and his improper methodology of "cherry picking" the data that fits his conclusion and rejecting the data that fails to.[99] It hardly needs to be said that this is inconsistent with the scientific method and lacks the reliability and scientific rigor of admissible scientific evidence.

The third hurdle is that Sutherland's medical history presents several potential and more likely causes of anosmia. She was using Zicam to treat a cold, perhaps the most common cause of anosmia known to medical science. She also has a history of rhinitis and sinusitis, depression, and GERD, all conditions which are either known to cause or have been associated with anosmia. Jafek rejects these and other potential and more likely causes almost entirely on the

[98] Exh. D (Jafek depo) at 321-328, 342-343.

[99] *See Cano v. Everest Minerals Corp.*, 362 F.Supp.2d 814, 850-853(W.D.Tex. 2005) (expert may not rely on favorable aspects of scientific literature and ignore or unreasonably reject aspects which fail to support theory); *Newton v. Roche Labs., Inc.*, 243 F.Supp.2d 672, 681 (W.D. Tex. 2002) (ignoring directly relevant data which undermines opinion is unreliable).

improper basis of temporal proximity.[100] Zicam is hypothesized by Jafek to be a cause of anosmia, based primarily on case reports and the inappropriate analogy to zinc sulfate, but it is not generally accepted in the medical or scientific community that Zicam can cause anosmia when used as directed.[101] Thus, Jafek has violated the rule of parsimony.[102] Moreover, Jafek has no evidence that any of the Zicam gel Sutherland applied made its way to her neuroepithelium, and the available data discussed above suggests it did not.[103] Under the circumstances, Jafek's

[100] Exh. C (Jafek supp. report) at 9; Exh. D (Jafek depo) at 320-322, 340, 342. It is improper to rely solely or primarily on temporality to select the most likely cause. *See Black v. Food Lion, Inc.,* 171 F.3d 308, 313 (5th Cir, 1999); *Leathers*, 233 F.R.D. at 695-696; *Newton*, 243 F.Supp.2d at 682-683.

[101] Jafek says it is, Exh. D (Jafek depo) at 363, 366-367, but his "bald assurance" is not sufficient. *See* McClain, 401 F.3d at 1243; *Moore*, 151 F.3d at 276. His own colleague, co-author of the case series, and co-expert in this case, Linschoten, does not concur. Exh. M (Linschoten depo) at 153-155. Neither does the other expert designated by Sutherland, James O'Donnell. Exh. AAA (O'Donnell depo) at 127-129, 137. Nor do others within the small community of experts testifying against Matrixx. Exh. D (Jafek depo) at 367-368.

[102] Rejection of simpler, more apparent and generally accepted explanations in favor of a novel and more complicated theory violates the rule of parsimony, also known as "Occam's Razor." *Kelley v. American Heyer-Schulte Corp*., 957 F.Supp. 873, 882 (W.D. Tex. 1997). *See also Justiss Oil Co. v. Kerr-McGee Refining Corp.*, 75 F.3d 1057, 1060-61 & n.10 (5th Cir. 1996) (approving use of Occam's Razor in analyzing causation evidence and listing cases that apply the rule). *See Cano*, 362 F.Supp.2d at 837-38 (where expert failed to scientifically rule out known causes and selected a cause that is not generally accepted as established, opinion was unreliable and inadmissible).

[103] Though Jafek's straight shot theory is irrelevant, given Sutherland's proper use, his effort to fit her within it is telling, because it again highlights both the subjectivity and bias of his analysis. Contemporaneous descriptions of Sutherland's nasal anatomy described anything but a straight shot; her septal deviation and enlarged turbinates were sufficiently substantial to prompt her treating physician to recommend surgical correction. Yet Jafek simply dissents, based on his personal observation and characterization of her anatomy four and one-half years later, and declares Sutherland a "straight shot.". Exh. NN (Caldwell 1/8/02 chart); Exh. SS (Caldwell depo) at 24-29; Exh. D (Jafek depo) at 334-339.

dismissal of established causes in favor of the controversial cause he was hired to promote, based largely on temporality, is unfounded, subjective, speculative, and inadmissible.

Several courts have excluded specific causation opinions which failed to properly account for other factors that could have caused the illness, and/or failed to demonstrate exposure to a dose sufficient to cause the illness.[104] The courts have also found that overly subjective selection of the most likely cause is too unreliable to be admitted,[105] and "temporal correlation" "is not scientifically valid proof of causation."[106] Dr. Jafek's analysis violates all these principles of science.

In coming to his conclusion as to the cause of Sutherland's alleged anosmia, Jafek ignored her testimony that she had used the product as directed on the package (and his own prior acknowledgment that such use does not cause anosmia), and disregarded the smell test data

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[104] *E.g., Nelson,* 243 F.3d at 252-253, 254 (other possible explanations for the condition were not adequately considered before the expert ruled them out, and expert's failure to establish (rather than assume) that plaintiffs had received a dose sufficient to cause the illness were significant flaws in methodology and rendered opinion unreliable). *See also Haggerty*, 950 F.Supp. at 1165-1166; *In re Meridia*, 328 F.Supp.2d at 804 (one issue for reliability is whether the expert has adequately accounted for obvious alternative explanations); *Downs v. Perstop Components, Inc.*, 126 F.Supp.2d 1090, 1126 (E.D. Tenn. 1999) (one red flag of inconsistency with the scientific method is "reaching a conclusion before the expert makes a reasonable attempt to eliminate some of the most obvious causes"), *aff'd* 2002 WL 22000(6th Cir. Jan. 4, 2002).

[105] *Nelson*, 243 F.3d at 253; *Haggerty* , 950 F. Supp. at 1166-67 (excluding testimony where expert "failed to eliminate many possible causes of Plaintiff's behavior. . . before arriving at her specific causation opinion.

[106] *McClain*, 401 F.3d at 1243 (drawing "a conclusion from temporal relationships leads to the blunder of the *post hoc ergo propter hoc* fallacy."); *Allison*, 184 F.3d at 1321. *See also Newton*, 243 F.Supp.2d at 683 (specific causation opinion based primarily on temporality amounted to speculation, of no assistance to the trier of fact); *Downs*, 126 F.Supp.2d at 1126 ("Forming a conclusion on the basis of temporal proximity, in the absence of some established scientific connection between substance and illness is inconsistent with the scientific method because the expert fails to consider other possible explanations – not to mention the unexplainable – that a scientist would want to look into before drawing a conclusion.").

obtained his own trusted colleague, apparently because it was inconsistent with the conclusion he was hired to offer. He has not submitted a report with any meaningful discussion of why the other risk factors present in Sutherland's medical history are not equally or more plausible than his theory that Zicam was the cause. Indeed, Sutherland was using Zicam because she was experiencing cold symptoms, and the cold, a well-established cause of smell loss, obviously bears a temporal relationship to the smell loss similar to that of Zicam.[107]

Jafek's subjective and standardless rejection of established alternative causes in favor of the proffered litigation cause, based primarily on temporality, is precisely the type of subjective, unscientific opinion that fails to satisfy Rule 702. In *Viterbo v. Dow Chem. Co*, the Fifth Circuit observed:

> We do not hold, of course, that admissibility of an expert opinion depends upon the expert disproving or discrediting every possible cause other than the one espoused by him. Here, however, Dr. Johnson has admitted that Viterbo's symptoms could have numerous causes and, without support save Viterbo's oral history, simply picks the cause that is most advantageous to Viterbo's claim. Indeed, Dr. Johnson's testimony is no more than Viterbo's testimony dressed up and sanctified as the opinion of an expert. Without more than credentials and a subjective opinion, an expert's testimony that "it is so" is not admissible.[[108]].

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[107] Jafek also argues that there is insufficient evidence that Sutherland had a cold, but this is entirely subjective and unsupported. Sutherland testified to her cold symptoms. Soon after her cold and smell loss, and prior to the evolution of litigation bias, Sutherland was referred to ENT Dr. Caldwell and described for Dr. Caldwell her symptoms of congestion, sore throat, and upper respiratory inflammation and infection. Despite his knowledge of Sutherland's history of Zicam use and her belief that it was the cause of her problem, Dr. Caldwell concluded that her URI was the most likely cause. Exh. SS (Caldwell depo) at 23, 37-38; Exh. NN (Caldwell 1/8/02 chart); Exh. D (Jafek depo) at 335-336, 351-352. But Jafek simply rejects the notion that she had a cold, because he does not personally consider her symptoms signs of a cold and because Sutherland personally denied to him, during the course of his litigation examination, that she had developed a cold. Exh. C (Jafek supp. report) at 3, 9; Exh. D (Jafek depo) at 331-332, 351-353, 364-365.

[108] 826 F.2d 420, 423-424 (5th Cir. 1987).

In sum, Dr. Jafek's specific causation opinion is not based on facts or data sufficient to reach his conclusion using proper and reliable scientific principles and methods, and he has not reliably applied the principles and methods of science to the facts of the case. Rule 702 requires the exclusion of his testimony.

CONCLUSION

The opinions of Jafek that Zicam causes smell disturbances, and caused Sutherland's smell disorder, contain multiple, disqualifying foundational flaws. They lack any reliable foundation in exposure and dose-response; they fail to consider background risk; they improperly rest on temporality, anecdote, and logical fallacy, rather than scientific experimentation; and they improperly rely on studies which investigate different scientific hypotheses with different compounds at different doses, under drastically different conditions of exposure, and often in different species. Moreover, they ignore or dismiss by *ipse dixit* directly relevant scientific and factual evidence that contradicts his assumptions and hypotheses. Both Jafek's hypothesis and the way he has set out to prove it are not generally accepted in the scientific community.

> While hypothesis is essential in the scientific community because it leads to advances in science, speculation in the courtroom cannot aid the fact finder in making a determination of whether liability exists.[109]

The "scientific knowledge" admissible under Rule 702 presupposes conscientious and well-grounded application of the methods and principles of science. Science is, above all, an objective discipline, and it has no room for advocacy. As Sir Thomas Huxley wrote at the turn

[109] *Dunn v. Sandoz Pharms. Corp.*, 275 F.Supp.2d 672, 684 (M.D.N.C. 2003)

of the last century, "Science commits suicide when it adopts a creed."[110] Jafek has embarked on a crusade, not a scientific inquiry. This is an exercise in justification, not the pursuit of scientific truth.

Dr. Jafek's opinions are speculative, lack basic reliability and adequate factual and scientific foundation, are not of assistance to the trier of fact, and they must be excluded pursuant to Federal Rule of Evidence 702 and the case law designed to keep real science in the courtroom and junk science like this out.

Respectfully submitted this 18th day of July, 2006.

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[110] *See* Thomas H. Huxley, APHORISM AND REFLECTIONS, no. LXXI, ed. by Henrietta A. Huxley (1907) reprinted by Kessinger Publishing.

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CERTIFICATE OF SERVICE

I hereby certify that I have served a copy of the above and foregoing pleading on the following counsel via ECF electronic filing and through United States First Class Mail on this the 18th day of July, 2006.

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U.S. DISTRICT COURT
N.D. OF ALABAMA

IN THE UNITED STATES DISTRICT COURT
FOR THE NORTHERN DISTRICT OF ALABAMA
MIDDLE DIVISION

JANIE SUTHERLAND,	}	
	}	
Plaintiff,	}	
	}	CIVIL ACTION NO.
v.	}	04-AR-0129-M
	}	
MATRIXX INITIATIVES, INC., et al.,	}	
	}	
	}	
Defendants.	}	

MEMORANDUM OPINION

Before the court are two motions filed by defendants, Matrixx Initiatives, Inc., Zicam, LLC, Botanical Laboratories, Inc. and McKesson Corp. (collectively "Matrixx"), who plaintiff, Janie Sutherland ("Sutherland"), sues, claiming that they manufactured and marketed a nasal spray that, when used as directed, caused her to lose her senses of smell and taste. Defendants' first motion asks this court to preclude Sutherland from using Bruce W. Jafek, M.D., as an expert witness to link defendants' product with plaintiff's alleged injuries. In tandem with their first motion, defendants have filed a motion for summary judgment. It is based upon their expectation that their motion targeting Dr. Jafek will be granted, it being well understood that a claim that a defective product caused personal injury of the "toxic tort" variety cannot proceed to trial without an expert to demonstrate not only its toxicity, but general and specific causation.

While conducting a hearing pursuant to Federal Rule of Evidence 702, and *Daubert v. Merrell Dowd Pharmaceuticals, Inc.*, 509 U.S. 579, 113 S.Ct. 2786 (1993), this court shared with the parties its reluctance to be the first court in the United States to perform the gatekeeping role with respect to Dr. Jafek. The court expressed its reason for its timidity, namely, that it had been the first court in the land to undertake, *albeit* unsuccessfully, the gatekeeping role with respect to the pharmacologist and the medical doctor who were proffered as experts by plaintiffs in *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1220 (11th Cir. 2005), and allowed by this court to state their opinions that an ephedra-based weight loss product manufactured and sold by defendant causes stroke. The Eleventh Circuit found that this court had abused its discretion by allowing these unreliable "expert" opinions to be expressed.

This court will not repeat the Eleventh Circuit's chastisement, and criticism of the two witnesses, whose testimony the court should not have permitted, but that persuaded the jury. Suffice it to say that the Eleventh Circuit made plain its mandatory rule for a strict and "conservative" examination of all proffered expert witnesses in order to close the gate on them if they do not meet the *Daubert* criteria. *McClain* requires trial courts to be as able as the Eleventh Circuit was there to pick apart an esoteric expert opinion, and to understand and apply

better than this court did the nuances of *Daubert* analysis. After *McClain* was remanded to this court, Metabolife filed for bankruptcy, creating an automatic stay of the case, and subsequently, the case was transferred to the multidistrict panel that is handling voluminous ephreda-related toxic tort cases, including a number against Metabolife. Thus, this court was protected from having to pass on the methodology and expertise of any substitute expert witness that might have been offered by McClain and his fellow plaintiffs, or on the right of the two experts eliminated for the moment by the Eleventh Circuit to express exactly the same ultimate opinions after they performed the requisite empirical studies, after being peer reviewed and after sufficient consensus in the scientific community had been achieved. In *McClain*, the Eleventh Circuit did not express itself on whether a cause of action for toxic tort that arises from the use of a new and untested product, implies, as a matter of "due process", a tolling of the statute of limitations while the required epidemiological studies are being performed, peer review is being conducted and general acceptance by the scientific community is being established, so as to meet the *Daubert* standards. It will be interesting when the inevitable case requiring an answer to this question comes along. For the moment, it is an academic question.

Deliberately hanging back to see if another court would

speak first on the subject of Dr. Jafek's right to state his opinion that Zicam causes smell loss, another court, on September 29, 2006, did just what this court was waiting for. Relying largely on what the Eleventh Circuit said in *McClain*, Honorable Thomas B. Russell of the Western District of Kentucky in *Hans, et al. v. Matrixx Initiatives, Inc., et al.*, Civil Action No. 3:04-CV-540-R, held: "Dr. Jafek may not testify as to the opinion that Plaintiffs' use of Zicam caused their permanent anosmia as it is unreliable and therefore inadmissible under FED.R.EVID. 702".

With this encouraging word from the Western District of Kentucky, this court's confidence was restored and it recovered its courage. It now believes that it can conduct the *Daubert* analysis required of it and which it was said to have abdicated in *McClain*.

Matrixx says, just as it argued to the Western District of Kentucky, that Dr. Jafek's report and testimony do not qualify as relevant scientific knowledge under Rule 702 and must be excluded. The question there was, and here is, whether Dr. Jafek articulates any sound scientific basis for his conclusion that a causal connection exists between Zicam, the product manufactured by Matrixx, and the loss of smell and taste experienced by Sutherland. Despite this court's admiration for Dr. Jafek's professional accomplishments, it concludes that the methods and

procedures he employed are not sufficiently reliable under *Daubert* and Rule 702 to allow him to share his opinions with a jury. His testimony fails to establish either general or specific causation, both of which must be established by expert testimony.

I. FACTS

Zicam No Drip Nasal Gel ("Zicam") is an intranasal, over-the-counter homeopathic cold remedy. The active ingredient, zinc gluconate, is delivered to the nasal epithelial membrane through a nasal pump. Although zinc gluconate can be taken orally, nasal application is arguably preferred because it delivers the allegedly beneficial effects of zinc directly to the nasal cavity, where most cold viruses first invade. The extent to which zinc gluconate is actually an effective remedy or prophylactic for the common cold is an open question.[1]

Sutherland is fifty-eight years old, is in good health, but has a history of mild sinus disease. She claims that on December 21, 2001, she used Zicam because she feared the onset of a cold. In the two days before shooting Zicam up her nose, she had been

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[1] Ronald B. Turner, *Ineffectiveness of Intranasal Zinc Gluconate for Prevention of Experimental Rhinovirus Colds*, 33 CLINICAL INFECTIOUS DISEASES 1865-70 (2001). *But See* D. Hulisz, *Efficacy of zinc against common cold viruses: an overview*, J. AM. PHARM. ASS'N 594-603 (2004) (concluding that the evidence supports the value of zinc in reducing the duration and severity of symptoms of the common cold when administered within 24 hours of the onset of common cold symptoms).

suffering from cold-like symptoms, including a scratchy throat and sneezing. She also testifies that she used Zicam in accordance with the package directions. She says that immediately after applying Zicam she felt a burning sensation in both nostrils and, in the minutes that followed, lost her senses of taste and smell. She says her condition has not improved.

Olfactory disorders are not uncommon. Estimates indicate that over two million Americans suffer from some form of smell dysfunction. David H. Freedman, *In the Realm of the Chemical*, DISCOVER, June 1993. There are many varieties of olfactory disorders, including anosmia (the total lack of the ability to smell) and hyposmia (a decreased ability to smell). There are also many causes, including "(1) intranasal swelling or other obstruction which prevents odors from gaining access to the olfactory area; (2) the olfactory neuroepithelium is destroyed, as in viral infections, atrophic rhinitis, [etc.] . . .; or (3) the olfactory nerve fila, bulbs and tracts, or central connections are destroyed, as by head trauma, intracranial surgery, [etc.]." MERCK MANUAL, *Anosmia*, 2347 (1992). Anosmia can also result from the introduction of a toxic substance into the nasal passage.

Sutherland's claim depends entirely upon her ability to prove that her use of Zicam caused her loss of smell and taste. In order to succeed, she must prove that Zicam was toxic and that

the toxicity caused her to lose her senses of taste and smell. In other words, she must prove both general and specific causation. In support of her claim, she offers the report and testimony of Dr. Jafek, a medical doctor, professor, and researcher. A frequent expert witness, Dr. Jafek not only proposes to testify to toxicity and causation in this case, but in other Zicam cases. One of the other cases was the Western District of Kentucky case in which his testimony was excluded.

II. LEGAL STANDARD

Matrixx contends that Dr. Jafek's testimony is unreliable because it is not supported by sufficient facts and data and because he failed to base his conclusions on proper scientific methods as required by Rule 702.[2] As made plain in *McClain*, it is the responsibility of the trial court to determine whether proffered expert testimony is scientifically valid and constitutes evidence of sufficient reliability to be received into evidence. As the proponent of Dr. Jafek's testimony,

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[2]Rule 702 states:
"If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case."

Sutherland bears the burden of establishing its admissibility. *United States v. Williams*, 95 F.3d 723, 729 (1996), *cert. denied* 519 U.S. 1082, 117 S. Ct. 750 (1997).

Rule 702 is designed to ensure that expert evidence has an adequate factual basis and meets a minimum standard of reliability. In *Daubert*, the Supreme Court made clear that Rule 702 requires of the trial court careful scrutiny of the reliability and relevancy of expert scientific evidence. *Daubert* and its progeny have established a test for determining the admissibility of expert scientific evidence. Under that test, the trial court must determine "whether the expert is proposing to testify to (1) scientific knowledge that (2) will assist the trier of fact to understand or determine a fact in issue." Id. at 592. In other words, the trial court, acting in its capacity as "gatekeeper," must make a "preliminary assessment of whether the reasoning or methodology underlying the testimony is scientifically valid and of whether that reasoning or methodology properly can be applied to the facts at issue." Id.

In order to satisfy its *Daubert* obligation, this court must "engage in a rigorous inquiry to determine whether: (1) the expert is qualified to testify competently regarding the matters he intends to address; (2) the methodology by which the expert reaches his conclusion is sufficiently reliable as determined by the sort of inquiry mandated by *Daubert*; and (3) the testimony

assists the trier of fact, through the application of scientific, technical, or specialized expertise, to understand the evidence or to determine a fact in issue." *Rink v. Cheminova, Inc.*, 400 F.3d 1286 (11th Cir. 2005) (internal quotations and citations omitted) It is this second inquiry, into reliability, that is primarily upon which this case turns.

To evaluate the reliability of proffered expert testimony, the methods, procedures, and reasoning used by the expert must be considered. As the Supreme Court held in *Kumho Tire Co., Ltd. v. Carmichael*, 526 U.S. 137, 152, 119 S. Ct. 1167, 1176 (1999), the trial court must ensure that "an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." It is not the role of the court to examine the credibility or honesty of the expert. "Rather, [it is] only to determine whether the principles and methodology underlying the testimony are valid." *United States v. Bonds*, 12 F.3d 540 (6th Cir. 1993). If the methodology is scientifically sound, then the conclusions are scientifically valid, even if the court might not believe them.[3] In other words, the focus of the court is "on how experts reach their conclusions and not on the conclusions themselves." BERT

[3] Scientifically valid evidence is not necessarily correct evidence. The ultimate veracity of evidence is to be determined by the jury.

BLACK & PATRICK LEE, EXPERT EVIDENCE: A PRACTITIONER'S GUIDE TO LAW, SCIENCE AND THE FJC MANUAL, 21 (West Group, 1991).

Daubert suggests several non-exclusive factors that should guide the trial court's reliability analysis, including: (1) whether the expert's theory has been subjected to scientific testing; (2) whether the expert's opinions and research has been reviewed by academic peers; (3) the rate of error and controls standards; and (4) the general scientific acceptance of the technique or theory. *Daubert* specifically stated that these factors are not a definitive check-list. Other factors may be considered.

In toxic tort cases like this one, the reliability analysis must include the questions of causation. As the Eleventh Circuit noted in *McClain*, when the general causal effect of a particular toxin is not in doubt, the court need only engage in a *Daubert* analysis of the testimony as it relates to the specific harm to the individual plaintiff. However, where, as in this case, there is no general consensus as to the harmful effect of the particular substance (in this case, zinc gluconate), the trial court's *Daubert* analysis must include "the general question of whether the drug or chemical **can** cause the harm the plaintiff alleges." Id. (emphasis in the original).

III. *DAUBERT* ANALYSIS

To recapitulate, evidence is admissible under Rule 702 if it

is (1) offered by a qualified expert; (2) the product of reliable scientific methods; and (3) relevant and of assistance to the trier of fact. This court's *Daubert* analysis begins with a clarification of what is **not** at issue. First, Dr. Jafek is unquestionably competent to testify to matters related to nasal health. His professional record provides ample basis for concluding, as this court does, that he is an expert in matters related to the treatment of nasal ailments. Therefore, this court has no difficulty in finding the first part of the three-part test to be satisfied. Dr. Jafek is not, however, a toxicologist or an epidemiologist, and his opinions on these matters is subject to careful scrutiny. It is at this point that this court fell down in the *Daubert* analysis it conducted in *McClain*. Dr. Jafek's testimony easily satisfies the third part of the test. What he wants to say is undoubtedly relevant to the case because his testimony, if allowed, would be central and evidence for the trier of fact. It therefore passes the third part of the test. However, after an analysis of the methods and procedures relied upon by Dr. Jafek in reaching his conclusions, this court finds that they are not sufficiently reliable to pass *Daubert* muster. This court has been told in *McClain* to be "conservative" in performing its gatekeeping role, and this court will do just that.

a) Dr. Bruce Jafek

Dr. Jafek is a professor of otolaryngology at the University of Colorado School of Medicine. He is an experienced educator and has written and edited a number of scholarly articles and treatises related to ear, nose, and throat conditions. As said, his distinguished and impressive medical qualifications are beside the point. The evidence he offers encompasses the fields of toxicology, epidemiology, physiology, chemistry, and clinical medicine. He is wearing several hats in this litigation, but not all of them fit.

His testimony relates to the issues of both general and specific causation. It is his opinion that Zicam, when used according to the directions contained on the package, can reasonably be expected to cause complete anosmia. It is also his opinion that Sutherland actually suffers from anosmia and that her condition was caused by the single dose of Zicam she took in December of 2001.

There is no general consensus that Zicam, or zinc gluconate, is harmful or dangerous to the human smell tissue. Dr. Jafek's assertion that such a consensus exists is challenged by many distinguished physicians who assert precisely the opposite. More telling than a difference of opinion among experts is the fact that Dr. Miriam Linschoten, a designated expert witness for Sutherland, and a colleague of Dr. Jafek, testified during her deposition that **she did not know** whether the hypothesis that

Zicam causes smell loss is generally accepted in the medical community. Nor has Sutherland presented evidence that could justify this court's independently identifying a general scientific consensus. Consequently, the court must conclude, as a conservative critic, that Zicam is not **generally thought** to cause smell loss.

b) General Causation:

Following the mode of analysis described in *McClain*, the court next examines the elements of general causation. A logical starting point for a discussion of general causation is with a definition. "General causation is concerned with whether an agent increases the incidence of disease in a group and not whether the agent caused any given individual's disease." Michael D. Green et al., *Reference Guide on Epidemiology, in* Reference Manual on Scientific Evidence 392 (Federal Judicial Center, 2d ed. 2000) (cited in *McClain*, 401 F.3d at 1233.). Simply put, general causation is a predicate for establishing a specific harm.

This means, in the context of this litigation, that Sutherland's burden is satisfied if her expert can reasonably conclude, after using proper scientific methodology, that Zicam can cause permanent anosmia. In this case, it is no easy task to establish general causation. To do so, two major assertions must be established by evidence. First, it must be shown that Zicam

can reach the olfactory neuroepithelium, the part of the nose that regulates the sense of smell. Second, Zicam, and zinc gluconate, must be shown to harm the neuroepithelium in such a way as to cause permanent anosmia. Neither of these assertions is facially implausible. Indeed, Dr. Jafek may ultimately be proven to be correct. However, until he can establish a sufficient scientific basis, his conclusions remain no more than an "intuitive, clinical hunch." *Leathers v. Pfizer, Inc.*, 233 F.R.D. 687, 695 (N.D. Ga. 2006).

1. Does Zicam Reach the Neuroepithelium?

The first step in evaluating the causal relationship claimed by Dr. Jafek is determining the route by which Zicam is delivered to the nasal membrane. In other words, how does Dr. Jafek think Zicam reaches the olfactory tissue? Given the complex anatomy of the nose, it is not sufficient to simply assume that a gel-like substance automatically travels to this remote patch of nerve receptors, high up in the nose.

The neuroepithelium is the tissue by which man detects the presence of odor. It consists of a small patch of cells located on the roof of the nasal cavity, located some seven centimeters above and behind the nostril openings. The probability that a substance like Zicam can reach the neuroepithilium is the subject of contention. Dr. Jafek himself seems have mixed thoughts on the matter. In 1983, he wrote in a scholarly paper that the

neuroepithelium is "almost anatomically inaccessible."[4] When asked about this conclusion in his deposition, he said that he no longer stands by the statement made in his 1983 paper.[5]

It is, of course, possible that what was thought to be inaccessible in 1983 may be thought more accessible in light of recent medical innovations. Nevertheless, it is uncontroverted that the neuroepithelium is remotely located within the human cranium, and whether Zicam is actually delivered to this remote area is an essential question in this litigation. Dr. Jafek recognizes as much. He testified that the path to the neuroepithelium is simply a "straight shot" within reach of Zicam. However, other more recent studies indicate that, when administered according to the directions, Zicam does not reach the neuroepithelium. Admittedly, these studies have received funding from Matrixx, potentially diminishing their credibility. Even so, Dr. Jafek offers no non-speculative evidence to support his opinion that Zicam is capable of reaching the neuroepithelium. Instead, he bases his conclusion on two independent observations: first, when sprayed in the air, "Zicam

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[4] The paper, entitled *Ultrastructure of Human Nasal Mucosa*, was published in *Laryngoscope*, the official journal of the American Larygological, Rhinological, and Otological Society, Inc. The American Larygological, Rhinological, and Otological Society is also known as the Triologic Society

[5] He did, however, note in his deposition that the paper had been awarded a prize by the Triologic Society.

squirts for a distance of 4 to 10 feet;" and second, the neuroepithelial tissue is located only seven centimeters into and behind the nostril. Therefore, according to Dr. Jafek, when sprayed into the nostril, Zicam is bound to reach the neuroepithelium. This conclusion, the product of thoroughly unconvincing reasoning, rests at the heart of Dr. Jafek's testimony. Why he did not conduct an experiment on a live human being using a pump and gel with Zicam's viscosity leaves this court stumped.

Dr. Jafek offers additional bases for his conclusion, the most outre of which is his defrosted cadaver study. Interestingly, this frozen cadaver study was conducted in March 2005, well into the development of the Zicam litigation and after Dr. Jafek had already appeared on "Good Morning America" to discuss the dangers of Zicam. The cadaver study was conducted with the bisected head of a defrosted cadaver. After removing the septum and placing a pane of plexiglass over half the head, Dr. Jafek placed a bottle of Zicam far up into the nostril and pumped gel into the nasal passage. According to Jafek, the study shows that "liquid nasal gel (with tracking dye) routinely crossed the inferior, middle, and superior turbinates to lodge in the olfactory cleft. . . covering the region of the olfactory epithelium." This is supposed to prove that Zicam travels far enough into the nostril to cause anosmia. However, the cadaver

study suffers from a number of major methodological flaws.

The timing of the study is this court's first major concern. The study was conducted in between Zicam-related depositions and, as mentioned, after Dr. Jafek's public appearances on the subject. One of the hallmarks of the scientific method is an unbiased pursuit of knowledge. Scientists are to observe and interpret the results of their experiments; they are not to engage in agenda-driven fact finding for the purposes of pending litigation. The sequence of events implicates not only credibility, a matter for the jury, but a scientific method, a matter for the court as gatekeeper. This court is unable to conclude that the cadaver study was an unbiased, scientific experiment. Dr. Jafek could not have initiated the cadaver experiment with an open mind. He had already concluded publicly that Zicam causes anosmia. His giving of deposition testimony demonstrated a need to provide something that could pass as a "scientific" foundation. There is no proof to counter the court's logical conclusion that Dr. Jafek's study was a *post hoc* attempt to justify a prior conclusion.

The court's second major concern about Dr. Jafek's prospective testing is also with methodology. This court's knowledge of human physiology is admittedly limited. The court has, however, seen the photographs contained in the cadaver study. Placing a Zicam bottle far up the nostril of one half of

a defrosted, septum-less cadaver head does not strike this court as a sufficient scientific basis for concluding that Zicam can be expected to reach the olfactory epithelium. Nor, it seems, would Dr. Jafek disagree with the court. During his deposition testimony, Dr. Jafek gave his opinion of a single cadaver study conducted by an expert retained by Matrixx. The following exchange occurred:

> Q: Do you have any criticism of the Dohar cadaver study?
>
> A: No. 1, it's a single cadaver study. I'm not sure what that has to do with much of anything. So I guess that would be the first concern. I'm not sure that that raises to the level of criticism without additional study, but to spray something into the nose of a cadaver, I'm not sure how that is a significant enough observation that Dr. Schwab could depend upon that in reaching his conclusions.
>
> ******
>
> Q: Well, why was their information suboptimal, in your words?
>
> A: Because it contains incomplete data. I don't think you can draw conclusions from one 79-year old cadaver study.

The court agrees with Dr. Jafek's criticism of a cadaver study. Although interesting and perhaps informative, the cadaver study provides little, if any, support for a conclusion that Zicam reaches the olfactory epithelium of a living person.

Dr. Jafek relies on two other studies which he says support his conclusion that Zicam causes smell loss. He refers to a study conducted at the University of Pittsburgh. However, in his

deposition, Dr. Jafek admitted to not having actually seen the results, but rather "having heard of them peripherally." He also purports to rely on a case study authored by Dr. Terence Davidson, another plaintiffs' expert in Zicam litigation. Again, there are a number of difficulties with Dr. Jafek's reliance on this paper. First, as is always true of case reports, there are inherent methodological concerns about their significance. Second, the study makes a number of conclusions that differ materially from Dr. Jafek's theory.[6] Third, there are a number of unresolved discovery disputes regarding Dr. Jafek's written reflections on this paper. Thus far, Dr. Jafek has refused to produce documents which memorialize his opinion on the paper. Without such documents, it would be inappropriate to find that Dr. Jafek actually relied on the paper in forming his opinion, even if the paper itself met the smell test.

Sutherland has failed to establish that Dr. Jafek's conclusions are sufficiently reliable to pass the *Daubert* test. The burden of proof was on her. In the words of Dr. Jafek, the basis for his opinion is "[his] examination of [Sutherland], the acute loss of smell, and the absence of preexisting loss of smell." Putting it another way, Dr. Jafek's methodology is based

[6] Most important, perhaps, is that the study's author admits that it is not a "straight shot" to the olfactory neuroepithilium and that a Zicam user would have to sniff before the gel would travel upwards in the nose.

on conclusions. They are tautological. In short, Dr. Jafek's opinion, whether correct or not, has no recognizable scientific basis. This court is therefore compelled to exclude the total testimony of Dr. Jafek.

2. Toxicity

Dr. Jafek is unable to offer a scientific basis for his assertion that Zicam actually causes anosmia. It is not, however, for want of effort. Indeed, he cites a body of scholarship that does raise the possibility that zinc gluconate may, in fact, be harmful to the nose. Under *Daubert*, however, this is not sufficient.

Courts who permit expert testimony regarding toxicity from non-toxicologists require that the expert employ the principles and methods of toxicology. *Cavallo v. Star Enter.*, 852 F. Supp 756, 771 (E.D. Va. 1996). Although Dr. Jafek reaches the questionable conclusion that zinc gluconate is toxic, his methodology does not conform to standard toxicological practice. His opinions are based on antiquated and irrelevant experiments from the 1930s and on extrapolation from tests conducted on mice and fish that do not involve zinc gluconate.

The keystone to Dr. Jafek's theory of toxicity is a series of polio prevention experiments performed in the 1930s. Conducted by the prominent scientist, E.W. Schultz, and others, these experiments involved the introduction of zinc sulfate into

human and simian nasal cavities in an attempt to prevent the spread of the polio virus. Although the results of these experiments suggested that zinc ions could harm the olfactory nerve endings, there are too many dissimilarities between the experimental application of zinc sulfate to prevent the spread of polio in the 1930s and the use of an over-the-counter cold treatment today. Most importantly, zinc sulfate is chemically distinct from zinc gluconate, the active ingredient in Zicam. Dr. Jafek fails to demonstrate experimentally that the two compounds have an identical chemical effect and fails to address the many differences between the two substances.[7]

In attempting to establish similarities between zinc gluconate and zinc sulfate, Dr. Jafek did conduct an experiment which ostensibly proved that zinc ions from the two compounds behaved similarly. In his medical report, Dr. Jafek states that he has

> "confirmed Schultz's zinc experiments in our laboratory, showing that zinc gluconate produces analogous effects to other zinc salts implying analogous pharmacodynamic mechanisms in its production of loss of smell to the original (and subsequent) zinc work. This work has been shared with the scientific community and submitted for

[7] Matrixx notes (1) there is less zinc in zinc gluconate than in zinc sulfate; (2) there is no proof that the gluconate and sulfate have identical effect; (3) zinc sulfate dissolves faster than zinc gluconate; and (4) zinc sulfate is a liquid whereas zinc gluconate is a gel.

additional presentation and possible publication."[8] Even if Dr. Jafek's findings are correct, they are irrelevant. As he himself recognizes, his "experiment" offers proof only by analogy and implication. It only **implies** that the two compounds have similar chemical effects. To establish toxicity under *Daubert*, more conclusive evidence is required.

There are other important differences between the 1930s polio studies and any study of Zicam. Because the experimental protocols differ radically from the directed use of Zicam, the Schultz experiments and others like it are of little value in this case. To illustrate the differences, a brief description of the actual experiments is helpful. In one 1930's experiment, the zinc sulfate was applied "by the use of a special atomizer tip introduced between the middle turbinate and the septum." This was as unpleasant as it sounds. The researchers found this method to be "difficult, especially with small children, and is not free from danger." Ashley, *Chemoprophylaxis Against Poliomyelitis*, 29 ARCHIVES OF OTOLARYNGOLOGY 104 (1939). The second method was equally distinctive: "Pentecost advises introducing the solution into the nasal cavity with the olive-tipped urethral

[8] Dr. Jafek seems to be making an implicit assurance that his study comports with the rigors of the scientific method. However, it is well established that "the expert's assurances that he has utilized generally accepted scientific methodology is insufficient." *Moore v. Ashland Chemical Inc.*, 151 F.3d 269, 276 (5th Cir. 1998).

catheter placed between the middle turbinate and the septum with the patient in the Proetz position so that the head is inverted with the chin and the external auditory meatus in a vertical plane." Id. Essentially, this second method flooded the nasal cavity with a zinc sulfate solution while the patient lay on his back, up-side down. Nothing like that happens when Zicam is used as directed.

While the Schultz studies might suggest that soluble zinc solutions are potentially dangerous to the olfactory nerves, they do not sufficiently establish a general causal effect under *Daubert* for zinc gluconate, a distinct compound. Unfortunately for Sutherland, they are her strongest evidence for a causal relationship. For example, to support Dr. Jafek's contention that the application of zinc gluconate produces permanent anosmia, he says in his report: "I was informed of a woman who participated in the Toronto experiments and remains anosmic, by history, 67 years after the application of zinc to her nose." Anecdotal hearsay cannot fill the gap left by the absence of the kinds of clinical and epidemiological proof required by *Daubert*.

Dr. Jafek cites an article he and his colleagues published in the American Journal of Rhinology. This piece, a case series, details the symptoms of a number of users of intranasal zinc who now suffer from anosmia. A case study does not prove causation. This is another lesson from *McClain*. A case study is a "mere

accoun[t] of medical events. [It] reflect[s] only reported data, not scientific methodology." *Rider v. Sandoz Pharmaceutical Corp.*, 295 F.3d 1194, 1199 (11th Cir. 2002); See also *Siharath v. Sandoz Pharmaceutical Corp.*, 131 F. Supp 2d 1344, 1359 (N.D. Ga. 2001). While case studies may bolster true toxicological data, they are not, standing alone, sufficient to establish general causation. *Haggert v. Upjohn Co.*, 950 F. Supp 1160 (S.D. Fla. 1996).

At most, Dr. Jafek's paper illustrates that there may be a correlation between intranasal zinc application and anosmia. However, a causal relationship cannot be inferred without evidence that the subject's anosmia was, in fact, caused by the Zicam rather than by the underlying cold virus that prompted the taking of Zicam. Without taking into account such factors, Dr. Jafek's results are too speculative and his methodology too tenuous, to satisfy a *Daubert* analysis.

Furthermore, there are a number of serious methodological flaws with the case series itself. Most troublesome is the method of diagnosis. Of the ten patients included, only two were actually examined by the authors. Dr. Jafek reached a diagnosis for the other eight patients through the use of an internet questionnaire. Although the internet is now in vogue, it does not substitute for hands-on investigation. The study can raise interesting questions regarding the possible relationship between

anosmia and Zicam. *McClain*, 401 F.3d at 1254 ("case reports raise questions, they do not answer them"), but it does not provide an adequate scientific basis for general causation.

3. Dose-Response

The notion of dose-response is fundamental to scientific toxicology. "Virtually every element or compound . . . is toxic above a certain level or dose." BLACK & LEE, EXPERT EVIDENCE, at 124. The primary job of the toxicologist is to determine at what levels a substance becomes toxic. Dr. Jafek does not establish this relationship. His discussion of the dose-response relationship includes a series of implausible analogies. First, he notes that the full dose of Zicam (140 microlitres) contains more than 17 times the amount of zinc that, when applied *directly* to a mouse's olfactory tissue, produces the least observable effect level ("LOEL"). Next, because the size of the neuroepithelium is approximately the same size in the mouse as in the human, he would extrapolate that effects in humans are similar to the effects produced in the mouse. Finally, he asserts that because Zicam is designed to deliver zinc gluconate to the *nasal epithelium* it must produce effects in the olfactory epithelium.

Dr. Jafek's assertions and analogies suffer from flaws on many levels. First, he has offered no proof that **any** amount of the 140 microliters of Zicam delivered by a single dose are

absorbed in the neuroepithelium. Nevertheless, he uses the **entire** 140 microliters as his base-line dose for establishing toxicity. Such a leap defies logic and enters the never-never land of conjecture and wishful thinking.

Next, he analogizes the dose at which a LOEL is observed in a mouse as the basis for showing toxicity in a human. Although the effect on humans may be similar to the effect observed in a mouse, Dr. Jafek has offered no basis for assuming such is the case here. Furthermore, he assumes that the levels at which the LOEL exist establish toxicity equivalent to that causing permanent anosmia. Because no scientific support for such a claim is provided, the court finds Dr. Jafek's assertion in this regard implausible.

Lastly, Dr. Jafek assumes that because Zicam is purposely designed to deliver a lasting dose of zinc gluconate to the nasal membrane, the alleged toxicity is enhanced by the prolonged exposure. With this assertion, Dr. Jafek conflates the nasal epithelium, the skin covering all of the inside of the nose and that contains no nerves relating to the sense of smell, with the olfactory neuroepithelium. Unless and until Dr. Jafek can prove that a dose of Zicam sufficient to cause a toxic effect is present in the olfactory neuroepithelium, the fact that zinc gluconate is delivered to the nasal membrane is irrelevant.

Dr. Jafek has offered no scientific proof for any of his

conclusions. He engages in repeated inferential leaps, he has conducted no tests, and he relies on no evidence, scholarship, or credible sources of information dealing with the relationship between dose and effect, all typical elements of a toxicological analysis. David L. Eaton, *Toxicology in Litigation*, 12 J.L. & POL'Y 5, 15 (2003). Nor has he offered any evidence as to the frequency or duration of the use of Zicam that might produce permanent anosmia in humans.

If an expert offers no evidence related to the dose-response relationship, there is an unsurmountable methodology problem. Id. Where there is a methodology problem, there is reliability problem. And where there is a reliability problem, there is a *Daubert* problem, especially when the *Daubert* examination is conducted from a conservative perspective as *McClain* requires. Even if Dr. Jafek could show with sufficient scientific basis that Zicam reaches the neuroepithelium (something he has not done), he has made no attempt to show that it does so in a dose sufficient to cause permanent anosmia.

In examining the dose-response relationship, the court is again mindful of what it learned in *McClain*. In that case, the Eleventh Circuit held that expert testimony was inadmissible where the witness "offered no testimony about the dose of [the substance] required to injure Plaintiff or anyone else. [The witness] could not say how much is too much. . . His lack of

testimony about the dose-response relationship . . . leaves a muddle of ambiguity that undermines his opinions." *McClain*, 401 F.3d at 1241. It is no different with Dr. Jafek's testimony. Dr. Jafek would simply have this court take his word that Zicam is toxic.

Whether further experimentation can remedy the shortcomings in Dr. `Jafek's testimony is not for the court to predict. The trial court must deal with the evidence it has before it. Dr. Jafek's failure to meet the strict *Daubert* requirements results in the exclusion of his evidence. Even if this court's discretion were broad, it would exclude as unreliable the evidence offered by Dr. Jafek pertaining to general causation

Specific Causation:

"Specific causation" addresses whether a particular plaintiff's injury was actually caused or exacerbated by the purported toxin manufactured by the defendant. *Amorgianos v. Nat'l R.R. Passenger Corp.*, 303 F.3d 256, 268 (2d. Cir. 2002). In order to establish specific causation, the complaining party must show that the purported toxin was the probable, not merely a possible, cause of injury. *Jones v. United States*, 933 F.Supp. 894 (N.D. Cal. 1996). If a plaintiff is unable to establish general causation, the need to consider whether the plaintiff has established specific causation disappears. The first is necessary to the second. *Dunn v. Sandoz Pharmaceuticals Corp.*,

275 F. Supp 672 (M.D. N.C. 2003). Even so, an examination of the more glaring flaws in the evidence proffered on specific causation is helpful in illustrating the dearth of scientific support for the conclusion that Zicam causes anosmia generally.

In this case, Dr. Jafek proposes to testify that Zicam not only is generally dangerous, but that it was the proximate cause of Sutherland's injuries. This court finds that Dr. Jafek's specific causal conclusions are not supported by sufficient facts and evidence and are not the product of a sufficiently reliable methodology to pass muster under Rule 702. His specific testimony is even more questionable than his general causal testimony.

Sutherland claims that after using Zicam she lost all sense of smell **and taste**. There is a serious question about the true nature and extent of her injuries, although the nature and extent of her injuries fall outside the *Daubert* analysis. Nevertheless, Dr. Jafek's unwillingness to address evidence which undermines his diagnosis raises questions regarding his methods and reliability.

1. Sutherland's Taste Loss:

It is common for sufferers of anosmia to report symptoms of taste-loss. The sense of smell shapes the human perception of taste. Indeed, much of what humans think of as "taste" is actually governed by the olfactory senses. However, the ability

to perceive the four basic tastes of salt, sweet, sour, and bitter is regulated by nerves in the tongue which are independent of the sense of smell. Anosmia does not affect an individual's ability to register these four basic tastes.

Sutherland claims to have completely lost her ability to receive the sensation of taste. In this respect, her condition defies explanation. In his expert report, Dr. Jafek concedes that he is "unable to account for gustatory loss." Plaintiff's own expert, Dr. Miriam Linschoten ("Linschoten"), is similarly unable to account for Sutherland's taste loss and testified that **it was not scientifically possible for Zicam to destroy a user's sense of taste.**

There are only three possible explanations for this puzzling state of affairs: (1) Sutherland's anosmia and taste loss, while occurring simultaneously, are entirely independent of one another; (2) the loss of both taste and smell was caused by an unidentified sensory or neurological impairment unrelated to Zicam; or (3) Sutherland is a malingerer. In testifying that Zicam caused Sutherland's anosmia, Dr. Jafek has implicitly gone with choice number one. He has not, however, made any attempt to explain the loss of taste or the bizarrely coincidental development of both ailments. Dr. Jafek's disregard for this puzzling aspect of Sutherland's conditions is convenient for his client's purposes. However, it seems to this court evidence of

the unreliability of his methodology.

2. Sutherland's Smell Test:

Dr. Jafek's diagnosis is based on the smell test conducted by Dr. Linschoten, his colleague and frequent collaborator. Dr. Linschoten, a researcher at the University of Colorado, is the co-author of the case study published by Dr. Jafek which links Zicam with anosmia. She is experienced with taste and smell tests and has written a number of scientific papers on the subject. Dr. Linschoten is understandably not proffered by Sutherland as an expert witness on general or specific causation.

On June 5, 2006, Dr. Linschoten examined Sutherland and administered a battery of taste and smell tests designed to determine the severity of her sensory dysfunction. According to Dr. Linschoten, the results of these tests indicate that Sutherland is a likely malingerer.

The smell test administered by Dr. Linschoten required Sutherland to chose between two bottles, one of which was scented, one of which was not. This was repeated twenty times. Sutherland correctly chose only three of the scented bottles, a highly improbable result given that a true anosmic would have a one in two chance of picking the scented bottle. Dr. Linschoten estimates that such a result would occur only seventeen times in every 10,000 cases of true anosmia. These results, coupled with Sutherland's conduct during the test, caused Dr. Linschoten to

believe that Sutherland was a malingerer.

The results of these tests and Dr. Linschoten's interpretation of them were ignored by Dr. Jafek. Indeed, while acknowledging that Dr. Linschoten found it "highly improbable" that the results were accurate, Dr. Jafek nevertheless based his medical diagnosis, in part, on the tests. At no time did Dr. Jafek seek to have Sutherland retested. Nor did he offer any explanation for the troubling results of the tests. Instead, he simply relied on his unsupported opinion that Zicam causes anosmia and jumped to the conclusion that because Sutherland had taken Zicam, she must have anosmia and a loss of gustatory function. This chain of reasoning is predicated upon the preconceived notion of the toxicity of Zicam and an inferential leap of faith. It is without sufficient foundation to be admitted under *Daubert* and Rule 702.

Other problems also exist with Dr. Jafek's specific causation methodology. Of these, perhaps the most troubling is his unwillingness to address Sutherland's medical history and nasal anatomy. These potentially serious confounding factors are, for the most part, ignored or dismissed by Dr. Jafek. Nor does he address the unequivocal testimony of Sutherland herself indicating that she applied the product in accordance with the packaged directions. This, too, is a serious flaw in his methodology, given that he cannot show how a toxic dose can reach

the smell tissue even when the product is over-aggressively applied.

Because Dr. Jafek cannot establish the elements necessary to show general causation, this court need not conduct a more exhaustive inquiry into specific causation.

IV. CONCLUSION:

Under *Daubert*, even the most distinguished scientist must adhere to the rigors of the scientific method. It is this court's responsibility, as gatekeeper, a responsibility it cannot abdicate, as this court did in *McClain*, under the influence of self-doubt, to evaluate the methodology and factual basis for the conclusions put forward by an expert. If the proffered evidence is the product of an unreliable methodology or contrary to the facts, and logical declaration, it must be excluded. After its review of the record, this court concludes that Dr. Jafek's testimony is methodologically unsound and must be excluded.

By separate order, the court will grant Matrixx's motion to exclude the testimony of Dr. Jafek and, as night must follow day, will grant Matrixx's motion for summary judgment because without an expert to connect a toxin to an injury, there is no toxic tort.

DONE this 7th day of November, 2006.

WILLIAM M. ACKER, JR.
UNITED STATES DISTRICT JUDGE