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

MAXINE BENKWITH, individually and on behalf of all other similarly situated persons,	)	
Plaintiff,	)	
v.	)	CASE NO. 2:04-cv-623-MEF
	)	(WO - Recommended for Publication)
MATRIXX INITIATIVES, INC., *et al.,*	)	
Defendants.	)	

MEMORANDUM OPINION AND ORDER

Plaintiff Maxine Benkwith brings this action against Matrixx Initiatives, Inc., Zicam, LLC, Botanical Laboratories, Inc., and McKesson Corporation (hereinafter collectively "Defendants"), claiming that a nasal spray designed, manufactured, marketed, and shipped by Defendants caused her to lose her senses of smell and taste. This cause is presently before the Court on Defendants' (1) Motion to Exclude the Expert Report and Testimony of Bruce W. Jafek, M.D. (Doc. # 90), and (2) Motion for Summary Judgment (Doc. # 93). Defendants argue that all or part of the reports or testimony of Dr. Jafek is inadmissible under Rule 702 of the Federal Rules of Evidence and the standards set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993), and *McClain v. Metabolife Int'l, Inc.*, 401 F.3d 1233 (11th Cir. 2005), and that, as a result, there exists no genuine issue of material fact and Defendants are entitled to judgment as a matter of law. Plaintiff contends that Dr. Jafek's opinion is admissible and therefore both motions should be denied. The Court has carefully considered the arguments in support of and in opposition to each motion. For the

reasons stated herein, the Motion to Exclude and the Motion for Summary Judgment are both due to be GRANTED.

I. Jurisdiction and Venue

The Court exercises subject matter jurisdiction over this action pursuant 28 U.S.C. §§ 1332 (diversity) and 1446 (removal). The parties contest neither personal jurisdiction nor venue, and the Court finds a sufficient factual basis for each.

II. Factual and Procedural Background

Zicam No-Drip Liquid Nasal Gel ("Zicam") is a homeopathic cold remedy intended to place zinc in direct contact with the nasal epithelial membrane. The active ingredient in Zicam is zinc gluconate, which is supposed to reduce the length and severity of a cold. A pump delivers the gel to the nasal membrane. The directions state that the applicator tip should be placed approximately one-eighth of an inch past the nasal opening. The nozzle should then be slightly angled outward. The purchaser should pump the applicator once in each nostril. Finally, the directions state that to avoid irritation, the purchaser should not "sniff up" the gel.

Plaintiff Maxine Benkwith is sixty-one years old with a history of sinusitis and nasal congestion. She has taken Flonase, Nasalcrom, and Sudafed for nasal congestion. She has taken medication for other medical problems, including hypertension, acid reflux, arthritis, bronchitis, and high cholesterol. She first used Zicam in the winter of 2002-2003, when she felt that she was coming down with a cold. She used Zicam twice between November 2002

and March 2003. She believes that she felt a burning sensation between her eyes each time she used Zicam. In November 2003, Plaintiff bought another bottle of Zicam, which she used in November and December 2003 and in January 2004. She states that she probably used Sudafed as well for these colds. In February 2004, Plaintiff realized that she had lost her senses of smell and taste.

Plaintiff testified that when she applied Zicam she followed the directions. She testified that she did not put the applicator tip very far inside her nose and that she tilted the applicator tip toward the outer side of her nostril. She does not recall whether she sniffed when applying the Zicam, but stated that she believed the directions said not to sniff.

Plaintiff filed this case as a class action on May 3, 2004 in the Circuit Court of Montgomery County, Alabama, against Matrixx Initiatives, Inc., Zicam, LLC, and Bruno's Supermarkets, Inc. She puts forward several grounds for relief, including products liability under the Alabama Extended Manufacturer's Liability Doctrine, negligent distribution, failure to warn, breach of warranty of merchantability, and negligence.

The case was removed to this Court by Matrixx and Zicam on June 24, 2004. (Doc. # 1.) The parties filed a stipulation of dismissal as to Bruno's (Doc. # 14), and the claims against it were dismissed (Doc. # 15). Plaintiff failed to file a motion for class certification, and Defendants' Motion to Strike Class Allegations (Doc. # 32) was denied as moot (Doc. # 34). Plaintiff filed an Amended Complaint (Doc. # 78) on April 25, 2006, which added as defendants Botanical Laboratories, Inc. and McKesson Corporation.

On August 31, 2006, Defendants filed a Motion to Exclude the Expert Report and Testimony of Bruce W. Jafek, M.D. and Miriam R. Linschoten, Ph.D. (Doc. # 90). On October 2, 2006, Defendants filed a notice of withdrawal of that portion of the motion pertaining to Miriam R. Linschoten, Ph.D. (Doc. # 109). Construing that notice as a motion to withdraw, the Court granted the motion (Doc. # 111) . On August 31, 2006, Defendants filed a Motion for Summary Judgment (Doc. # 93) on the basis of a lack of expert testimony regarding causation.

IV. Defendants' Motion to Exclude the Expert Report and Testimony of Bruce W. Jafek, M.D.

A. Standard

The admissibility of expert opinion is governed by Rule 702 of the Federal Rules of Evidence, which lays the foundation for a trial court's *Daubert* analysis. *See McClain*, 401 F.3d at 1237.

> 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.

Fed. R. Evid. 702. In applying Rule 702, district courts must consider 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 conclusions is sufficiently reliable as determined by the sort of inquiry mandated in *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." *United States v. Frazier*, 387 F.3d 1244, 1260 (11th Cir. 2004). The Eleventh Circuit has stated that the primary purpose of any *Daubert* inquiry is to determine whether 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.'" *McClain*, 401 F.3d at 1255 (quoting *Kumho Tire Co., Ltd., v. Carmichael*, 526 U.S. 137, 152 (1999)).

Rule 702 imposes upon a district court the duty to act as a "gatekeeper" for expert scientific testimony before it may be admitted into evidence. *See Kumho Tire*, 526 U.S. at 147; *Gen. Elec. v. Joiner*, 522 U.S. 136, 142 (1997). As a gatekeeper, the trial judge must "insure that speculative and unreliable opinions do not reach the jury." *McClain*, 401 F.3d at 1237. Where the scientific support for expert opinions or testimony is sufficiently called into question, the district court must determine whether the testimony "has a reliable basis in the knowledge and experience of the relevant discipline." *Kumho Tire*, 526 U.S. at 149 (quotation marks and alteration omitted). "[T]he burden of establishing qualification, reliability, and helpfulness rests on the proponent of the expert opinion." *McClain*, 401 F.3d at 1238 (quoting *Frazier*, 387 F.3d at 1260).

The district court, before admitting expert testimony, 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." *Daubert,* 509 U.S. at 592. To do so, the court

must assess whether the reasoning or methodology underlying the opinion is scientifically valid and whether the reasoning or methodology can properly be applied to the facts of the case. *See id.* at 592-93. The "overarching subject" of this inquiry is the scientific validity–and thus the relevance and reliability–of the principles underlying the testimony. *Id.* at 594-95.

The requirement that the proposed evidence or testimony "assist the trier of fact to understand or determine a fact in issue" relates primarily to relevance. *Id.* at 591. The Supreme Court has described this consideration as one of "fit." *Id.* "'Fit' is not always obvious, and scientific validity for one purpose is not necessarily scientific validity for other, unrelated purposes." *Id.* "[A] court may not admit evidence when there is 'simply too great an analytical gap between the data and the opinion proffered.'" *Rider v. Sandoz Pharm. Corp.*, 295 F.3d 1194, 1197 (11th Cir. 2002) (citing *Joiner*, 522 U.S. at 146). "Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility." *Daubert*, 509 U.S. at 591-92.

"[T]he trial judge must ensure that any and all scientific testimony or evidence admitted is not only relevant, but reliable." *Daubert,* 509 U.S. at 589. To be reliable, "an expert's testimony [must] pertain to 'scientific knowledge,'" which "implies a grounding in the methods and procedures of science." *See id.* at 590. An expert's "inference or assertion must be derived by the scientific method" and "supported by appropriate validation–*i.e.*, 'good grounds,' based on what is known." *Id.*

While acknowledging that many factors are relevant to the reliability inquiry, the Court has set out several factors for consideration: (1) whether the theory or technique "can be (and has been) tested;" (2) "whether the theory or technique has been subjected to peer review and publication;" (3) "the known or potential rate of error;" and (4) "general acceptance" in the relevant scientific community. *Daubert*, 509 U.S. at 593-94. These factors should be considered "where they are reasonable measures of the reliability of expert testimony." *Kumho Tire*, 526 U.S. at 152. "[A]ny step that renders the analysis unreliable under the *Daubert* factors renders the expert's testimony inadmissible." *McClain*, 401 F.3d at 1245 (quotation and emphases omitted). These factors, however, are only a starting point for the reliability analysis; the Eleventh Circuit and other courts have also considered "reliance on anecdotal evidence (as in case reports), temporal proximity, and improper extrapolation (as in animal studies)." *Allison v. McGhan Med. Corp.*, 184 F.3d 1300, 1312 (11th Cir. 1999).

The focus of the inquiry under Rule 702 "must be solely on principles and methodology, not on the conclusions that they generate." *Daubert*, 509 U.S. at 595. However,

> nothing in either *Daubert* or the Federal Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert. A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered.

Joiner, 522 U.S. at 146. "The expert's assurances that he has utilized generally accepted scientific methodology are insufficient." *McClain*, 401 F.3d at 1244 (quotation and

alteration omitted).

"[T]he proponent of the testimony does not have the burden of proving that it is scientifically correct, but that by a preponderance of the evidence, it is reliable." *Allison*, 184 F.3d at 1312. The expert must "know[] of facts which enable him to express a reasonably accurate conclusion as opposed to conjecture or speculation. However, absolute certainty is not required." *Jones v. Otis Elevator Co.*, 861 F.2d 655, 662 (11th Cir. 1988) (internal citations omitted).

B. Qualifications, Relevance, and Reliability

The Court first addresses whether Dr. Jafek has sufficient qualifications and experience for his opinion to be admissible under Rule 702. In their motion and brief in support thereof, Defendants do not challenge the qualifications of Dr. Jafek to testify competently to the matters he intends to address. The Court has some concern regarding his qualifications and experience in certain fields other than rhinology and otolaryngology. The Court will assume *arguendo* that he is qualified to render an opinion, even though this Court concludes that his opinion does not meet the relevance and reliability requirements of Rule 702.

Dr. Jafek proposes to testify that Zicam is capable of causing permanent anosmia in humans and that use of Zicam caused Plaintiff's permanent anosmia. For convenience of analysis, the Court will view Dr. Jafek's opinions as conclusions that two types of causation are present in this case: (1) general causation, meaning that Zicam can cause permanent

anosmia when used as directed; and (2) individual causation, meaning that Zicam, and not some other factor, did in fact cause permanent anosmia in Plaintiff.

The Eleventh Circuit has recognized two broad categories of toxic tort cases: (1) those in which the medical community generally recognizes the toxicity of the substance in question, and (2) those in which it does not recognize both the toxicity of the substance and the cause of the alleged injury. *See McClain*, 401 F.3d at 1239. In the first category of cases, there is no need for the district court to undertake an extensive *Daubert* inquiry. *Id.* In the second category, the court must address general causation as part of the *Daubert* inquiry. *Id.* It is clear from the evidence presented in this case that the scientific community does not generally recognize that zinc gluconate is toxic to the human olfactory epithelium. Therefore, the Court will analyze Dr. Jafek's methodology with regard to both general and individual causation.

C. General Causation

"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." *McClain*, 401 F.3d at 1239 (quoting Michael D. Green, D. Michal Freedman, & Leon Gordis, *Reference Guide on Epidemiology, in Reference Manual on Scientific Evidence* 392 (Federal Judicial Center, 2d ed. 2000)). To find general causation, Dr. Jafek relies on epidemiological studies, his own observations and experiments, other experiments and papers, and animal studies.

Using Dr. Jafek's analysis in his report as a general guide, the Court will divide this topic into three inquiries: (1) whether Zicam can reach the human olfactory epithelium when used as directed; (2) whether zinc gluconate is toxic to the olfactory epithelium such that it can cause permanent anosmia; and (3) whether a dose of Zicam sufficient to cause permanent anosmia can reach the olfactory epithelium.

1. Can Zicam reach the olfactory epithelium when used as directed?

Dr. Jafek opines that Zicam, when used as directed, can reach the human olfactory epithelium. He claims several bases for this opinion. First, he asserts, based upon his own personal observations, that Zicam travels approximately four to ten feet in a straight liquid stream when dispensed; he cites texts on anatomy for the proposition that the olfactory epithelium is approximately five centimeters into the nose. Dr. Jafek also relies on his own research into whether there is a "straight shot" to the olfactory epithelium from the nostril and on an experiment he performed with two cadavers. He further bases his opinion on a 1937 article published in the Journal of the American Medical Association.

The Court first notes that it is questionable whether Dr. Jafek's opinion "fits" the data given his interpretation of the Zicam directions. The directions indicate that the nozzle should be pointed outward toward the side of the nose after insertion into the nostril; indeed, this is how Plaintiff interpreted them. It would be very unlikely that Zicam could reach the olfactory epithelium were the pump turned outward toward the side of the nose.[1] However,

[1] Dr. Jafek testified in deposition as follows:

even accepting Dr. Jafek's interpretation of the directions, his methods do not meet the minimum level of scientific rigor required by *Daubert*.

The Court turns to Dr. Jafek's observations regarding the distance Zicam is propelled and the distance from the opening of the nose to the olfactory epithelium. The validity of this method depends first upon Dr. Jafek's contention that in most people there is a straight pathway or "straight shot" from the outer opening of the nose to the site of the olfactory epithelium. He published an award-winning paper in 1983 that he claims was the first to demonstrate that such a pathway exists. *See* Bruce W. Jafek, *Ultrastructure of Human Nasal Mucosa*, Laryngoscope, Dec. 1983. In that paper, he stated that the human olfactory epithelium is "almost anatomically inaccessible in living humans . . . . To reach it, the biopsy instrument must pass approximately 7 cm deep to the nostril . . . into a 1.0 mm crevasse between adjacent nasal bones." *Id.* at 1576. Despite the difficulty of doing so, he was evidently able to use a straight biopsy instrument to access the site of the olfactory

---

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.

(Jafek depo. (Lusch) at 237-38; Doc. 92 Ex. F.)

epithelium. *Id.* He therefore contends that it is possible, although difficult, to reach the olfactory epithelium with a straight biopsy instrument. Based on that insight, he claims that there is a straight pathway in some people from the opening of the nose to the olfactory epithelium. Based on Dr. Jafek's published article and his expertise in rhinology, the Court will accept that it is difficult, but not impossible, to access the site of the olfactory epithelium in some people in a straight path from the opening of the nose.[2] However, the Court's acceptance of a straight pathway or "straight shot" from the nasal opening to the olfactory cleft in some people, by itself, does not show that Zicam can reach the olfactory cleft when applied as directed.

Building upon his "straight shot" theory of nasal anatomy, Dr. Jafek supports his contention that Zicam can reach the olfactory epithelium with the following observations: (1) Zicam was propelled four to ten feet when he dispensed it into the air; (2) the human olfactory epithelium is approximately five centimeters into the nose; and (3) Zicam travels in a straight liquid stream when dispensed. Even accepting Dr. Jafek's "straight shot" theory of nasal anatomy, his methodology lacks sufficient reliability; it is not "ground[ed] in the methods and procedures of science." *See Daubert,* 509 U.S. at 590. *See, e.g., Kumho Tire*, 526 U.S. at 153-155 (questioning the reliability of an expert's use of visual and tactile inspection to determine the cause of a tire's separation); *Allison*, 184 F.3d at 1317-19

[2] This does not mean that the Court accepts Dr. Jafek's "straight shot" theory that Zicam can reach the olfactory epithelium; rather, the Court accepts the "straight shot" theory only as it relates to the anatomy of the nose.

(affirming the district court's exclusion of an expert's opinion that silicone causes autoimmune disease because it was based on unreliable methodologies). It is evident that other researchers have performed similar experiments, of which Dr. Jafek is apparently aware, with human subjects, using liquid without Zicam's alleged toxic properties. Dr. Jafek's experiment does not demonstrate the level of intellectual rigor of an expert in the relevant field.

To support his "straight shot" theory of Zicam distribution, Dr. Jafek also relies on a 1937 article by Drs. Max Peet, Dean Echols, and Harry Richter. Entitled "The Chemical Prophylaxis for Poliomyelitis," this article attempted to demonstrate prophylactic treatment for children using a chemical solution to protect them from the polio virus. *See* Max M. Peet *et al.*, *The Chemical Prophylaxis for Poliomyelitis*, 108 J. Am. Med. Ass'n 2184 (1937). The chemical solution was to be applied to the olfactory epithelium, a procedure which the authors found to be difficult. In fact, the authors noted that "[d]irect nasal examination after spraying a large number of children with methylene blue showed that in practically all instances the solution did not go above the middle turbinate if an ordinary atomizer was used with the tip of the spray introduced only slightly within the nostril." *Id.* at 2186. In order to successfully apply the solution, the authors stated that the subject should have the head tilted backwards to about 45 degrees. Then, the physician should insert a atomizer with a long, narrow tip "until definitely past the middle turbinate." *Id.* She should then pump the atomizer "a number of times." *Id.* The authors stated that the technique must be performed

by someone trained in it; a parent or physician unfamiliar with intranasal work would be insufficient. There is simply no "fit" between the this article and the facts of this case. *See Rider*, 295 F.3d at 1202 ("[S]cientific evidence must 'fit' the plaintiff's theory of causation."). The Court concludes that the Peet study does not provide support for Dr. Jafek's conclusion.

Dr. Jafek performed an experiment with two cadavers to determine whether Zicam could reach the olfactory epithelium. The hypothesis to be tested was "whether there is a clear, straight anatomic pathway from the external opening of the nose to the olfactory cleft, location of the olfactory epithelium." (Doc. 92 Ex. Q.) Dr. Jafek sagittally sectioned the head of each cadaver and removed the septum from one of them. He clamped a pane of glass onto one of the halves of the sectioned head so he could observe the passage of fluid through the nose. Dr. Jafek added blue dye to a bottle of Zicam. He positioned the bottle in the cadaver's nose and sprayed the Zicam into the nose. He found that Zicam reached the olfactory epithelium.

The Court finds that this experiment is not sufficiently relevant or reliable to survive scrutiny under Rule 702. The Court has several concerns about Dr. Jafek's methodology. It appears from the pictures accompanying the study that the Zicam bottle was put a considerable distance into the cadaver's nose; the instructions state that the nozzle should be placed approximately one-eighth of an inch past the nasal opening. According to Defendants' expert Robert C. James, the mucosa in a cadaver will be smaller than that of a

living human, creating wider passageways in the nose. In addition, as Defendant's expert Dr. James Schwob notes, glass is a substance more likely to transmit the Zicam upward toward the olfactory cleft than is human mucosa. The cadavers used were 69 and 70 years old. It is unclear why Dr. Jafek could not have performed a study with living humans using a substance similar to Zicam but without its alleged toxic properties, as other experts have done. The facts of this case involve the nose of a living human, and Dr. Jafek's study on a cadaver using a pane of glass does not "fit" those facts.

Finally, the timing of this experiment is suspect. Dr. Jafek performed this experiment in March 2005. By that time, Dr. Jafek had already concluded and was testifying that Zicam could reach the olfactory epithelium. Scientific methodology "is based on generating hypotheses and testing them to see if they can be falsified." *Daubert*, 509 U.S. at 593 (quoting E. Green & C. Nesson, *Problems, Cases, and Materials on Evidence* 645 (1983)). This experiment appears to have been undertaken more to bolster a conclusion than to test a hypothesis. It is does not meet the requirements of Rule 702.

Dr. Jafek cites a distribution study of Zicam in live individuals performed at the University of Pittsburgh. Dr. Jafek testified in deposition that he had not seen the results of the study; rather, he had "heard of them peripherally." (Jafek Depo. at 342; Doc. 92 Ex. D.) Relying on studies based not on reading them, but on what one hears about them does not fall within Rule 702's standards for expert scientific testimony. Plaintiff claims that Dr. Jafek relied on a study performed by Dr. Terrance Davidson, a defense expert in the Zicam

litigation. However, Dr. Jafek does not mention this study in his report. It appears that he discussed in his deposition a paper that he was writing in response to the Davidson study. Dr. Jafek refused to provide this paper to Defendants' counsel. He testified that he disagreed with Dr. Davidson's opinion that most patients did not have a "straight shot." In light of these facts, it is not clear how this study provides support for Dr. Jafek's opinion, except to the extent that he disagrees with its conclusions.

2. Is zinc gluconate toxic to the olfactory epithelium such that it can cause permanent anosmia?

In order to show that Zicam can cause permanent anosmia, Plaintiff must demonstrate that zinc gluconate is toxic to the cells of the olfactory epithelium in such a way as to cause permanent anosmia. Dr. Jafek claims to do so through epidemiological evidence, experiments he and others have performed, animal studies, his personal observations, case reports, and anecdotal evidence. The Court concludes that Dr. Jafek's opinion does not meet the requirements of *Daubert*.

The Court first addresses Plaintiff's proffered epidemiological evidence. "Epidemiology, a field that concerns itself with finding the causal nexus between external factors and disease, is generally considered to be the best evidence of causation in toxic tort actions." *Rider*, 295 F.3d at 1198. However, "the lack [of epidemiological studies] is not fatal to a plaintiff's case." *Id.*

Dr. Jafek first cites a paper he published in the American Journal of Rhinology. *See*

Bruce W. Jafek *et al.*, *Anosmia After Intranasal Zinc Gluconate Use*, 18 Am. J. Rhinology 137 (2004). The paper describes the "Methods" of the study as follows: "The case report of a typical patient is presented and analyzed in detail, followed by a series of patients with severe hyposmia or anosmia after the use of intranasal zinc gluconate." *Id.* The paper states that based on its "numerous inquiries from patients with chemosensory dysfunction," the authors identified "a number of patients with loss of smell after the use of intranasal zinc gluconate." *Id.* at 138. The "study series" was comprised of seven men and three women. The authors used a questionnaire to rule out other causes of chemosensory loss.

After discussing a case report and briefly mentioning the "study series," the paper canvasses various experiments with zinc sulfate. It barely mentions the "study series" at all. The study is best seen as a series of case reports, with some analysis of studies conducted with zinc sulfate, not zinc gluconate. This is demonstrated by the "Conclusions" section: "Zinc ions are toxic to olfactory epithelium [sic]. Reports of severe hyposmia with parosmia or anosmia have occurred after intranasal use of zinc gluconate." This study does not appear to employ the methods of epidemiology.

Dr. Jafek also lists two other epidemiological studies as supporting his opinion. One is "[a]n increasing group of patients, enrolled in an ongoing epidemiologic, analytical, observational, cohort-observational study." Dr. Jafek does not, however, provide any further details on this study and the Court cannot conclude that it is any more epidemiological than the study published in the American Journal of Rhinology. Dr. Jafek also relies on

testimony that over 500 patients have reported anosmia to Matrixx following use of Zicam. This is not an epidemiological study. These complaints are even less persuasive than case reports. Discussing an expert's reliance on anecdotal consumer complaints, the Eleventh Circuit stated, "Uncontrolled anecdotal information offers one of the least reliable sources to justify opinions about both general and individual causation." *McClain*, 401 F.3d at 1250.

These studies do not support Dr. Jafek's opinion. There is no evidence that any of these studies had control groups, which are part of the epidemiological method. *See Reference Manual on Scientific Evidence* 338-340 (Federal Judicial Center, 2d ed. 2000). Further, before determining whether an agent causes a disease, an epidemiologist will first address whether there is an association between the agent and the disease. *See id.* at 348. This association is often expressed as the relative risk, the odds ratio, or the attributable risk. *See id.* at 348-52. Dr. Jafek does not appear to have attempted to quantify an association between zinc gluconate exposure and anosmia, nor has he presented any epidemiological studies demonstrating such an association.

The Court turns to Dr. Jafek's reliance on the work of E. W. Schultz in the 1930s and 1940s in attempting to use intranasal application of zinc sulfate to control the polio virus. Dr. Jafek states that his opinion that zinc is toxic to the human olfactory epithelium is founded on this work. The main problem with reliance on the polio experiments is the fact that the substance used in those experiments was zinc sulfate, not zinc gluconate.

The Eleventh Circuit has emphasized that careful scrutiny is required when an expert

attempts to demonstrate general causation through analogy to a different, though similar, substance. "[E]ven minor deviations in chemical structure can radically change a particular substance's properties and propensities." *Rider*, 295 F.3d at 1201 (quoting *Glastetter v. Novartis Pharm. Corp.,* 252 F.3d 986, 990 (8th Cir. 2001)). Such "small differences in chemical structure can sometimes make very large differences in the type of toxic response that is produced." *McClain*, 401 F.3d at 1246 (quoting David Eaton, *Scientific Judgment and Toxic Torts–A Primer in Toxicology for Judges and Lawyers*, 12 J. L. & Pol'y 1, 10-11 (2003)). To rely on studies using zinc sulfate, Dr. Jafek must show that the analogy to zinc gluconate is valid by demonstrating that the dissimilarities in chemical structure make no difference in the toxic effect on the olfactory epithelium.

Dr. Jafek performed an experiment in which he attempted to show that zinc gluconate has the same effect on the olfactory epithelium as zinc sulfate. He claims that he has confirmed Dr. Schultz's zinc experiments. He found that zinc gluconate "produces analogous effects to other zinc salts (protein precipitation), implying analogous pharmacodynamic mechanisms in its production of loss of smell to the original (and subsequent) zinc work." Given that "[e]ven minor deviations in chemical structure can radically change a particular substance's properties and propensities," *Rider*, 295 F.3d at 1201, this experiment is not sufficient to demonstrate that zinc ions in zinc gluconate, rather than zinc sulfate, are toxic to the olfactory epithelium.

Dr. Jafek also states that the similar solubility of zinc sulfate and zinc gluconate

suggests that zinc gluconate will be similarly toxic to the olfactory epithelium. He further argues that sulfuric acid cannot be toxic to the olfactory epithelium because zinc sulfate does not react with water to form zinc oxide or sulfuric acid except at very high temperatures; rather, Dr. Jafek contends, it is the zinc ion that is toxic to the olfactory epithelium. This reasoning ignores differences in chemical structure between the two substances. For example, as Dr. Jafek admits, zinc ions disassociate better from zinc gluconate than from zinc sulfate. Dr. Jafek's observations are not sufficient, whether considered separately or in conjunction with his experiment, to meet Rule 702's requirements. In approximating zinc sulfate and zinc gluconate, Dr. Jafek "leap[s] from an accepted scientific premise to an unsupported one." *See Allison*, 184 F.3d at 1314.

The Court next turns to the animal studies Dr. Jafek cites in support of his opinion. He cites experiments exposing the olfactory tissue of fish to zinc sulfate and an article containing a table listing publications that have discussed zinc toxicity in various animals. While Plaintiff has not provided the Court with the article containing the table, it is nevertheless clear that his reliance on the animal studies suffers from two significant errors. First, Dr. Jafek has not specifically identified in his report any animal studies using zinc gluconate instead of zinc sulfate. Second, he has not provided evidence sufficient for the Court to conclude that zinc sulfate would have similar effects on humans and the animals studied. Dr. Burton Slotnick, a consultant for Matrixx, whom Dr. Jafek cites in his report, notes a significant difference between mice and rats in the effects of zinc sulfate on olfactory

function. *See* Kathleen McBride, Burton Slotnick, & Frank L. Margolis, *Does Intranasal Application of Zinc Sulfate Produce Anosmia in the Mouse? An Olfactometric and Anatomical Study*, 28 Chem. Senses 659, 668 (2003). Dr. Jafek gives no reason why there should not be an equal or greater difference in the effects of zinc sulfate between humans and the animals used in these experiments.

Dr. Jafek relies as well on the use of zinc ions as a "standard method to produce loss of smell in animals." As in the case of the animal studies, however, he does not specify what substance containing zinc ions is used or provide evidence that this substance would have a similar effect upon humans as on animals.

Another problem with Dr. Jafek's reasoning and opinion concerns the dose-response relationship, which is "the hallmark of basic toxicology." *McClain*, 401 F.3d at 1242 (quoting Eaton, *supra*, at 15). District courts should pay careful attention to an expert's consideration of the dose-response relationship when analyzing her methodology in toxic tort cases. *Id.* at 1241. "The dose-response relationship is a relationship in which a change in amount, intensity, or duration of exposure to an agent is associated with a change–either an increase or decrease–in risk of disease." *Id.* at 1241-42 (quoting Green, Freedman, & Gordis, *supra*, at 390) (quotation marks and alteration omitted). The reliability of an expert's methodology is suspect if she avoids or neglects the dose-response relationship. *Id.* at 1242.

In his report, Dr. Jafek discusses the dose-response relationship. He offers evidence that the olfactory epithelia of mice and humans are of approximately the same area. He then

claims that 140 microliters of Zicam liquid can reach the olfactory cleft when Zicam is applied. Toxicologists consider toxic effect levels in terms of the No Observable Effect Level ("NOEL") and the Least Observable Effect Level ("LOEL"), according to Dr. Jafek. He claims that the dose of zinc ions delivered to the nose of humans by Zicam is approximately 15.7 times the LOEL per centimeter squared for the mouse. He therefore concludes that the dose of zinc ions delivered by Zicam is over fifteen times the toxic dose in mice. He also states that prolonged exposure to a toxic substance increases the toxic effect, and claims that Zicam is designed to be in contact with the nasal mucosa for at least ten minutes.

This analysis suffers from several flaws. First, Dr. Jafek makes no attempt to demonstrate that his comparison between the olfactory epithelia of humans and mice is valid despite differences in body size and biological systems. *See Quiet Tech. DC-8, Inc. v. Hurel-Dubois UK Ltd.*, 326 F.3d 1333, 1348 (11th Cir. 2003) (quoting *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 743 (3rd Cir. 1994)) ("[I]n order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans, just as the methodology of the studies must constitute good grounds to reach conclusions about the animals themselves."). His claim that 140 microliters of Zicam liquid reaches the olfactory cleft when Zicam is applied is supported by unpublished data that Plaintiff has not provided to the Court. Dr. Jafek's evidence of the dose of Zicam sufficient to cause damage to the olfactory epithelium, as noted earlier, is based on experiments with

zinc sulfate. He has not articulated an adequate explanation of the dose-response relationship.

An expert should consider the disease's background risk, which is "the risk a plaintiff and other members of the general public have of suffering the disease or injury that plaintiff alleges *without* exposure to the drug or chemical in question." *McClain*, 401 F.3d at 1243. Thus, "the likelihood that the chemical caused the disease or illness in an individual should be considered in the context of other known causes." *Id.* (quoting Eaton, *supra*, at 40). Dr. Jafek admits in his report that there are hundreds of reported causes of anosmia. However, Dr. Jafek has not identified the additional risk that Zicam exposure poses over the risk of anosmia to the general population.

Dr. Jafek's opinion that zinc gluconate can cause permanent anosmia also lacks sufficient relevance and reliability to meet the standards of Rule 702. Dr. Jafek first cites the polio experiments. These experiments, though, involved zinc sulfate rather than zinc gluconate. In addition, the source Dr. Jafek relies on, *Polio and Its Problems* by Roland Berg, does not do much to support his opinion. The strongest evidence in that source for permanent anosmia after spraying with zinc sulfate is the following: "It was many months later that Dr. Schultz began receiving complaints from physicians that many of their patients had suffered a complete and evidently permanent loss of the sense of smell." Roland H. Berg, *Polio and Its Problems* 42 (1948). Dr. Jafek also cites Schultz's reports of "several cases in adults in whom the sense of smell has not yet returned after a period of more than

six months." These uncontrolled, anecdotal reports do not meet the reliability standards of *Daubert*.

Dr. Jafek cites two authorities reporting persistent anosmia in approximately one percent of patients treated with zinc sulfate. However, Dr. Jafek's opinion is contradicted by an expert he mentions in his report. He cites an article by Dr. Slotnick to demonstrate that zinc ions are toxic to the olfactory epithelium. Dr. Slotnick testified that "[w]e have never produced a permanent anosmia [with any type of zinc], nor has anybody else on record." (Slotnick Depo. at 134-35; Doc. # 92 Ex. VV.) In an article, Dr. Slotnick found that intranasal application of zinc sulfate caused only "somewhat variable and short-duration anosmia." *See* Burton M. Slotnick & Lois A. Gutman, *Evaluation of Intranasal Zinc Sulfate Treatment on Olfactory Discrimination in Rats*, 91 J. Comp. & Physiological Psychol. 942, 948 (1977). Furthermore, the study Dr. Jafek cites involved spraying with zinc sulfate, and it therefore cannot support his opinion with regard to zinc gluconate in the absence of an adequate foundation for extrapolation.

Finally, Dr. Jafek seeks to establish that zinc gluconate causes permanent anosmia in humans by stating that he was told about a woman who still had anosmia 67 years after being treated with zinc sulfate. This anecdotal report does not meet the requirements of Rule 702. Reliance on this evidence simply does not reflect the level of intellectual rigor characterizing the practice of a toxicology expert.

3. Can a dose of Zicam sufficient to cause permanent anosmia reach the olfactory epithelium?

In addition to the other faults with his opinion, Dr. Jafek has not shown that a dose of Zicam sufficient to cause permanent anosmia can reach the olfactory epithelium when Zicam is used as directed. As discussed earlier, he has failed to present sufficient evidence in support of his theory of the dose-response relationship. He provides no support for his contention that 140 microliters of Zicam gel reach the olfactory cleft when applied as directed. He further fails to demonstrate that even if 140 microliters reached the olfactory cleft, that amount can cause permanent anosmia. Dr. Jafek cannot show that a toxic dose of Zicam can reach the olfactory epithelium.

There is another methodological problem with much of Plaintiff's evidence relating to the amount of Zicam that actually reaches the olfactory cleft. The application of zinc sulfate to animals' olfactory tissue by scientists or children's olfactory epithelia by trained rhinology experts is very different from the directed application of Zicam. For example, Dr. Jafek relies on the polio experiments. However, the method of application of the solution in those experiments is too dissimilar from the application of Zicam to support Dr. Jafek's opinion. In the polio experiments, the zinc sulfate spray would have to be administered by experts in nasal anatomy to ensure that it reached the olfactory epithelium. Further, the subjects often had their heads inverted while their olfactory epithelium was bathed with the zinc sulfate solution. The animal studies also involved the intentional application of zinc

sulfate to the olfactory epithelium. While these experiments might show that zinc sulfate can cause anosmia, they do not support the contention that Zicam can cause anosmia when used as directed.

The Court next considers the *Daubert* factors. Viewing his conclusions as a whole, and considering all of the evidence on general causation, the Court concludes that Dr. Jafek's opinion does not meet the requirements for expert scientific testimony based on the aforementioned factors. The published and peer reviewed studies he cites can only support his opinion by strained and ultimately unacceptable analogy. His opinion has not been tested except to the extent that case reports could be considered testing. He has not presented evidence of the known or potential rate of error of his theory. His opinion does not enjoy general acceptance in the relevant scientific community. Whether considered separately or in combination, the reasoning, authorities, and experiments upon which Dr. Jafek relies to support his opinion on general causation do not demonstrate the level of scientific rigor required by Rule 702.

D. Individual Causation

The Court turns to Dr. Jafek's opinion regarding individual causation. Individual, or specific, causation is concerned with "[w]hether exposure to an agent was responsible for a given individual's disease." Green, Freedman, & Gordis, *supra*, at 396. To find individual causation, Dr. Jafek relies on temporal association and the burning sensation Plaintiff experienced following her use of Zicam. He states that because there is no suggestion that

Plaintiff previously experienced anosmia, the only possible causes of the anosmia are Zicam use and a cold virus. He concludes that the fact that Plaintiff never developed a cold rules out a virus as the cause of her anosmia.

The first problem with Dr. Jafek's opinion is that he has failed to establish general causation. *See Norris v. Baxter Healthcare Corp.*, 397 F.3d 878, 881 (10th Cir. 2005) ("Plaintiff must first demonstrate general causation because without general causation, there can be no specific causation."). There are also, however, flaws specific to his methodology and reasoning, which the Court will address.

Dr. Jafek relies on the temporal proximity between Plaintiff's use of Zicam and the onset of her anosmia. He has testified that he believes that the temporal relationship is probably the most important consideration in arriving at a causation relationship. The Eleventh Circuit, however, has disapproved of reliance on this factor. Crediting a temporal relationship with proving a causal relationship leads to the *post hoc ergo propter hoc* fallacy, which "assumes causality from temporal sequence." *McClain*, 401 F.3d at 1243. Dr. Jafek's heavy reliance on the temporal relationship between Plaintiff's Zicam use and her subsequent anosmia is misplaced.

Dr. Jafek further points to the fact that Plaintiff felt a burning sensation following her use of Zicam. He contends that the burning sensation, along with the temporal proximity, proves that it was Zicam that caused Plaintiff's anosmia. While perhaps more convincing than temporal proximity, this reasoning similarly suffers from the *post hoc ergo propter hoc*

fallacy. Dr. Jafek states that burning pain is a recognized sign of injury, but fails to demonstrate that this pain reflects injury to the olfactory epithelium, or that the burning sensation is not consistent with intranasal application of Zicam in the absence of injury. The burning sensation experienced by Plaintiff, whether or not in conjunction with temporal proximity, is not sufficient to demonstrate that Zicam caused her injury.

Dr. Jafek states that absent evidence of past history of anosmia in Plaintiff, there are only two possible causes of her injury: her use of Zicam and postviral anosmia. He then concludes that postviral anosmia should be ruled out because she testified that she never developed a cold. Here Dr. Jafek appears to perform a differential etiology. Differential etiology is "the investigation and reasoning that leads to the determination of external causation, sometimes more specifically described by the witness or court as a process of identifying external causes by a process of elimination." *McClain*, 401 F.3d at 1252 (citing Mary Sue Henifin *et al.*, *Reference Guide on Medical Testimony, in Reference Manual on Scientific Evidence* 439, 481 (Federal Judicial Center, 2d ed. 2000)). This process "only satisfies a *Daubert* analysis if the expert can show the general toxicity of the drug by reliable methods." *See McClain*, 401 F.3d at 1253.

The Court questions Dr. Jafek's reasoning with respect to the possibility of postviral anosmia. Plaintiff took Zicam when she began to have cold symptoms. She generally used Zicam for at least two days when she felt that she was coming down with a cold. It is not clear to the Court that Plaintiff never had a cold based on her testimony. While Plaintiff may

have had a less severe cold than usual, Dr. Jafek fails to demonstrate that she did not have a cold or that the cold symptoms she experienced could not cause postviral anosmia. His conclusion that postviral anosmia can be ruled out is therefore suspect. In addition, despite the apparently acute nature of the anosmia, Plaintiff had a history of medical conditions associated with anosmia. She has taken medication that is associated with anosmia. Finally, Dr. Jafek's differential etiology is flawed because he has not shown Zicam's general toxicity through reliable methods. *See McClain*, 401 F.3d at 1253.

In addition, the Court notes that Plaintiff testified that she applied Zicam as directed. She pointed the nozzle of the applicator outward toward the side of the nose after insertion into the nostril. It is unlikely that the Zicam liquid could even reach the olfactory epithelium as Plaintiff applied it, and Dr. Jafek has not demonstrated otherwise.

E. Conclusion

The Court concludes that Dr. Jafek's causation opinion must be excluded because it does not meet the standards for the admissibility of expert scientific testimony. While Dr. Jafek has impressive credentials in the fields of otolaryngology and rhinology, his opinion in this case is not sufficiently relevant or reliable. He attempts to use animal studies without support for extrapolation to humans, cites "epidemiologic studies" that fail to follow the fundamentals of epidemiology, makes unsupported analogies between different chemical substances, performs unsound experiments, draws impermissible conclusions from other scientists' articles and experiments, and relies on irrelevant and unreliable data. In short, Dr.

Jafek has not "employ[ed] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field." *Kumho Tire*, 526 U.S. at 152. His causation opinion must be excluded, and Defendants' motion is therefore due to be granted.

V. Motion for Summary Judgment

Under Rule 56(c) of the Federal Rules of Civil Procedure, summary judgment is appropriate "if the pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact and that the moving party is entitled to a judgment as a matter of law." Fed. R. Civ. P. 56(c). "A genuine issue of material fact does not exist unless there is sufficient evidence favoring the nonmoving party for a reasonable jury to return a verdict in its favor." *Chapman v. AI Transp.,* 229 F.3d 1012, 1023 (11th Cir. 2000) (*en banc*) (quoting *Haves v. City of Miami,* 52 F.3d 918, 921 (11th Cir. 1995) (internal quotation marks and citations omitted)).

The exclusion of Dr. Jafek's report and testimony necessitates granting Defendants' Motion for Summary Judgment. That motion was based on Defendants' contention that Dr. Jafek's report and testimony should be excluded. Without proof of causation, Plaintiff cannot prevail on any of her claims. *See McClain*, 401 F.3d at 1237 (proof of general and individual causation in toxic tort cases requires expert testimony); *Armstrong Bus. Servs., Inc. v. AmSouth Bank*, 817 So. 2d 665, 679 (Ala. 2001) (causation is an element of a negligence claim); *Brushwitz v. Ezell*, 757 So. 2d 423, 432-33 (Ala. 2000) (proximate

causation is an element of a wantonness claim); *Sears, Roebuck and Co. v. Harris*, 630 So. 2d 1018, 1030 (Ala. 1993) (proximate causation is an element of a failure to warn claim); *Volkswagen of Am., Inc. v. Marinelli*, 628 So. 2d 378, 385 (Ala. 1993) (causation is an element of a claim under the Alabama Extended Manufacturer's Liability Doctrine); *Clark v. Allied Healthcare Prods., Inc*., 601 So. 2d 902, 903 (Ala. 1992) (causation is an element of a breach of warranty claim). Defendants have therefore met their burden to demonstrate that there is no genuine issue of material fact and that they are entitled to judgment as a matter of law.

Plaintiff argues that summary judgment should be denied on her failure to warn claim because a jury could infer, without testimony from an expert, that use of Zicam could cause injury about which consumers should have been told. She contends that she does not need an expert on warnings. As she admits, though, she must present expert evidence on general causation. *See McClain*, 401 F.2d at 1237. Without proof of causation, she cannot prevail on her claims, *see Harris*, 630 So. 2d at 1030, and she has failed to provide such proof. Defendants' Motion for Summary Judgment is due to be granted.

VI. Conclusion

For the reasons set forth above, it is hereby ORDERED that:

(1) Defendants' Motion to Exclude the Expert Report and Testimony of Bruce W. Jafek, M.D. (Doc. # 90) is GRANTED.

(2) Defendants' Motion for Summary Judgment (Doc. # 93) is GRANTED.

(3) The trial and pretrial hearing are CANCELED.

(4) This Court will enter a separate final judgment taxing costs.

DONE this the 27th day of December, 2006.

/s/ Mark E. Fuller
CHIEF UNITED STATES DISTRICT JUDGE