J-A20012-15

NON-PRECEDENTIAL DECISION – SEE SUPERIOR COURT I.O.P 65.37

IN RE: DENTURE ADHESIVE CREAM LITIGATION	:	IN THE SUPERIOR COURT OF PENNSYLVANIA
APPEAL OF: GARY L. BROWN, EUGENE BUCKLER AND ESTHER BUCKLER, THOMAS M. FILLHART AND ANNA M. FILLHART, LOLISA JOYNER AND JEROME JOYNER, GREGORY N. McCOMMON, DONNA OLESKA, JAMES C. THOMAS AND SHARRON R. THOMAS, LORI WADSWORTH, WILLIAM WATKINS, PAMELA WORSHAM AND DANA YOUNGBLOOD	:	No. 915 EDA 2014

Appeal from the Order entered February 18, 2014,
Court of Common Pleas, Philadelphia County,
Civil Division at No. 04534 June Term 2009

BEFORE: DONOHUE, SHOGAN and WECHT, JJ.

MEMORANDUM BY DONOHUE, J.: **FILED NOVEMBER 12, 2015**

This appeal is filed on behalf of the twelve remaining plaintiffs ("Appellants") in the Dental Adhesive Cream Litigation consolidated in the Court of Common Pleas of Philadelphia County. The Appellants contend that their use of Fixodent, a denture adhesive cream manufactured and sold by the Appellees, resulted in a neurological condition identified as copper deficiency myeloneuropathy ("CDM"). According to the Appellants, Fixodent contains zinc, the ingestion of which causes copper deficiency, which in turn causes CDM. The trial court, pursuant to ***Frye v. United States***, 293 F. 1013 (D.C. Cir. 1923), excluded the opinions of the Appellants' expert

causation witnesses and granted summary judgment in favor of the Appellees[1]. For the reasons that follow, we affirm the trial court's orders.

In its written opinion, the trial court provided the following useful background information for this appeal:

> On July 2 , 2009, the coordinating judge of the Complex Litigation Center created the ***In re Dental Adhesive Cream*** mass tort master-docket. The Third Amended Master Long Form Complaint contains allegata against eight defendants, which can easily be distilled into three groups – 1) The Proctor & Gamble Manufacturing Company and its subsidiaries, which manufacture and distribute Fixodent, 2) GlaxoSmithKline and its subsidiaries, which manufactured and distributed Super Poligrip, and 3) Defendant Rite-Aid Corporation, which sold both Fixodent and Super Poligrip. ***See*** Third Amended Master Long Form Complaint at ¶¶ 17-52.
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> By September 2013, only twelve cases, all filed by the law firm of Chaffin and Luhana LLP, remained in the ***In re Dental Cream*** mass tort program, and GlaxoSmithKline and its subsidiaries were no longer defendants in these cases. On September 17, 2013, [Appellees] filed an omnibus Motion to Exclude all of [Appellants'] general causation experts in these remaining cases. Following extensive briefing by the parties and the reception of live testimony from Dr. Lautenbach, the [trial court] heard oral argument on the Motion.
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> In these cases, [Appellants] allege their use of zinc containing denture adhesive creams manufactured by Proctor and Gamble caused them to develop an irreversible neurologic condition known as [CDM[1]]. The parties agree each gram of Fixodent contains

[1] The Appellees in the present case consist of the Rite Aid Corporation, Proctor & Gamble Distributing, LLC, The Proctor & Gamble Manufacturing Company, and The Proctor & Gamble Company.

> approximately 17 milligrams of zinc bound within a Gantrez polymer. From this starting point, [Appellants] allege the following causal chain: 1) Fixodent contains zinc, 2) some zinc from Fixodent is absorbed into the blood, 3) excessive zinc in the blood blocks copper absorption, causing copper deficiency, 4) sustained copper deficiency for a prolonged period of time results in [CDM].
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> [Appellants] identified eight causation experts, Martyn T. Smith, PhD., Frederick K. Askari, M.D., PhD, Ebbing Lautenbach, M.D., M.P.H., Carl F. Cranor, PhD, M.S.L., David Grainger, PhD, Steven A. Greenberg, M.D., M.S., Joseph R. Prohaska, PhD, and Elizabeth A. Shuster, M.D. Although [Appellants] offer eight experts to support their theory of causation, only four experts, Dr. Smith, Dr. Lautenbach, Dr. Askari, and Dr. Greenberg, submitted opinions linking Fixodent to [CDM]. Three of the remaining experts, Dr. Cranor, Dr. Grainger, and Dr. Prohaska authored expert reports which buttress the conclusion of those experts who do link Fixodent to [CDM]. For example, Dr. Prohaska's report discusses how excess zinc ingestion can lead to [DCM]; however, Dr. Prohaska's report does not link Fixodent to excessive zinc ingestion. Since their opinions do not link Fixodent to [CDM], but serve only to bolster the testimony of the experts who do make such a link, this opinion will not address the testimony of Dr. Cranor, Dr. Grainger, and Dr. Prohaska.
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> [Appellants] also present the testimony of Dr. Shuster, who treated one of the patients in the contemporaneous Federal Multi-District Litigation, ***In re Denture Cream Products Liability Litigation***, 795 F. Supp. 2d 1345 (S.D. Fla. 2011). In the Multi-District Litigation, Dr. Shuster opined Fixodent caused her patient to develop [CDM]. Notably, Dr. Shuster did not file an expert report offering an opinion as to general causation in these cases; rather, [Appellants attach] excerpts of her deposition transcript from the Multi-District Litigation. ***See***

> Moving Defendants Motion at Ex. 13. The fact Dr. Shuster did not author a general causation expert report is hardly surprising in light of the fact [Appellants] candidly admit Dr. Shuster's employment contract prohibits her from serving as a general causation expert. ***See*** Plaintiffs' Response in Opposition at p. 103 n.33. Nonetheless, [Appellants'] argue Dr. Shuster's prior testimony supports general causation because it logically follows if Fixodent caused Dr. Shuster's patient to develop [CDM], then Fixodent must cause [CDM] generally. In light of the fact Dr. Shuster did not author a report offering an opinion as to general causation in any of the cases currently pending before this [trial court], Dr. Shuster's opinions will not be addressed. Accordingly, this Opinion only addresses the expert opinions of Dr. Lautenbach, Dr. Askari, Dr. Smith, and Dr. Greenberg.
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> [1] The [trial court] notes the parties and witnesses use a number of distinct, yet related, medical terms to describe the neurological injuries suffered by [Appellants]. These terms include 1) myelopathy - a spinal cord disease; 2) neuropathy - peripheral nerve disease; 3) myeloneuropathy - a combination of spinal cord disease and peripheral nerve disease, and 4) copper deficiency myeloneuropathy – a type of myeloneuropathy caused by copper deficiency.

Trial Court Opinion, 2/7/2014, at 1-3.

In its ruling, the trial court concluded that the Appellants' "experts have failed to establish in a methodologically sound manner that denture cream use, in general, results in [CDM]." ***Id.*** at 23. More specifically, Appellants' experts "failed to utilize sound methodology to establish a link between Fixodent and [CDM]." ***Id.*** On appeal, the Appellants raise the following four issues for our review and determination:

1. Did the trial court abuse its discretion or err as a matter of law by concluding that it is novel science that the zinc in denture cream can cause zinc-induced [CDM] and applying a ***Frye*** inquiry to [Appellants'] general causation experts' opinions?

2. Even if evaluating the scientific evidence was appropriate under ***Frye***, did the trial court abuse its discretion or err as a matter of law by holding that Dr. Ebbing Lautenbach's Cohort Study was inadmissible evidence that [Appellants'] general causation experts could not rely upon for their expert opinions?

3. Even if evaluating the scientific evidence was appropriate under ***Frye***, did the trial court abuse its discretion or err as a matter of law by holding that the Fixodent Blockade Study was inadmissible evidence that [Appellants'] general causation experts could not rely upon for their expert opinions?

4. Did the trial court abuse its discretion or commit an error of law by granting [Appellees'] Motion for Summary Judgment after erroneously granting [the Appellees''] Frye motion?

Appellants' Brief at 6-7.

Our standard of review with respect to a trial court's decision to grant or deny a motion for summary judgment is as follows:

> A reviewing court may disturb the order of the trial court only where it is established that the court committed an error of law or abused its discretion. As with all questions of law, our review is plenary.
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> In evaluating the trial court's decision to enter summary judgment, we focus on the legal standard articulated in the summary judgment rule. Pa.R.C.P. 1035.2. The rule states that where there is no genuine issue of material fact and the moving party is entitled to relief as a matter of law, summary

> judgment may be entered. Where the non-moving party bears the burden of proof on an issue, he may not merely rely on his pleadings or answers in order to survive summary judgment. Failure of a non[-]moving party to adduce sufficient evidence on an issue essential to his case and on which it bears the burden of proof establishes the entitlement of the moving party to judgment as a matter of law. Lastly, we will view the record in the light most favorable to the non-moving party, and all doubts as to the existence of a genuine issue of material fact must be resolved against the moving party.

Thompson v. Ginkel, 2014, 95 A.3d 900, 904 (Pa. Super 2014) (quoting ***JP Morgan Chase Bank, N.A. v. Murray***, 63 A.3d 1258, 1261–62 (Pa. Super. 2013)), *appeal denied*, 108 A.3d 36 (Pa. 2015).

Rule 702 of the Pennsylvania Rules of Evidence governs the admissibility of expert testimony on scientific knowledge:

> **Rule 702. Testimony by experts.**
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> If scientific, technical or other specialized knowledge beyond that possessed by a layperson 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.

Pa.R.E. 702. To exclude expert testimony based upon a challenge to the scientific evidence, a party must file a motion pursuant to Rule 207.1 of the Pennsylvania Rules of Civil Procedure, which provides as follows:

> **Rule 207.1 Motion to Exclude Expert Testimony Which Relies upon Novel Scientific Evidence.**

(a) If a party moves the court to exclude expert testimony which relies upon novel scientific evidence, on the basis that it is inadmissible under Pa.R.E. 702 or 703,

(1) the motion shall contain:

(i) the name and credentials of the expert witness whose testimony is sought to be excluded,

(ii) a summary of the expected testimony of the expert witness, specifying with particularity that portion of the testimony of the witness which the moving party seeks to exclude,

(iii) the basis, set forth with specificity, for excluding the evidence,

(iv) the evidence upon which the moving party relies, and(v) copies of all relevant curriculum vitae and expert reports;

(2) any other party need not respond to the motion unless ordered by the court;

(3) the court shall initially review the motion to determine if, in the interest of justice, the matter should be addressed prior to trial. The court, without further proceedings, may determine that any issue of admissibility of expert testimony be deferred until trial; and

(4) the court shall require that a response be filed if it determines that the matter should be addressed prior to trial.

(b) A party is not required to raise the issue of the admissibility of testimony of an expert witness prior to trial unless the court orders the party to do so.

Pa.R.C.P. 207.1. The proponent of expert scientific evidence has the burden of establishing all of the elements required for submission. ***Grady v. Frito–Lay, Inc.***, 839 A.2d 1038, 1045 (Pa. 2003).

In ***Commonwealth v. Topa***, 369 A.2d 1277 (Pa. 1977), our Supreme Court adopted the standard originally set forth in ***Frye v. U.S.***, 293 F. 1013 (D.C.Cir. 1923), for the admissibility of scientific evidence. In ***Frye***, the Court of Appeals for the District of Columbia concluded that scientific evidence may be admitted only if it is generally accepted in the relevant scientific community:

> Just when a scientific principle or discovery crosses the line between the experimental and demonstrable stages is difficult to define. Somewhere in this twilight zone the evidential force of the principle must be recognized, and while courts will go a long way in admitting expert testimony deduced from a well-recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field in which it belongs.

Frye, 293 F. at 1014; ***Commonwealth v. Nazarovitch***, 496 97, 101, 436 A.2d 170, 172 (Pa. 1981). In ***Topa***, the Supreme Court described the ***Frye*** standard as follows: "Admissibility of the [scientific] evidence depends upon the general acceptance of its validity by those scientists active in the field to which the evidence belongs." ***Topa***, 369 A.2d at 1281.

Our Supreme Court has reaffirmed Pennsylvania's continued adherence to the ***Frye*** test on several occasions, including recently in ***Betz***

v. Pneumo Abex, LLC, 44 A.3d 27 (Pa. 2012), rather than adopt the federal standard in ***Daubert v. Merrell Dow Pharmaceuticals, Inc.***, 509 U.S. 579 (1993). In ***Betz***, the Supreme Court provided the following general guidance when applying ***Frye***:

> There is inherent tension among the various measures for admissibility of expert testimony. The threshold common law test requires merely some reasonable pretension to specialized knowledge. Our evidentiary rules, on the other hand, suggest trial courts may take a greater role in assessing whether the testimony will assist the trier of fact to understand the evidence or determine a fact in issue, ***see*** Pa.R.E. 702, and in screening evidence to avoid unfair prejudice, confusion of the issues, or misleading of the jury, ***see*** Pa.R.E. 403. For better or for worse, however, in the context of the more conventional realms of science, the Pennsylvania decisions tend to downplay the courts' screening function. A manifestation of this trend is that challenges generally are vetted through the ***Frye*** litmus, which winnows the field of the attacks by application of the threshold requirement of novelty.
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> Various reasons underlie the preference to limit the courts' involvement in determining the admissibility of scientific evidence. There is the concern that liberality in allowing challenges would substantially increase the number of challenges (and cases in which lengthy pre-trial proceedings would ensue). The competency of trial judges to accept or reject scientific theories remains a legitimate subject of controversy. Additionally, a claim or defense in many cases may rise or fall based upon expert testimony and, therefore, there is some reluctance on the part of courts to deprive litigants of their day in court.
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> On the other hand, this Court has recognized the influential nature of expert testimony on complex

> subjects, and the potential that distortions have to mislead laypersons. It would be naïve, in this regard, to assume that the possibility for distortion is limited to the very newest realms of science.

Id. at 52-53. Because ***Frye*** is an exclusionary rule of evidence, "it must be construed narrowly so as not to impede admissibility of evidence that will aid the trier of fact in the search for truth." ***Trach v. Fellin***, 817 A.2d 1102, 1104 (Pa. Super. 2003) (en banc).

A ***Frye*** motion requires a trial court to engage in a two-step process. First, the trial court must determine whether the evidence the moving party seeks to exclude is "novel scientific evidence." ***Id.*** at 1109. To do so, the trial court must consider, inter alia, the proffered basis for excluding the evidence and the evidence presented in support of that basis (per Rule 207.1(a)(1)(iii) & (iv)), and decide whether the moving party has demonstrated that there is a legitimate dispute regarding the reliability of the expert's conclusions. ***See, e.g.***, ***Commonwealth v. Foley***, 38 A.3d 882, 888-90 (Pa. Super. 2012). If the trial court determines that the proponent has offered "novel scientific evidence," then it must proceed to the second step, namely to apply the ***Frye*** standard to decide whether the expert's methodology "has general acceptance in the relevant scientific community." ***Grady***, 839 A.2d at 1043–44. Ultimately, the focus is on the methodologies utilized, not on the conclusions reached. ***Id.*** at 1045.

This two-step process ensures that scientific evidence admitted at trial is the product of sound scientific research, but is not "senselessly restrictive" by prohibiting testimony inconsistent with currently prevailing orthodoxy. ***See Blum ex rel. Blum v. Merrell Dow Pharmaceuticals, Inc.***, 764 A.2d 1, 5 (Pa. 2000) (Cappy, C.J., dissenting). The rationale behind ***Frye*** is to measure the quality of scientific evidence prior to its admission because "there is the danger that the trial judge or jury will ascribe a degree of certainty to the testimony of the expert ... which may not be deserved.'" ***Id.*** at 1317 (quoting ***Topa***, 369 A.2d at 1281).

In applying this two-step process, judges should generally be deferential to the scientists, "who are in the best position to evaluate the merits of scientific theory and technique." ***Grady***, 839 A.2d at 1045. As this Court acknowledged in ***Trach***,

> Judges, both trial and appellate, have no special competence to resolve the complex and refractory causal issues raised by the attempt to link low-level exposure to toxic chemicals with human disease. On questions such as these, which stand at the frontier of current medical and epidemiological inquiry, if experts are willing to testify that such a link exists, it is for the jury to decide whether to credit such testimony.

Trach, 817 A.2d at 1117 (quoting ***Ferebee v. Chevron Chemical Co.***, 736 F.2d 1529, 1534 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984)). Moreover, "[i]n a courtroom, the test for allowing a plaintiff to recover … is not scientific certainty but legal sufficiency," and "the fact that another jury

might reach the opposite conclusion or that science would require more evidence before conclusively considering the causation question resolved is irrelevant." ***Id.*** (quoting ***Ferebee***, 736 F.2d at 1535-36).

Before proceeding to consideration of the issues raised by the Appellants in this appeal, we must note that a prior panel of this Court affirmed the trial court's grant of a previous ***Frye*** motion to exclude expert causation testimony by Drs. Lautenbach, Askari and Smith in another case on the ***In re Dental Adhesive Cream*** mass tort master-docket. In ***Jacoby v. Rite Aid Corp. et al.***, 1508 EDA 2012 (Pa. Super. December 9, 2013) (unpublished memorandum), this Court agreed that the trial court properly subjected the expert testimony to a ***Frye*** analysis because it was novel scientific evidence. The panel determined that while the links between excess zinc and copper deficiency, and between copper deficiency and neurological injuries, have been well established over many years, "the real question before this Court was whether Fixodent releases sufficient zinc to cause [CDM]." ***Id.*** at 10-11. With regard to this question, the panel recognized that the proffered expert testimony contained significant analytic gaps, including the lack of any basis on which to opine regarding (1) how much zinc is absorbed into the body from Fixodent ingestion, (2) how much zinc would have to be absorbed from Fixodent use to result in copper deficiency, and (3) how low a person's copper level must be, and for what duration, before CDM may result. ***Id.*** at 15-16. These analytic gaps existed

in large part because the expert witnesses relied on reviews of case reports and case series, which is not a generally accepted methodology on which to base conclusions about the causes of disease. ***Id.*** at 17. In one of his own publications, Dr. Lautenbach had recognized that case reports are anecdotal and thus at most may serve to "generate hypotheses that may be tested in future analytic studies." ***Id.*** Dr. Lautenbach also acknowledged that "since a case report or case series does not include a comparison group, one cannot determine which characteristics in the description of the cases are unique to the illness." ***Id.***

Dr. Smith and Dr. Askari employed ill-defined methodologies they respectively described as "weight of the evidence" and "totality of the evidence." The panel in ***Jacoby*** determined that these methodologies are not generally accepted within the scientific community, and are in fact not scientific methodologies at all. ***Id.*** at 14. These methodologies "are not verifiable or replicable, but rather are based on subjective judgment", and reflect only a "seat of the pants qualitative assessment." ***Id.*** The ***Jacoby*** panel was somewhat less critical of Dr. Lautenbach's methodology, pursuant to which he reviewed case reports and classified the results on the Naranjo adverse drug reaction probability scale. This methodology was not generally accepted either, however, both because Dr. Lautenbach relied on the same case reports and case series as did Drs. Smith and Askari, and because he admitted during his deposition that he was unaware that the Naranjo scale

had ever been used in attempting to verify a hypothesis that an essential trace element (like zinc) causes long-term injury. ***Id.*** at 19.

In an effort to fill the analytic gaps and other shortcomings identified in ***Jacoby***, in the present case the Appellants offered new evidence to supplement the previously submitted expert reports. This supplemental evidence consisted of: (1) a peer-reviewed article by Alemayehu A Gabreyes and others, published in the European Journal of Haematology in 2013 (the "Gabreyes Article"); (2) a cohort study performed by Dr. Lautenbach (the "Cohort Study") based upon the data in the Gabreyes Article; and (3) a Fixodent Blockade Study performed by Dr. Askari. ***See*** Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 32 (Alemayehu A Gabreyes et al., *Hypocupremia associated cytopenia and myelopathy: a national retrospective review*, 90 European Journal of Haematology (2013)); Exhibit 11 (Lautenbach 2013 Expert Report); Exhibit 3 (Askari 2013 Expert Report).

In the Gabreyes Article, the authors identified twenty-two patients who fit the study's pre-determined parameters: they did not have a pre-existing cytopenia blood condition, they had their blood copper levels tested by the Scottish Trace Element and Micronutrient Reference Laboratory (STEMRL), and their blood copper levels were less than or equal to 6µm. Gabreyes Article at 2. Of these twenty-two, four were excluded because of a lack of documentation, and the treating physician(s) for two others declined to

admit their patients for participation. Of the sixteen participating patients, the Gabreyes Article reported that "[t]welve of the sixteen remaining patients had high serum zinc concentrations (>18µm/L), including nine "due to zinc-containing dental fixatives." ***Id.*** In addition, twelve of the sixteen patients "had both haematological and neurological features of copper deficiency." ***Id.*** The Gabreyes authors did not identify the overlap between the nine patients who had used zinc-containing denture adhesives and the twelve who had neurological symptoms. In its concluding discussion section, the Gabreyes Article noted that its findings "again highlight[] the association between long-term zinc exposure through dental fixatives and the subsequent haematological and neurological symptoms …." ***Id.*** at 8. The authors also noted that "copper deficiency is under diagnosed," and if better recognized and properly diagnosed, "the actual prevalence is likely to be higher." ***Id.***

At the ***Frye*** hearing, Dr. Lautenbach testified that he performed his Cohort Study to determine "the association between denture cream and [CDM]." N.T., 11/12/2013, at 20. A "cohort study" compares two groups of people, one exposed to a substance considered to be a possible cause of a disease, and another not so exposed. ***Hamilton v. Breg, Inc.***, 2011 WL 833614, at *4 (S.D. Ohio 2011). While cohort studies are typically prospective in nature, where the researcher follows the progress of both groups over a period of time, ***id.***, Dr. Lautenbach's Cohort Study was

retrospective in nature[2] and was based upon the information in the Gabreyes Article:

> So what really enabled me to do the cohort study was the Gabreyes study. And the reason for that is that the Gabreyes authors identified the source – the clear source population, which is the population of Scotland, and within that population identified all patients who in a given time period, from '05 to 2010, developed copper deficiency, and within that group those that developed copper deficiency – signs and symptoms consistent with [CDM].

N.T., 11/12/2013, at 20.

In his Cohort Study, Dr. Lautenbach compared two cohort groups, namely those who used denture cream in Scotland between 2005 and 2010 and those who did not, to determine the rates of development of CDM in each group. He concluded that the rate of development of CDM was higher among denture cream users based upon the following analysis: the Gabreyes Article identified twelve of the sixteen patients with low copper levels as suffering from CDM, and of these twelve, between six and nine used denture cream. Based upon statistics regarding the incidence of denture cream use in the United Kingdom, he estimated that a similar percentage (10%) of the population of Scotland used denture cream. Given a Scottish population of 5.2 million, Dr. Lautenbach estimated that roughly

[2] At the ***Frye*** hearing, Dr. Lautenbach testified that performing a prospective cohort study would be unethical "because you would be assigning people to excessive amounts of denture cream exposure. N.T., 11/12/2013, at 15.

500,000 people used denture cream between 2005 and 2010. Using the more conservative number from the Gabreyes Article, six out of 500,000 denture cream users is a much higher rate of developing CDM than is six out of 4.7 million who did not use denture cream. Accordingly, Dr. Lautenbach opined that the rate of development of CDM is much higher among denture cream users than is the same rate among non-denture cream users, even using the most conservative assumption from the Gabreyes Article data (six rather than nine). Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 11.

Finally, Dr. Askari performed his Fixodent Blockade Study to test his hypothesis that ingestion of zinc-containing Fixodent blocks copper absorption, resulting in decreased blood (serum) copper levels and increased copper levels in urine and feces. Twenty-four individuals on controlled diets received three pills per day for 30 days, during which time blood, urine and feces levels were regularly monitored. Twelve participants ingested encapsulated Fixodent, six ingested encapsulated zinc acetate, and the final six ingested an encapsulated placebo. At the end of the 30-day period, contrary to Dr. Askari's assumptions, there were no statistically significant differences in copper levels in the blood or urine of those ingesting Fixodent and those ingesting the placebo. On days 31-33, however, there was a statistically significant difference between the copper levels in the fecal excretions of those two groups. From this latter finding, Dr. Askari opined

that the study confirmed his initial hypothesis. Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 3.

For their first issue on appeal, the Appellants argue that the trial court abused its discretion or erred as a matter of law in subjecting the opinions of their expert causation witnesses to a ***Frye*** inquiry. According to the Appellants, the science that zinc-containing denture adhesives can cause CDM is "now widely accepted among scientists," and thus is not novel. Appellants' Brief at 26. The Appellants' contend that "today 23 textbooks in hematology, neurology, internal medicine and other disciplines have concluded that zinc, including the zinc in denture adhesives like Fixodent, can cause copper deficiency and resulting hematological and neurological injuries, including CDM." ***Id.*** at 34. Because diverse and widely respected sources agree that the science at issue is not novel, the Appellants insist that no ***Frye*** inquiry was necessary or appropriate. ***Id.*** at 36.

In ***Jacoby***, this Court considered and rejected a substantially similar contention based upon a review of most of the same textbooks and related sources now cited by the Appellants. ***Jacoby***, 1508 EDA 2012 at 10-11. The law of the case doctrine provides, inter alia, that judges of equal jurisdiction sitting in the same case should not overrule each other's decisions. ***Commonwealth v. Starr***, 664 A.2d 1326, 1331 (Pa. 1995); ***Ario v. Reliance Ins. Co.***, 980 A.2d 588, 597 (Pa. 2009); ***Mohney v. Am. Gen. Life Ins. Co.***, 116 A.3d 1123, 1132 (Pa. Super. 2015). As a technical

matter, the law of the case doctrine does not apply here, as this is not the "same case" as ***Jacoby***. The Appellants, however, have provided us with no basis to reach a result contrary to that of the ***Jacoby*** panel. The publications cited by the Appellants acknowledge the widely-accepted associations between the ingestion of zinc and the incidence of low copper levels, and between low copper levels and CDM. They do not, however, firmly establish an association between the use of Fixodent and CDM. Most of these publications do not mention denture adhesives at all, and those that do fail to mention Fixodent in particular.

More importantly in this regard, in ***Betz*** our Supreme Court reminded us that the test for novelty is whether the trial court "has articulable grounds to believe that an expert witness has not applied accepted scientific methodology in a conventional fashion in reaching his or her conclusions." ***Betz***, 44 A.3d at 53. To the extent that the publications cited by the Appellants do suggest a causal link between Fixodent and CDM,[3] they provide no indication of the scientific methodologies used to establish such a link, including whether the methodologies employed were mere reviews of

[3] The Appellants cite to a publication from the U.S. National Institutes of Health (NIH) that, while not mentioning Fixodent specifically, does indicate that while regular use of zinc-containing denture adhesive creams as directed is not of concern, "chronic, excessive use can lead to zinc toxicity, resulting in copper deficiency and neurologic disease." Appellants' Brief at 33. The NIH publication does not identify what levels of denture cream use would constitute "chronic, excessive use" or describe the bases for this opinion (including the methodologies employed or by whom).

case reports and case series, which, as noted in ***Jacoby***, has routinely been rejected as not constituting a generally accepted methodology. ***See, e.g.***, ***Betz***, 44 A.3d at 55. As a result, to determine the novelty (or lack thereof) regarding the science at issue here, we will look only to the new evidence proffered by the Appellants, including Dr. Lautenbach's Cohort Study and Dr. Askari's Fixodent Blockade Study, to determine whether they, per ***Betz***, apply accepted scientific methodology in a conventional fashion. As we conclude hereinbelow, they do not, and thus the trial court did not err in proceeding with its ***Frye*** analysis.

For their second issue on appeal, the Appellants claim that the trial court erred in its ruling that Dr. Lautenbach's Cohort Study does not provide a methodologically sound basis for an opinion that the use of Fixodent causes CDM. According to the Appellants, Dr. Lautenbach designed and conducted the Cohort Study using generally accepted methodologies and population data routinely employed by epidemiologists, and that any criticisms of the Cohort Study go to its weight rather than its admissibility. Appellants' Brief at 27-28.

Based upon our review of the certified record, we must agree with the trial court that Dr. Lautenbach's Cohort Study is not based upon generally accepted methodologies. In their appellate brief, the Appellants attempt to support the general acceptance of Dr. Lautenbach's methodologies in constructing his cohort study by citing to excerpts from *Methods in*

Observational Epidemiology by Jennifer L. Kelsey. ***Id.*** at 48. Dr. Kelsey's book, however, suggests that the data contained in the Gabreyes Article was insufficient to provide the basis for conducting a retrospective cohort study.

> As in prospective cohort studies, selection of the most appropriate groups to study in retrospective cohort studies requires careful attention to both practical and theoretical issues. … **The group selected must be one in which a large number of people has been exposed to the agent of interest.** A sufficient number of these people must have been exposed at high enough levels that important excess incidence for the diseases under investigation is likely to be detected.

Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 85 at 115 (emphasis added). The Gabreyes Article involved a mere sixteen participants, only twelve of whom reported neurological symptoms, with as few as six of these twelve having used zinc-containing denture cream. The Appellants have not directed us to any evidence that it is a generally accepted methodology to perform a retrospective cohort study based upon the exposure of just six individuals to the agent of interest.

In addition, contrary to the Appellants' contentions, the Gabreyes Article does not itself contain any epistemological evidence based upon generally accepted methodologies. The Appellants claim that the Gabreyes Article "itself found an association between long-term zinc exposure through dental cream use and subsequent neurological injuries such as CDM."

Appellants' Brief at 25. The authors of the Gabreyes Article made no similar claim, however, describing their work "as a retrospective audit of clinical practice rather than clinical research" and indicated that "the audit was observational, based on retrospective review of case records." Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 59 at 2. As such, the Gabreyes Article was a review of a small number of case reports, which even Dr. Lautenbach concedes does not constitute the basis for an epidemiological finding of causation.

This lack of epidemiological support is significant. In ***Trach***, this Court agreed that the expert's use of extrapolation was a generally accepted methodology because it was based upon sound epidemiological evidence. In particular, we permitted an expert to extrapolate, based upon evidence generated from methodologically sound clinical trials, that a medication known to cause certain adverse effects at a lower (recommended) dose could cause increased levels of the same effects if taken in a massive overdose. ***Trach***, 817 A.2d at 117-18. More recently, however, our Supreme Court refused to permit an expert to extrapolate based upon unsound epidemiological data ("case reports, animal studies, and regulatory standards"). ***Betz***, 44 A.3d at 55-57. Here, as in ***Betz***, Dr. Lautenbach's Cohort Study is not based upon any supporting epidemiological evidence produced using generally accepted scientific methodologies.

The trial court focused on another of Dr. Kelsey's requirements for conducting a generally accepted retrospective cohort study, namely the need for sufficient data to obtain an accurate measure of exposure. Trial Court Opinion, 2/7/2014, at 13. The trial court criticized Dr. Lautenbach's use of the Gabreyes Article as the basis for the Cohort Study because it failed to provide Dr. Lautenbach with certain types of seemingly important data, including the type of denture adhesive used, the amount used, the frequency of use, the time-frame between use and the onset of neurological injuries, and whether the use preceded the neurological symptoms. ***Id.*** at 13-14. Particularly troubling for the trial court was the failure to distinguish between the use of Fixodent and Super Poligrip, in substantial part because Super Poligrip contained twice as much zinc as did Fixodent. ***Id.*** According to the trial court, even one of the Appellants' own experts (Dr. Grainger) agreed that the use of Super Poligrip resulted in the delivery of a greater amount of zinc into the body than did Fixodent. ***Id.*** at 13 n.4 (citing Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 7 at 9). Given the difference in exposure levels and the lack of data regarding which denture adhesive the Cohort Study participants used, the trial court found that Dr. Lautenbach's conclusion that 45% of the neurological injuries reported in the Gabreyes Article were caused by the use of Fixodent (because Fixodent had 45% of the relevant market share) constituted "faulty logic and clear litigation bias." ***Id.*** at 14.

At the ***Frye*** hearing, however, Dr. Lautenbach testified that the lack of data identified by the trial court had no effect on his ability to use the Gabreyes Article as the basis for his Cohort Study. N.T., 11/12/2013, at 105. According to Dr. Lautenbach, this data was unnecessary because the authors of the Gabreyes Article relied upon the diagnoses of the treating physicians that their patients' high zinc levels (and low copper levels) resulted from the use of denture adhesives over time. ***Id.*** In other words, it was not necessary for Dr. Lautenbach or the authors of the Gabreyes Article to make independent determinations that the high zinc/low copper levels were caused by the use of denture adhesives because the patients' treating physicians, as a normal part of their clinical practices (including taking patient histories), had made these causation determinations. ***Id.*** at 106. According to Dr. Lautenbach, in each reported case, the treating physician assessed all possible causes and made a clinical assessment that the use of zinc-containing denture adhesives was the cause of the patient's high zinc and low copper levels. ***Id.*** at 112.

Dr. Lautenbach testified that reliance on the diagnoses of treating physicians when performing a cohort study is a generally accepted methodology. ***Id.*** at 157 ("Yes. That's very, very commonly what we do."). On appeal, the Appellants likewise insist that Dr. Lautenbach's reliance on the diagnoses of treating physicians is "unquestionably methodologically sound." Appellants' Brief at 44. Other than citing to Dr. Lautenbach's own

testimony, however, the Appellants provide no substantial support for this contention, as their various citations to the record refer us back to their briefs filed in the trial court and to publications apparently not contained in the certified record on appeal.

Moreover, Dr. Lautenbach's testimony at the ***Frye*** hearing, including both during cross-examination and in response to questioning by the trial court, provided several reasons for the trial court to question the credibility of Dr. Lautenbach's contention that his reliance on the diagnoses of treating physicians is a generally accepted methodology. For example, Dr. Lautenbach admitted that the treating physicians did not apply consistent diagnostic criteria for diagnosing copper deficiency, and the authors of the Gabreyes Article agreed that they were unaware of the "extent the treating clinician applied … diagnostic criteria in the management of their patients."[4] N.T., 11/12/2013, at 108-09. At the completion of the study, the authors of

[4] In addition, the treating physicians in the Gabreyes Article lacked a consistent case definition of CDM. N.T., 11/12/2013, at 108-09. The Gabreyes Article does not even refer to CDM specifically, instead reporting only that twelve patients displayed "neurological features of copper deficiency." Gabreyes Article at 2. Despite this, Dr. Lautenbach assumed that the twelve patients suffering from said "neurologic features" all suffered from CDM, even though (given the lack of a consistent case definition) some of these patients may not have had the same symptoms or even the same disease. Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 11 (Lautenbach 2013 Expert Report) ¶ 43. ***Cf. In re Denture Cream Products Liability Litigation***, 795 F. Supp. 2d 1345, 1361 (S.D.Fla. 2011) ("There are very good reasons to believe the cases reported in the literature suggesting an association between denture cream and neurological symptoms included people who were not suffering from [CDM].").

the Gabreyes Article destroyed the clinical records of the patients, and thus Dr. Lautenbach could not independently evaluate the correctness of the treating physicians' diagnoses. ***Id.*** at 103. The Gabreyes Article also did not identify the treating physicians by name, and thus Dr. Lautenbach could not assess the skill level or ability of these particular physicians to diagnose the causes of disease generally or CDM specifically, including, among other things, whether the treating physicians adequately considered alternatives to the use of denture adhesives to explain their patients' high zinc levels. ***Id.*** at 149.

Finally, while the Gabreyes Article purported to identify cases from 2005 through 2010, it did not identify **when** specifically the patients identified as having copper deficiency caused by the use of zinc-containing denture adhesives were identified and included in the study. ***Id.*** at 149. This left open the possibility that most or all of the treating physicians may have diagnosed the use of denture adhesives as the cause of the low copper levels after 2008, when articles speculating on a possible association between denture cream and CDM began to appear, including an influential June 2008 article in Neurology that reviewed four case reports. Global Frye Motion to Exclude General Causation Expert Testimony, 9/17/2013, Exhibit 37 (S.P. Nations et al., *Denture Cream: an unusual source of excess zinc, leading to hypocupremia and neurologic disease*, 71 Neurology 639 (2008)). As the authors of the Nations article acknowledged, "[w]e **speculate** that

the copper deficiency in these four patients was secondary to ingestion of denture cream."). ***Id.*** at 642 (emphasis added).

For these reasons, we must agree with the trial court's determination that Dr. Lautenbach's Cohort Study is not based upon generally accepted methodologies. As described herein, the Gabreyes Article did not provide sufficient data on exposure to the agent of interest (zinc-containing denture cream) to provide the basis for a retrospective cohort study. To this end, we do not agree with the Appellants' contention that the trial court's criticisms of the Cohort Study go to its weight rather than to its admissibility. A ***Frye*** analysis requires the trial court to evaluate whether the expert's methodologies have general acceptance in the relevant scientific community. The trial court here properly concluded that Dr. Lautenbach did not apply generally accepted methodologies, and instead attempted to convert a limited number of case reports into a retrospective cohort study without sufficient data to do so. No relief is due.

For their third issue on appeal, the Appellants claim that the trial court abused its discretion or erred as a matter of law in its ruling that Dr. Askari's Fixodent Blockade Study does not provide a methodologically sound basis for an opinion that the use of Fixodent increases zinc exposure and blocks the retention of copper in the body. As described in detail hereinabove, in the Fixodent Blockade Study, twelve participants ingested encapsulated Fixodent three times a day, six ingest encapsulated zinc acetate three times a day,

and six ingested an encapsulated placebo three times a day. While there were no statistically significant differences in copper levels in the blood or urine of those ingesting Fixodent and those ingesting the placebo, there was a statistically significant difference between the copper levels in the fecal excretions of those two groups. From this data, Dr. Askari opined that Fixodent blocks copper retention and thus causes CDM.

The trial court found that the Fixodent Blockade Study provides no firm basis for concluding that the ingestion of Fixodent causes CDM. Trial Court Opinion, 2/7/2014, at 18-19. We agree. At best, Dr. Askari's analysis of the results of the testing of fecal excretions establishes that the ingestion of Fixodent may result in a temporary negative copper balance for a short time immediately after ingestion, during which the body excretes more copper than it retains. There is a significant "analytical gap" between a narrow finding that the ingestion of Fixodent may result in a temporary negative copper balance in feces excretions and the broad proposition that the ingestion of zinc-containing Fixodent every day for many years may result in a copper deficiency in the entire body severe enough to result in neurologic injuries.

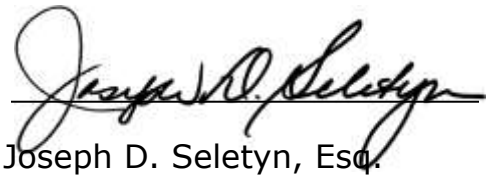
Identifying Fixodent as a cause of a temporary negative copper balance could potentially be one intermediate step in proving that Fixodent causes CDM, but it would, at a minimum, also require proof of a demonstrable link between a temporary negative copper balance and a

copper deficiency of sufficient severity to cause neurologic injury. Because Dr. Askari's Fixodent Blockade Study does not establish any such link, it cannot serve as the basis for a scientific opinion that the ingestion of Fixodent causes CDM. Accordingly, we conclude that the trial court did not abuse its discretion or err in its decision to exclude the Fixodent Blockade Study on the grounds that it failed to utilize a generally accepted methodology to opine as to a causal link between Fixodent and CDM.

For their fourth issue on appeal, the Appellants argue that the trial court erred in granting the Appellees' motion for summary judgment. Having concluded hereinabove, however, that the trial court properly excluded the reports and testimony of the Appellants' expert witnesses on causation, the Appellants' fourth issue on appeal is without merit. The Appellants do not contest that proof of causation is an element of all of the causes of action asserted against the Appellees, and contend instead only that the trial court erred in excluding the testimony and reports of their general causation witnesses. Appellants' Brief at 62. Having concluded that the trial court did not so err, the trial court properly granted summary judgment in favor of the Appellees.

Orders affirmed.

Judgment Entered.



Joseph D. Seletyn, Esq.
Prothonotary

Date: 11/12/2015