SUPERIOR COURT OF CALIFORNIA

COUNTY OF LOS ANGELES

COORDINATION PROCEEDING SPECIAL TITLE (Rule 2.550) ACTOS PRODUCT LIABILITY CASES	LASC Case No: JCCP4696 COURT'S RULING AND ORDER RE: 1) DEFENDANTS' MOTION TO STRIKE THE SPECIFIC CAUSATION OPINIONS OFFERED BY DR. NORM SMITH, M.D.; AND 2) DEFENDANTS' MOTION FOR NONSUIT
THIS DOCUMENT RELATES TO: *Jack Cooper et al. v. Takeda Pharmaceuticals America, Inc., et al.*, San Francisco Superior Court Case No. CGC-12-518535	Trial: February 19, 2013

I.

BACKGROUND

In this coordinated litigation, Plaintiffs have sued the Defendants, manufacturers of the prescription drug Actos (the trade name for pioglitazone HC1 tablets), which is used to treat type 2 diabetes mellitus. Plaintiffs allege that they developed bladder cancer from ingesting the drug. The Plaintiffs in these cases allege various theories for products liability (including claims for negligence, strict liability – failure to warn, strict liability – defective design, breach of the

implied warranty for a particular purpose, breach of the implied warranty of merchantability, violation of the Unfair Competition Law ("UCL") and False Advertising Law ("FAL"), deceit by concealment, negligent misrepresentation, and violation of the Consumer Legal Remedies Act ("CLRA")).

Jack Cooper and Nancy Cooper are Plaintiffs in one of the coordinated cases. This Court granted a preference trial due to Plaintiff Jack Cooper's health on October 30, 2012. Trial commenced on February 19, 2013, with opening statements occurring on February 28, 2013.

Prior to commencement of the trial, Defendants moved for an order *in limine* to exclude the opinions of Dr. Norm Smith, who has been proffered by Plaintiffs as an expert on genotoxicity, general causation, and specific causation. On February 11, 2013, the Court deferred a ruling on the motion *in limine*, pending a hearing pursuant to Evidence Code §402 to assess the admissibility of Dr. Smith's opinions. On March 18, 2013, the Court held the §402 hearing. The Court has ruled that Dr. Smith's opinions are admissible with respect to his opinion on general causation, and has excluded Dr. Smith's opinions on the genotoxicity of Actos.

In the instant Ruling and Order, the Court addresses the admissibility of Dr. Smith's opinion on specific causation – that Actos ingestion was, to a reasonable degree of medical certainty[1], the cause of Plaintiff Jack Cooper's bladder cancer. Following the §402 hearing, the Court had tentatively found that Dr. Smith had not established a foundation for his opinion on specific causation. The Court requested the parties brief the issue further, and entertained argument from both sides on the admissibility of Dr. Smith's specific causation opinion on March 22, 2013.

Subsequently, on March 25, 2013, the Court deferred ruling on the admissibility of Dr.

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[1] March 18, 2013 Transcript of §402 Hearing of Dr. Norm Smith, dated March 18, 2013 ("§402 Hearing Transcript") at 149:5-7.

Smith's specific causation opinion, and permitted Plaintiffs to call Dr. Smith to the stand for examination. The Court made this order, subject to providing Defendants the opportunity to file a motion to strike Dr. Smith's opinion on specific causation.

Defendants moved to strike Dr. Smith's specific causation opinion. Concurrently, Defendants filed a motion for judgment of nonsuit, on the following grounds:

> 1) All of Plaintiffs' claims fail because specific causation is an essential element of each of their causes of action, and that Plaintiffs have no admissible expert testimony to establish that Actos (pioglitazone HC1) caused Plaintiff Jack Cooper's bladder cancer; and
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> 2) Plaintiff Nancy Cooper's cause of action for Loss of Consortium is derivative of Plaintiffs' substantive claims and fails for the same reasons as those claims.

The Court deferred a ruling on these issues, as well. In the interim, the jury returned a verdict in favor of Plaintiffs on April 26, 2013.

For the reasons discussed *infra,* the Court, having considered Dr. Smith's deposition transcript; his testimony at the §402 hearing; all exhibits duly admitted; Dr. Smith's specific causation testimony at trial; and the written and oral arguments of the parties addressing the issue, determines that Dr. Smith's specific causation opinion is not admissible and must be excluded. As such, the Court grants Defendants' motion to strike Dr. Smith's opinions on specific causation.

The motion for a judgment of nonsuit is granted.[2]

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[2] In light of the Court's order granting the motion for nonsuit, the Defendants' motion for a directed verdict, filed April 12, 2013, is moot.

II.

MOTION TO STRIKE DR. SMITH'S SPECIFIC CAUSATION OPINION

Standards on Admissibility of Expert Opinion

Evidence Code §801(b) provides:

> If a witness is testifying as an expert, his testimony in the form of an opinion is limited to such an opinion as is:
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> ....
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> **(b)** Based on matter (including his special knowledge, skill, experience, training, and education) perceived by or personally known to the witness or made known to him at or before the hearing, whether or not admissible, that is of a type that *reasonably may be relied upon* by an expert in forming an opinion upon the subject to which his testimony relates, unless an expert is precluded by law from using such matter as a basis for his opinion. (Emphasis added.)

Under Evidence Code §802, "[a]witness testifying in the form of an opinion may state on direct examination the reasons for his opinion and the matter (including, in the case of an expert, his special knowledge, skill, experience, training, and education) upon which it is based, unless he is precluded by law from using such reasons or matter as a basis for his opinion. The court in its discretion may require that a witness before testifying in the form of an opinion be first examined concerning the matter upon which his opinion is based."

In *Jennings v. Palomar Pomorado Health Systems, Inc.* (2003) 114 Cal.App.4th 1108, 1117, the Court of Appeal noted:

> [E]ven when the witness qualifies as an expert, he or she does not possess a carte blanche to express any opinion within the area of expertise. For example, an expert's opinion based on assumptions of fact without evidentiary support, or on speculative or conjectural factors, has no evidentiary value and may be excluded from evidence. Similarly, when an expert's opinion is purely conclusory because unaccompanied by a reasoned explanation connecting the factual predicates to the ultimate conclusion, that opinion has no evidentiary value because an "expert opinion is worth no more than the reasons upon which it rests." (Internal citations omitted).

The matter relied on "must provide a reasonable basis for the particular opinion offered,

and...an expert opinion based on speculation or conjecture is inadmissible." *Geffcken v. D'Andrea* (2006) 137 Cal.App.4th 1298, 1311. In determining reliability, the emphasis should be on the "factors considered and the reasoning employed." *Id.* "Where an expert bases his conclusion upon assumptions which are not supported by the record, upon matters which are not reasonably relied upon by other experts, or upon factors which are speculative, remote or conjectural, then his conclusion has no evidentiary value." *Id.*; *see also Bushling v. Fremont Med. Ctr.* (2004) 117 Cal.App.4th 493, 510.

""Exclusion of expert opinions that rest on guess, surmise or conjecture is an inherent corollary to the foundational predicate for admission of the expert testimony: will the testimony assist the trier of fact to evaluate the issues it must decide?"" *Sargon Enters., Inc. v. Univ. of Southern California* (2012) 55 Cal.4th 747, 770 ("*Sargon*") (citing *Jennings v. Palomar Pomorado Health Systems, Inc., supra,* 114 Cal.App.4th at 1117). "[U]nder Evidence Code sections 801, subdivision (b), and 802, the trial court acts as a *gatekeeper* to exclude expert opinion testimony that is (1) based on matter of a type on which an expert may not reasonably rely, (2) based on reasons unsupported by the material on which the expert relies, or (3) speculative. Other provisions of law, including decisional law, may also provide reasons for excluding expert opinion testimony." *Id.* at 771-772 (emphasis added).

The *Sargon* court further expanded on the Court's "gatekeeper" role, stating as follows:

> [C]ourts must also be cautious in excluding expert testimony. The trial court's gatekeeping role does not involve choosing between competing expert opinions. The high court warned that the gatekeeper's focus "must be solely on principles and methodology, not on the conclusions that they generate." (*Daubert v. Merrell Dow Pharmaceuticals, Inc.* [(1993)] 509 U.S. [579,] 595.) The advisory committee on the 2000 amendments to Federal Rules of Evidence, rule 702 (28 U.S.C.), which codified the rule established in *Daubert*, noted that the trial court's task is not to choose the most reliable of the offered opinions and exclude the others: "When a trial court, applying this amendment, rules that an expert's testimony is reliable, this does not necessarily mean that contradictory expert testimony is unreliable. The amendment is broad enough to permit testimony that is the product of competing principles or methods in the same field of expertise." (Advisory Com. Notes to Fed. Rules Evid., rule 702, 28 U.S.C.)

> The trial court's preliminary determination whether the expert opinion is founded on sound logic is not a decision on its persuasiveness. The court must not weigh an opinion's probative value or substitute its own opinion for the expert's opinion. Rather, the court must simply determine whether the matter relied on can provide a reasonable basis for the opinion or whether that opinion is based on a leap of logic or conjecture. The court does not resolve scientific controversies. Rather, it conducts a "circumscribed inquiry" to "determine whether, as a matter of logic, the studies and other information cited by experts adequately support the conclusion that the expert's general theory or technique is valid." [Citation.] The goal of trial court gatekeeping is simply to exclude "clearly invalid and unreliable" expert opinion. [Citation.] In short, the gatekeeper's role "is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom *the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.*" [Citation.] *Sargon, supra,* 55 Cal.4th at 772 (emphasis added).

As part of the Court's duties under Evidence Code §802, as set forth in *Sargon,* the Court "may inquire into...not only the type of material on which an expert relies, but also whether that material *actually supports the expert's reasoning.* 'A court may conclude that there is simply too great an analytical gap between the data and the opinion proffered.'" *Sargon,* 55 Cal.4th at 771 (citing *General Electric Co. v. Joiner* (1997) 522 U.S. 136, 146) (emphasis added).

Discussion

With all of these standards in mind, Defendants argue that Dr. Smith lacks a reliable foundation to opine that Actos specifically caused Mr. Cooper's bladder cancer.

Under California law, Plaintiffs must prove that Actos was a substantial factor in bringing about Mr. Cooper's injury. *Bockrath v. Aldrich Chemical Co.* (1999) 21 Cal.4th 71, 79. "[T]he substantial factor standard is a relatively broad one, requiring only that the contribution of the individual cause be more than negligible or *theoretical.*" *Id.* (Emphasis added.) To arrive at his specific causation opinion, Dr. Smith testified at the 402 hearing and later at trial that he performed what is known as a differential diagnosis.[3]

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[3] Dr. Smith did not use this term at his December 17, 2012 deposition.

Differential diagnosis is "the *patient-specific process* of elimination that medical practitioners use to identify the 'most likely' cause of a set of signs and symptoms from a list of possible causes" and is "undoubtedly important to the question of specific causation." See Matthew Bender, *Drug Product Liability*, §5.01(b) (2012) (emphasis added).

"Differential diagnosis is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated. *It is typically performed after taking physical examinations and medical histories, and reviewing clinical tests*." *Id.* (Emphasis added.)

"The technique has widespread acceptance in the medical community, and the overwhelming majority of courts have held that a medical opinion on causation based upon a reliable differential diagnosis provides a valid foundation for expert testimony[.]" *Id.*

Importantly, "[m]ost courts require that a reliable differential diagnosis at least *consider* other factors that could have been the sole cause of the plaintiff's injury. Nevertheless, the expert need not rule out every conceivable cause for his or her differential-diagnosis-based opinion to be admissible." *Id.*

Dr. Smith, when asked at the §402 hearing if he performed a differential diagnosis on the possible causes of Mr. Cooper's bladder cancer, stated that he did. Dr. Smith further testified at trial to having performed a differential diagnosis.[4] He testified in pertinent part that he "ruled out" potential causes, as follows:

> A. Particularly smoking, environmental exposures, occupational exposure. And sometimes those that are hard to define, you know, a single agent that [Mr. Cooper] may have been exposed to. But if you look once again at all of that, you don't really get the hazard ratios out of the ones whereas in the Mamtani article, that seems to fit Mr. Cooper very well with his, you know, 50-plus thousand milligrams cumulative dose greater than five years that has a hazard ratio of almost seven. So I think in [Mr. Cooper's] case when you try to weigh that all in, that's really what is formative of the opinion that Actos caused bladder cancer for

[4] March 26, 2013 Trial Transcript at 10:24-11:22.

Mr. Cooper.[5]

The following exchange also occurred between Plaintiff's counsel, Mr. Miller, and Dr. Smith during the §402 hearing:

> Q....Is there anything in Mr. Cooper's history that's even half as risky [as Actos] scientifically? Former smoking?
>
> A. Again, the relative risks of that go down to the ones, and this new article would suggest maybe even lower than that if you quit at age 40.
>
> Q. Any literature out there that shows a retired Pacific phone supervisor would have a risk of even half the Actos risk?
>
> A. Not to my knowledge, no.
>
> Q. The fact that he has diabetes in and of itself, is diabetes a risk factor for bladder cancer?
>
> A. I would say it's a little bit controversial. There are some papers that say it causes a slight risk. Other papers refute that.[6]

Further, Dr. Smith testified as follows in response to Mr. Miller's questioning:

> Q. Dr. Smith, in the studies we went through when they factor in the relationship to Actos and bladder cancer, people on both sides of the study had diabetes; right?
>
> A. Yes.
>
> Q. And people on both sides of the study were older white males in spots; right?
>
> A. Yes.
>
> Q. And so the association of Actos to bladder cancer was irrespective of the fact that they had old white men with diabetes.
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> A. That's where in those studies, it says adjusted for sex, race, smoking, hemoglobin, A1c, et cetera, yes.
>
> Q. So after you completed your differential diagnosis, filed your evidence-based

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[5] March 18, 2013 §402 Hearing Transcript at 52:25-53:8.

[6] March 18, 2013 §402 Hearing Transcript at 53:18-54:4.

medicine, do you hold the opinion to a reasonable degree of medical certainty that a substantial increasing factor, a cause of Mr. Cooper's bladder is Actos –

A. Yes.

Q. –his long term use? ….[7]

However, it is evident to the Court that the manner in which Dr. Smith conducted his differential diagnosis is based on speculation, is not reliable, not done with the intellectual rigor expected of an expert, and is therefore inadmissible under prevailing California law.

Dr. Smith's own peer-reviewed study, entitled "Bladder Cancer Risk From Occupational and Environmental Exposures" (also referred to as the "Kiriluk study"[8]) identifies several possible causes of bladder cancer. In particular, the potential "causative factors" are identified in the Kiriluk study as cigarette smoking; cigar/pipe smoking; 1-Naphthylamine, 2-naphthylamine, benzidine, 4-aminobiphenyl, ortho-toluidine and chloroaniline; high arsenic levels; polyaromatic hydrocarbons; ionizing radiation; schistosoma haematobium; chronic inflammation; immunosuppression; oxazophosphorines; phenacetin; and *aristolochia fangchi*. The "indeterminate" factors are identified as second-hand smoke; chlorinated water; halogentated hydrocarbons; low arsenic levels; HPV; pioglitazone; nitrates and nitrites; and Vitamin D deficiency. Dr. Smith confirmed at deposition that "there is a huge, huge list of things that have been listed as risk factors for bladder cancer[.]"[9]

There is nothing before the Court, in the form of Dr. Smith's deposition testimony, his testimony before the Court during the §402 hearing, or his trial testimony demonstrating that Dr. Smith exercised the care of a professional expert or displayed the intellectual rigor expected of such an expert.

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[7] March 18, 2013 §402 Hearing Transcript at 54:22-55:18.

[8] Master trial exhibit 1678.

[9] Deposition of Dr. Norm Smith at 42:9-11.

He did not sufficiently consider these causes, and then rule them out *as to Mr. Cooper specifically*, in order to reach his specific causation opinion based on a differential diagnosis.

Critically, the following exchange occurred during the §402 hearing between Defendants' counsel, Mr. Parker, and Dr. Smith:

> Q. In your paper, not to pull it back up, your Kirulik paper, there were a long list of known causes of bladder cancer; correct?
>
> A. Yes.
>
> Q. And you did not sit down with the Coopers and do a medical history to find out to what extent he – Mr. Cooper – may or may not have been exposed to any of those.
>
> A. I reviewed the medical history.
>
> Q. So what you get in the medical history is what somebody like Dr. Brunsting is commenting on as Mr. Cooper comes in to him each week or whatever may be causing a problem.
>
> A. Or his oncologist.
>
> Q. And did you see anybody undertaking a history for purposes of assessing the underlying cause of bladder cancer at any point in [Mr. Cooper's] medical history?
>
> A. You do that as part of social history, family history, et cetera.
>
> Q. My question is when you went through the medical records, you didn't find any such history of someone attempting to look to see if he had been exposed to things that you've determined are causes of bladder cancer.
>
> A. The oncologist specifically mentions no occupational exposures, no history of occupational exposures.
>
> Q. And who is it that you're referring to?
>
> A. The patient's medical oncologist [Dr. Xavier].
>
> ....
>
> Q. [In] Dr. Xavier's notes we will find a comprehensive history where she went into the list of known causes of bladder cancer. Is that what you're telling us?

A. *I don't know the answer to that.*[10]

Dr. Smith, at deposition, when asked what Mr. Cooper did for a living, testified that he could not recall.[11] When asked whether he knew if Mr. Cooper had any exposures at his workplace that had any sort of association with bladder cancer, Dr. Smith testified that it was "a difficult question to answer because…we don't understand all the exposures."[12] Absent a foundational basis for ruling in, and then ruling out, these occupational and environmental exposures (potential exposures which Dr. Smith identifies as belonging to a "huge list"), Dr. Smith could not reliably perform a differential diagnosis to arrive at his specific causation opinion.

Further, the following exchange occurred at the §402 hearing:

> Q. By Mr. Miller: And the basis for your opinion that Actos is a substantial contributing factor to Mr. Cooper, Actos is a substantial contributing factor to Mr. Cooper having bladder cancer is based upon, as you describe in your record, Takeda's own studies; right, sir?
>
> A. It's a combination of all the published literature, the Takeda studies, experience of taking care of bladder cancer patients, experience of having written on exposures and risks for bladder cancer.[13]

In the Court's view, while such testimony may demonstrate a basis for Dr. Smith's general causation opinion, it confirms that the methodology employed by Dr. Smith in reaching his *specific* causation opinion is inherently unreliable.

Dr. Smith testified at the §402 hearing that, prior to his deposition, he did not meet with the Coopers or examine Mr. Cooper before he rendered his opinion in this case; never spoke to

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[10] March 18, 2013 §402 Hearing Transcript at 138:15-139:23 (emphasis added).

[11] December 17, 2012 Deposition Transcript at 182:19-22.

[12] December 17, 2012 Deposition Transcript at 182:23-183:4.

[13] March 18, 2013 §402 Hearing Transcript at 148:20-149:1.

Mr. Cooper's doctors; did not read the depositions of Mr. or Mrs. Cooper before he reached his opinion in this case; and did not read the deposition of Dr. Brunsting (Mr. Cooper's prescribing doctor).[14] Dr. Smith confirmed the same during his trial testimony.[15]

Plaintiffs maintain that Dr. Smith need not have personally interviewed Mr. Cooper or his physicians in order for his specific causation opinion to be admissible. To be sure, the "Comments" section of Evidence Code §801(b) provides that "[a] physician may…rely on reports and opinions of other physicians." Evidence Code §801, "Comments" (citing *Kelley v. Bailey* (1961) 189 Cal.App.2d 728; *Hope v. Arrowhead & Puritas Waters, Inc.* (1959) 174 Cal.App.2d 222). Witkin states that a doctor may base an opinion on a diagnosis or examination made by another doctor. 1 Witkin, California Evidence, §34 (5th Ed. 2012) (citing *Christiansen v. Hollings* (1941) 44 Cal.App.2d 332, 347; *Hope v. Arrowhead & Puritas Waters* (1959) 174 Cal.App.2nd 222, 230 *Kelley v. Bailey* (1961) 189 Cal.App.2nd 728, 737 *People v. Campos* (1995) 32 Cal.App.4th 304, 308; and *Shugart v. Regents of Univ. of Calif.* (2011) 99 Cal.App.4th 499, 505).

As such, the fact that Dr. Smith did not examine or interview Mr. Cooper does not, by itself, render his specific causation inadmissible. However, Dr. Smith *was* required to otherwise establish a reliable foundation for his differential diagnosis, which he did not do as to Mr. Cooper. Dr. Smith's testimony that Dr. Xavier mentioned "no history of occupational exposures", and his reliance on that mere statement, is not sufficient, from a foundational standpoint, to rule in, and rule out, such potential exposures to reach a differential diagnosis as to the specific cause of Mr. Cooper's bladder cancer.

The problems with the foundation for Dr. Smith's differential diagnosis were further

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[14] March 18, 2013 §402 Hearing Transcript at 137:22-138:14.

[15] March 26, 2013 Trial Transcript at 35:22-38:21.

illustrated at his deposition, where he stated he could not testify as to whether, *inter alia*, Mr. Cooper was exposed to secondhand smoke at his workplace, whether he may have had any exposures at his workplace that have any association with bladder cancer, and whether he may have had exposure to anything during his Army service.[16] Ultimately, Dr. Smith testified that he had not taken a history from Mr. Cooper regarding his exposures to potential bladder carcinogens over time; instead, he "simply reviewed [Mr. Cooper's] medical record."[17] Again, ruling in, and ruling out, potential causes of Mr. Cooper's bladder cancer is critical for purposes of establishing a foundation as to Dr. Smith's specific causation opinion by way of a differential diagnosis.

With respect to Dr. Smith's opinion ruling out Mr. Cooper's smoking as a cause of his bladder cancer, the following exchange occurred at trial between Takeda's counsel and Dr. Smith:

> Q. All right. Now, you told the jury this morning that you reviewed that large notebook that we were given this morning of medical records, correct?
>
> A. And that was present at the deposition back in December.
>
> ...
>
> Q. And yet, Dr. Smith, sir, despite reading those records, you were totally unaware that they were records reporting that [Mr. Cooper] had stopped smoking in the 1990's. Isn't that true, sir?
>
> A. There's discrepancies within the chart which we talked about before. There are places in the chart that say never smoker. There are also places that say 1990's.
>
> Q. Doctor, I'm going to ask you a specific question. Isn't it true that as of the time we took your deposition, you were unaware of any record reporting that he had stopped in the 1990's?

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[16] December 17, 2012 Deposition Transcript at 182:16-183:11 (testifying, *inter alia*, that he did not know that Mr. Cooper was in the Corps of Army Engineers in the 1950s, and that he could not opine whether Mr. Cooper was exposed to anything during his Army service).

[17] December 17, 2012 Deposition Transcript at 184:8-13.

A. My impression was that he had stopped in the 1970's, correct.

Q. So you saw no record. This is my question. Despite claiming that you read the records, you saw no record that reported that he had stopped in the 1990's. Isn't that true?

A. I did not recall at that time, correct.

Q. … [Y]ou can then agree that for purposes of forming your opinion, you did not weigh whether and to what extent if he smoked for 20 years or 40 years would factor into your opinion because you didn't know then. Isn't that true?

A. I was under the impression, once again, that he had quit in 1974. I was not aware of any documentation at that time of 1990 something.[18]

It is evident to the Court that the disparities in the record as to the date Mr. Cooper stopped smoking do not provide a reliable basis for Dr. Smith's differential diagnosis. In fact, Dr. Smith testified that his information that Mr. Cooper stopped smoking in the 1970s came from Plaintiff's counsel, Mr. Miller.[19] This information, according to Dr. Smith, came from having "met with counsel for Mr. Cooper many times, [having] had many discussions [with Plaintiffs' counsel], and [having] had many e-mails [with Plaintiffs' counsel]" in the year leading up to Dr. Smith's deposition.[20]

However, Mr. Cooper's records, which have been duly admitted into evidence, all state that Mr. Cooper ceased smoking at various dates in the 1990s.[21] Ultimately, without knowing the date Mr. Cooper ceased smoking, Dr. Smith could not (and did not) properly rule out

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[18] March 26, 2013 Trial Transcript at 39:22-40:27.

[19] March 26, 2013 Trial Transcript at 42:3-6.

[20] March 26, 2013 Trial Transcript at 41:27-42:2.

[21] See, e.g. trial exhibits 1014-236 (December 8, 2011 record from Scripps Mercy Hospital, stating that Mr. Cooper quit smoking in 1994 with a 40-year history of smoking 1 pack per week); 1012-269 (December 17, 1999 record from Scripps Physicians-Mercy Medical Group stating that he quit smoking seven years prior); 1011 (December 9, 2011 record from San Diego Heart and Vascular Associates, stating that Mr. Cooper stopped smoking in 1994); and 2011 (November 1, 2001 record from Hillcrest Urological Medical Group, indicating that Mr. Cooper stopped smoking in 1995).

smoking as a potential cause of Mr. Cooper's bladder cancer in conducting his differential diagnosis – given Dr. Smith's trial testimony that: 1) smoking is a significant risk factor for bladder cancer[22]; and 2) the time since cessation of smoking is important in assessing smoking as a risk factor.[23]

An expert physician, evaluating a patient's medical records, would thoroughly study them, noting anything of significance, and follow up on every detail necessary to come up with an accurate diagnosis. Since the date Mr. Cooper stopped smoking and his level of tobacco consumption is a critical fact in the diagnosis, an expert would do all he or she could to resolve any ambiguities. Pursuant to *Sargon,* Dr. Smith was required to "employ[] in the courtroom *the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.*" *Sargon, supra,* 55 Cal.4th at 772 (emphasis added).

For instance, Mr. Cooper's medical record from Dr. Xavier dated September 17, 2012[24] indicates that Mr. Cooper was suffering from "[m]oderate emphysema."

Dr. Smith was questioned by Takeda's counsel:

> Q. And emphysema, as we just discussed, would be some indication of the burden that tobacco, either in cigarettes or pipes, might have in some who smoked 40 years. Would you agree?
>
> A. I would certainly not quantify myself as a – as an emphysema expert, a COPD expert, a radiologic expert. I don't feel I have an opinion on the question.[25]

Yet, Dr. Smith, not having noticed the multiple medical record entries indicating smoking cessation in the 1992-4 timeframe or Mr. Cooper's history of moderate emphysema, steadfastly continued to use as basis for his opinion the statement of Mr. Cooper's attorney that Mr. Cooper

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[22] March 26, 2013 Trial Transcript at 16:16-17:12.

[23] March 26, 2013 Trial Transcript at 16:16-17:12, 17:21-18:8.

[24] See trial exhibit 1015b-002.

[25] March 26, 2013 Trial Transcript at 54:5-12

stopped smoking in the 1970s.

Aside from the Court's determination that Dr. Smith did not adequately rule out smoking as a cause of Mr. Cooper's bladder cancer, there are other portions of Mr. Cooper's medical history which Dr. Smith did not consider. Other medical records that were not reviewed by Dr. Smith (and which therefore did not aid in the formulation of his differential diagnosis) indicate that Mr. Cooper has a history of chronic kidney disease[26] and that he experienced skin cancer at various times.[27] There is nothing in the record to indicate that Dr. Smith reviewed these records in reaching his differential diagnosis.[28] These records in particular are important because if diabetes is a risk factor for bladder cancer, they are a measure of the seriousness of Mr. Cooper's diabetes.

Even so, the medical records that Dr. Smith *did* review are limited in time and in scope. Notwithstanding Dr. Brunsting's testimony that Mr. Cooper had been a patient of his for twenty years, the oldest record from Dr. Brunsting in trial exhibit 2047 dates from 2006.[29] Exhibit 2047 also includes Dr. Brunsting's lab results and progress notes from visits in 2009, 2010, and 2011.[30]

Again, an expert physician, evaluating a patient's medical records, would thoroughly study them, note anything of significance, and follow up on every detail necessary to formulate

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[26] March 26, 2013 Trial Transcript at 83:18-84:4

[27] See, e.g., trial exhibit 1011-014, record from Dr. Brunsting (noting, *inter alia,* "basal cell carcinoma on left side of nose" on February 20, 2002 and "basal cell carcinoma on right shin" on November 16, 2009); trial exhibit 006-00005, progress note of September 19, 2012 (indicating "history of basal cell carcinoma of the skin"); trial exhibit 006-00046, progress note of October 18, 2012 (also indicating "history of basal cell carcinoma of the skin").

[28] The mere fact that Dr. Smith testified at trial that he was "aware" of the record reflecting that Mr. Cooper was diagnosed with "moderate emphysema" does not indicate that Dr. Smith actually considered exhibit 1015b-002 as part of his review of Mr. Cooper's medical records.

[29] Trial exhibit JC-22-000001-000006

[30] Trial exhibit JC-07-000012-07-000014; JC-07-000196-JC-07-000216.

an accurate diagnosis. Once the expert realized that the records were incomplete, the expert would require records going back, if possible, to the 1970s. Reviewing medical histories taken during this time period could provide a definitive answer as to when Mr. Cooper stopped smoking, as well as other possible environmental exposures. Instead, Dr. Smith either did not notice the time limitations of the medical records or assumed the records would show no exposure. This is speculation and any such opinion would necessarily be based on a leap of logic or conjecture.

At both the §402 hearing and at trial, Dr. Smith, when stating the basis for his differential diagnosis, did not discuss the risk factors of age, race and gender, saying that these were not risk factors, but rather "demographics." However, at Dr. Smith's deposition, he stated differently, indicating that all three were indeed risk factors:

> Q. Doctor, other risk factors for bladder cancer include being over the age of 60, correct?
>
> A. Yes.
>
> Q. Being a male, correct?
>
> A. Yes.
>
> Q And being white?
>
> A. Yes.[31]

Dr. Smith provided no justification for his change of opinion, nor did he provide any study, any research paper, or any basis whatsoever for his elimination of these patient-specific three risk factors from his differential diagnosis.

At his deposition, Dr. Smith avoided considering the severity of Mr. Cooper's diabetes by simply indicating it was not a risk factor because of unspecified "conflicting studies":

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[31] Deposition of Dr. Norm Smith at 40:2-8.

Q. Okay. By the way, do you – do you consider diabetes itself to be a risk factor for bladder cancer?

A. I don't.

Q. Okay. Why not?

A. You know, I think that the evidence for it is just not strong enough in my mind.

Q. Okay. There is some – there are some studies that have come to that conclusion?

A. There are some, yeah.

Q. Okay. What is it about that body of – you know, there has been about 20 papers now on the topic. Are you aware of that?

A. I wouldn't be able to give you an exact count but . . .

Q. But there has been a number?

A. But there are definitely various studies. But I think that, you know, they're conflicting to a degree.

Q. When you say they're conflicting, what do you mean?

A. Some find that there is an association, others don't find that. There's you know, papers. The methodology of them are different. And, again, I haven't reviewed this for a while but when we were reviewing it for our paper, it's – it struck me that I didn't consider it a risk factor.[32]

Dr. Smith has ruled out diabetes as a risk factor without citing any study, and without differentiating or identifying which conflicting studies he based his opinion on, or identifying even one study that supports his view. A competent expert who claims a foundation for evaluating general causation by critically analyzing research studies cannot throw up his hands and declare "no opinion" because the studies are conflicting. More importantly, as will be discussed *infra*, the very epidemiological studies upon which Dr. Smith relies for his Actos

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[32] Deposition of Dr. Norm Smith at 73:16 - 7418

causation opinion treat the level of the underlying diabetes as a cause of bladder cancer.[33]

The epidemiological studies relied on by Dr. Smith are further emblematic of the problems with Dr. Smith's differential diagnosis. Putting aside the issue of whether epidemiological studies can generally be utilized as a basis for a differential diagnosis, Dr. Smith's reliance on the KPNC nested case control study[34] as a basis for his diagnosis is problematic. The authors of the study cautioned against use of the data in the study for making risk assessments, as Dr. Smith himself acknowledged.[35]

Another example of the flaw in Dr. Smith's reliance on medical literature as a basis for his differential diagnosis is illustrated through the study entitled "Association Between Longer Therapy with Thiazolidinediones and Risk of Bladder Cancer: A Cohort Study", Ronac Mamtani, et al. ("the Mamtani Study"),[36] published in the Journal of the American Cancer Institute. Dr. Smith testified during his §402 hearing that the article concludes that five (5) years of Thiazolidinedione ("TZD") use increases the risk of bladder cancer.[37] Because Mr. Cooper used Actos for "slightly more than five years,"[38] and ingested "50-plus thousand milligrams cumulative dose greater than five years that has a hazard ratio of almost seven," Dr. Smith testified "that's really what is formative of the opinion that Actos caused bladder cancer for Mr. Cooper."[39] Critically, however, Dr. Smith testified during the §402 hearing that he did not

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[33] March 26, 2013 Trial Transcript at 85:1 – 86:6

[34] Master Exhibit 504.

[35] March 26, 2013 Trial Transcript at 74:20-75:10; March 18, 2013 §402 Hearing Transcript at 102:07-104:27.

[36] Trial exhibit 677.

[37] March 18, 2013 §402 Hearing Transcript at 44:14-16.

[38] March 18, 2013 §402 Hearing Transcript at 44:22-24.

[39] March 18, 2013 §402 Hearing Transcript at 53:3-5.

receive the Mamtani article until February 2013 – a date *subsequent* to his deposition.[40] Under such circumstances, Dr. Smith cannot base his specific causation opinion on the Mamtani article. *See* CCP §2034.260; *Kennemur v.* State (1982) 133 Cal.App.3d 907; *Bonds v. Roy* (1999) 20 Cal.4th 140, 148-149.[41]

Other studies upon which Dr. Smith relied in forming his specific causation opinion are also flawed. Dr. Smith, as a general matter, admitted during the §402 hearing that: 1) "when conducting an epidemiological study, scientists go about before they begin the study to identify what the primary [and] secondary endpoints of that study are going to be"; and 2) "secondary end point data is data that must be viewed with caution."[42] However, notwithstanding that testimony, Dr. Smith's opinions were primarily based on such secondary endpoint data.

Further, Dr. Smith was questioned at the §402 hearing as to three additional studies: 1) "Secondary Prevention of Macrovascular Events in Patients with Type 2 Diabetes in the PROactive Study (PROspective Pioglitazone Clinical Trial in macroVascular Events): A Randomized Controlled Trial," by Dormandy, J., et al. (the "PROactive Study" or the "Dormandy Study")[43]; 2) "Risk of Bladder Cancer Among Diabetic Patients Treated With

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[40] March 18, 2013 §402 Hearing Transcript at 129:11-19.

[41] In *Bonds,* the California Supreme Court noted:

> [T]he statutory scheme as a whole envisions timely disclosure of the general substance of an expert's expected testimony so that the parties may properly prepare for trial. Allowing new and unexpected testimony for the first time at trial so long as a party has submitted any expert witness declaration whatsoever is inconsistent with this purpose. We therefore conclude that the exclusion sanction of subdivision (j) applies when a party unreasonably fails to submit an expert witness declaration that fully complies with the content requirements of subdivision (f)(2), including the requirement that the declaration contain "[a] brief narrative statement of the general substance of the testimony that the expert is expected to give." (Subd. (f)(2)(B).) This encompasses situations, like the present one, in which a party has submitted an expert witness declaration, but the narrative statement fails to disclose the general substance of the testimony the party later wishes to elicit from the expert at trial. *Bonds v. Roy, supra,* 20 Cal.4th at 148-149.

[42] March 18, 2013 §402 Hearing Transcript at 94:12-22.

[43] Trial exhibit 1568.

Pioglitazone," by Lewis, J., et al. ("the Lewis Paper")[44]; and 3) "Assessing the Association of Pioglitazone Use and Bladder Cancer Through Drug Adverse Event Reporting," by Piccini, C., et al. (the "Piccini Study").[45] These studies were reviewed by Dr. Smith prior to his retention as an expert (and constituted "the universe of information" Dr. Smith had prior to his co-authoring the Kiriluk study).[46] When questioned whether the body of information in those studies "would not allow [him] to conclude that pioglitazone is a cause of bladder cancer," Dr. Smith stated that it was "indeterminate at that time[.]"[47]

During the §402 hearing, Dr. Smith also testified that there were two studies whose primary endpoints were statistically significant (i.e., a positive association in the primary end point)[48]: "The Use of Pioglitazone and the Risk of Bladder Cancer in People with Type 2 Diabetes: Nested Case-Control Study", by Laurent Azoulay, et al. (known as "the Azoulay Study")[49], and the study entitled "Pioglitazone and Risk Of Bladder Cancer Among Diabetic Patients In France: A Population-Based Cohort Study", by A. Neumann, et al. This latter study is alternatively known as the "Neumann Study" and the "French Study."[50]

The Neumann Study, which frames itself as a cohort study, concludes that "[i]n this cohort of diabetic patients from France, pioglitazone exposure was significantly associated with

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[44] Trial exhibit 1606.

[45] Trial exhibit 685.

[46] March 18, 2013 §402 Hearing Transcript at 96:16-97:24.

[47] March 18, 2013 §402 Hearing Transcript at 99:1-4.

[48] March 18, 2013 §402 Hearing Transcript at 94:23-95:5.

[49] Trial exhibit 691.

[50] Trial exhibit 686.

increased risk of bladder cancer."[51] However, as Dr. Smith admitted during his trial testimony, the study was originally done involving approximately 170,000 people.[52] Dr. Smith further admitted that when the authors did the full study, they were unable to find a statistically elevated risk in the primary end point for bladder cancer and Actos.[53] Dr. Smith admitted that when the authors of the Neumann study looked at the data, they dropped 250,000 people from the study.[54] Dr. Smith further admitted that such a post hoc rejection of data by investigators undisclosed to the scientific community is not good science.[55]

Even aside from Dr. Smith's own testimony about the unreliability of the Neumann study, the authors themselves acknowledged "several limitations," including the fact the study "lacks data on tobacco use, know to be the third main risk factor for bladder cancer after age and male sex[.]"[56] Further, the authors stated that they did "not report data on the duration of diabetes[.]"[57]

The Azoulay Study also suffers from fundamental flaws which the Court wishes to highlight. The Azoulay Study utilized a study cohort, whose incidence rate the authors stated "is consistent with data suggesting an association between type 2 diabetes and an increased risk of bladder cancer."[58] Critically, in discussing the limitations of the Azoulay study, the authors

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[51] Trial exhibit 686 at 1.

[52] March 18, 2013 §402 Hearing Transcript at 113:11-13.

[53] March 18, 2013 §402 Hearing Transcript at 113:14-17.

[54] March 18, 2013 §402 Hearing Transcript at 113:22-24.

[55] March 18, 2013 §402 Hearing Transcript at 114:7-14.

[56] Neumann Study, trial exhibit 686 at 8.

[57] *Id.*

[58] Trial exhibit 691 at 3.

noted that "[a]nother limitation of the general practice research database is the lack of information on certain risk factors for bladder cancer. These include exposure to arsenic, *occupational exposures*, *race/ethnicity*, and family history of bladder cancer."[59] While the authors stated that "it is unlikely that these variables were differentially distributed between ever users of pioglitazone and ever users of other oral hypoglycaemic agents," and opined "that the absence of these variables [did not affect] the internal validity of the study,"[60] the non-consideration of such risk factors pose significant limitations of the study. Moreover, while the Azoulay study did identify smoking as a variable, the Azoulay study did not control for smoking, based on the number of years the subject smoked, when they smoked, or how much they smoked. All of these limitations are problematic with respect to Dr. Smith's reliance on the Azoulay study in forming a specific causation opinion.

In the Court's view, and for the reasons discussed, neither the Neumann study nor the Azoulay study (which, again, were the only two studies relied on by Dr. Smith whose primary endpoints were statistically significant) serve as "reasonable [bases]" for Dr. Smith's specific causation opinion. *Sargon, supra,* 55 Cal.4th at 772. In other words, these studies do not "actually support" Dr. Smith's reasoning. *Id.* at 772.

As discussed *supra,* Dr. Smith testified at deposition that in forming his opinion, he did not rule out the factors of being a white male over the age of 60 – notwithstanding his admission at deposition that these were also risk factors for bladder cancer[61] (and notwithstanding the Neumann study's identification of age and male sex as the first and second main risk factors for

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[59] Trial exhibit 691 at 5.

[60] Trial exhibit 691 at 5.

[61] December 17, 2012 Deposition Transcript at 40:2-12.

bladder cancer, respectively[62]). He confirmed this during his trial testimony.[63] As such, Dr. Smith's contrary opinion, expressed at different points of his testimony that these are not risk factors but are "demographic factors"[64] is not persuasive, in light of CCP §2034.260 and *Bonds v. Roy, supra,* 20 Cal.4th 148-149.

To the extent Plaintiffs assert that Dr. Smith's general causation opinion renders reliable (and admissible) his specific causation opinion, the Court is not persuaded. There is nothing in Dr. Smith's deposition transcript, nor anything stated at the §402 hearing or during his trial testimony, which demonstrates that Dr. Smith could disregard the identified risk factors as they specifically relate to Mr. Cooper. Again, a differential diagnosis is a *patient-specific* process. It is evident to the Court that Dr. Smith did *no* patient-specific analysis that satisfies the admissibility standards under Evidence Code §§801 and 802.

Moreover, instead of his differential diagnosis being patient specific, based upon a review the patient's medical history, clinical tests, biological and physiological markers, and physical examination of the patient, Dr. Smith rendered a diagnosis based upon speculation, conjecture and leaps of logic. His sole remaining risk factor is not patient-specific, but is instead based upon statistical studies. Dr. Smith's diagnosis would virtually apply to any male, non-smoker who took Actos for more than five years, since he has no physiological or biological markers to distinguish Mr. Cooper's bladder cancer from the myriad of bladder cancer patients he treats with no known causes.

In sum, the Court determines that the bases for Dr. Smith's opinion that Actos caused Mr. Cooper's bladder cancer are inherently unreliable. The studies and other information Dr. Smith

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[62] Neumann Study, trial exhibit 686 at 8.

[63] March 26, 2013 Trial Transcript at 69:16-70:1.

[64] March 26, 2013 Trial Transcript at 79:6-9.

relied on, as outlined *supra* and as discussed thoroughly in Dr. Smith's deposition, the §402 hearing, and the trial testimony, do not support Dr. Smith's conclusion that Actos was a specific cause of Mr. Cooper's bladder cancer. *Sargon, supra,* 55 Cal.4th at 772. Since Dr. Smith's specific causation opinion is based on assumptions of fact without sufficient evidentiary support, as well as on speculative or conjectural factors, that opinion has no evidentiary value. *Jennings v. Palomar Pomorado Health Systems, Inc., supra,* 114 Cal.App.4th at 1117.

In assessing the admissibility of Dr. Smith's opinion on specific causation, the Court emphasizes it is not making a determination as to the weight of that opinion, as *Sargon* commands. *Sargon, supra,* 55 Cal.4th at 772. The only task with which the Court is entrusted is assessing whether his opinion is admissible. To be admissible, it must satisfy the strictures of Evidence Code §801 and 802. In the Court's view, Dr. Smith's specific causation opinion does not satisfy those standards, and on the record before the Court, it must be excluded.

III.

MOTION FOR JUDGMENT OF NONSUIT

Standards on Motions for Nonsuit

"A nonsuit motion tests the sufficiency of the plaintiff's evidence before the defense is presented.... The granting of a nonsuit motion is warranted when, disregarding conflicting evidence, giving plaintiff's evidence all the value to which it is legally entitled, and indulging in every legitimate inference that may be drawn from the evidence, the trial court determines that there is no sufficiently substantial evidence to support a verdict in plaintiff's favor...." *County of Kern v. Sparks* (2007) 149 Cal.App.4th 11, 16.

In determining a motion for nonsuit, courts may not weigh evidence or consider witness credibility. *Castaneda v. Olsher* (2007) 41 Cal.4th 1205, 1214.

"Only after, and not before, the plaintiff has completed his or her opening statement, or

after the presentation of his or her evidence in a trial by jury, the defendant... may move for a judgment of nonsuit." CCP §581c.

Discussion

Under California law, "in a personal injury action causation must be proven within a reasonable medical probability based upon competent expert testimony. Mere possibility alone is insufficient to establish a prima facie case." *Jones v. Ortho Pharma. Corp.* (1985) 163 Cal.App.3d 396, 402-403. Specific causation is an element to each of the Plaintiffs' claims in this litigation.

As noted *supra,* the central basis for Takeda's motion for judgment of nonsuit is premised on the assertions that Dr. Smith's specific causation opinion is inadmissible, and that without Dr. Smith's opinion being admissible, Plaintiffs have not presented at trial any additional evidence that Actos specifically caused Plaintiff Jack Cooper's bladder cancer.

Aside from Dr. Smith's testimony, there is no additional evidence before the Court of specific causation. Given the Court's finding that Dr. Smith's specific causation opinion is not admissible, Plaintiffs did not offer evidence at trial to prove their claims. Further, Plaintiff Nancy Cooper's claim for loss of consortium "is dependent on the existence of a cause of action for tortious injury to [Plaintiff Jack Cooper]." *Hahn v. Mirda* (2007) 147 Cal.App.4th 740, 746; *Taylor v. Elliott Turbomachinery Co., Inc.* (2009) 171 Cal. App. 4th 564, 596 n.16.

For these reasons, the Court grants the motion for nonsuit.

IV.

CONCLUSION AND ORDER

For the reasons discussed *supra,* the Court, in its mandated role as a "gatekeeper" pursuant to *Sargon*, finds that Dr. Smith's specific causation opinion is without foundation, and does not comply with the admissibility standards under Evidence Code §§801 and 802, and

California law. Accordingly, Defendants' motion to strike Dr. Smith's opinions on specific causation is granted. The Court, having determined that Dr. Smith's opinion on specific causation is not admissible, grants the motion for judgment of nonsuit. Defendants shall submit a proposed judgment forthwith. Plaintiffs shall have ten (10) days from the receipt of said judgment to object to the form of the judgment.

Dated: May 1, 2013

KENNETH R. FREEMAN

Kenneth Freeman
Judge of the Superior Court