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APPROVAL OF THE APPELLATE DIVISION

SUPERIOR COURT OF NEW JERSEY
APPELLATE DIVISION
DOCKET NO. A-2633-08T3

KAMIE S. KENDALL,

Plaintiff-Respondent,

v.

HOFFMAN-LA ROCHE, INC.; ROCHE LABORATORIES, INC.; F. HOFFMAN-LA ROCHE LTD.; and ROCHE HOLDING LTD.,

Defendants-Appellants.

Argued April 14, 2010 - Decided August 5, 2010

Before Judges Graves, Sabatino, and J. N. Harris.

On appeal from the Superior Court of New Jersey, Law Division, Atlantic County, Docket No. L-8213-05.

Paul W. Schmidt (Covington & Burling LLP) of the Washington, D.C. bar, admitted pro hac vice, argued the cause for appellants (Gibbons P.C., attorneys; Michael X. Imbroscio (Covington & Burling LLP) of the Washington, D.C. bar, admitted pro hac vice, and Mr. Schmidt, of counsel; Michelle M. Bufano, on the brief).

David R. Buchanan argued the cause for respondent (Seeger Weiss LLP, attorneys; Michael D. Hook (Hook & Bolton, P.A.) of the Florida bar, admitted pro hac vice, of counsel; Mr. Buchanan, of counsel and on the brief).

PER CURIAM

In this products liability case involving the acne medication Accutane, defendants appeal a final judgment entered in favor of plaintiff following a jury trial. Although we affirm the trial court's determinations in most respects, we vacate the judgment and remand for a new trial because of the trial court's erroneous restriction of certain quantitative proofs and related defense arguments.

I.

A. Accutane and IBD

Defendants, Hoffman-La Roche, Inc., Roche Laboratories, Inc., F. Hoffman-La Roche Ltd., and Roche Holding Ltd. (collectively, "Roche" or "defendants"), have manufactured Accutane since the 1980s.[1] Also known as isotretinoin, Accutane is a retinoid, derived from vitamin A.

In 1982 the Food and Drug Administration ("FDA") approved the use of Accutane to treat recalcitrant nodular acne, after research showed that retinoids were effective in abating acne that had been resistant to other forms of treatment. The

[1] At oral argument before us, defense counsel indicated that Roche discontinued producing Accutane in 2009, and that its existing stock of the drug is being sold off. Counsel also indicated that generic versions of Accutane continue to be produced and sold by other drug companies.

precise method by which Accutane suppresses nodular acne is not clearly known, although it apparently reduces the production of oil and waxy material in the sebaceous glands. Accutane is commonly administered in capsule form.

Patients using Accutane have reported a number of common side effects. Those side effects include, among other things, dry skin, lips, and eyes; reduced night vision; conjunctivitis; joint and muscle aches; and elevated triglycerides. The product also presents a high risk of birth defects in the children of pregnant women who ingest the drug. Additionally, some patients have become depressed or suicidal after taking Accutane.

The side effect that is centrally at issue in this case is the alleged propensity of Accutane to cause patients to suffer from inflammatory bowel disease ("IBD"). IBD is a condition involving the chronic idiopathic inflammation of the small bowel and colon. IBD primarily manifests as one of two diseases: Crohn's disease or ulcerative colitis. Ulcerative colitis, the particular medical condition that plaintiff in this case developed, entails a chronic inflammation of the inner lining of the colon cells.

IBD is triggered by an immune reaction, or an inflammation, which the patient's body is unable to arrest. The common symptoms of IBD include diarrhea, gastrointestinal bleeding, and

rectal bleeding. Patients suffering from ulcerative colitis ordinarily have frequent—often bloody—bowel movements. They often experience fatigue, dehydration, anemia, cramping, abdominal pain, and bloating. Although these symptoms can wax and wane, IBD is regarded as a permanent condition. The peak age of onset of IBD generally occurs in patients between the ages of fifteen and thirty-five.

The exact scientific causes of IBD have not been conclusively established. IBD has been statistically associated with several factors, including family history, prior infections, frequent use of antibiotics, and possibly the use of contraceptives and nonsteroidal anti-inflammatory drugs.

Before obtaining FDA approval for Accutane, Roche performed various clinical studies on the drug which, among other things, generated information concerning potential stomach or intestinal side effects. In one such pre-approval study on 523 patients, 21.6 percent of them reportedly suffered some gastrointestinal problems after using Accutane. Additionally, certain pre-approval studies of Accutane revealed gastrointestinal bleeding in dogs who were administered the drug.

These pre-approval studies suggesting a potential linkage between Accutane and gastrointestinal symptoms raised some concern with the FDA. That concern was documented by a May 3,

1978 memorandum authored by M.J. Schiffrin, a Roche employee, who had received a telephone call about this possible link from Manfred M. Hein, an FDA pharmacologist. Nevertheless, the FDA approved Accutane for sale and did not require Roche to include warnings about IBD on the original 1982 Accutane label.

B. Post-Market Monitoring of Accutane

Roche monitored side effects reported by Accutane users after it began marketing the drug. As part of that monitoring process, Roche received post-marketing reports about a number of patients who developed IBD following their use of the drug. Roche collected adverse drug reaction ("ADR") reports, through its call center, from physicians, pharmacists, patients, family members, and attorneys. It also received these reports indirectly through MedWatch, the FDA's voluntary reporting program. Roche employees, generally nurses and drug safety associates, recorded the responses on a MedWatch form. This form listed the duration of therapy, dosage, age and sex of patient, family history, medical history, onset of symptoms, ultimate outcome, and a description of the adverse event.

Staff at Roche also recorded whether the adverse event abated after the patient stopped using Accutane and whether it returned after reintroduction. A Roche medical reviewer, generally a physician, examined the ADR reports and contacted

the patient, doctor, or other reporter to request any missing information, including the patient's medical reports. Kasia Petchel, M.D., the global head of safety risk management for Roche, stated that it was "very critical" to obtain as accurate information as possible to enable Roche to "monitor the safety appropriately."

Data from the ADR reports was input into what was known as the ADVENT database. If a reporter provided an assessment of an alleged relationship between Accutane and the adverse event, Roche would record that assessment in an ADVENT data field. The ADVENT database also contained a field that reflected Roche's assessment of relatedness. It further utilized a data field developed by the Council for International Organizations of Medical Sciences ("CIOMS"), in which Roche would insert a narrative discussion of the potential causal relationship.

As part of its assessment of potential causality, Roche utilized what is known as "the Naranjo algorithm," a questionnaire created to help determine the likelihood of whether an adverse drug reaction is related to a drug's use.[2] The Naranjo algorithm consists of ten questions that capture information concerning the reported adverse event. It includes

[2] See A.C. Naranjo, et al., A Method for Estimating the Probability of Adverse Drug Reactions, 30 Clinical-Pharmacology & Therapeutics 239 (1981).

such factors as: prior adverse reports, the timing of the adverse reaction, whether the adverse reaction ceased when usage of the drug was discontinued and whether it reappeared if that usage was resumed, dosage levels, possible alternative causes, and other considerations. The algorithm uses a point system, with assigned points being added or subtracted to the overall score depending on the questionnaire responses. These calculations yield a total score classified as either "highly probable," "probable," "possible," or "doubtful."

Roche's director of drug safety, Daniel Reshef, M.D., performed a final review of the information generated by the ADR reports and causality assessments. If he determined that a patient had suffered a serious adverse event, the case would be forwarded for immediate medical review by a Roche physician serving as a product specialist. Roche did not supply its internal causality assessments to the FDA, because drug companies are not required to do so, even though they are apparently required to report them to regulators in Europe.

In one such internal causality assessment, Roche stated that, from 1982 to January 6, 1994, 104 cases of colitis and related syndromes, including Crohn's disease, had been reported in Accutane users. Of those cases, thirty-three were given a "possible" or "probable" causality rating by Roche. Based on

that information, Henri Lefrancq, a physician with Roche, stated in an internal memorandum dated February 24, 1994, that "[i]t is reasonable to conclude from this data that, in rare cases, ROACCUTANE[3] may induce or aggravate a preexisting colitis." Lefrancq further explained in his memorandum that "[i]t is reasonable to assume that [Accutane] has the same effect on the intestinal mucosa as on the other mucosae in the body such as the oral or nasal mucosae." He recommended that Accutane use should be discontinued for a patient suffering from ulcerative colitis until the disease was "no longer in an active phase."

In another internal Roche document, the company reported a comprehensive search of "the Roche safety database[,] with a cut-off date of December 31st, 2002[.]" This search yielded 159 reports of adverse events from exposure to Accutane received from worldwide sources. Of those patients, sixty-four had developed Crohn's disease. Roche assessed causality as "related" in twenty-seven of those sixty-four cases, with the remainder designated as "either unrelated or unknown."

Roche also prepared quarterly periodic safety update reports ("PSURs") and annual evaluations of the ADR reports, which it submitted to the FDA. For example, in a 1985 PSUR the

[3] ROACCUTANE, also spelled "Roaccutan," is the brand name for Accutane in Europe and is used interchangeably by Roche with the Accutane brand name.

reviewer found that "[t]here were 474 entries on the database referring to Ro[a]ccutane adverse reactions[,]" of which four were reports of hemorrhagic colitis.

Additionally, in a semi-annual report dated February 25, 1987, Peter Schifferdecker, a physician and product specialist for Roche, detailed the 241 ADR reports received from patients using Accutane from July 1, 1986 to December 31, 1986. He wrote that Roche had "previously received [reports of four] cases of ileitis, [four] cases of proctitis, and [ten] case reports of colitis in association with [Accutane] treatment." Dr. Schifferdecker concluded that, "[p]atients who experience rectal bleeding, or abdominal pain, should be advised to discontinue [Accutane] therapy, although a causal relationship between [Accutane] and bowel disorders remains uncertain."

In a similar report, dated February 9, 1988, Dr. Schifferdecker reviewed the ADR reports received from patients using Accutane from July 1, 1987 to December 31, 1987. He reported that "[s]ince marketing introduction[,] R[oche] Drug Safety received [nine] case reports of Crohn's disease in association with [Accutane] treatment." However, of those cases, Dr. Schifferdecker felt that only three "may have a reasonable association with [Accutane]." He wrote that:

> [e]stimates of the incidence of Crohn's disease are approximately 2 per 100,000

> population per year.[] Since introduction of [Accutane] in 1982, more than one million patients have been treated with [Accutane]. When comparing cases of Crohn's disease reported to R[oche] Drug Safety in association with [Accutane] with the incidence rates in the general population, it appears that case reports reported to R[oche] although probably underreported, are well within the background incidence rates in the general population, and not due to [Accutane] therapy.

In a later semi-annual report, dated August 17, 1988, Dr. Schifferdecker reviewed the ADR reports received from patients using Accutane for the period from January 1, 1988 to June 30, 1988. He reported that "[s]ince introduction [of Accutane,] R[oche] Drug Safety received [thirty-eight] case reports of colitis and proctitis in association with [Accutane] treatment." He wrote that, as a matter of comparison:

> [u]lcerative colitis and proctitis has an incidence rate of approximately 6-8 cases per 100,000 population per year (U.S.A. and western Europe).[]
>
> It appears that cases of colitis and proctitis reported to R[oche] Drug Safety are within the spontaneous incidence rates of the background population, although underreporting of such cases may occur. It should be stressed that approximately one half of the patients were at a certain risk for the development of colitis prior to [Accutane] treatment. Although there is evidence from in vitro and animal experiments that [Accutane] may protect the organism from experimental colitis,[] R[oche] Drug Safety will further monitor closely cases of colitis and proctitis

> reported in association with [Accutane] treatment.
>
> [Footnotes omitted.]

Later, in a report dated December 30, 1996, Dr. Schifferdecker reviewed the ADR reports submitted for September 1, 1995 to August 31, 1996. During that period, it was "estimated that 1.1 to 1.4 million patients [had] been treated with [Accutane]," and that Roche had received 153 reports of gastrointestinal disorders (including two cases of Crohn's disease), of which thirty-two were "considered serious."

Subsequently, in a report dated October 15, 1997, Dr. Schifferdecker reviewed the ADR reports submitted from September 1, 1996 to August 31, 1997. During that period, it was estimated that 1.2 to 1.5 million patients had used Accutane, and that Roche had received 171 reports of gastrointestinal system disorders, including eight cases of colitis, six reports of ileitis, and two reports of aggravated ulcerative colitis.

John LaFlore, a physician employed by Roche who replaced Schifferdecker, reviewed the ADR reports submitted up to October 31, 1999. Dr. LaFlore concluded, in a report issued in January 2000, that "[t]here is not sufficient information to recommend additional label changes related to inflammatory bowel disease. Some patients with known active symptoms and diagnosis of IBD are treated with Accutane for their severe recalcitrant acne

without clinical sequel." Dr. LaFlore further observed that "[s]ince the recognition of ulcerative colitis and Crohn's disease, the incidence has increased in all populations around the world." He cautioned that Crohn's disease, but not ulcerative colitis, showed a familial tendency. Dr. LaFlore also noted that, from 1982 to 1999, Roche received 206 case reports of IBD from patients taking Accutane, the majority of whom fell within the peak age range (ages twenty to twenty-nine), although some cases of IBD manifested before taking the drug and others did not have a confirmed IBD diagnosis.

C. The Accutane Product Warnings

The FDA initially did not require Roche to include warnings about the potential risks of IBD. Consequently, no warnings about IBD were included on the original Accutane label in 1982.

In the year after Accutane was approved by the FDA for marketing, Public Citizen, a nonprofit consumer advocacy group, petitioned the FDA in a letter dated September 8, 1983, seeking enhanced warnings on Accutane about a variety of adverse reactions, including IBD. In that letter, which was admitted into evidence at trial solely for the purpose of proving notice, Public Citizen expressed its concerns about what it characterized as the FDA's "fast approval" of Accutane. Public Citizen noted that the FDA had received three reports of

patients developing Crohn's disease, three reports of colitis, and five reports of bleeding from the rectum. The group asserted that "these clusters of serious reactions are unlikely to be related to factors other than the drug." Public Citizen further asserted that "[s]ince many FDA officials believe that only one out of every [ten] adverse drug reactions is reported to the FDA, these reports probably represent only a fraction of the . . . problems associated with the drug."

Public Citizen argued that the original patient brochure approved by the FDA for Accutane was "dangerously inaccurate," "fails to mention the more serious risks of Accutane," and "trivializes side effects which may be early warning signs of serious adverse reactions." Despite these assertions by Public Citizen, the FDA did not require any immediate change to the Accutane product warnings.[4]

In March 1984, prior to the use of Accutane by plaintiff in the present matter, Roche revised the various warnings that it supplied concerning the drug. In particular, Roche circulated a "Dear Doctor" letter to physicians who were prescribing Accutane, informing them that:

[4] The record suggests, although it does not clearly document, that Roche had been discussing a proposed label change with the FDA at that time.

> Ten Accutane patients have experienced gastrointestinal disorders characteristic of inflammatory bowel disease (including [four] ileitis and [six] colitis). While these disorders have been temporally associated with Accutane administration, i.e., they occurred while patients were receiving the drug, a precise cause and effect relationship has not been shown. Roche is continuing to monitor adverse experiences in an effort to determine the relationship between Accutane . . . and these disorders.

Additionally, Roche amended the "WARNINGS" section of the Accutane package insert provided to physicians, to include the following language:

> Inflammatory Bowel Disease: Accutane has been temporally associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. Patients experiencing abdominal pain, rectal bleeding[,] or severe diarrhea should discontinue Accutane immediately.

Meanwhile, Roche's Sales Desk Reference, a manual used by its sales personnel, similarly was revised to indicate that some patients had experienced symptoms characteristic of IBD, and that "[t]hese disorders have been temporally associated with Accutane administration, that is to say, the symptoms occurred while the patients were receiving the drug. A precise cause and effect relationship has not been shown."

Eileen Leach, a nurse and the medical director of dermatology at Roche, testified in her deposition, which was

moved into evidence at trial, that the term "temporal" contained in these revised warnings meant that "during the time that the patient was taking Accutane, they developed symptoms, or they reported symptoms." This definition of "temporal" echoed the definition set forth in the sales manual.

However, Martin Huber, M.D., Roche's global head of drug safety, differed with that definition of "temporal," contending instead that the term meant that symptoms would occur "in a reasonable temporal association[,]" or within a reasonable time after taking the drug. Similarly, Heather Mayer, the product knowledge manager for Accutane at Roche, testified that temporal meant that symptoms manifested "[a]t or near the time" a patient took the drug.

In 1994, Roche issued a patient brochure, warning, among other things, that "ACCUTANE MAY CAUSE SOME LESS COMMON, BUT MORE SERIOUS SIDE EFFECTS" and patients should "BE ALERT FOR . . . SEVERE STOMACH PAIN, DIARRHEA, [and] RECTAL BLEEDING . . . ." Patients were advised that if they "EXPERIENCE ANY OF THESE SYMPTOMS" they should discontinue taking Accutane and check with their doctor. The brochure also warned that these symptoms "MAY BE THE EARLY SIGNS OF MORE SERIOUS SIDE EFFECTS WHICH, IF LEFT UNTREATED, COULD POSSIBLY RESULT IN PERMANENT EFFECTS." The same warnings were reprinted on the blister packaging that

contained individual Accutane pills. These warnings remained unchanged until 2000.

In another "Dear Doctor" letter, dated August 1998, which was sent to board-certified dermatologists, Roche warned that patients taking Accutane should be monitored for several serious adverse events, including IBD. However, Roche maintained that, based on the available data, Accutane "does not cause" IBD.

Roche subsequently revised its product warnings for Accutane, also with FDA approval, in 2000 and again in 2002. The 2000 revisions, among other things, removed the modifier "temporally" from the "WARNINGS" section of the Accutane package insert, thereby creating a more direct connection for the reader between the use of Accutane and the risks of IBD. The 2002 revision further strengthened the warnings, in a manner which we will discuss in more detail in the forthcoming pages.

D. Plaintiff, Her Use of Accutane, and Her Diagnosis of IBD

Plaintiff in the present litigation, Kamie Kendall,[5] is a resident of Utah and resided in that state when she first was prescribed with Accutane in 1997.

[5] Plaintiff is now known by her married name, Kamie Rees. We will refer to her as Kamie Kendall, consistent with the caption and briefs on appeal.

On January 13, 1997, plaintiff, who was then twelve years old, began treatment with Accutane for cystic and scarring acne, which had not resolved after twenty-one months of treatment with antibiotics. She then received a daily dose of forty milligrams of Accutane. Stephen Thomson, M.D., plaintiff's dermatologist in Utah, testified that he discussed Accutane and various side effects with plaintiff and her mother, Karla Kendall, including teratogenicity, elevated cholesterol and triglycerides, dry eyes, dry skin, dryness of the mucus membranes of the nose resulting in nosebleeds, chapped lips, musculoskeletal aches, thinning hair, and the potential for sunburn. Plaintiff, who contends that she was relying on her mother to make informed decisions on her behalf, recalled that Dr. Thomson had stressed that she should not become pregnant while taking the drug.

The record indicates that Dr. Thomson did not advise plaintiff or her mother of the risk of developing IBD. Dr. Thomson did, however, give plaintiff a copy of the Accutane patient brochure as it existed in 1997, which warned, as set forth above, that patients should be "ALERT" for "SEVERE STOMACH PAIN, DIARRHEA, [and] RECTAL BLEEDING," and that if they experienced any of these symptoms they should discontinue taking Accutane and check with their doctor. Plaintiff received similar warnings on the blister pack. Plaintiff signed a

consent form, acknowledging that she had received and read the patient brochure. No specific reference to IBD was contained in either the patient brochure or the blister pack.

Dr. Thomson, who had read Roche's 1984 "Dear Doctor" letter, testified that he understood at the time that there "was no documented cause-and-effect relationship" between Accutane use and IBD. At trial, Dr. Thomson acknowledged that he had not been made aware of Roche's internal causality assessment from 1994, in which Roche had noted that of the 104 reported cases of colitis and related syndromes, including Crohn's disease, thirty-three had been given a "possible" or "probable" causality rating. Dr. Thomson considered this data to be important information, and he stated that he would have made his patients, including plaintiff, aware of Roche's assessment.

During plaintiff's initial four-month treatment with Accutane, from January 13, 1997 to May 9, 1997, she experienced several side effects from Accutane use—including dry lips, cracking at the corner of her mouth, bloody noses, dry eyes, and back and knee pain—but no gastrointestinal effects. Over the next two years, plaintiff underwent three more courses of Accutane treatment: July to September 1997; February to April 1998; and July to September 1998.

In April 1999, plaintiff, who was then fifteen years old, and had been suffering from abdominal pain for approximately one year, experienced a severe case of bloody diarrhea, abdominal pain, and cramping, for which she was hospitalized. On April 14, 1999, Linda Book, plaintiff's treating pediatric gastroenterologist, diagnosed plaintiff as suffering from severe ulcerative colitis, an IBD. Plaintiff's family medical history indicated that plaintiff's grandmother had also previously suffered from colitis.

Dr. Book discussed plaintiff's Accutane use with plaintiff and her mother. According to Dr. Book, she told them that she "did not know about the relationship of colitis and Accutane[.]" However, Dr. Thomson's medical records indicate that, on May 17, 1999, plaintiff's mother informed his office that plaintiff had been diagnosed with an IBD, and that "[h]er ulcerative [c]olitis has nothing to do with her Accutane [use], <u>according to her G.I. doctors</u>." (emphasis added).[6]

After her release from the hospital, plaintiff took various medications to treat her IBD symptoms, including prednisone, which caused her to gain approximately forty pounds and suffer

[6] At some point in late 2003, plaintiff, who by that time was an adult, stopped seeing Dr. Book, who is a pediatric specialist, and began seeing Brian Pugh, also a gatroenterologist. Dr. Pugh did not testify in this case, and his medical charts for plaintiff are not in the appellate record.

from mood swings—and Remicade, which caused her to go into anaphylactic shock. Plaintiff's IBD symptoms disappeared and reappeared frequently, as is typical of the disease.

On October 17, 2000, plaintiff returned to Dr. Thomson for treatment of more uncontrolled acne. Dr. Thomson wrote in his office notes, at the time, that he intended to consult with Dr. Book before restarting plaintiff on Accutane. During that subsequent consultation, Dr. Book expressed to Dr. Thomson no objections to plaintiff's restarting treatment with Accutane, provided that Dr. Thomson monitored plaintiff's liver enzymes.

Plaintiff asserted in her testimony that neither Dr. Book nor Dr. Thomson told her that her Accutane use had caused her IBD. Nor had they told her that continued use of the drug could exacerbate her condition.

On December 11, 2000, plaintiff started her fifth course of Accutane, which she took until March 2001. By that point, the "WARNINGS" section of the label or package insert, provided to physicians, not patients, had been amended, removing the word "temporally," and warning that Accutane had been associated with IBD. Plaintiff was given a copy of the patient brochure, which apparently remained unchanged since 1997, and contained no reference to IBD. Dr. Thomson did not warn plaintiff that her Accutane use had caused, or could exacerbate, her IBD.

Plaintiff again experienced several side effects, including dry lips, cracking at the corner of her mouth, dry hands, red eyes, nosebleeds, and back aches, but no diarrhea or other gastrointestinal effects.

At the age of nineteen, plaintiff took her sixth and final course of Accutane from September 2003 to January 2004. She again suffered many of the same side effects. Prior to this last course of treatment, Dr. Thomson warned plaintiff about some of these side effects, including birth defects, dry eyes, sun sensitivity, and nosebleeds, but again not IBD. Dr. Thomson testified that he did not believe that there was a significant risk of developing IBD from taking Accutane.

Additionally, prior to this final course of treatment, plaintiff signed a "Patient Information/Consent" form, confirming that she had read and understood the written patient information and had watched a video accompanying the product about contraception. An additional "Informal Consent/Patient Agreement" form, signed by plaintiff, listed several side effects of Accutane use, including birth defects, and the risk of depression and suicide, but not IBD. The written materials included a patient brochure presented as a large, purple-colored ring binder entitled "Be Smart, Be Safe, Be Sure," which contained extensive warnings regarding not becoming pregnant

while taking Accutane. The binder materials stated in relevant part, that:

> You should be aware that certain SERIOUS SIDE EFFECTS have been reported in patients taking Accutane. Serious problems do not happen in most patients. If you experience any of the following side effects or any other unusual or severe problems, stop taking Accutane right away and call your prescriber because they may result in permanent effects.
>
> . . . .
>
> Abdomen (stomach area) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the liver, pancreas, bowel (intestines), and esophagus . . . . If your organs are damaged, they may not get better even after you stop taking Accutane. Stop taking Accutane and call your prescriber if you get severe stomach, chest, or bowel pain; have trouble swallowing or painful swallowing; get new or worsening heartburn, diarrhea, rectal bleeding, yellowing of your skin or eyes, or dark urine.

Plaintiff also received a "Medication Guide," from her pharmacist. This guide consisted of a printed two-sided page and contained identical warnings regarding "Abdomen (stomach area) problems." The blister pack with the drug doses contained a similar warning. There was no specific reference to IBD,

ulcerative colitis, or Crohn's disease in these patient materials.[7]

In early 2005, plaintiff suffered from excessive diarrhea, bowel incontinence, bloody diarrhea, fatigue, cramping, and abdominal pain. As 2005 progressed, plaintiff's symptoms worsened, and she often had fifteen to twenty bloody bowel movements a day, with diarrhea, and she frequently experienced bowel incontinence.

In January 2006, plaintiff, who was then twenty-one years old, underwent a proctocolectomy, in which her entire colon and rectum was surgically removed. Her small intestine was then attached to the anal canal, creating a ileoanal pouch. In order to give the pouch time to heal, the surgeon also performed an ileostomy, in which a portion of plaintiff's small intestine was brought through the abdominal wall to drain into a ileostomy bag, thereby temporarily diverting the fecal stream. After the surgery, plaintiff, who was hospitalized for three weeks, continued to experience problems with incontinence. She also suffered from leakage of fecal matter and stomach acid from the bag, skin irritation, excess gas, pain, and humiliation resulting from the leakage and noises emanating from the bag.

[7] At our request, counsel supplied to us exemplars of these written materials, which were photocopied in the appendices in modified, black-and-white, form.

Six weeks after her initial surgery, plaintiff underwent a second surgery to reverse the ileostomy. In that second operation, plaintiff's intestine was placed back into her abdominal cavity, and the bag was removed. She continued to suffer numerous complications including pain, fatigue, dehydration, incontinence, and diarrhea, and on an average day had ten to twelve bowel movements. On a bad day, she had thirty to forty bowel movements, and, as she put it, essentially had to "live in [her] bathroom," lying on the floor with a blanket and drinking fluids. She was hospitalized numerous times for dehydration. She also suffered from two or three episodes of pouchitis, an inflammation of the ileal pouch.

At the time of trial, plaintiff, who got married approximately one year after her surgery, continued to experience pain, incontinence, diarrhea, and fatigue. Dr. Craig Foley, plaintiff's treating colorectal surgeon, testified that, as a result of her surgeries, plaintiff was at risk of suffering from dehydration, bowel obstruction, incontinence, and a narrowing of the pouch. She was also at risk of developing recurrent pouchitis, which could result in the need for a permanent ileostomy bag. Dr. Foley predicted that plaintiff would experience frequent bowel movements for the remainder of her life.

Plaintiff contends that if she had been warned that Accutane use could cause, or exacerbate, her IBD, she would not have taken the drug. She stresses that there was no specific reference to IBD, or that Accutane use could cause IBD, in any of the materials she received from 1997 to 2003. She does, however, acknowledge that there was reference to certain symptoms of IBD, including rectal bleeding and diarrhea. Plaintiff also asserts that none of her treating physicians warned her that Accutane use could be associated with IBD, or that she should not take Accutane after being diagnosed with ulcerative colitis.

Plaintiff, who had done some Internet research about her medical condition in 1999, admitted that she knew ulcerative colitis was a medical term for damage to the intestines and a type of IBD. She also acknowledged on cross-examination at trial that:

> Q. And you knew then [in 2003, after she had developed ulcerative colitis] that if there was damage to your intestines, that could trigger the need for surgery, right?
>
> A. I believe so.
>
> Q. . . . [S]o, in 2003, you knew that there could be abdominal problems, including damage to your bowel or your intestines, right?
>
> A. Right.

Q. And you took Accutane.

A. Yes.

However, she testified that in 2003 she had not understood the warnings regarding "Abdomen (stomach area) problems," to mean that Accutane could cause IBD.

In January 2004, plaintiff cut out an advertisement from a magazine which listed a number of risks of taking Accutane, including IBD. At that point, plaintiff "started to think" that her Accutane use might have caused her IBD, and that she might have a basis for a lawsuit.

Thereafter, in April 2004, plaintiff's grandmother told plaintiff's mother about an advertisement that she had seen on television linking Accutane use to IBD. At her parents' suggestion, plaintiff called the telephone number of an attorney's office listed in the ad.

E. Plaintiff's Complaint and the Present Litigation

Plaintiff filed suit against Roche, whose principal place of business is in New Jersey, in the Law Division on December 21, 2005. At the time, she was twenty-one years of age.

In her complaint against Roche, plaintiff sought both compensatory and punitive damages. In essence, plaintiff alleged that Roche was liable to her—under principles of products liability and other applicable laws—because the

warnings that she and her doctors had received from Roche concerning Accutane were inadequate and, in particular, failed to sufficiently disclose the risks of her contracting IBD. Roche denied liability.

The case was filed as a mass tort action, pursuant to Rule 4:38A and a May 2005 order of the Supreme Court, in the Law Division in Atlantic County, where approximately 500 products liability cases against Roche involving Accutane are centrally managed.

Roche filed several dispositive and evidentiary motions before trial. These motions, several of which are germane to the present appeal, included a motion to dismiss the complaint as time-barred; motions for summary judgment as to the adequacy of the Accutane product warnings; motions to exclude the trial testimony of plaintiff's causation expert and, to exclude proofs concerning Roche's internal causality assessments; and a motion to admit certain background information concerning the number of Accutane users into evidence. The trial court denied all of these motions. The statute of limitations motion was denied following an evidentiary hearing, after which the trial court decided to toll the pertinent two-year limitations period on equitable grounds, pursuant to Lopez v. Swyer, 62 N.J. 267, 272 (1973).

F. The McCarrell Litigation

Before the trial in the instant case commenced, a jury rendered a verdict for the plaintiff in McCarrell v. Hoffman-La Roche, Inc., No. L-1951-03 (Law Div. Mar. 12, 2008), the first of the Accutane mass tort cases venued in Atlantic County to go to trial. The plaintiff in McCarrell, a resident of Alabama, developed IBD after being prescribed Accutane. McCarrell sued Roche, similarly contending, as in the present case, that the warnings Roche provided with the drug were inadequate. McCarrell was represented by the same law firm that is representing Kamie Kendall in the instant case, and Roche was represented by the same defense counsel.

The jury in McCarrell found the product warnings for Accutane inadequate and awarded that plaintiff compensatory damages. Roche appealed, raising several of the same issues it now advances here. While the appeal in McCarrell was pending, the present case was tried and went to verdict.

Ultimately, in March 2009, a panel of this court issued an opinion in McCarrell, vacating the judgment for the plaintiff and remanding that matter for a new trial because the court had erroneously restricted the quantitative evidence that Roche was allowed to present to the jury in an effort to contest its liability. See McCarrell v. Hoffman-La Roche, Inc., No. A-3280-

07 (App. Div. Mar. 12, 2009), certif. denied, 199 N.J. 518 (2009).[8] We note that the trial court did not have the benefit of this court's extensive opinion in McCarrell before it proceeded with the instant trial in Kendall.[9]

G. The Trial

The proofs in this case at trial, which consumed thirteen intermittent days in April 2008 after the jury was selected, were extensive. In addition to the live testimony of several witnesses, counsel played the videotaped depositions of nine witnesses, and also read aloud a transcript of the deposition testimony of another witness.

Plaintiff testified in person and recounted her experience in using Accutane and her symptoms and treatment for IBD. Plaintiff also presented the testimony of her dermatologist, Dr.

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[8] On remand, the McCarrell case was retried and reportedly produced a significantly larger verdict than the first trial. We understand that an appeal of that second verdict in McCarrell is forthcoming.

[9] We shall refer several times to the unpublished Appellate Division opinion in McCarrell, not because it is precedential, see R. 1:36-3, but because the panel's opinion in McCarrell provides useful background information common to both cases. We also refer to McCarrell in the interest of brevity because, as noted, infra, we adopt in this case various legal analyses and conclusions previously set forth by the panel in McCarrell. We have generally adopted that reasoning from McCarrell, not because we are bound by principles of preclusion or stare decisis to do so, but because we agree substantially with the other panel's analysis of the overlapping legal issues.

Thomson; her pediatric gastroenterologist, Dr. Book; her colorectal surgeon, Dr. Foley; her mother; and her husband. In addition, plaintiff presented evidence of statements from several fact witnesses at Roche who had been involved in various aspects of Accutane's development and marketing, or in the processing of case reports from Accutane users.

Plaintiff presented two expert witnesses: David Sachar, M.D., concerning issues of causation, and Cheryl Blume, Ph.D., concerning issues of drug development and labeling.

Dr. Sachar is a board-certified internal medicine specialist and a Professor of Medicine at Mount Sinai School of Medicine. He is the past chairman of the FDA advisory committee on gastroenterology, and has authored or co-authored over two hundred articles on IBD, ulcerative colitis, and Crohn's disease.

After the trial court denied Roche's application to bar Dr. Sachar's testimony under Rule of Evidence 702, the jury heard Dr. Sachar opine that "Accutane and its metabolites directly cause gastrointestinal damage." Dr. Sachar based his expert opinions on causation upon a variety of sources, including, among other things, pre-market toxicity studies in which dogs were administered Accutane; the aforementioned 1981 pre-approval study on 523 patients; the post-market MedWatch reports with so-

called "challenge," "dechallenge," and "rechallenge"[10] events; published scientific literature;[11] Roche's internal causality assessments; the background incidence rates within the population for IBD; data reporting side effects with Vesanoid another retinoid produced by Roche to treat leukemia, and plaintiff's own medical history. Noting that plaintiff's IBD had worsened after each course of Accutane and that plaintiff's family history and prior medical history did not contain markers for IBD, Dr. Sachar concluded that plaintiff's IBD was caused by her use of Accutane rather than by genetic or other factors.

Dr. Blume, plaintiff's labeling expert, is a pharmacologist and an adviser on new drug applications presented to the FDA. She opined that Roche had received many "signals," both prior to and after the marketing of Accutane, which should have alerted

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[10] In the parlance of the drug field, a "challenge" occurs when a patient suffers an adverse event while taking a prescription drug. A "dechallenge" occurs when a patient stops taking the drug and the adverse effects abate. Lastly, a positive "rechallenge" occurs when the drug is readministered and the adverse effects reappear.

[11] The principal article discussed by Dr. Sachar was a peer-reviewed publication, Deepa Reddy, M.D. et al., Possible Association Between Isotretinoin and Inflammatory Bowel Disease, 101 Am. J. Gastroenterology 1569 (2006). Dr. Sachar also relied upon other articles, including: Denise E. Reniers & John M. Howard, Isotretinoin-Induced Inflammatory Bowel Disease in an Adolescent, 35 Annals Pharmacotherapy 1214, 1215 (2001); and P. Martin et. al., Isotretinoin-Associated Proctosigmoiditis, 93 Gastroenterology 606 (1987).

it to the need for stronger product warnings about IBD. According to Dr. Blume, Roche did not adhere to applicable standards of care—either in the 1984 product materials, or in the subsequently-revised warnings in 2000—to alert Accutane users sufficiently about the risks of developing IBD.

Dr. Blume opined that the amended warnings contained in the 2000 label were inadequate. As we have noted, the warnings sections of the Accutane package insert provided to physicians, was amended in 2000, to remove the word "temporally," in warning that Accutane had been associated with IBD. As Dr. Blume explained it, a drug label generally contains three sections: black-box warnings, contraindications, and warnings. She opined that Roche should have included information in the black-box section of the label, specifically warning of the risk of developing IBD.

Further, Dr. Blume asserted that, in the contraindications section, Roche should have warned that Accutane can never be given to patients with preexisting Crohn's disease or ulcerative colitis. As to the warnings section, Dr. Blume opined that Roche should have disclosed that Accutane can "induce" or "cause" IBD. She contended that Roche should also have included: (1) reference to the positive challenge/dechallenge/rechallenge events, (2) revealed the

results its internal causation assessments, and (3) listed the side effects of taking Vesanoid, a "sister drug."

Dr. Blume stated that Roche should have provided stronger warnings that would have communicated the risks of contracting IBD more clearly and prominently. As Dr. Blume noted, such stronger warnings are especially warranted because Accutane is commonly prescribed by dermatologists and primary care physicians, doctors who may not be "as versed in the intricacies of [IBD] as a gastroenterologist[.]"

In its defense proofs, Roche presented testimony from several fact witnesses, including Dr. Huber, its former global head of drug safety; Alan Bess, M.D., Roche's head of drug safety within the United States; Dr. Reshef, a Roche director of drug safety; and Dr. Petchel, the company's vice-president and global head for safety risk management. Roche also moved into evidence numerous documents and other exhibits.

As its defense expert on causation and what was characterized in its proffer as "clinical investigation" issues, Roche presented the testimony of Richard Blumberg, M.D., a board-certified gastroenterologist. Dr. Blumberg is a Professor of Medicine at Harvard Medical School, where he is the chief of its gastroenterology department. His scientific research has predominantly focused upon IBD. Dr. Blumberg has been funded as

an investigator by the National Institutes of Health. He has also served as the scientific chairperson of the Crohn's and Colitis Foundation of America.

In the opinion of Dr. Blumberg, there is no "experimental evidence to support the biological plausibility for Accutane causing IBD." Dr. Blumberg noted in his testimony that the rate of incidence of IBD had peaked in the 1970s, twelve years before Accutane entered the drug market, and that since that time the rate had been largely "either flat, [or in] some regions of the country . . . actually decreasing." Dr. Blumberg explained that the "major effects of Accutane are anti-inflammatory[,]" and that, as a retinoid, Accutane actually could prevent, not trigger, IBD, by inhibiting intestinal inflammation.

Dr. Blumberg disagreed with Dr. Sachar that the published literature signifies that Accutane causes IBD. Given the state of the scientific research, Dr. Blumberg opined that the manner in which Roche had communicated the risks of contracting IBD in its product warnings was scientifically accurate, and that those warnings conservatively "err[ed] on the side of patient safety."

With respect to plaintiff and her particular medical history, Dr. Blumberg concluded that Accutane had not caused her IBD. He noted that plaintiff's manifestation of the disease was very abrupt, which he explained was "absolutely typical" of the

manner in which ulcerative colitis normally presents in an adolescent. Dr. Blumberg acknowledged that plaintiff had suffered abdominal pain and constipation—symptoms of IBD—for one year prior to developing the disease. Nonetheless, plaintiff had taken four courses of Accutane before she developed IBD, with no apparent gastrointestinal effects. He further noted that plaintiff took two courses of Accutane after she developed IBD, with "no evidence of exacerbation" of the IBD. Additionally, Dr. Blumberg cited the fact that plaintiff did not develop IBD until six months after she had completed treatment with Accutane.

On the whole, Dr. Blumberg concluded that there was no "medical reasonability to conclude that there was any relationship between the Accutane [doses] and [plaintiff's] unfortunate diagnosis of ulcerative colitis." Dr. Blumberg further concluded that it would have been "inappropriate," given the state of the scientific research for Roche to have advised plaintiff's dermatologist in 2000 not to prescribe Accutane for her, notwithstanding that she had already been diagnosed with IBD by that point.

After the parties rested, the trial judge issued a jury charge which, by stipulation of the parties, substantively instructed the jury on the elements of a failure-to-warn claim

under the Utah products liability statute, Utah Code Ann. §§ 78B-6-701 to -707 (2010).[12]

H. The Verdict and Post-Trial Motions

The jury returned a verdict for plaintiff. In its various answers to special interrogatories posed to them, the jury unanimously found that: (1) "the use of Accutane [is] a cause of inflammatory bowel disease in some people who take it"; (2) that Roche had failed "to provide an adequate warning" to plaintiff's prescribing physician "about the risks of IBD from Accutane that Roche either knew or should have known about prior to April 1999"; and (3) that Roche's failure to warn was "a proximate cause of [plaintiff] developing inflammatory bowel disease[.]" By a seven-to-two vote, the jurors awarded plaintiff $10.5 million in compensatory damages, in addition to a stipulated sum of $78,500 for past medical expenses. Pursuant to a ruling it had made while the jurors were deliberating, the trial court declined to allow plaintiff to present proofs on punitive damages.

[12] The parties agreed at the time of trial that Utah law, rather than New Jersey law, applied to plaintiff's substantive claims of products liability. We note that this application of foreign substantive law is similar to that which occurred at the first trial in McCarrell, supra, No. A-3280-07 (slip op. at 107-08), in which the substantive law of Alabama, the plaintiff's home state, was charged to the jury, rather than New Jersey's products liability laws.

Following the verdict, Roche moved to set aside the jury's decision on various grounds, and for other post-trial relief. The trial court rejected the defense's post-trial motions in their entirety, and this appeal ensued.

I. The Appeal

Roche raises the following points on appeal for our consideration: (1) the trial court erred in denying Roche's motion to dismiss plaintiff's lawsuit as time-barred; (2) the court abused its discretion in preventing Roche from adducing evidence as to the number of Accutane users and in limiting Roche's arguments to the jury concerning such data; (3) the court likewise abused its discretion in allowing plaintiff to place into evidence Roche's causality assessments, the Accutane adverse case reports, and certain testimony and arguments as to Roche's failures to conduct testing and its alleged corporate emphasis on marketing over safety; (4) the warnings that Roche provided during the time periods in question were adequate as a matter of law, and plaintiff failed to establish that a different warning would have altered or prevented her use of Accutane; and (5) the court erred in denying Roche's motion in limine to preclude Dr. Sachar from testifying on causation issues.

II.

As a threshold issue, Roche argues that plaintiff's lawsuit, which she filed on December 21, 2005, should have been dismissed as time-barred, and that the trial court erred in applying equitable principles under Lopez, supra, to toll the applicable two-year statute of limitations. In reviewing this issue, we need not engage in a comparative choice-of-law analysis, given that both New Jersey and Utah have a two-year statute of limitations applicable to products liability actions. See N.J.S.A. 2A:14-2 and Utah Code Ann. § 78B-6-706 (2010); see also Rowe v. Hoffman-La Roche, Inc., 189 N.J. 615, 621 (2007) (noting that, in the absence of a conflict between the laws of the respective states involved, the court will apply the law of New Jersey as the forum state).

Because plaintiff was a minor at the time she started taking Accutane in 1997 and also a minor at the time of her initial diagnosis with ulcerative colitis in 1999, the two-year limitations statute did not begin to run until at least January 28, 2002, when plaintiff reached the age of eighteen. See N.J.S.A. 2A:14-21; Green v. Auerbach Chevrolet Corp., 127 N.J. 591, 598 (1992). This means that plaintiff was obligated to file her complaint against Roche by January 28, 2004, unless

equitable tolling principles under Lopez are applied to extend that time period.

As noted, plaintiff filed her complaint on December 21, 2005. The pivotal question then becomes whether, as of the two years before that actual filing date—i.e., as of December 21, 2003—her cause of action had accrued. Specifically, the court must determine whether if, by that point, plaintiff knew or reasonably should have known that she had been injured due to the actions or inactions of Roche. Lopez, supra, 62 N.J. at 272. This analysis requires the equitable application of what is known, under Lopez and its progeny, as the "discovery rule." Ibid.

The discovery rule has been crafted and applied as an equitable device "to avoid the potentially harsh effects of the 'mechanical application' of statutes of limitations." Guichardo v. Rubinfeld, 177 N.J. 45, 51 (2003) (quoting Vispisiano v. Ashland Chem. Co., 107 N.J. 416, 426 (1987)). "Under the discovery rule . . . the limitations period does not commence until the injured party actually discovers or should have discovered through reasonable diligence the fact essential to the cause of action." R.A.C. v. P.J.S., Jr., 192 N.J. 81, 98 (2007).

The discovery rule "prevents the statute of limitations from running when injured parties reasonably are unaware that they have been injured, or, although aware of an injury, do not know that the injury is attributable to the fault of another." Baird v. Am. Med. Optics, 155 N.J. 54, 66 (1998). "Although the discovery rule does not require 'knowledge of a specific basis for legal liability or a provable cause of action,' it does require 'knowledge not only of the injury but also that another is at fault.'" Guichardo, supra, 177 N.J. at 51 (quoting Martinez v. Cooper Hosp.-Univ. Med. Ctr., 163 N.J. 45, 52 (2000)). "Once a person knows or has reason to know of this information, his or her claim has accrued since, at that point, he or she is actually or constructively aware 'of that state of facts which may equate in law with a cause of action.'" Abboud v. Viscomi, 111 N.J. 56, 63 (1988) (quoting Burd v. N.J. Tel. Co., 76 N.J. 284, 291 (1978)). The fundamental question in a discovery rule case, therefore, is "whether the facts presented would alert a reasonable person, exercising ordinary diligence, that he or she was injured due to the fault of another." Caravaggio v. D'Agostini, 166 N.J. 237, 246 (2001).

A.

To resolve the timeliness and tolling issues implicated by Roche's motion to dismiss, the trial court conducted an

evidentiary hearing ("Lopez hearing") shortly before the jury was empanelled in this case. Such a plenary hearing is customary in equitable tolling matters, "since credibility is usually at issue." J.L. v. J.F., 317 N.J. Super. 418, 429 (App. Div.), certif. denied, 158 N.J. 685 (1999). The sole witness who was presented at the hearing was plaintiff herself.

In her testimony at the Lopez hearing, plaintiff asserted that she did not make an ultimate connection in her mind between her Accutane use and her IBD until April 2004, when her grandmother contacted her parents about a television ad by a law firm pursuing Accutane products liability cases. According to plaintiff, her parents then told her that the ad had indicated that Accutane was associated with colitis, although the ad allegedly did not provide any other information about that disease or the drug.

Plaintiff also acknowledged reading a magazine ad in January 2004, which listed a number of risks of taking Accutane, including IBD, but she contended that it was not until she was advised of the ad spotted by her grandmother three months later in April 2004 that she reached the point of perceiving a link between her IBD and her use of Accutane.

During the course of the plenary hearing, defense counsel underscored—both in his cross-examination of plaintiff and in

his arguments to the trial court—that when plaintiff resumed taking Accutane in the fall of 2003, she received several warning documents. Those documents contained, among other things, warnings about the potential adverse side effects to a patient's abdomen and bowels. Those documents included: (1) the multi-page, purple-colored patient brochure entitled "Be Smart, Be Safe, Be Sure;" (2) the double-sided "Medication Guide;" and (3) the blister pack containing the Accutane capsules. All of those materials mention potential side effects from Accutane to a patient's abdomen and bowels, although none of them specifically refer to IBD or ulcerative colitis.

Roche also emphasized that plaintiff signed, on August 26, 2003, two informed consent forms,[13] after she had been provided the patient brochure by Dr. Thomson: one form to be completed by all patients and a second form for all female patients. The all-patient version of the consent form contains twelve paragraphs, each of which plaintiff initialed. In paragraph eleven of that consent form, plaintiff acknowledged that:

> I have read the Patient Product Information, Important Information Concerning Your Treatment with Accutane® (isotretinion) and other materials my prescriber gave me containing important safety information

[13] The "Patient Signature" line on both forms is blank, as plaintiff mistakenly signed the "Prescriber Signature" line instead.

about Accutane. I understand all the information received.

Initials: s/KK

In addition, the all-patient consent form contains a place for the signature of the prescriber, Dr. Thomson, in which he is to attest that he had "fully explained" to plaintiff "the nature and purpose of Accutane treatment, including its benefits and risks[,]" that he had given plaintiff the patient brochure and had asked her if she had "any questions regarding [her] treatment with Accutane[,]" and that he had answered such questions "to the best of [his] ability."[14]

The female-patient version of the consent form contained similar recitals, but it was focused on pregnancy and birth defect concerns. By signing and initialing that version of the consent form, plaintiff specifically confirmed that she understood that it was her "responsibility not to get pregnant during Accutane treatment or for [one] month after [she] stop[ped] taking Accutane." (Emphasis in original). In paragraph twelve of this separate consent form for female patients, plaintiff reaffirmed that she had read the patient

[14] The section was actually filled out and signed by plaintiff, inaccurately identifying her as the prescriber and bearing her apparent signature on the line that follows "Prescriber Signature." Dr. Thomson's name and signature appear nowhere on either document.

brochure, and also that she had watched a videotape about contraception accompanying the materials.

When asked during the Lopez hearing whether she had read the Accutane patient brochure when she took the drug in 2003, plaintiff stated that she had just "skimmed over it." Plaintiff explained that she had only skimmed the material "[b]ecause [she] had taken Accutane three times before."

On cross-examination at the Lopez hearing, plaintiff recalled very little of the contents of the product warnings. She acknowledged that she had received the double-sided Medication Guide from her pharmacy every month between September and December 2003, when she received her final prescription for Accutane. She acknowledged that she "probably" read the Medication Guide in 2003 at least one time. She also acknowledged that the Medication Guide, like the patient brochure and the blister pack, refers to symptoms of diarrhea, rectal bleeding or stomach pain, which could indicate that Accutane is damaging to the patient's bowel.

Plaintiff emphasized in her testimony at the Lopez hearing that none of her physicians up through 2003 ever stated to her that Accutane could have caused her IBD. The only warning that plaintiff remembered receiving was from Dr. Thomson, her

dermatologist, and it was "not to get pregnant."[15] Plaintiff did acknowledge, however, that her IBD symptoms worsened in 2003 when she began taking Accutane again.

Plaintiff's counsel argued at the Lopez hearing that his client's failure to appreciate by the end of calendar year 2003 that her use of Accutane could have resulted in her IBD condition flowed out of her reasonable reliance upon her physicians' silence and their continued re-prescribing of—or acquiescing in the prescription of—Accutane in spite of her IBD.

Defense counsel, meanwhile, attempted to neutralize these proofs, by establishing through plaintiff that her physicians had not told her specifically that her colitis was not caused by Accutane. Plaintiff agreed that, with respect to Dr. Book, "[s]he didn't say one way or the other," and she gave a similar response with respect to Dr. Thomson.

B.

Several days later, after considering these proofs from the Lopez hearing, the trial judge issued a lengthy oral decision. The judge denied Roche's motion to dismiss the complaint under

[15] Although they did not testify at the Lopez hearing, deposition testimony of Dr. Thomson and Dr. Book was partially read into the record. These depositions similarly indicate that neither of those physicians specifically recalled telling plaintiff that her use of Accutane could lead to IBD or other gastrointestinal problems.

the statute of limitations, and applied equitable principles to toll the statute, at least through December 21, 2003, two years before the complaint was filed on December 21, 2005. The judge recognized that the written Accutane warnings included language that instructed the patient to contact his or her physician if he or she experienced any side effects, including diarrhea. The judge found that such warnings should be read in light of the fact that plaintiff had been diagnosed with IBD, had suffered from diarrhea, and was approved for Accutane treatment—even though her dermatologist was aware of her symptoms.

The court also noted that the product materials supplied to plaintiff had predominantly discussed pregnancy and the risks of birth defects, not abdominal or bowel problems. In particular, the judge observed that the "Be Smart, Be Safe, Be Sure" pamphlet said nothing about abdominal or bowel problems on its cover, and that in the approximately 3,000 words typed on the first five pages of that brochure, only eighty of them related to gastrointestinal side effects and none of those words were in boldface print. The judge further noted that the two consent forms signed by plaintiff only mentioned the risks of birth defects and of suicide, and said nothing about IBD, bowel, or stomach problems.

In her Lopez analysis, the judge also took into account plaintiff's youth, and the fact that plaintiff had been taking Accutane periodically since she was twelve years old. The judge specifically found credible plaintiff's testimony that, although she was "counsel[ed] about pregnancy repeatedly" by her physicians when she was using Accutane, "she was not told that IBD . . . was caused by or would be exacerbated by Accutane treatment." The judge further noted that the testimony of plaintiff's doctors was consistent with her recollections.

Given these factual circumstances, the judge reasoned:

> I think that when you look at these things out of context and you take just the warning . . . and you say . . . what would a reasonable person have taken this to mean, the focus is a lot different than what the focus of a reasonable person would be who has taken a drug for years and who is being warned about pregnancy, pregnancy, pregnancy and who signs a book where it says "pregnancy." And there's a small section [in the brochure] . . . that talks about diarrhea and . . . damage to the intestines, but it does not say "ulcerative colitis," it does not say "IBD," it doesn't say something that would pull her attention to her disease.
>
> [Emphasis added.]

Additionally, the judge found there was no indication that plaintiff had discovered a causal connection between Accutane and IBD before 2004 through her independent internet research about ulcerative colitis. As a result, the judge concluded that

there was no evidence that plaintiff, who knew she had been injured in 1999 when she developed IBD, "had any inclination that there was wrongdoing or fault" on the part of Roche, until she saw the lawyer's advertisement in early 2004.

The judge did not find it pivotal that plaintiff's symptoms from IBD "somewhat" increased when she resumed taking Accutane. The judge rejected the defense's suggestion that plaintiff reasonably could have educated herself about the risks of Accutane before December 2003 by utilizing online research resources. Additionally, none of the medical information that had been supplied to plaintiff specifically referred to "IBD."

The trial judge considered whether Roche would be unfairly prejudiced in its defense of this case by equitably tolling the statute of limitations. The judge found no such prejudice had been demonstrated, particularly since the pertinent records had been produced and the witnesses with relevant knowledge were still available to testify. The judge also noted that the product risks of Accutane were "an ongoing issue" for the drug company.

In sum, the trial judge recognized that the tolling issues in the present case were "complicated." Even so, she concluded that, although plaintiff knew by December 2003 that she had IBD and was injured, a reasonable person would not have "put

together Accutane and that [injury]," given plaintiff's circumstances. "[T]he bottom line," as the judge phrased it, "is [that] I don't believe that this patient knew [as of December 2003] based on what I have heard here that her IBD was caused by Accutane."

C.

In appealing the trial court's ruling on equitable tolling, Roche maintains that the statute of limitations began to run "no later than 2003," and that the court improperly extended the permissible filing period to plaintiff's advantage. The drug manufacturer contends that the various written warnings that plaintiff received in 2003, when she restarted taking Accutane, "unequivocally told [her] that the condition she had experienced—IBD—may be linked to her Accutane use." Roche urges that the combination of warnings sufficiently placed plaintiff on notice of at least the "possibility" that Accutane "may have caused" her injury. It argues that the trial court was too indulgent in finding that a reasonable person in plaintiff's situation would not have realized by December 2003 that Accutane was potentially responsible for her IBD.

Roche also faults the trial judge for treating plaintiff's exposure to the lawyer advertisement in early 2004 as a triggering event for plaintiff's awareness, noting that the

information contained in the lawyer's ad was no more detailed or specific about abdominal or stomach side effects than the Roche product warnings that plaintiff was given in 2003.

As we evaluate these arguments on appeal, we recognize that the question of whether a particular cause of action is barred by a statute of limitations is a decision for a judge rather than for a jury. See Lopez, supra, 62 N.J. at 275; Estate of Hainthaler v. Zurich Commercial Ins., 387 N.J. Super. 318, 325 (App. Div.), certif. denied, 188 N.J. 577 (2006). In that vein, we examine the trial judge's application of the relevant legal principles de novo. See Manalapan Realty, L.P. v. Twp. Comm. of Manalapan, 140 N.J. 366, 378 (1995); Estate of Hainthaler, supra, 387 N.J. Super. at 325. However, with respect to the trial judge's evaluation of plaintiff's credibility at the Lopez hearing, we defer to the judge's first-hand assessment, so long as it has substantial support in the record. Rova Farms Resort, Inc. v. Investors Ins. Co., 65 N.J. 474, 483-84 (1974).

In performing our review function, we add another consideration that was not specifically raised in the original briefs, but as to which we received helpful supplemental briefs from both parties at our invitation following oral argument. That additional consideration stems from the fact that the State Legislatures in both Utah and New Jersey have enacted a

rebuttable presumption that product warnings approved for a prescription drug by the FDA, or in accordance with such regulatory standards, should be deemed adequate as a matter of law.

In New Jersey, that rebuttable presumption is codified at N.J.S.A. 2A:58C-4, a provision within our State's Product Liability Act ("PLA"). Section 4 of the PLA states:

> In any product liability action the manufacturer or seller shall not be liable for harm caused by a failure to warn if the product contains an adequate warning or instruction or, in the case of dangers a manufacturer or seller discovers or reasonably should discover after the product leaves its control, if the manufacturer or seller provides an adequate warning or instruction. An adequate product warning or instruction is one that a reasonably prudent person in the same or similar circumstances would have provided with respect to the danger and that communicates adequate information on the dangers and safe use of the product, taking into account the characteristics of, and the ordinary knowledge common to, the persons by whom the product is intended to be used, or in the case of prescription drugs, taking into account the characteristics of, and the ordinary knowledge common to, the prescribing physician. If the warning or instruction given in connection with a drug or device or food or food additive has been approved or prescribed by the federal Food and Drug Administration under the "Federal Food, Drug, and Cosmetic Act," 52 Stat. 1040, 21 U.S.C. § 301 et seq. or the "Public Health Service Act," 58 Stat. 682, 42 U.S.C. § 201 et seq., a rebuttable presumption shall arise that the warning or instruction

> is adequate. For purposes of this section, the terms "drug", "device", "food", and "food additive" have the meanings defined in the "Federal Food, Drug, and Cosmetic Act."
>
> [N.J.S.A. 2A:58C-4 (emphasis added).]

When it adopted the PLA in 1987, the Legislature of our State declared that "there is an urgent need for remedial legislation to establish clear rules with respect to certain matters relating to actions for damages for harm caused by products, including certain principles under which liability is imposed and the standards and procedures for the award of punitive damages." N.J.S.A. 2A:58C-1. On the whole, the Legislature "intended for the Act to limit the liability of manufacturers so as to 'balance[] the interests of the public and the individual with a view towards economic reality.'" Zaza v. Marquess & Nell, Inc., 144 N.J. 34, 47-48 (1996) (quoting Shackil v. Lederle Labs., 116 N.J. 155, 188 (1989)). As the Supreme Court reaffirmed in Rowe, supra—an Accutane product liability case raising choice-of-law issues—the PLA "limits the liability of manufacturers of FDA-approved products by reducing the burden placed on them by product liability litigation. The Legislature carefully balanced the need to protect individuals against the need to protect an industry with a significant relationship to our economy and public health." Rowe, supra, 189 N.J. at 626.

Our Supreme Court has also made clear that the statutory presumption in Section 4 of the PLA, although it is rebuttable, is not a minor or inconsequential barrier. Compliance with FDA regulations serves "as compelling evidence that a manufacturer satisfied its duty to warn the physician about potentially harmful side effects of its product." Perez v. Wyeth Labs., Inc., 161 N.J. 1, 24 (1999). In Perez, the Court noted that "absent deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects, compliance with FDA standards should be virtually dispositive" of failure-to-warn claims. Id. at 25; see also Rowe, supra, 189 N.J. at 626.

The strength of the statutory presumption may be lessened, however, if the warning at issue is not the initial warning approved by the FDA for the drug, but rather is a modified warning that was negotiated post-market between the manufacturer and the FDA. As we recognized in McDarby v. Merck & Co., Inc., 401 N.J. Super. 10, 65 (App. Div. 2008), appeal dismissed, 200 N.J. 267 (2009), prior to the enactment of certain amendments to federal law in 2007, "the FDA 'did not have the [statutory] authority to compel labeling changes, but instead had to negotiate changes with the drug's sponsor.'" (quoting David A. Kessler & David C. Vladeck, A Critical Examination of the FDA's Efforts to Preempt Failure-To-Warn Claims, 96 Geo. L.J. 461, 466

(Jan. 2008)). Given the manufacturers' common resistance to such labeling changes, a revised label may be the result of a compromise, rather than a unilateral expression of the FDA's preferred regulatory approach. Ibid.

In light of the ongoing regulatory dynamics between drug companies and the FDA, the presumption of adequacy under the PLA arguably should be easier to overcome for a negotiated, post-market label than for the original warning accompanying the drug, which was not, to the same extent, the result of "conciliatory processes." Id. at 69.

The Utah Product Liability Act ("UPLA"), Utah Code Ann. §§ 78B-6-701 to -707 (2010), similarly contains what has been described in that State as a rebuttable presumption of "non-defectiveness" for a warning adopted "in conformity with government standards established for that industry." Id. at § 703(2). In particular, the Utah statute specifies that:

> There is a rebuttable presumption that a product is free from any defect or defective condition where the alleged defect in the plans or designs for the product or the methods and techniques of manufacturing, inspecting and testing the product were in conformity with government standards established for that industry which were in existence at the time the plans or designs for the product or the methods and techniques of manufacturing, inspecting and testing the product were adopted.
>
> [Ibid.]

The statutory presumption in Utah, unlike New Jersey, is not limited to warnings for pharmaceutical products.

As the Utah Supreme Court has described it, the Utah Legislature "must have intended to benefit the manufacturer by creating [this] presumption of nondefectiveness" for a product warning fashioned in compliance with governmental standards. Egbert v. Nissan N. Am., Inc., 167 P.3d 1058, 1062 (Utah 2007). "The presumption therefore gives a kind of legal imprimatur to the significance of compliance with federal [product safety] standards." Ibid. Even so, the Utah Supreme Court has construed the UPLA's statutory presumption as one that can be overcome by the traditional civil burden of a preponderance of the evidence, rather than by a heavier evidentiary burden, such as clear and convincing proof. Ibid.

Accordingly, both the New Jersey and Utah[16] products liability statutes establish, in an effort to recognize a manufacturer's regulatory burden, a rebuttal presumption that a warning label complying with governmental standards is

[16] We have no need to consider at this point, under choice-of-law rules, which State's statutory presumption applies, or which State's public policies should weigh more heavily in the court's analysis, in this equitable tolling context. We are satisfied that neither State's statutory presumption requires reversal of the trial judge's ruling in this case.

"adequate" or "nondefective." Here, it is undisputed that the FDA approved each of the product warnings for Accutane that were provided to plaintiff and her treating physicians, including the final—and arguably-stronger—written set of warnings that plaintiff was given in 2003.[17] The question then becomes whether these statutory presumptions should somehow play a role in a judicial analysis of whether a plaintiff supplied with those warnings acted reasonably in delaying the filing of his or her lawsuit. We believe that the public policies underpinning the statutory presumptions should at least be considered when weighing the panoply of factors and the overall reasonableness of a plaintiff's delay in filing suit.

If the FDA-approved warnings that a consumer received are presumed—as a matter of law and legislative mandate—sufficient to place an adult consumer on reasonable notice of a pharmaceutical drug's risks before ingesting it, those warnings also bear upon what that same consumer knew, or reasonably should have known, about the drug and its potential adverse side effects for purposes of contemplating potential litigation against the drug manufacturer.

[17] The record indicates that the amended version of the product brochure that plaintiff received in 2003 was approved by the FDA in 2002.

The warnings are designed to alert the reader to the potential for harm. If they are presumed adequate for purposes of a consumer deciding whether to use a product, they are logically also relevant to the user's reasonable awareness of whether the product has caused or will cause her harm, for purposes of an equitable tolling analysis. It also stands to reason that the legislative desire to lessen a drug manufacturer's potential liability for using an FDA-sanctioned warning also would extend to protecting that same manufacturer from an open-ended burden of defending belatedly-filed product liability lawsuits.

We are not suggesting that a plaintiff is routinely obligated to call labeling or causation experts as witnesses at a Lopez hearing,[18] or that the hearing in such equitable tolling cases should be converted into a "mini-trial" about the adequacy of an FDA-approved warning every time that a plaintiff receiving such a warning waits to file a products liability action more than two years after receiving such a warning from a drug manufacturer. What we are saying is that the trial court—at

[18] Plaintiff's experts at trial, Dr. Blume and Dr. Sachar, did not comment specifically about the 2003 warnings for Accutane in their trial testimony. The summation of plaintiff's counsel and the verdict sheet did not specifically address the 2003 warnings, as opposed to the earlier warnings.

least in a preliminary fashion and subject to the jury's potential ultimate[19] findings of adequacy or inadequacy—should not ignore the public policies supporting the statutory presumption when it decides whether or not the applicable statute of limitations should be equitably tolled. These public policy concerns are germane under the more general notion of prejudice to the defendant, a decisional criterion that the Supreme Court identified when it issued its seminal opinion in Lopez.

As the Court wrote in Lopez, "statutes of limitation are statutes of repose and the principal consideration underlying their enactment is one of fairness to the defendant. So in each case the equitable claims of opposing parties must be identified, evaluated[,] and weighed." Lopez, supra, 62 N.J. at 274 (internal citations omitted). "The interplay of the

[19] The trial court in the Lopez hearing need only make a preliminary finding that the public policies underlying the presumption of adequacy are outweighed by the particular facts and circumstances presented, and that plaintiff has supplied a reasonable basis for overcoming the presumption for purposes of extending the statute of limitations. A jury may ultimately find, after a plenary examination of the proofs, that the presumption of adequacy has not been overcome. In the present case, plaintiff's labeling expert, Dr. Blume, focused on the wording of the 1984 and 2000 warnings, and the jury was not specifically charged to evaluate the adequacy of the 2003 warnings. Plaintiff did not make an effort at trial to try to show that her resumed ingestion of Accutane in 2003 had exacerbated her previously-diagnosed IBD condition.

conflicting interests of the competing parties must be considered." Id. at 275. The public policies that generated the statutory presumptions in Utah and in this State represent, in our view, a pertinent aspect of such "conflicting interests." We are not saying that the statutory presumptions strictly apply in the equitable tolling context, but at least the legislative policies that underlie those statutes should be factored into the court's analysis.

D.

Having made these observations, we are nonetheless satisfied that the trial court's determination on the equitable tolling issues here was sound, and that it does not undermine the statutory policies that we have identified. In her cogent and detailed oral opinion, the trial judge identified many persuasive reasons for treating plaintiff's delay in filing suit beyond the two-year statute of limitations as a reasonable one.

We agree with the trial judge that the written warnings that plaintiff received in the latter part of 2003 predominantly focused upon pregnancy, and to a lesser degree, upon suicide risks. The materials alluded to abdominal and bowel problems in a far less conspicuous or pointed manner. Defendant's reliance on the two consent forms signed by plaintiff is substantially undercut by the fact that neither of those forms says a word

about abdominal or bowel symptoms. Plaintiff, who the judge found to be credible, consistently stated that her doctors had said nothing to her about the risks of IBD, abdominal or bowel problems at the time her sixth course of Accutane was prescribed in the fall of 2003. We also agree that it was appropriate for the trial judge to take into account plaintiff's young age, and the fact that she had been repeatedly prescribed Accutane by her physicians since she was twelve years old, and even after she had been diagnosed with IBD.

It was not unreasonable, in these particular circumstances, for plaintiff to not yet appreciate by December 2003 that her use of Accutane had produced her IBD or that it had exacerbated that condition. The last set of warnings that she received in 2003, in spite of their presumptive adequacy, were demonstrably insufficient in this factual setting for this plaintiff's cause of action to have accrued before December 21, 2003.

Because we are satisfied that equitable tolling was justifiably extended by the trial court to at least December 21, 2003, we do not have to resolve whether plaintiff's subsequent exposure to the lawyer's advertisement in 2004 did or did not trigger an ultimate accrual. Consequently, we need not address Roche's argument that the trial court improperly treated the lawyer's advertisements as the limitations trigger date. Cf.

Martinez, supra, 163 N.J. at 52 (noting that the discovery rule does not require that a plaintiff "have knowledge of a specific basis for legal liability . . . before the statute of limitations begins to run").

Conversely, we also do not have to address plaintiff's competing contention that even if, as a matter of law, the statutory presumptions of adequacy and nondefectiveness are pertinent to an equitable tolling analysis, Roche forfeited the benefits of such presumptions with respect to Accutane. In particular, we need not examine plaintiff's contention that Roche—according to proofs that plaintiff was foreclosed from adducing on punitive damages—allegedly misled the FDA about the reported incidents of adverse effects of Accutane after the drug went to market.[20]

[20] We are mindful that, on June 3, 2010, the New Jersey Supreme Court granted certification in Blessing v. Johnson & Johnson, ____ N.J. ____ (2010), arising out of an unreported decision of this court which was brought to our attention by Roche pursuant to Rule 2:6-11(d) before certification was granted. See Blessing v. Johnson & Johnson, No. A-3561-08 (App. Div. Mar. 5, 2010) (affirming the dismissal of a lawsuit against a suture manufacturer filed more than two years after those sutures were surgically removed). The plaintiff's petition for certification in Blessing urges the Court to consider, among other things, whether "the statute of limitations should be equitably tolled in a products liability action involving a medical device, when a manufacturer intentionally conceals information about a product defect."

In sum, although we have adopted a more expansive approach to the tolling issue that incorporates the legislative policies relating to the statutory presumptions of adequacy or nondefectiveness, we affirm the trial court's denial of Roche's motion to dismiss the complaint as time-barred.

III.

The next significant matter for our consideration is what the parties refer to as the "numbers" issue.

In both her trial proofs and in her counsel's arguments to the jury, plaintiff relied heavily upon the number of adverse case reports for Accutane and other quantitative evidence as proof of at least two critical issues: (1) that a patient's use of Accutane can cause IBD and other gastrointestinal problems, and (2) that Roche acted too slowly and ineffectively in responding to those risks with more forceful product warnings. Roche contends that the trial court unfairly curtailed its ability at trial to defend that numbers-oriented evidence and advocacy.

The curtailment at issue arose out of a restrictive pretrial order governing the defense proofs that was only partially relaxed on the eighth day of trial; a jury instruction in the midst of a key company witness characterizing as "unscientific" certain uses of the background rates of IBD in

the general population; and limitations upon defense counsel's summation when he was discussing the "numbers" issues. Roche contends that these limitations on its defense proofs and arguments were unduly restrictive and inconsistent with the appellate panel's opinion in McCarrell, supra, in which a new trial was ordered for arguably similar reasons.

A.

This is the pertinent chronology. Prior to the trial in this case, plaintiff moved to bar defense counsel from presenting certain proofs and arguments concerning the background incident rates of IBD in the general population. In essence, plaintiff argued, those general background rates are unreliable because symptoms of IBD are frequently underreported. Plaintiff noted an estimate that the actual number of persons with IBD may be ten or a hundred times higher than, for example, the number of persons who actually report such medical problems to drug companies or other data collectors. Plaintiff also noted that in a different Accutane trial conducted in another state and in certain deposition testimony, Roche and its witnesses had previously taken the position that such background data cannot be scientifically used or formulaically applied to prove or disprove causation.

Roche opposed plaintiff's pretrial application. Although Roche's counsel agreed that the numbers do not prove causation, he argued that Roche should not be curtailed in its defense against plaintiff's case from explaining its "business practice of how it looks at incoming complaints" and in looking for "signals" in the data that might call for stronger product warnings.[21]

Over the objection of Roche, the trial court entered a pretrial order on the numbers issue, which provided as follows:

> ORDERED that [p]laintiff['s] request to preclude any witness testimony, documentary evidence[,] or argument stating the background rates of IBD in the general population as compared to the rate of IBD in Accutane users support [d]efendants' position that Accutane use does not cause IBD is granted, but [d]efendants' position that they acted reasonably based on background rates is allowed if it is factual testimony describing what they did by their present or former employees, and the numbers are not told to the jury; . . . .

[21] In its motion papers before this pretrial issue was argued to the trial court, Roche asserted that "the total number of Accutane users is relevant to [p]laintiff['s] causation case," and resisted a ruling "that these [background] numbers may not be introduced in response to [p]laintiff['s] causation arguments." (Emphasis added). However, defense counsel qualified their position about the potential relevance of the numbers to causation, by stating, at the end of Roche's motion papers, that "Roche stands prepared, if the [c]ourt deems it necessary to admissibility in spite of Roche's contrary views, to have the [c]ourt limit Roche's use of this evidence to its affirmative presentation of its actions in monitoring the IBD case reports that it received." (Emphasis added).

[(Emphasis added.)]

As noted, this directive precluded Roche from referring at trial to the background rates of IBD in the general population to disprove causation. The order did allow Roche to present "factual testimony" to show that it acted reasonably based on such background rates, but only if "the numbers are not told to the jury[.]" The trial court did not, however, impose any restrictions upon plaintiff in her own use of numerical proofs at trial, other than a restriction against using the numbers in a formula.

As anticipated, plaintiff extensively presented a host of quantitative proofs at trial, in her dual effort to both prove causation and to prove the inadequate response by Roche to the adverse data that, as plaintiff's counsel phrased it, was "piling up" after Accutane was on the market. For example, during opening statements, plaintiff's counsel noted that she would present proof that Roche was aware of at least 104 reported cases of IBD, of which thirty-three cases were given a causality rating of possible or probable. Plaintiff's counsel also cited in his opening argument to an internal Roche report stating that, in 2002, there had been sixty-four reports of Crohn's disease.

This emphasis on numbers continued during the evidentiary phase of the trial during plaintiff's case-in-chief. Plaintiff's counsel and her witnesses repeatedly cited to the number of adverse events and causality assessments. Plaintiff also successfully moved into evidence various exhibits containing figures about gastrointestinal diseases and symptoms suffered by Accutane users. For example, plaintiff's counsel asked Dr. Sachar about: the specific number of ADR reports referred to in an article; the sixty-four cases of Crohn's disease; and the number of challenge, dechallenge, and rechallenge reports. Dr. Sachar testified that Roche had received about fifty such challenge/dechallenge/rechallenge reports annually. Dr. Sachar also testified that, even accounting for underreporting, the eighty-five cases of IBD reported in the article could indicate that there were actually anywhere from 850 to 8500 cases of IBD in the exposed population. Similarly, Dr. Blume testified on direct examination that the thirty-three cases of IBD, as reported in the Lefrancq memorandum, could indicate that there were likely 330 to 3300 actual cases.

The pretrial order's limitations on the defense's own use of numbers manifestly restricted Roche's counsel at trial, in both opening statements to the jury and in the cross-examination

of plaintiff's witnesses. For instance, during his opening statement, defense counsel described the method by which Roche had compared the number of reported IBD cases among Accutane users against the background rate of IBD in the unexposed population. He stated to the jury that such a comparison could show whether there was a "connection" between Accutane use and IBD, and was "important" to place the ADR reports, which plaintiff claimed had "piled up," in context.

Plaintiff's counsel objected to these statements, and the judge sustained the objection. The judge ruled that defense counsel had improperly suggested to the jury that Roche's use of the background rate was a scientifically-accepted method of evaluating a drug. As the judge perceived it, the evidence established that such a comparison "cannot be used as a scientific basis for making a decision." Although the judge found it appropriate for defense counsel to argue that Roche had considered the number of ADR reports against the background rate of IBD in deciding whether to conduct a further investigation or issue a stronger warning, Roche could not argue that such a comparison was a scientifically-valid way to evaluate the risk of a drug. The judge warned that, if Roche made such an argument again during the trial, she would give the jury a

cautionary instruction. Defense counsel promised to try to adhere to that limitation during the trial.

The trial court's pretrial restriction on the numbers evidence again came into play when defense counsel attempted to cross-examine plaintiff's witnesses. For example, during the cross-examination of Dr. Blume, plaintiff's labeling expert, defense counsel asked her to comment about a document reflecting how Roche had analyzed certain data on Accutane that it had presented to the FDA. When Dr. Blume then began to comment upon the background incidence rates for IBD that Roche had examined, and certain calculations that Roche had made based upon that data, defense counsel stopped her, indicating that he was "trying to adhere to the rules of the [trial] [c]ourt" by limiting such numerical references. At that point, the trial judge sent the jury out and then reinforced the restrictions that had been imposed in the pretrial order. Defense counsel responded that, although he would "love to go on and go to the numbers," he understood the court's limitations and would abide by them in his cross-examination. When the cross-examination of Dr. Blume resumed, defense counsel obliquely referred the witness to the IBD background rates conceptually, but steered clear of the actual figures, at one point instructing the witness, "I don't want you to read [aloud] the numbers."

B.

On the eighth day of trial, prior to the close of plaintiff's case, the judge, over plaintiff's objection, decided to re-visit the issue of the admission of the numbers evidence. At defense counsel's request, the judge addressed the issue after further written submissions by the parties, which included deposition testimony, scientific articles, and FDA regulations. After reflecting upon these additional materials and arguments, the judge partially reconsidered her pretrial ruling as to the numbers evidence. The judge found, on reflection, that it would be "unfair to the defense not to let them present" evidence of the methodology that Roche had used in comparing the reported events to the background rate of IBD. The judge thus modified her earlier ruling, and allowed Roche to submit specific numerical evidence of background rates, and evidence as to how it used these rates in connection with monitoring IBD and Accutane, but not to show causation. The judge further indicated she would give the jury a cautionary instruction concerning such proofs.

Thereafter, Dr. Huber testified in the defense's case-in-chief that Roche had modified its warnings in 1984, in response to reports of IBD among Accutane users. Dr. Huber maintained that no stronger warnings were required because the incidence

rate of IBD in Accutane users was "well within" the expected rate of IBD in the general population. In making that determination, Roche had compared the rate of IBD in the population exposed to Accutane to the rate of IBD in the unexposed population. Dr. Huber stressed that the comparison was only used to assess "signals," but not "causation."

Dr. Huber highlighted several internal Roche reports that detailed the number of users, adverse reports, and background rates. Those documents reflect an incidence rate of ulcerative colitis in the unexposed population of approximately six to eight cases per 100,000. Meanwhile, reported incidence of Crohn's disease in the unexposed population was approximately two per 100,000.[22]

Dr. Huber explained to the jury that, in calculating the number of IBD cases in the exposed population, Roche had assessed the reported adverse events. Then, because it was estimated that only one to ten percent of such events are

[22] Although it was difficult to determine exactly how many individuals had taken Accutane, Dr. Huber highlighted various reports and articles that presented estimated numbers of the patients treated with Accutane and the prescriptions written. The number of patients were estimated as: 1 million (1982 to 1987); and 850,000 to 915,000 (September 1998 to August 1999). The number of estimated prescriptions ranged from 32 million globally to 15 million in the United States, for the years 1982 to 1999. Another estimate set the number of prescriptions in the United States at 20 million from 1982 to 2000.

reported, Roche factored in underreporting. Dr. Huber compared these numbers. He testified that in calendar year 1988, when approximately one million patients took Accutane, there were only seven reports of IBD. From 1982 to 1999, when more than 32 million patients took the drug, there were only 206 case reports of IBD. According to Dr. Huber, most of the instances occurred in the age demographic in which IBD was most prevalent, and, as Dr. Huber asserted, well within the background rate.

The weight of this defense evidence concerning background rates was diluted, however, when on cross-examination Dr. Huber admitted that, by factoring in underreporting, the number of actual cases of IBD may have been much higher. For example, there had been nine reported cases of Crohn's disease from 1982 to 1987. Factoring in underreporting, Dr. Huber admitted that the actual cases of the disease may have actually ranged from 90 to 900. In addition, from 1982 to 1999, Roche received 206 reports of IBD, which he admitted could relate to a range from 2060 to 20,600 cases.

C.

Roche argues that the court's mid-trial change of heart concerning the defense's use of numbers evidence was inadequate to undo the prejudice that it had already suffered by the restrictions originally imposed by the pretrial order. Roche

further argues that the trial court unfairly prejudiced it by issuing a cautionary instruction during Dr. Huber's testimony. That instruction advised the jurors, in pertinent part, as follows:

> [t]he comparison of a background incidence of . . . IBD, in the general population, to the reported incidence of IBD in patients taking Accutane, is not a scientifically accepted method of proving whether a particular product . . . acts as a trigger for, and, therefore, is a cause of a particular side effect.
>
> So, you cannot use this as evidence of whether it does or doesn't cause [sic], you can't use this kind of comparison. However, the comparison of background incidence of [IBD] in the general population . . . to the reported incidence of IBD in patients taking Accutane, is not being offered as a method of proving or disproving causation. You couldn't use it for that.
>
> And it cannot be considered as evidence of whether there is causation [sic] relation between Accutane and IBD. However, it is offered and is evidence of one of the methods that Roche claims it used to conduct its post-marketing surveillance of Accutane, and you can consider it in evaluating or as evidence of how Roche conducted their business.
>
> [Emphasis added.]

This instruction differed from an alternative instruction that defense counsel had proposed, which omitted any reference to "science."

Roche argues that the trial court's version of the jury instruction was especially harmful, in accentuating to the jurors that Roche's internal corporate use of background numbers was, at least in some respects, unscientific. To be sure, the court's instruction was literally confined to causation matters, rather than to Roche's corporate conduct, or what at times is referred to in the record as "signal detection." Even so, Roche argues, the trial court's directive to the jurors that at least one use of the background numbers was not "scientifically accepted," placed a prejudicial and unnecessary spin on the proofs, to Roche's detriment. Roche argues that the limiting instruction, as it was phrased, compounded the potential for prejudice that had already been created by the pretrial order restricting the use of quantitative data.

D.

The prejudice arising out of the numbers issue resurfaced again in closing arguments. In closing argument, plaintiff's counsel repeatedly emphasized the quantitative proofs. As part of that summation, plaintiff's counsel used an analogy to the Wachovia Center arena, which he had first raised in cross-examining Dr. Blumberg, Roche's expert. In this regard, plaintiff's counsel alluded to the 206 adverse case reports linking Accutane to IBD which had been stated in the LaFlore

report. Extrapolating from that figure, plaintiff's counsel suggested that the actual number of patients with IBD could have been a hundred times that sum, or 20,600, which counsel characterized as "enough to fill up the Wachovia Center where the [Philadelphia] Flyers play hockey." In summation, plaintiff's counsel repeated that analogy, reminding the jurors that the calculations could yield enough cases of IBD to "fill the Wachovia Center," and that "[i]t would be standing room only."

In his own summation, defendant's trial attorney was accorded some leeway to refer to the background rates, and to contest plaintiff's assertions that the adverse case reports and other statistics were meaningful. However, when defense counsel was in the midst of discussing such numbers in his summation, plaintiff's counsel interrupted and raised an objection to his adversary "running through [Accutane] usage numbers each year." The judge sustained that objection, and defense counsel ceased that line of argument.

E.

As we evaluate Roche's argument on appeal that these various rulings and events deprived it of a fair trial, we consider—for comparative but not precedential purposes—this court's treatment of related, although not identical,

circumstances that prompted the remand for a new trial in McCarrell. In McCarrell, supra, No. A-3280-07 (slip op. at 92), the trial judge excluded any comparison of the number of reported adverse events to the number of people taking Accutane for the purpose of proving causation. The trial judge did allow the plaintiff in McCarrell to present evidence, "in a numerical fashion, about a host of adverse incidents in which Accutane users contracted or manifested symptoms associated with IBD." Id. (slip op.at 93). The jurors in McCarrell were not allowed, however, "to hear certain competing figures and expert testimony that Roche had proffered, in an effort to put the adverse numbers stressed by plaintiff in a better light." Id. (slip op. at 97). For example, Dr. Huber, who the defense also called as a witness in that case, was barred from testifying in McCarrell that from 1982 to 1995, five million people had been treated with Accutane. Id. (slip op. at 100).

The appellate panel in McCarrell held, with respect to this "numbers" issue, that the trial court had:

> erred in forbidding Roche from placing into evidence statistics about Accutane usage that could have made Roche's conduct and labeling decisions appear far more reasonable to the jury. For instance, the "five million users" statistic proffered by Dr. Huber could have given the jurors very relevant contextual background, and possibly led the jury to be more indulgent of Roche's

> delay in upgrading the risk information on Accutane's label and package insert.
>
> Even accepting, for the sake of argument, Dr. Sachar's contention that adverse events are heavily under-reported, the quantity of actual users of a drug logically is a significant part of the numerical landscape. At a minimum, the actual usage data for Accutane would go to "safety signaling" concerns, i.e., whether Roche had received sufficiently frequent adverse "signals" to take corrective action.
>
> Whether or not the excluded proof would ultimately have altered the jurors' thinking about the reasonableness of the company's conduct, we are persuaded that the trial court unduly impeded Roche from offering this context-supplying evidence. Although the jury did learn from Dr. Cunningham that there were 300,000 Accutane users by 1983, it would have been far more powerful to the defense presentation if Dr. Huber had been allowed to inform the jury that five million people had taken Accutane by 1995, when plaintiff began his own treatment. Five million is a far cry from three hundred thousand.
>
> Had Roche been allowed to present the statistics showing five million Accutane users and other related counter-proofs, the jury would have had a fuller and more balanced picture of the data bearing upon the company's delay in changing its label.
>
> [Id. (slip op. at 101-02) (emphasis added; internal footnote omitted).]

Because of the trial court's erroneous limitation on Roche's presentation of numerical proofs and arguments in McCarrell, we vacated the judgment in favor of that plaintiff, and remanded

the case for a new trial.[23] See also Rand v. Hoffman-La Roche, Inc., 291 Fed. Appx. 249 (11th Cir. 2008) (affirming, among other things, a federal district judge's determination about the relevancy of the background incidence of IBD in the general population, in assessing whether Roche was liable for failing to provide adequate product warnings about IBD with Accutane).

This case differs from the first trial in McCarrell, inasmuch as we are presented here, not with a continuous preclusion of the defense's use of numerical proofs, but rather an initial restriction, which was partially lifted on the eighth day of trial. Even so, we similarly lack confidence that this trial, when considered as a whole, provided a full and fair opportunity for Roche to contest, present, and advocate the relevant "numbers" evidence. The trial judge's mid-course correction of her pretrial ruling, although reflective in nature and indicative of the judge's overall conscientious effort to be fair, was insufficient to compensate for, in effect, the uneven playing field that was used for the first two-thirds of the contest. The trial court's corrective measure was also weakened by the jury instruction's pointed designation of Roche's

[23] As we have already noted, the retrial verdict in McCarrell resulted in a higher damages award than the original trial.

methodology as "unscientific" and also by the curtailment of defense counsel's numerical arguments during his summation.

F.

The hallmark of our system of civil justice is fairness. Pellicer ex rel. Pellicer v. St. Barnabas Hosp., 200 N.J. 22, 40 (2009). No matter who wins or loses a trial, we fall short of our institutional obligations and aspirations if the process that generated a civil judgment is not, at bottom, one that gave both litigants a fair opportunity to present, within the confines of the Rules of Court and Rules of Evidence, their own "side of the story."

In reviewing contentions on appeal that a trial process did not fulfill these goals, we are equally mindful of our limited role as an appellate tribunal. We bear in mind the general deference that we rightfully owe to trial judges, who must make difficult rulings as the parties' arguments and evidence dynamically unfold. Green v. N.J. Mfrs. Ins. Co., 160 N.J. 480, 492 (1999) (noting the deference generally accorded to trial judges on the admission or exclusion of evidence).

Recognizing these overarching institutional considerations, we conclude that Roche was unduly impeded at this particular trial from adducing and advocating numerical proofs that could have potentially and reasonably led a jury to reach a different

verdict. We do not reach that conclusion lightly. We appreciate that this is a very difficult issue. The arguments raised by Roche are less powerful here than those it raised in McCarrell, where its "numbers" presentation was even more restricted by the trial judge. Nevertheless, a remand for a new trial in this case is likewise warranted.

Even though Roche ultimately was permitted in this case to get before the jury a substantial amount of "numbers" counterproofs through Dr. Huber's testimony, the trial court's original prohibition upon counsel referring to those numbers—up through that late point in the trial—easily could already have done its damage. It is not unreasonable to presume that the defense's presentation would have been stronger if Roche's counsel had been allowed to preview the numbers evidence in his opening statement to the jurors, and to explore such proofs with specificity in cross-examining Dr. Blume and plaintiff's other witnesses. See Jamgochian v. N.J. State Parole Bd., 394 N.J. Super. 517, 536 (App. Div. 2007) (emphasizing "[t]he importance of cross-examination, 'one of the greatest engines that the skilled man has ever invented,' for ascertaining the truth of a matter" (quoting 6 Wigmore on Evidence § 1838 (Chadbourn Rev. 1976))), aff'd as modified, 196 N.J. 222 (2008).

We recognize that Roche and its witnesses have taken somewhat different approaches concerning the significance or insignificance of the "numbers" proofs in the various Accutane cases that have been litigated. Some of those differences may well be attributable to litigation tactics or experimentation.

In any event, we reject plaintiff's contention that defense counsel waived any right to present the numbers proofs here in a more expansive fashion. Although defense counsel did state repeatedly to the trial judge, after she had entered her restrictive pretrial order, that the defense would hew to the order's limitations, those statements do not mean that Roche had abandoned its desire to use the numbers evidence without such restriction. Indeed, as we have noted, defense counsel advised the court during plaintiff's case-in-chief that he would "love" to make greater use of the numbers proofs. Roche ultimately tried to do so in the latter portion of the trial, through Dr. Huber's testimony, after the pretrial restriction was partially abated. But that late development did not eliminate the disadvantage that had been imposed upon Roche at the outset.

We recognize that the conceptual boundary between using background data for purposes of evaluating "signals" and company conduct, but not for "causation," is a technical and somewhat elusive distinction. In fact, there logically appear to be some

implicit causation aspects of a drug company using background incidence data for evaluating signal strength. Increased reports of a medical condition occurring in a drug's users, as contrasted with the general population, may well provoke a drug maker to strengthen its labeling, because such adverse reports may suggest that the product is, in fact, "causing" such adverse results. In any event, we need not here draw the boundaries between causation and conduct with precision or with definiteness. The point remains that, even accepting, arguendo, as reasonable the trial court's prohibition upon Roche using background numbers to disprove causation,[24] the trial as a whole did not provide Roche with a sufficient opportunity to make full and legitimate uses of such contextual evidence as part of its trial advocacy.

The jury instruction issued by the court during Dr. Huber's examination went too far in characterizing to the jurors the use of background numbers to prove or disprove causation as "unscientific." Although that verbiage about science was consistent with at least some of what Roche's representatives

[24] On remand, the defense is not foreclosed by this opinion from attempting to use the numbers evidence to show not only that the company acted reasonably in the manner in which it developed and modified the Accutane product warnings, but also to attempt (if it chooses to do so) to disprove causation—subject, of course, to appropriate impeachment and cross-examination by plaintiff and the application of N.J.R.E. 702.

had previously asserted in this and other litigation, it was unnecessary to include the phraseology in the special jury charge.

Moreover, the limitations imposed on defense counsel's summation were likewise excessive. Indeed, the objection to the summation may not have arisen had Roche been allowed to develop its numbers proofs in a plenary fashion from the outset of the trial. The restrictions impeded defense counsel's ability to take full advantage of his advocacy concerning the "numbers" proofs, and to respond to the vivid, numbers-oriented "Wachovia Center" analogy that had been presented during the trial by plaintiff's counsel.

In remanding this matter for a new trial because of the inappropriate handling of the numbers issue, similar to what this court did in McCarrell, we do not wish to be misunderstood about the significance of that directive. The trial judge presided over this case without the benefit of this court's opinion in McCarrell, which undoubtedly would have guided the court accordingly in its handling of the numbers issue. We also are mindful that there are other Accutane cases in the mass tort pipeline in the Law Division that will be affected by what we have done here, and thus we anticipate that the additional guidance will be helpful to both the court and counsel.

We commend the trial judge for attempting a mid-course correction of her pretrial ruling. Unfortunately, that correction came too late to give us full and final comfort in the soundness of the process that produced the jury's verdict. Having stated these points, we vacate the judgment in plaintiff's favor, and remand for a new trial, consistent with the direction about "numbers" evidence provided in this opinion and in McCarrell.

IV.

We have fully considered the balance of the arguments presented by Roche on appeal. Many of those arguments were unsuccessfully raised by Roche in McCarrell, and we discern no reason to treat them differently in this case. On the whole, defendants' remaining arguments are unpersuasive, and only warrant some brief comments.

A.

Roche argues, as it did in McCarrell, that the trial court erred in admitting proofs of adverse case reports for Accutane and its internal causality assessments. For the reasons stated by the panel in McCarrell, which we adopt and incorporate here by reference, the admission of such proofs—particularly as it was explained and used to support, in part, Dr. Sachar's expert opinions on causation—was not improper. See McCarrell, supra

(slip op. at 75-76). By way of a caveat, however, we do endorse and repeat the panel's acknowledgment in McCarrell that "causality assessments, standing alone, are not sufficient to support an admissible scientific opinion on causation." Id. (slip op. at 76).

We likewise are satisfied that the trial court did not exceed its discretion in admitting Dr. Sachar's expert testimony in this case, and allowing plaintiff's related arguments highlighting the lack of human clinical studies on whether Accutane increases the risks of contracting IBD. Although it is uncertain whether such clinical studies—if they had been performed or could have been feasibly performed in accordance with ethical principles—would have shown or disproven a causal link between Accutane and IBD, it was not improper for plaintiff to allude to the absence of such studies as part of the overall factual landscape. Moreover, it does not appear that defendant made a contemporaneous objection to these particular references at trial. We detect no error, much less plain error, in the trial court's allowance of proofs and arguments on this subject.

Similarly, we are unpersuaded by defendant's contentions that the court abused its discretion in allowing plaintiff to introduce selective testimony from Roche's former employee, Dr. Bess, recounting an internal disagreement about Accutane within

the company between its marketing and drug safety departments. This evidence, even though it directly related to a different side effect than IBD, i.e., suicide, was relevant because it tended to corroborate plaintiff's overall theme that marketing had played a role in Roche's decision not to issue stronger warnings with the drug. See N.J.R.E. 401 (providing that relevant evidence only needs to create a "tendency" to prove or disprove a fact of consequence).

We have examined Roche's other arguments alleging various trial errors, including its claim that the company was unfairly criticized by Dr. Sachar and plaintiff's counsel for its interactions with the FDA; its claim that plaintiff's counsel improperly made comparative references to the inclusion of hepatitis and liver side effects in the Accutane package inserts; and other alleged singular and cumulative errors. None of these arguments, separately or in combination, requires a new trial. We are satisfied that, but for the aforementioned errors relating to the "numbers" proofs, see Point III, supra, the trial was, on the whole, fair.

B.

We reject Roche's contention, one which it had previously asserted in McCarrell, that Dr. Sachar's methodology was manifestly unscientific and unsound, particularly because of its

partial reliance on animal studies, and that the trial court thus should have rejected his expert testimony under N.J.R.E. 702. We agree with the McCarrell panel's lengthy analysis and determination that Dr. Sachar's expert methodology did indeed satisfy the prerequisites for the admission of expert proof in this State. See McCarrell, supra, (slip op. at 44-86). Dr. Sachar's testimony in the present case substantially replicated his explanation of his methodology in McCarrell. We perceive no palpable abuse of discretion, nor any manifest denial of justice, in the admission of his expert opinions, particularly when his testimony is taken as a whole. See Hisenaj v. Kuehner, 194 N.J. 6, 12 (2008) (limiting the scope of appellate review of the trial court's rulings on expert admissibility).[25]

[25] We are unpersuaded that the two published research articles supplied to us on appeal by Roche's counsel, pursuant to Rule 2:6-11(d), render Dr. Sachar's expert testimony inadmissible. See Seth D. Crockett et al., Isotretinoin Use and the Risk of Inflammatory Bowel Disease: A Case-Control Study, Am. J. Gastroenterology (published online Mar. 30, 2010); Seth D. Crockett et al., A Causal Association Between Isotretinoin and Inflammatory Bowel Disease Has Yet to Be Established, 104 Am. J. Gastroenterology 2387 (2009). Although both of these articles appear to lend some support to Roche's contention that the use of Accutane has not conclusively been scientifically proven to cause IBD, the research in these articles also arguably lends some credence to plaintiff's competing position on causation, in light of findings that higher doses of isotretinoin, dose escalation, and longer duration of therapy were correlated with higher incidences of ulcerative colitis in the case-control group.

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C.

Roche further argues that the trial court should have entered judgment in its favor because its warnings were adequate as a matter of law. On this point, Roche cites to several New Jersey authorities, including the statutory presumption of adequacy under the PLA, N.J.S.A. 2A:58C-4. It does so, even though Roche had argued in the trial court that the substantive law of Utah, rather than of New Jersey, applies.

We do not need to resolve any issues about the substantive choice-of-law applicable to this case, as we are satisfied that the trial proofs here reasonably supported a verdict for plaintiff under either Utah or New Jersey law. However, on remand prior to the new trial that we have ordered, the parties and the court are free to re-visit the relevant choice-of-law

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In any event, because this recent scientific literature was not presented to the trial judge, nor addressed by any of the experts at trial, we decline to make any conclusions or inferences from the articles. Nieder v. Royal Indem. Ins. Co., 62 N.J. 229, 234 (1973). Of course, on the retrial we have ordered, the parties' respective experts may update their opinions to take into account the Crockett articles and any appropriate implications that should be derived from them. Additionally, the trial judge is not foreclosed from reexamining the admissibility of any expert's testimony in light of these articles, or any other new developments in the published literature.

We are also satisfied that the additional New Jersey cases and out-of-state legal authorities supplied to us by counsel in correspondence pursuant to Rule 2:6-11(d) do not affect our analysis of the issues.

questions in light of supervening case law, including the Supreme Court's November 2008 opinion in P.V. ex rel. T.V. v. Camp Jaycee, 197 N.J. 132, 135-36 (2008) (rejecting the "governmental interest" test for choice-of-law issues and substituting the "most significant relationship" test as set forth in the Restatement (Second) of Conflicts of Laws (1971)).

Whether Utah or New Jersey substantive law is applied here, we are satisfied that plaintiff adduced sufficient evidence at this trial to overcome the presumption of adequacy or nondefectiveness occasioned by the FDA's approval of the product warnings. There is ample factual proof in the present record to justify the jury's determination that the warnings supplied with Accutane, even though they had been approved by the FDA, were inadequate to have reasonably alerted plaintiff and her physicians to the risks that plaintiff would contract IBD from using the drug.

According, as we must, all reasonable inferences from the record in favor of plaintiff, the court had sufficient reason to deny Roche's requests for the entry of judgment in its favor. See R. 4:37-2(b), R. 4:40-1, and R. 4:40-2(b); see also Estate of Roach v. TRW, Inc., 164 N.J. 598, 612 (2000). Among other things, the expert testimony of plaintiff's labeling expert, Dr. Blume (who was not countered by an equivalent defense expert

specifically called to opine exclusively on labeling issues) was sufficiently persuasive and tied to the proofs that a reasonable juror could have found the statutory presumptions were overcome. We also find that the evidence at trial sufficed to support a reasonable circumstantial inference that a stronger warning would have discouraged plaintiff from using the drug.

D.

We have carefully examined all of the remaining points raised on appeal by Roche, and are satisfied they lack sufficient merit to warrant discussion in this written opinion. R. 2:11-3(e)(1)(E).

Affirmed in part, vacated in part, and remanded for a new trial.