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Supreme Court of New Jersey.

IN RE: ACCUTANE LITIGATION

A-26/27 September Term 2017
|
079933
|
Argued April 23, 2018
|
Decided October 3, 2018

On certification to the Superior Court, Appellate Division.

Attorneys and Law Firms

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Adam M. Slater argued the cause for amicus curiae New Jersey Association for Justice (Mazie Slater Katz & Freeman, attorneys; Adam M. Slater, of counsel and on the brief).

Opinion

JUSTICE ALBIN delivered the opinion of the Court.

This appeal arises from 532 product-liability claims filed against defendants Hoffmann-La Roche Inc. and Roche Laboratories Inc. (collectively Roche), corporations with their principal places of business in New Jersey. Roche developed, manufactured, marketed, and labeled Accutane, a prescription medication for the treatment of severe and persistent cases of acne. Plaintiffs allege that Accutane, prescribed by their physicians for the treatment of acne, caused them to contract inflammatory bowel disease (IBD) and that Roche failed to give adequate label warnings to advise them of the known risks of the medication. Of the 532 plaintiffs, 18 are New Jersey residents and 514 are residents of 44 other jurisdictions. Plaintiffs' claims are designated as Multicounty Litigation (MCL) and consolidated in the Atlantic County Superior Court, Law Division, for administrative purposes.

Two issues are before us. The first is what law governs whether Roche's label warnings were adequate -- the law of each of the 45 jurisdictions where plaintiffs were prescribed and took Accutane or the law of New Jersey where the 532 cases are consolidated for MCL purposes. The second issue is the adequacy of the label warnings for the period after April 2002. Because Roche's warnings received the approval of the federal Food and Drug Administration (FDA), those warnings enjoy a "rebuttable presumption" of adequacy under New Jersey's Products Liability Act (PLA). See N.J.S.A. 2A:58C-4. That presumption provides pharmaceutical companies greater protection in New Jersey than in many other jurisdictions.

After conducting a choice-of-law analysis, the trial court determined that New Jersey's PLA applies to each of the 532 consolidated cases and then concluded that plaintiffs failed to overcome the presumption of adequacy that attached to Roche's Accutane warnings. Accordingly, the court granted summary judgment in favor of Roche.

The Appellate Division came to a different result. The panel held that the law of each jurisdiction where plaintiffs were prescribed and took Accutane would govern the adequacy of the label warnings. After conducting a state-by-state legal analysis, the panel concluded that summary judgment in favor of Roche was improvidently granted in

all cases except those governed by the laws of California, Colorado, Indiana, Maryland, Mississippi, New York, Texas, and Virginia. In other words, under New Jersey's PLA and the laws of thirty-six other jurisdictions, the panel maintained that a genuine issue of material fact remained concerning the adequacy of the warnings.

***6** We now reverse in all those cases in which the Appellate Division reinstated plaintiffs' actions against Roche. Like the trial court and Appellate Division, we apply the Restatement (Second) of Conflict of Laws (Am. Law Inst. 1971, amended 1988) ("Restatement"), adopted for personal injury cases in McCarrell v. Hoffmann-La Roche, Inc., 227 N.J. 569, 593-94 (2017), and P.V. ex rel. T.V. v. Camp Jaycee, 197 N.J. 132, 143 (2008). Unlike the Appellate Division, we hold that New Jersey has the most significant interests, given the consolidation of the 532 cases for MCL purposes in Atlantic County. The aggregation of hundreds of cases under MCL allows the resolution of common issues of law. A trial judge cannot be expected to gain a mastery of the law of forty-five different jurisdictions. Construing New Jersey's PLA is challenging enough. New Jersey's interest in consistent, fair, and reliable outcomes cannot be achieved by applying a diverse quilt of laws to so many cases that share common issues of fact.

The PLA's presumption of adequacy for medication warnings approved by the FDA gives a reasonable measure of protection to pharmaceutical companies, which are researching and developing medications to combat diseases and maladies that afflict people around the world. New Jersey also has an interest in ensuring that its companies are producing safe medications and attaching warnings that advise the public of their risks and benefits. On the record before us, even when viewed in the light most favorable to plaintiffs, we do not find that Roche withheld from the FDA material information that would have altered the nature of the warnings or engaged in economically driven manipulation of the regulatory process. We also find that plaintiffs did not present clear and convincing evidence that Roche knew or should have known that the label warnings were inadequate. Plaintiffs therefore have not overcome the statutory presumption of adequacy.

Consequently, as a matter of law, the warnings provided physicians with adequate information to warn their patients of the risks of IBD. We therefore reverse in part and affirm in part the judgment of the Appellate Division and dismiss all plaintiffs' complaints.

I.

A.

In this appeal, we address the adequacy of Roche's FDA-approved post-April 10, 2002 warnings for Accutane, the brand name for isotretinoin, a prescription drug developed and marketed nationwide by Roche for the treatment of severe cases of acne. See Kendall v. Hoffmann-La Roche, Inc., 209 N.J. 173, 180 (2012). Plaintiffs are 532 individuals from 45 jurisdictions, including New Jersey, who were prescribed Accutane by their treating physicians for their acne conditions. After taking the medication, plaintiffs claim they developed IBD, which encompasses "a number of chronic, relapsing inflammatory diseases of the gastrointestinal tract." See Tabor's Cyclopedic Medical Dictionary 1252 (23d ed. 2017) ("Tabor's").

The two most common forms of IBD are ulcerative colitis and Crohn's disease. The 532 plaintiffs in this case state that they suffer from ulcerative colitis, "a chronic condition characterized by ulceration of the colon and rectum," which leads to frequent and bloody bowel movements as well as fatigue, dehydration, anemia, and abdominal pain. See Kendall, 209 N.J. at 181. "The symptoms often wax and wane, but the condition is regarded as permanent." Ibid.

The heart of this case is plaintiffs' contention that the taking of Accutane caused their IBD and that Roche failed to adequately warn of that risk. A Long Form Complaint, filed on behalf of all plaintiffs, alleges that Roche knew or should have known that taking Accutane "was causally related" to IBD based on information contained in its adverse event database and the conclusions drawn by its scientists. Plaintiffs further allege Roche "did not adequately inform physicians or consumers of [Accutane's] propensity to induce, aggravate or cause IBD." Plaintiffs contend that Roche's failure to provide adequate warnings is the proximate cause of the "permanent physical and emotional injuries" they continue to suffer, and therefore they seek compensatory and punitive damages.

***7** Roche moved for summary judgment, claiming that the warnings were adequate as a matter of law.[1] We start with the relevant facts from the summary judgment record.

B.

In 1982, the Food and Drug Administration approved Roche's application to market Accutane for the treatment of recalcitrant nodular acne. As part of the FDA pre-approval process, Roche conducted a human clinical study involving 523 patients who took Accutane. No reports of IBD arose from that clinical study, although approximately twenty-two percent of the patients suffered certain gastrointestinal side effects. Roche submitted the study to the FDA.

When Roche launched Accutane commercially, the label warnings did not mention IBD. By 1983, during the postmarketing phase and while monitoring the safety of Accutane use, Roche received reports of six to eight patients -- out of a total population of 300,000 -- who had taken Accutane and developed IBD. Those reports prompted Roche to issue label warnings in 1984 to prescribing physicians, generally dermatologists, stating that Accutane "has been temporally associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders."

Roche collected additional data as it continued to monitor the effects of Accutane on patients. Between 1985 and 2001, Roche received at least twenty case reports called "challenge," "dechallenge," and "rechallenge" events. The reports described patients who, while taking Accutane, suffered intestinal disorders, with symptoms such as abdominal cramping and rectal bleeding (the "challenge" event), which subsided when Accutane use was discontinued (the "dechallenge" event), but reappeared when the medication regimen resumed (the "positive rechallenge" event). Those reports, many filed by the patients' treating physicians, were registered with MedWatch, an FDA-administered database that compiles adverse events concerning medications approved by the FDA.

In February 1999, the FDA asked Roche whether its data demonstrated the "reversibility" of Accutane-associated IBD. By that time, Roche had received information concerning nearly 300 cases that associated Accutane usage with the onset of IBD. An internal Roche email explained that approximately two-thirds of 188 patients who stopped using Accutane recovered. Although Roche responded to the FDA inquiry by stating that there was "not sufficient information to recommend additional label changes related to [IBD]," the FDA nevertheless requested that Roche remove from its label warning the word "temporally" and add that symptoms of IBD "have been reported to persist after Accutane treatment has stopped." Roche complied.

By April 10, 2002, Roche had generated a variety of FDA-approved warning labels and materials for a target audience of prescribing physicians, pharmacists, and patients. The information provided to physicians is of particular importance because New Jersey has adopted the "learned intermediary" doctrine, which recognizes that a prescribing doctor has the primary responsibility of advising the patient of the risks and benefits of taking a particular medication. See N.J.S.A. 2A:58C-4; see also Niemiera v. Schneider, 114 N.J. 550, 565-66 (1989) ("[I]t is the physician's responsibility to pass on to the parties the information that enables the patient to use the product safely.").

***8** Presented below are the five key warning tools that were provided to physicians, pharmacists, and patients.

1.

Roche's primary means of communicating to healthcare providers such information as Accutane's dosages, drug interactions, commonly occurring side effects, and serious side effects is through the physician label (also known as a package insert). Roche's approximately twenty-four-page package insert provided medical professionals with specific IBD warnings.

Physician Label

WARNINGS:

...

Inflammatory Bowel Disease: Accutane has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. In some instances, symptoms have

been reported to persist after Accutane treatment has been stopped. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue Accutane immediately. (see ADVERSE REACTIONS: *Gastrointestinal*). [2]

Importantly, this warning advises prescribing physicians that not only has IBD been associated with the taking of Accutane, but that symptoms of the disease "have been reported to persist after Accutane treatment has been stopped."

2.

In addition, Roche provided physicians with a Best Practices Guide, which, although mostly focused on the risks of Accutane causing birth defects, also identified IBD as a specific risk associated with Accutane use. The Guide advised physicians to fully counsel their patients "about the warnings and precautions in the Accutane package insert."

Best Practices Guide

Accutane use is associated with other potentially serious adverse events, as well as more frequent, but less serious side effects.

....

Adverse Event Warnings include ... inflammatory bowel disease ....

....

Patients should be reminded to read the Medication Guide, distributed by the pharmacist at the time Accutane is dispensed.

3.

Roche also prepared a Patient Safety Packet for physicians to give to their patients that explained in plain language the risks and possible side effects of taking Accutane. An attached Informed Consent Form required the patient to acknowledge in writing that he or she read and understood the Patient Safety Packet. It also required the prescribing doctor to certify that the "benefits and risks" of Accutane treatment were "fully explained" to the patient. [3]

Patient Safety Packet

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.

***9** ....

Abdomen (stomach area) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the ... bowel (intestines). 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 or bowel pain, diarrhea, [or] rectal bleeding ....

4.

Roche also developed, in conjunction with the FDA, a Medication Guide for pharmacists to distribute to Accutane patients when they received their prescriptions. Like the Patient Safety Packet, the Medication Guide warned of "possible serious side effects" from Accutane and described IBD symptoms in simple and plain language.

Medication Guide

Accutane has possible serious side effects

....

Abdomen (stomach area) problems. Certain symptoms may mean that your internal organs are being damaged. These organs include the ... bowel (intestines) .... 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 ... diarrhea, [or] rectal bleeding ....

....

> Serious permanent problems do not happen often. However, because the symptoms listed above may be signs of serious problems, if you get these symptoms, stop taking Accutane and call your prescriber. If not treated, they could lead to serious health problems. Even if these problems are treated, they may not

clear up after you stop taking Accutane. The Medication Guide makes clear the potential permanency of harm to the patient's bowels and intestines by taking Accutane, indicating to the patient that "[i]f your organs are damaged, they may not get better even after you stop taking Accutane" and that symptoms "may not clear up after you stop taking Accutane."

5.

Last, Roche required pharmacists to dispense Accutane pills in "blister packaging" that again warned the patient that Accutane could have serious gastrointestinal side effects.

Blister Packaging

> *Other serious side effects to watch for*
>
> Stop taking Accutane and call your prescriber if you develop any of the problems on this list or any other unusual or severe problems. If not treated, they could lead to serious health problems. Serious permanent problems do not happen often.
>
> ....
>
> • Severe stomach pain, diarrhea, rectal bleeding, or trouble swallowing.
>
> ....
>
> Other important information is found in the Medication Guide and in the booklet from your prescriber.

Accordingly, by 2002, before taking Accutane, patients received the IBD warnings from their prescribing physicians and from their pharmacies when they filled their prescriptions. The FDA, moreover, reviewed and approved each of Roche's warning tools mentioned. One senior FDA official commented before the House Committee on Energy and Commerce that the agency took its "regulatory responsibilities concerning [Accutane] very seriously," as evidenced by its involvement in monitoring adverse reactions and updating the drug's warning labels. Issues Relating to the Safety of Accutane: Hearing Before the Subcomm. on Oversight & Investigations of the H. Comm. on Energy & Commerce, 107th Cong. 27 (2002) (statement of Janet Woodcock, Director, Center for Drug Evaluation and Research, U.S. Food and Drug Administration).

***10** In 2009, Roche discontinued the marketing of Accutane in the United States. In 2010, the FDA issued an official Notice, stating that the "FDA has independently evaluated relevant literature and data for possible postmarketing adverse events and has found no information that would indicate that [Accutane] was withdrawn from sale for reasons of safety or effectiveness." 75 Fed. Reg. 39,024, 39,025 (July 7, 2010).

In 2012, the FDA approved Absorbica, another brand-name formulation of isotretinoin manufactured by a different company. Absorbica's FDA-approved physician label warnings about IBD are functionally identical to those used by Roche in its post-2002 Accutane physician labels. [4]

C.

From the voluminous record in this case, plaintiffs focus our attention on excerpts from several internal Roche documents that reference Accutane and the potential risk of IBD as evidence that Roche should have given better warnings. Additionally, plaintiffs state that Roche failed to share the "internal conclusions" in those documents with the FDA.

One excerpt provided by plaintiffs is from a 1994 internal Roche document that indicates that colitis is a "possible [s]ide effect" of taking Accutane. The document notes that the "reason for inclusion [of colitis] as a side effect and not as a contraindication is probably the fact that the data regarding occurrence or aggravation of this condition ... is contradictory." [5] The document's author refers to published and unpublished data about Accutane and IBD-related disorders and reaches some tentative conclusions: (1) "Enterocolitis is a possible side effect of [Accutane] in very rare cases, possibly in

patients predisposed to inflammatory gastro-intestinal diseases"; (2) "[i]n patients with ileitis, enteritis or colitis in the active phase of the disease [Accutane] is basically contraindicated"; and (3) "a careful risk analysis should be made" before administering Accutane to patients with a "history of severe gastro-intestinal inflammatory diseases."

Another document referenced by plaintiffs is a 1994 memorandum from Dr. H. Lefrancq, a Roche physician, to an inquirer within Roche concerning "the administration of [Accutane] in patients with colitis." In that memorandum, Lefrancq mentions information from a safety database, which disclosed "a total of 33 cases of colitis [that] have been spontaneously reported up to January 6, 1994, which were rated as 'possibly' or 'probably' related to the administration of [Accutane]." Based on the data, Lefrancq believed it was "reasonable to conclude ... that, in rare cases, [Accutane] may induce or aggravate a preexisting colitis." Significantly, however, Lefrancq recommended to the inquirer that he could re-administer Accutane to his patient when the patient's ulcerative colitis reached the "inactive phase."

***11** Plaintiffs also highlight less than one page of an 1197-page report that Roche prepared for European regulatory authorities in 2000 that describes a particular patient's case. In that case, a seventeen-year-old patient developed ulcerative colitis one month after she stopped taking Accutane. In the analysis of that single case, a Roche physician noted that Accutane "has been found to be causally associated with inflammatory bowel disease, including colitis."

Finally, plaintiffs allude to a debate inside Roche between the marketing and drug-safety employees about whether to strengthen warnings about the psychiatric side effects of Accutane. IBD was not at issue. In a general sales presentation, the marketing department had described Accutane as "the goose that lays the golden eggs" -- an obvious reference to Roche's strong financial interest in the continued success of Accutane sales. Despite the discussions, Roche strengthened the warning, indicating that Accutane use could cause depression. At an earlier Accutane trial, Roche's former chief medical officer testified that the marketing department did not make the call over labeling decisions.

II.

A.

In 2005, for administrative purposes, this Court designated all pending and future New Jersey product-liability actions involving Accutane as Mass Tort Litigation -- now referred to as Multicounty Litigation (MCL), see R. 4:38A -- and consolidated all such actions in Atlantic County. The law firm Seeger Weiss LLP, which had requested that the Accutane cases be given the designation of Mass Tort Litigation, was later appointed plaintiffs' liaison counsel. In making that request, counsel for Seeger Weiss wrote: plaintiffs' "claims share common issues of law and fact, including whether ... [Roche] violated the New Jersey Products Liability Act in its marketing and sale of Accutane."

In 2015, in a series of rulings, the trial court concluded that the New Jersey PLA governed not only the 18 in-state claims but also the 514 claims that involved plaintiffs who were prescribed and took Accutane in 44 other jurisdictions. [6] The court then granted Roche's motion for summary judgment, determining that plaintiffs failed to overcome the presumption of adequacy that attached to the post-2002 Accutane label warnings approved by the FDA.

In making its choice-of-law determination, the court referenced the Seeger Weiss letter in which counsel represented that the sixty-eight cases then pending in 2005, only two of which were brought by New Jersey residents, shared a common issue of law -- whether Roche violated New Jersey's PLA. The court emphasized that nothing in Seeger Weiss's correspondence with this Court suggested that the out-of-state plaintiffs "wish[ed] to bring the law of their states with them to New Jersey" or that the court would have to engage in a state-by-state choice-of-law analysis. [7] The court did not find it reasonable for our judiciary to apply the law of scores of jurisdictions, "many of which express standards incompatible with the NJPLA," to thousands of claims involving cutting-edge issues of science and law.

***12** The court noted that Accutane filings grew from less than 100 in March 2005 to more than 7500 by February 2015. More than 4600 Accutane cases remained

on the docket when the court determined that applying each state's law "is neither practical ... nor would it promote 'the values of uniformity and predictability,' " quoting Camp Jaycee, 197 N.J. at 154. The court cited "the inability to assemble 'bellwether' cases from multiple jurisdictions which would produce meaningful results" as another reason for applying the New Jersey PLA. It also asserted that applying the conflicting law of another state would undermine the Legislature's intent in passing the FDA presumption-of-adequacy provision of the PLA, which was to "reduc[e] the burden placed on [New Jersey manufacturers] by product liability litigation," quoting Rowe v. Hoffmann-La Roche, Inc., 189 N.J. 615, 626 (2007).

In concluding that the presumption of adequacy governing Accutane's FDA-approved warnings had not been overcome, the court maintained that plaintiffs' proofs did not establish either a "deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects," citing Perez v. Wyeth Labs., Inc., 161 N.J. 1, 25 (1999), and Rowe, 189 N.J. at 626, or a "manipulation of the post-market regulatory process," citing McDarby v. Merck & Co., 401 N.J. Super. 10, 63 (App. Div. 2008). In addition, the court concluded that Roche's label warnings, in their totality, communicated a "clear, accurate and unambiguous" message to physicians that Accutane "is associated with risk of serious side effects." For those reasons, the court dismissed the 532 product-liability actions brought against Roche.

B.

The Appellate Division reversed in part and affirmed in part. The panel found that the trial court erred in its choice-of-law analysis by applying New Jersey's PLA to the 514 cases in which plaintiffs were prescribed and took Accutane in 44 other jurisdictions. The panel rejected the trial court's position that the representations made by the attorney seeking mass-tort designation for the then less than 100 Accutane cases waived the right of the now thousands of out-of-state plaintiffs to the customary choice-of-law analysis. The panel pointed to the wording of the later-filed Long Form Complaint designated for MCL cases, which indicates that plaintiffs' claims are based on the violation of New Jersey's PLA or "the analogous law" of the jurisdictions where Accutane was ingested or prescribed. In short, the panel held that counsel did not have the authority to stipulate the choice of law for thousands of plaintiffs.

Applying the relevant sections of the Restatement (Second) of Conflict of Laws, adopted by this Court, the panel concluded that each individual case had to be judged under the substantive law of the jurisdictions where each plaintiff was prescribed and took Accutane -- forty-five jurisdictions in all. The panel dismissed the notion that plaintiffs, by participating in mass-tort litigation in New Jersey, surrendered their right to an individual choice-of-law analysis and the application of their states' laws. The panel maintained that although plaintiffs' claims were consolidated for administrative purposes, each plaintiff filed a separate complaint.

The panel considered New Jersey's PLA to be "sufficiently different from most, if not all, [of] the other competing jurisdictions," and therefore reasoned that a choice-of-law analysis was required. The panel observed that, under section 146 of the Restatement, the law of the state where the injury occurred is presumed to govern unless another state has "a more significant relationship" to the litigation in light of the principles enunciated in sections 145 and 6 of the Restatement. The panel ruled that this State did not have a more significant relationship to the litigation than those jurisdictions where the "injury" occurred. In the panel's view, New Jersey's PLA gives greater protection to pharmaceutical companies than analogous laws in other jurisdictions and therefore application of our State's law "might frustrate the other states' policies in deterring a broader scope of inadequate warnings" and be inconsistent with the reasonable expectations of the parties. The panel "reject[ed] the argument that simplification of procedures and uniformity of results should govern the choice-of-law questions presented." According to the panel, "[i]nterests of judicial administration should not be accorded undue weight," and the demand for "efficient results" should not yield to the strong state interests of other jurisdictions. The panel concluded that the law in each of the forty-five jurisdictions where plaintiffs resided and ingested Accutane would apply to their cases.

***13** The panel affirmed the grant of summary judgment in favor of Roche in those cases involving plaintiffs who were prescribed and took Accutane in California, Colorado, Indiana, Maryland, Mississippi, New York, and Virginia because "[i]t is enough in these jurisdictions

that IBD was referenced" in Roche's label warnings to render them adequate as a matter of law. The panel also affirmed the grant of summary judgment in those cases involving the Texas plaintiffs because they had not overcome that jurisdiction's presumption of adequacy. The panel, however, found that the trial court improvidently granted summary judgment in favor of Roche in the cases of those plaintiffs from the remaining thirty-seven jurisdictions because "the adequacy of the warnings could not be resolved as a matter of law."

Under New Jersey's PLA, the panel held that plaintiffs had presented sufficient evidence to overcome the presumption of adequacy attached to Accutane's FDA-approved warnings and therefore genuine issues of material fact needed to be resolved by a jury. In particular, the panel stated that, based on Perez and McDarby, the summary judgment record rebutted the presumption of adequacy because Roche not only failed to disclose to the FDA "after-acquired knowledge of Accutane's harmful effects," but also engaged in an "economically-driven manipulation of the post-market regulatory process." The panel specifically determined that a factfinder could conclude that, after FDA approval, Roche did not disclose critical information in its post-2002 warnings -- that Roche "had internally concluded there was a causative effect" between Accutane and IBD.

The panel also disagreed with the trial court's assertion that, even if the presumption of adequacy had been overcome, the label warnings were "clear enough to negate a trial on the issue."

C.

We granted Roche's petition for certification, 231 N.J. 419 (2017), and plaintiffs' cross-petition, 231 N.J. 428 (2017). We also granted the motion of the New Jersey Association for Justice to participate as amicus curiae. The HealthCare Institute of New Jersey, which participated as amicus curiae before the Appellate Division, was allowed to appear in that role before this Court pursuant to Rule 1:13-9(d).

III.

A.

1.

Roche argues that the Appellate Division erred in failing to apply the New Jersey PLA to the 514 claims of out-of-state plaintiffs. Roche submits that a proper choice-of-law analysis requires this Court to recognize New Jersey's strong interest -- expressed through the PLA's presumption of adequacy -- in protecting this State's pharmaceutical companies from unmeritorious product-liability litigation from out-of-state residents. Roche also claims that the effective administration of justice through the consolidation of many claims in a single county under MCL calls for the application of this State's PLA to adequacy challenges brought by non-New Jersey plaintiffs. On that point, Roche emphasizes that plaintiffs sought MCL designation on the basis that they shared a common issue of law -- whether Roche violated the PLA.

The interests in applying New Jersey law, Roche contends, are not outweighed by plaintiffs' home-state interests. According to Roche, "a large number of states lack a clear standard for determining precisely when pharmaceutical warnings are adequate as a matter of law" and "nearly all other states lack a clearly-defined presumption of adequacy like New Jersey's." Roche further contends that the application of the PLA to all 532 claims will promote "certainty, predictability and uniformity of result," quoting Restatement § 6(2)(f). In sum, Roche urges this Court to find, in analyzing the Restatement factors, that New Jersey, where Accutane was labeled, "has the most significant relationship to the adequacy issue" in this appeal.

***14** Roche submits that the Appellate Division mistakenly determined that non-dismissed plaintiffs had overcome the presumption of adequacy attached to Accutane's FDA-approved warnings. It claims that "the FDA helped formulate, repeatedly reviewed, and consistently approved Accutane's safety communication tools," which "repeatedly and directly addressed the risk" of IBD. Roche asserts that there is no evidence that it concealed evidence from the FDA or engaged in "intentional post-market manipulation of the FDA for economic reasons." Roche claims that plaintiffs "plucked isolated statements from [its] internal documents" and wrongly accused Roche of intentionally concealing them,

even though the information in those statements was known to the FDA through its submissions.

Roche also states that "the overwhelming scientific record now demonstrably fails to show any connection" between Accutane and IBD, further validating the accuracy of its label warnings, which it insists clearly and unambiguously warned physicians and patients of the risk of IBD. [8]

2.

Amicus curiae the HealthCare Institute of New Jersey echoes many of the arguments advanced by Roche. It asserts that the fallout from the Appellate Division's decision is "that potentially hundreds of juries [will] separately determine whether Accutane's FDA-approved IBD warnings are adequate, presenting the risk of divergent outcomes regarding the same warnings." It also posits that the panel's decision undermines the effectiveness of the PLA's presumption of adequacy and will burden pharmaceutical companies with unmeritorious lawsuits that will threaten "the development of prescription medical devices and drugs."

B.

1.

Plaintiffs urge this Court to uphold the Appellate Division's choice-of-law determination, which requires the application of the law of the jurisdiction where each plaintiff was prescribed and took Accutane. Plaintiffs agree with the panel that the trial court erred in deciding to apply New Jersey law based on the 2005 letter written by the attorney -- later selected as liaison counsel -- as support for consolidating the Accutane cases into an MCL matter. Plaintiffs point to the Long Form Complaint in which plaintiffs expressly invoked the analogous law of the states where plaintiffs were prescribed and took Accutane. Those states' laws are implicated, plaintiffs contend, because "Roche deliberately marketed and sold [Accutane] in those jurisdictions." Plaintiffs maintain that an analysis under the guiding principles of the Restatement favors applying the law of the jurisdictions where Accutane was prescribed and taken because those states have strong interests in regulating commerce within their borders. In plaintiffs' view, New Jersey's interest in effective judicial administration should yield to the interests of interstate comity. Plaintiffs submit that, under each of those states' laws, summary judgment should have been denied because of the abundant evidence of the inadequacies of Roche's 2002 label warnings.

Plaintiffs also maintain that the "Appellate Division correctly determined that a reasonable jury could find that substantial evidence overcomes [the PLA's] rebuttable presumption of adequacy" that attaches to Roche's FDA-approved label warnings. They further claim that the evidence supports a finding of inadequacy under the laws of all the jurisdictions at issue. Plaintiffs assert that they have presented "[substantial] evidence of Roche's non-disclosure of critical safety information and its economic motivation to thwart the regulatory process," both bases for overcoming the presumption of adequacy of Roche's label warnings. Plaintiffs charge Roche with withholding documents from the FDA that would have revealed "that Roche had internally determined that there was a causal link between Accutane and IBD/[ulcerative colitis]." According to plaintiffs, "[d]espite internal admissions that Accutane 'induces,' 'may cause,' and is 'causally associated with' IBD, Roche did not disclose this knowledge to physicians in its warnings."

***15** Plaintiffs insist that our jurisprudence does not "establish[ ] a nearly irrebuttable presumption that exculpates pharmaceutical manufacturers from failure-to-warn liability." Plaintiffs conclude we should affirm the Appellate Division, which denied summary judgment in the cases of those plaintiffs bound by the laws of thirty-seven jurisdictions, including New Jersey, and reverse its grant of summary judgment in the cases of those plaintiffs bound by the laws of eight other jurisdictions.

2.

Amicus curiae the New Jersey Association for Justice lends support to the arguments made by plaintiffs. It suggests the "typical rebuttable presumption" of adequacy afforded to label warnings was heightened in Perez based on an incomplete understanding of the role the FDA plays in regulating and approving label warnings after a prescription drug has been marketed. The Association submits that Perez's declaration that "compliance with FDA standards should be virtually

dispositive" of failure-to-warn claims does not account for the reality that the FDA -- particularly in the postmarketing phase of a prescription drug -- does not have "the financial, technological, and human capital resources to fulfill its mission."

IV.

A.

We first address the choice-of-law issue. We must decide which law or laws govern the 532 cases before us -- New Jersey's PLA or the failure-to-warn laws of each of the forty-five jurisdictions where individual plaintiffs were prescribed and took Accutane.

The decisions of the trial court and Appellate Division offer starkly different choice-of-law options. The trial court ruled that New Jersey's PLA applies to all 532 cases. The Appellate Division reversed and determined that the law of the jurisdiction where each plaintiff was prescribed and took Accutane -- in all, forty-five jurisdictions -- governs each action. We review those choice-of-law decisions de novo, owing no deference to the legal conclusions reached by either court, unless persuaded by their reasoning. McCarrell, 227 N.J. at 583-84.

B.

We apply New Jersey's choice-of-law rules in determining whether this State's or another state's law governs the action. Id. at 583. In doing so, the first inquiry "is whether the laws of the states with interests in the litigation are in conflict." Id. at 584. If there is not "an actual conflict" in "the substance of the potentially applicable laws" of the two jurisdictions, then "there is no choice-of-law issue to be resolved," Camp Jaycee, 197 N.J. at 143, and the forum state applies its own law, McCarrell, 227 N.J. at 584. A conflict of law arises when the application of one or another state's law may alter the outcome of the case, see id. at 584, or when the law of one interested state is "offensive or repugnant" to the public policy of the other, see Continental Ins. Co. v. Honeywell Int'l, Inc., 234 N.J. 23, 46 (2018) (quoting DeMarco v. Stoddard, 223 N.J. 363, 383 (2015)).

Here, we must compare New Jersey's PLA with the product-liability laws or analogues of forty-four other jurisdictions.[9] New Jersey's rebuttable presumption of adequacy, which specifically attaches to FDA-approved warnings, sets our law apart from most other states' laws. Texas also has a presumption of adequacy for FDA-approved warnings, but its presumption is evidently more difficult to overcome than New Jersey's presumption.[10] Indiana, Kansas, North Dakota, Oklahoma, Oregon, Tennessee, Utah, and Wisconsin have a general rebuttable presumption that applies to all product warnings, which can be overcome either by a mere preponderance of the evidence or by sufficient evidence.[11]

***16** The laws of the remaining jurisdictions do not protect a product's warnings with a presumption of adequacy.[12] Nevertheless, in Alabama, California, Colorado, Indiana, Maryland, Louisiana, Mississippi, New York, and Virginia, a drug warning is adequate as a matter of law if it provides clear and specific information about a potential risk, such as IBD.[13] New Jersey's presumption of adequacy for FDA-approved label warnings seemingly gives greater protection to pharmaceutical companies than the laws of other states, but not necessarily so. The Appellate Division granted summary judgment in favor of Roche in the cases of plaintiffs governed by the laws of eight states but denied summary judgment in the cases of those plaintiffs governed by New Jersey's PLA and the laws of the thirty-six remaining jurisdictions.

***17** Discerning the precise meaning of the laws of forty-four jurisdictions -- other than New Jersey's -- is an arduous and burdensome task. Our treatment of those laws here is far from comprehensive or definitive. We proceed under the assumption that the application of New Jersey's PLA may lead to an outcome different from the application of the laws of those other jurisdictions. Recognizing that the substantive laws of New Jersey and the other jurisdictions are in conflict requires that we choose the law or laws that govern the 532 cases before us.

In Camp Jaycee, we adopted the Restatement's most-significant-relationship test set forth in sections 146, 145, and 6 as the paradigm for deciding which state's substantive law applies in personal injury cases involving more than one state. 197 N.J. at 142-43. The

Restatement's most-significant-relationship test embodies all the elements of this Court's former governmental-interest test and adds "a series of other factors deemed worthy of consideration." Id. at 142 n.4. [14] That more nuanced approach is the one we apply here.

In Camp Jaycee, the plaintiffs -- parents of a young woman with mental disabilities from New Jersey -- brought suit in our Superior Court, Law Division, against a New Jersey not-for-profit corporation operating a summer program in which the parents had enrolled their daughter. Id. at 136-37. While under the defendant's care at a Pennsylvania summer camp, the plaintiffs' daughter was sexually assaulted by another camper. Ibid. The parents alleged that the defendant was negligent in its supervision of their daughter. Id. at 137. The defendant was shielded from tort liability under New Jersey's Charitable Immunity Act, but not under Pennsylvania law, which had expressly abolished the doctrine of charitable immunity. Id. at 135, 143-44. The case thus presented a true conflict of substantive law. Id. at 143-44. In applying the Restatement principles, we affirmed the Appellate Division's determination to apply Pennsylvania's law. Id. at 155-56. We held that a weighing of all relevant factors did not overcome section 146's presumption that the law of the place of injury applied. Id. at 156. We found that Pennsylvania, which has a specific policy of encouraging the exercise of due care by those residing within its borders and assuring that those who suffer injuries from the negligent acts of others receive compensation, had a more significant relationship to the case. Id. at 155-56.

Unlike Camp Jaycee, where the only question was whether the law of New Jersey or Pennsylvania governed in a single personal injury action, in this MCL setting, New Jersey's PLA intersects with the laws of 44 other jurisdictions in 514 cases. The case before us, therefore, presents challenges not posed in Camp Jaycee.

In Ginsberg v. Quest Diagnostics, Inc., "[w]e acknowledge[d] that a defendant-by-defendant choice-of-law analysis is not feasible in every matter," particularly "[i]n a complex case with many parties from different states." 227 N.J. 7, 20 (2016). In such a scenario, "the trial court retains the discretion to decline a defendant-by-defendant approach and, utilizing a Restatement §§ 146, 145 and 6 analysis ... apply the law of a single state to claims asserted against all defendants." Ibid. [15] It also bears mentioning that, among academic experts in the field of conflict of laws, there is a "consensus, at least, that ordinary choice-of-law practices should yield in suits consolidating large numbers of claims and that courts should apply a single law in such cases" -- but there are dissenting voices. See Larry Kramer, Choice of Law in Complex Litigation, 71 N.Y.U. L. Rev. 547, 547 (1996). [16]

***18** With those principles and concerns as background, we turn to the Restatement sections that apply the most-significant-relationship test in personal injury cases. Under that test, the analysis begins with section 146 and the presumption that the law of the state where the injury occurred applies. Camp Jaycee, 197 N.J. at 135-36. That presumption may be overcome if "some other state has a more significant relationship with the parties and the occurrence based on an assessment of each state's contacts" viewed through the prism of section 145, which sets forth general principles for tort actions, and section 6, which lists overarching choice-of-law principles. McCarrell, 227 N.J. at 590.

Section 146 provides:

> In an action for a personal injury, the local law of the state where the injury occurred determines the rights and liabilities of the parties, unless, with respect to the particular issue, some other state has a more significant relationship under the principles stated in § 6 to the occurrence and the parties, in which event the local law of the other state will be applied.
>
> [Restatement § 146.]

Because Roche marketed Accutane nationwide, it is not surprising that plaintiffs hail from forty-four jurisdictions other than New Jersey. The place of injury for the 532 plaintiffs whose cases are before us is where their physicians prescribed Accutane, where they took the medication, and where they developed IBD. Typically, all three events occurred in the same jurisdiction, but not necessarily. Thus, the place of injury may not be so easily identified.

In the case of 514 plaintiffs, the place of injury is a jurisdiction other than New Jersey. Therefore, we must determine whether New Jersey has a more significant relationship "to the occurrence and the parties," first looking to section 145, the general principles for tort actions, and then to section 6, the universal guiding

principles for choice-of-law issues. Camp Jaycee, 197 N.J. at 140-41.

Under Restatement section 145, the contacts weighed in making that assessment include:

> (a) the place where the injury occurred,
>
> (b) the place where the conduct causing the injury occurred,
>
> (c) the domicil[e], residence, nationality, place of incorporation and place of business of the parties, and
>
> (d) the place where the relationship, if any, between the parties is centered. [Restatement § 145.]

"These contacts are to be evaluated according to their relative importance with respect to the particular issue." Ibid. A weighing of those contacts yields mixed results. The injuries caused by the putative failure to give adequate warnings occurred in forty-four other jurisdictions, but New Jersey is "where the [alleged] conduct causing the injury occurred" -- the manufacturing and labeling of Accutane. See ibid. "When both conduct and injury occur in a single jurisdiction, with only 'rare exceptions, the local law of the state where conduct and injury occurred will be applied' to determine an actor's liability." Fu v. Fu, 160 N.J. 108, 125-26 (1999) (quoting Restatement § 145 cmt. d). The logic is that "a state has an obvious interest in regulating the conduct of persons within its territory and in providing redress for injuries that occurred there." Id. at 126 (quoting Restatement § 145 cmt. d). Thus, in Camp Jaycee the conduct (the failure of the defendant to act with due care) and the injury (the sexual assault of the plaintiff) both occurred in Pennsylvania, the jurisdiction whose law we applied in that case. 197 N.J. at 136. Unlike Camp Jaycee, in 514 cases, we do not have the convergence in one jurisdiction of both the conduct causing the injury and the occurrence of the injury.

***19** In this case, moreover, 514 plaintiffs are residents of 44 other jurisdictions, and Roche is a corporation that has its principal place of business in New Jersey. That indicates a rather diffuse interest among the states. Although the relationship between the parties is not centered in one place, Roche marketed Accutane in the jurisdictions where plaintiffs resided. Had plaintiffs brought their actions in the states where they were prescribed and took Accutane, those state courts presumably would have applied the law of their jurisdictions because each state has a strong interest in ensuring that safe products are marketed within its borders. See, e.g., McLennan v. Am. Eurocopter Corp., 245 F.3d 403, 426 (5th Cir. 2001) ("Texas has a strong interest in enforcing its products liability laws against manufacturers operating in the State."); Fed. Ins. Co. v. J.K. Mfg. Co., 933 F. Supp. 2d 1065, 1077 (N.D. Ill. 2013) ("Indiana has an interest in ensuring that safe products are used within its borders."). Overall, the section 145 contacts do not point to one ineluctable result.

We next review the overarching principles of section 6 to guide us in deciding whether New Jersey "has a more significant relationship ... to the occurrence and the parties." Restatement § 146. Section 6 prescribes that

> the factors relevant to the choice of the applicable rule of law include
>
> (a) the needs of the interstate and international systems,
>
> (b) the relevant policies of the forum,
>
> (c) the relevant policies of other interested states and the relative interests of those states in the determination of the particular issue,
>
> (d) the protection of justified expectations,
>
> (e) the basic policies underlying the particular field of law,
>
> (f) certainty, predictability and uniformity of result, and
>
> (g) ease in the determination and application of the law to be applied.
>
> [Restatement § 6(2).]

Our interstate system recognizes that the forum state should not apply its choice-of-law principles in a way that discriminates against out-of-state residents. That is the essence of comity. The tort systems of all the jurisdictions involved share the same general goals -- ensuring that pharmaceutical companies market drugs that are reasonably safe for consumption by the public and that the drugs' label warnings adequately inform the physicians who prescribe the medications and the patients who use them of the medications' potential benefits and risks. Each jurisdiction regulates, in some way, a pharmaceutical company's responsibility for the

accuracy of its label warnings in the initial marketing and postmarketing phases of a drug. The differences in each jurisdiction's law are sometimes subtle, and the precise meaning of another jurisdiction's law is many times far from self-evident. In some instances, we have difficulty construing our own State's laws, particularly when legislation is written in broad terms and legislative history gives little guidance for the interpretive process. Our discussion of New Jersey's PLA later in this opinion illustrates the challenges of applying a broadly worded statute to specific circumstances.

The parties' expectations "ordinarily play[ ] little or no part in a choice-of-law question in the field of torts." Fu, 160 N.J. at 123 (citing Restatement § 145 cmt. b). Nonetheless, to the extent that the parties' expectations are relevant, is it realistic that plaintiffs should expect to carry with them the forty-four different laws of their home states or the state where their injuries occurred when their cases are consolidated for administrative purposes under the umbrella of MCL -- a designation intended to make more manageable the processing of hundreds and sometimes thousands of cases? One of the reasons for joining together so many cases before a single judge is to gain the benefits of administrative efficiency.

Under Rule 4:38A, "[t]he Supreme Court may designate a case or category of cases as [MCL] to receive centralized management in accordance with [promulgated] criteria and procedures." MCL is a grouping of "mass tort" cases that typically involve substantial numbers of claims associated with a single product, a mass disaster, or a complex environmental event. MCL Resource Book 1. One of the criteria for MCL status is whether the cases "involve[ ] many claims with common, recurrent issues of law and fact." Id. at 4. Other criteria include "whether centralized management is fair and convenient to the parties, witnesses and counsel" and "whether the cases require specialized expertise and case processing." Id. at 4-5. [17]

***20** The two most significant Restatement factors in this MCL matter are section 6 factors f ("certainty, predictability and uniformity of result") and g ("ease in the determination and application of the law to be applied"). Applying a single standard to govern the adequacy of the label warnings in the 532 individual cases will ensure predictable and uniform results -- rather than disparate outcomes among similarly situated plaintiffs, who took the same medications and were presumably advised by their physicians of the same risks and benefits based on the label warnings. Removed from the equation will be the fortuity of the place where individual plaintiffs reside and where the injury occurred. Of course, each plaintiff controls his or her fate. Plaintiffs can choose to bring suit in the state where they reside and the injury occurred and probably enjoy the benefit -- if it is a benefit -- of their own state law. See Bristol-Myers Squibb Co. v. Superior Court, ___ U.S. ___, ___, 137 S. Ct. 1773, 1783 (2017).

There can be no question that administrative ease and efficiency favor the application of New Jersey's PLA. A single judge presiding over highly complex Multicounty Litigation cannot be expected to gain a mastery of the laws of forty-five jurisdictions. That is a wholly unworkable scheme. It would lead to more errors and more appeals, and therefore greater delays in resolving cases -- cases that would languish in our court system for many years.

In the long run, applying New Jersey's PLA in such circumstances as here is not an approach that advantages one side or the other. In this case, plaintiffs apparently believe that New Jersey law is not as beneficial to their cause as the laws of other jurisdictions. However, as viewed by the Appellate Division, the Roche warnings are adequate under the laws of eight other jurisdictions. Today, plaintiffs complain about the application of New Jersey law in this MCL case. Tomorrow, in another such case, defendants may be the disappointed party. Interestingly, in McCarrell, the out-of-state plaintiff clamored for the application of New Jersey's statute of limitations whereas Roche angled for the application of the law of the plaintiff's home state. See 227 N.J. at 582-83. In Rowe, the plaintiff did not want Michigan's law to govern because Michigan had an irrebuttable presumption of adequacy for FDA-approved label warnings. 189 N.J. at 618.

It is understandable that the parties want to apply the law of the jurisdiction that will give them the greatest advantage. In this case, we are not picking sides or winners, but merely establishing a reasonable rule of law that can be implemented by our courts and that can best advance the administration of justice.

Here, we find that, under the principles stated in section 6, New Jersey has the most significant relationship to the occurrence and the parties, thus overcoming section 146's

presumption that the law of the place of injury governs. We therefore apply this State's PLA to the 532 cases before us.

V.

We now address the standard for overcoming the presumption of adequacy of FDA-approved warnings during the postmarketing phase of a prescription medication.

A.

In 1987, New Jersey passed the Products Liability Act, L. 1987, c. 197, codified at N.J.S.A. 2A:58C-1 to -11. In enacting the PLA, the Legislature intended to both codify the existing common law and provide "some sense of order and clarity to products liability cases within New Jersey." Governor's Statement to S. 2805; accord N.J.S.A. 2A:58C-1; see also In re Reglan Litig., 226 N.J. 315, 335 (2016) ("The PLA is a codification of tort-law principles, where the state has traditionally exercised its historic police powers.").

Under N.J.S.A. 2A:58C-4, the manufacturer or seller is not liable if a product "contains an adequate warning or instruction" about the dangers of the product. (emphasis added). The PLA defines "an adequate warning or instruction" as

> ***21** 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.
>
> [N.J.S.A. 2A:58C-4 (emphasis added).]

In the case of prescription drugs, the PLA codifies what is commonly referred to as the learned intermediary doctrine -- a doctrine that acknowledges that "the physician acts as the intermediary between the manufacturer and the [patient]." Niemiera, 114 N.J. at 559. The prescribing physician -- as a learned intermediary -- generally is in the best position to advise the patient of the benefits and risks of taking a particular drug to treat a medical condition. See Perez, 161 N.J. at 17-18. Under the learned intermediary doctrine, "a pharmaceutical manufacturer generally discharges its duty to warn the ultimate user of prescription drugs by supplying physicians with information about the drug's dangerous propensities." Id. at 10 (quoting Niemiera, 114 N.J. at 559).

Under the PLA, a presumption of adequacy attaches to a product's label warnings approved by the Food and Drug Administration. N.J.S.A. 2A:58C-4 provides that

> [i]f 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 [federal laws], a rebuttable presumption shall arise that the warning or instruction is adequate.
>
> [(emphasis added).]

The Legislature, by attaching a presumption of adequacy to FDA-approved warnings, "recognized the preeminent role of federal regulation of drugs and medical devices." Cornett v. Johnson & Johnson, 211 N.J. 362, 387 (2012); accord Rowe, 189 N.J. at 625 (noting that PLA accepts FDA regulation and enforcement mechanisms as ordinarily "sufficient ... to deter New Jersey pharmaceutical companies from manufacturing unsafe prescription drugs"). Given the importance of the federal regulatory process in relation to the PLA, a brief overview of the relevant FDA premarketing and postmarketing regulations governing prescription drugs will be helpful.

B.

The FDA is responsible for "promot[ing] the public health by promptly and efficiently reviewing [drug manufacturers'] clinical research and taking appropriate action on the marketing of regulated products in a timely manner." 21 U.S.C. § 393(b)(1). Before a pharmaceutical company can market any new drug, it must complete the process for a New Drug Application (NDA), during which the FDA conducts a rigorous review to ensure that the drug is "safe and effective." See 21 C.F.R. § 314.2; see generally, 21 C.F.R. § 314.1 to .170. As part of the

NDA, the FDA requires extensive information, including the ingredients of the drug, its biological mechanisms, and the results of animal studies and clinical tests. 21 C.F.R. § 314.50. The FDA also ensures that the drug label summarizes "the essential scientific information needed for the safe and effective use of the drug" and describes potential safety hazards associated with use of the drug. 21 C.F.R. § 201.56(a); accord 21 C.F.R. § 314.50 (requiring that NDA include content for labeling).

***22** The FDA's oversight is at its peak before a new drug goes to market. See 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, 465 (2008) ("Kessler & Vladeck") (noting that when FDA approves new drug, it "is in the best position to be the exclusive arbiter of a drug's safety and effectiveness" because it then "has had access to and has devoted considerable resources to reviewing carefully all of the extant health and safety data relating to the drug"). [18] The clinical trials of a drug, however, may not identify all of the drug's risks by the time of FDA approval. [19] Id. at 470. After the drug goes to market, the manufacturer may receive critical new information about the risks, benefits, and optimal use of the drug. See 21 U.S.C. § 314.80(b). During the postmarketing period, when the drug is widely prescribed, risks emerge that were not "foreseen by the drug's manufacturer or the FDA and, for that reason, are not addressed on the label." Kessler & Vladeck at 466.

Under federal law, the manufacturer is responsible for the adequacy of a drug label's warnings not only when it files an NDA, 21 U.S.C. § 355(b)(1), (d), (j)(2)(A), but also during the period when the drug is on the market after FDA approval, see 21 C.F.R. § 314.70. After a manufacturer becomes aware of a previously unknown significant risk about a drug, the manufacturer must update the label to account for that risk in accordance with 21 C.F.R. §§ 314.70 ("Supplements and other changes to an approved NDA") and 601.12 ("Changes to an approved application"). The FDA requires a manufacturer to change a drug's "labeling to reflect newly acquired information" in certain circumstances. 21 C.F.R. § 314.70(c)(6)(iii). For example, a manufacturer must "add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under [21 C.F.R.] § 201.57(c)." 21 C.F.R. § 314.70(c)(6)(iii)(A). In turn, 21 C.F.R. § 201.57(c)(6) requires that a drug's "labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug; a causal relationship need not have been definitely established." 21 C.F.R. § 201.57(c)(6).

Thus, federal regulations make clear that drug manufacturers are responsible for the postmarketing surveillance of their products, 21 C.F.R. § 314.80(b), and have a continuing responsibility "to maintain their labeling and update the labeling with new safety information," 73 Fed. Reg. 49,603, 49,605 (Aug. 22, 2008). See Wyeth v. Levine, 555 U.S. 555, 570-71 (2009).

In Wyeth, the United States Supreme Court focused on the federal regulatory process that holds drug manufacturers accountable for revising their warning labels after a new drug has been on the market and on the role state tort law plays in enforcing that regulatory process. 555 U.S. at 567-68, 577-79. The Court in Wyeth held that federal law did not preempt a state-law tort action against a manufacturer of a prescription brand-name drug for its failure to give adequate warnings about the significant risks of administering the drug. Id. at 563, 581. Indeed, one of the central premises of the Federal Food, Drug, and Cosmetic Act (FDCA) and FDA regulations is "that the manufacturer bears responsibility for the content of its label at all times" and "is charged both with crafting an adequate label and with ensuring that its warnings remain adequate as long as the drug is on the market." Id. at 570–71. The Court noted that under the "changes being effected" (CBE) regulation, 21 C.F.R. § 314.70(c), a manufacturer can unilaterally strengthen label warnings before the FDA's approval. Id. at 568-71. The CBE regulation, in defined circumstances, provides that a manufacturer may make a label change when it files a supplemental application with the FDA -- and before FDA approval -- "that is intended to increase the safe use of the drug product." Id. at 568 (citing 21 C.F.R. § 314.70(c)(6)(iii)(A), (C)). [20] In Wyeth, when the risk became apparent to the manufacturer that its drug might cause serious harm, "[the manufacturer] had a duty to provide a warning that adequately described that risk, and the CBE regulation permitted it to provide such a warning before receiving the FDA's approval." Id. at 571.

***23** Significantly, the Supreme Court concluded that failure-to-warn lawsuits against manufacturers provide "a complementary form of drug regulation" in the

postmarketing phase. Id. at 578. In that phase, the Court recognized, the FDA's monitoring is far from foolproof. As the Court observed,

> [t]he FDA has limited resources to monitor the 11,000 drugs on the market, and manufacturers have superior access to information about their drugs, especially in the postmarketing phase as new risks emerge. State tort suits uncover unknown drug hazards and provide incentives for drug manufacturers to disclose safety risks promptly. They also serve a distinct compensatory function that may motivate injured persons to come forward with information. Failure-to-warn actions, in particular, lend force to the FDCA's premise that manufacturers, not the FDA, bear primary responsibility for their drug labeling at all times.
>
> [Id. at 578–79 (footnote omitted).]

C.

With the federal regulatory process as prologue, we turn to the rebuttable presumption of adequacy that attaches to an FDA-approved warning. N.J.S.A. 2A:58C-4. The presumption of adequacy necessarily "helps to ensure that manufacturers are not made guarantors against remotely possible, but not scientifically-verifiable, side-effects of prescription drugs," Perez, 161 N.J. at 25, and "reduc[es] the burden placed on [manufacturers of medications with FDA-approved warnings] by product liability litigation," Rowe, 189 N.J. at 626. The Legislature, however, gave no precise guidance either in the Products Liability Act or in its legislative history suggesting the proofs necessary to overcome the rebuttable presumption of adequacy of FDA-approved warnings.

In Feldman v. Lederle Laboratories, the Court acknowledged that the PLA's "plain language defies the conclusion that the presumption cannot be overborne." 125 N.J. 117, 157 (1991). Feldman, however, did not detail the proofs necessary to overcome the presumption, despite its reference to the general means of overcoming a presumption. Ibid. (citing McCormick on Evidence § 344, at 978–79 (E. Cleary ed., 3d ed. 1984)). The Court in Perez for the first time addressed the role of the federal regulatory process in relation to the PLA's presumption of adequacy that attaches to FDA-approved drugs. 161 N.J. at 25.

In Perez, the Court primarily focused on the learned intermediary doctrine, holding that the doctrine did not apply when a pharmaceutical company engaged in direct marketing of a product to consumers. Id. at 11-22. Within that context, the Court also declared that "in the area of direct-to-consumer advertising of pharmaceuticals, the same rebuttable presumption [of adequacy] should apply when a manufacturer complies with FDA advertising, labeling and warning requirements." Id. at 24.

The Court made clear that "FDA regulations are pertinent in determining the nature and extent of any duty of care that should be imposed on pharmaceutical manufacturers" and that "FDA regulations serve as compelling evidence that a manufacturer satisfied its duty to warn the physician about potentially harmful side effects of its product." Ibid. Significantly, the Court generally cited FDA advertising regulations and did not distinguish between FDA regulations governing pharmaceutical drugs in the premarketing and postmarketing phases. See id. at 22-24.

***24** In the absence of statutory language or legislative history suggesting the standard to overcome the rebuttable presumption, the Court in Perez turned to the punitive damages section of the PLA for guidance. Id. at 25. N.J.S.A. 2A:58C-5(c) states in part that punitive damages are not available "if a drug ... is generally recognized as safe and effective pursuant to" the FDA's "packaging and labeling regulations," except "where the product manufacturer knowingly withheld or misrepresented information required to be submitted under the agency's regulations, which information was material and relevant to the harm in question." Adapting that language to the rebuttable presumption of adequacy accorded to FDA-approved label warnings, the Court held that "absent deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects, compliance with FDA standards should be virtually dispositive of [product-liability and failure-to-warn] claims." Perez, 161 N.J. at 25. The Court acknowledged that "[t]his presumptive effect is in accordance with legislative intent that we discern from the punitive damages provision of the [PLA]" concerning "FDA labeling and pre-marketing requirements." Ibid. (emphasis added).

Notably, Perez was decided twenty years before Wyeth's expansive discussion of a manufacturer's duty to

update label warnings under FDA regulations in the postmarketing phase. Indeed, the Appellate Division in McDarby "note[d] that close scrutiny of the FDA and its regulatory power in a labeling context commenced only after Perez was decided, and that scrutiny disclosed flaws in the regulatory system." 401 N.J. Super. at 64. The McDarby court surveyed the FDA's role in the postmarketing phase of a drug and came to conclusions similar to those of the Wyeth Court. 401 N.J. Super. at 63-66. It observed that "[c]ommentators and courts have since [Perez] recognized that, whereas pre-market approvals of drugs are generally thorough in nature, the ability of the FDA, postmarket, 'to detect unforeseen adverse effects of [a] drug and to take prompt and effective remedial action' is considerably less." Id. at 64 (third alternation in original) (quoting Kessler & Vladeck at 465); see also Reglan, 226 N.J. at 337 (noting that Wyeth acknowledged "that the FDA does not have the resources to monitor the labeling of thousands of drugs after they are marketed").

The "flaws in that post-marketing oversight process," the Appellate Division reasoned, "render[ed] the dictum of Perez less all-encompassing than it might then have appeared" and "provide[d] the foundation for [a] further exception to the presumption of adequacy" enunciated in McDarby. McDarby, 401 N.J. Super. at 64.

McDarby did not deal with a manufacturer deliberately concealing or not disclosing after-acquired knowledge of a drug's harmful effects from the FDA, the bases for overcoming the presumption of adequacy of FDA-approved label warnings recognized in Perez. See id. at 63. In McDarby, the manufacturer had disclosed information about the drug's cardiovascular risk to the FDA but deliberately delayed amending the warning label to identify that risk, "despite the universal opinions of the FDA's advisory committee and medical reviewers – - and indeed, initially, the FDA regulators, themselves -- that a warning was appropriate."[21] Id. at 69. In light of the limitations of the FDA postmarketing oversight process and the evidence in that case, the Appellate Division articulated a further basis for overcoming the presumption of adequacy: a manufacturer's "economically-driven manipulation of the postmarket regulatory process." Id. at 63-64. In Cornett, 211 N.J. at 388, this Court recognized the McDarby exception.

D.

***25** The FDA's postmarketing oversight of drug label warnings is still hobbled by resource problems, according to a December 2015 report by the Government Accountability Office (GAO). That report indicated that the "FDA's lack of reliable, readily accessible postmarket safety data has prevented the agency from publishing required reports in a timely manner and has restricted its ability to conduct systematic oversight." U.S. Gov't Accountability Office, Drug Safety: FDA Expedites Many Applications, But Data for Postapproval Oversight Need Improvement 22 (Dec. 2015).[22]

We are mindful of Perez's general directive that federal regulations are of the utmost significance in determining whether "a manufacturer satisfied its duty to warn the physician about potentially harmful side effects of its product." See Perez, 161 N.J. at 24. Those regulations, in the postmarketing phase of a drug, require a manufacturer to revise a label to include a warning "about a clinically significant hazard as soon as there is reasonable evidence of a causal association with a drug." 21 C.F.R. § 201.57 (c)(6);[23] see also 21 C.F.R. § 314.70(c)(6)(iii)(A) (stating that, based on "newly acquired information," manufacturers must "add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under [21 C.F.R.] § 201.57(c)").

Even when manufacturers forward newly acquired information about a drug's risks to the FDA, Wyeth and the federal regulatory system make clear that manufacturers bear the ultimate responsibility for monitoring the effects of the drugs they place on the market. 555 U.S. at 570-71. The manufacturer's postmarketing obligation to update a label's warnings consistent with 21 C.F.R. § 201.57(c) and 21 C.F.R. § 314.70(c) is especially significant given that the FDA's oversight capabilities are limited due to overstretched resources in monitoring thousands of drugs on the market. Id. at 578.

Thus, an FDA-approved warning for a drug on the market for many years may grow stale in light of "newly acquired information" about "a clinically significant hazard" in the use of the drug by certain consumers. 21

C.F.R. § 201.57(c); 21 C.F.R. § 314.70(c). Prior FDA approval of a label's warning is not a license for a manufacturer to withhold updating and revising that warning in accordance with federal regulations. See ibid.

The PLA provides manufacturers with the protection of a rebuttable presumption of adequacy of an FDA-approved label warning. N.J.S.A. 2A:58C-4. An adequate warning for a prescription drug is one that "a reasonably prudent" manufacturer would have provided concerning dangers related to the drug's use "taking into account the characteristics of, and the ordinary knowledge common to, the prescribing physician." Ibid. "A duty to warn arises if [a manufacturer] actually knew or should have known of the need to issue a particular warning." N.J. Model Civil Jury Charges 5.40C (Model Civil Jury Charges Comm. 2017) (model charge for Failure to Warn/Instruct); see also McDarby, 410 N.J. Super. at 72 (finding that jury appropriately directed "to consider what [manufacturer] knew or should have known, when facts sufficient to require a warning became known, and whether it acted reasonably, given the information that it possessed").

***26** Consistent with Perez and McDarby, and the federal regulatory scheme, we hold that the rebuttable presumption of adequacy attaching to an FDA-approved drug label is overcome when a plaintiff presents clear and convincing evidence that a manufacturer knew or should have known, based on newly acquired information, of a causal association between the use of the drug and "a clinically significant hazard" and that the manufacturer failed to update the label accordingly. See 21 C.F.R. § 201.57(c); 21 C.F.R. § 314.70(c). We add one caveat. A manufacturer that acts in a reasonable and timely way to update its label warnings with the FDA, in accordance with its federal regulatory responsibilities, will receive the protection of the rebuttable presumption. If not, it cannot seek shelter behind it.

The heightened standard of clear and convincing evidence is in keeping with the high threshold set by Perez. Clear and convincing evidence is evidence that produces "a firm belief or conviction" in the truth of the alleged facts. N.J. Model Civil Jury Charges 1.19 (Model Civil Jury Charges Comm. 2017) (model charge for Burden of Proof -- Clear and Convincing Evidence). More descriptively, "it is evidence so clear, direct, weighty in terms of quality, and convincing as to cause [one] to come to a clear conviction of the truth of the precise facts in issue." Ibid. We reject the argument by amicus curiae New Jersey Association for Justice that the usual evidentiary standard for overcoming the presumption should apply.

The standard articulated here is a natural extension of the decisions in Perez and McDarby. It is a standard protective of responsible drug manufacturers. Faced with clear and convincing evidence of a label warning's inadequacy based on the FDA's label warning updating requirements set forth in 21 C.F.R. § 201.57(c) and 21 C.F.R. § 314.70(c), a responsible drug manufacturer will take action to revise its drug label warnings.

The PLA's rebuttable presumption of adequacy that attaches to label warnings gives pharmaceutical companies the protection necessary to research and develop the drugs that will improve and extend the lives of people around the world. The presumption of adequacy protects manufacturers from unmeritorious lawsuits. See Perez, 161 N.J. at 25; Rowe, 189 N.J. at 626.

The Legislature, however, envisioned that, in appropriate circumstances, the presumption would be overcome. See Feldman, 125 N.J. at 157 ("[The PLA's] plain language defies the conclusion that the presumption cannot be overborne."). In passing the PLA, the Legislature affirmed New Jersey's "substantial interest in deterring its manufacturers from developing, making, and distributing unsafe products, including inadequately labeled prescription drugs." See McCarrell, 227 N.J. at 597; Governor's Statement to S. 2805 (July 23, 1987) ("This legislation responds to the well documented need for the establishment of clear rules regarding legal actions seeking damages for harm caused by products.").

The high standard for overcoming the rebuttable presumption of adequacy of an FDA-approved label warning represents a balance that protects pharmaceutical companies that act responsibly and the public that consumes their products.

VI.

With the above principles in mind, we must now determine whether plaintiffs have presented the necessary evidence to overcome the presumption of adequacy that attaches to the FDA-approved post-April 2002 label warnings for Accutane. See N.J.S.A. 2A:58C-4.

Three pathways are available to overcome the presumption of adequacy. The first pathway is if a plaintiff can establish "deliberate concealment or nondisclosure of after-acquired knowledge of harmful effects." Perez, 161 N.J. at 25. The second is if a plaintiff can demonstrate "economically-driven manipulation of the post-market regulatory process." McDarby, 401 N.J. Super. at 63. The third is if a plaintiff can prove by clear and convincing evidence that a manufacturer knew or should have known in the postmarketing phase that the drug warnings were inadequate based on the label warning updating requirements in 21 C.F.R. § 201.57(c), 21 C.F.R. § 314.70(c), or any other pertinent federal regulation.

***27** On the record before us, plaintiffs have failed to show any of those bases for overcoming the presumption of adequacy. In the absence of evidence sufficient to rebut the presumption, as a matter of law, the warnings adequately conveyed to medical professionals -- as well as to patients -- that usage of Accutane was associated with a risk of IBD.

The post-April 2002 label warnings expressly informed physicians and, through them, patients that Accutane had been associated with a risk of IBD. Nevertheless, our focus is not only on the physician label, the primary means by which Roche communicated to prescribing physicians the risks of Accutane, but also on other IBD-related warnings that informed patients.

Roche used multiple warning tools: the physician label and Best Practices Guide, intended for physicians, and the Patient Safety Packet, Medication Guide, and blister packaging, intended for patients. The physician label -- written for trained healthcare professionals -- identified IBD by name ("Accutane has been associated with inflammatory bowel disease ....") and listed the most common symptoms of IBD ("Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue Accutane immediately."). Moreover, the physician label noted the potentially permanent nature of the condition ("In some instances, symptoms have been reported to persist after Accutane treatment has been stopped."). It also specifically warned prescribing physicians that patients with no prior history of intestinal problems might be at risk of IBD ("Accutane has been associated with [IBD] in patients without a prior history of intestinal disorders.").

Plaintiffs' principal criticism is that the physician label and other warning materials should have used the language "causes" instead of "has been associated with" to describe the relationship between Accutane and IBD. Plaintiffs, however, have failed to present clear and convincing evidence that Roche's use of the word "associated" to describe the relationship between Accutane and IBD was inadequate. We look to the scientific understanding of "association" as a physician would understand the term. According to the Reference Manual on Scientific Evidence, an association includes the possibility of causation but is not in itself causation. Reference Manual on Scientific Evidence 619 (3d ed. 2011) ("Association does not necessarily imply a causal relationship."). By use of the word "associated," Roche informed physicians that it was possible -- though not proven -- that, in the case of some patients, Accutane may have caused IBD. Roche had reports that some patients, after taking Accutane, developed symptoms of IBD. That one followed the other does not prove cause and effect. See In re: Accutane Litig., ___ N.J. ___, ___ (2018) (slip op. at 12-15).

Moreover, we do not find that the isolated examples plaintiffs have exhumed from the volumes of evidence support a showing of deliberate nondisclosure to the FDA, economically driven manipulation of the regulatory process, or clear and convincing evidence that Roche knew or should have known of the inadequacy of the warnings in light of the relevant federal regulations. Plaintiffs cite to the 1994 memorandum in which Dr. Lefrancq, a Roche physician, notes that Accutane "may induce or aggravate a preexisting colitis." Another 1994 excerpted internal Roche document noted that colitis was identified as a "possible" side effect of Accutane. Those memoranda are far from clear and convincing evidence that the language "Accutane has been associated with [IBD]" was an inadequate warning. [24]

***28** Plaintiffs argue that Roche had internally concluded that Accutane was causally -- not just possibly -- related to IBD. However, plaintiffs have failed to establish that Roche had in fact made such a determination, engaged in deliberate concealment or nondisclosure of such knowledge, or otherwise knew or should have known under the standard articulated above that the use of the word "associated" was inadequate. Rather, in support of that claim, plaintiffs point to another isolated statement

from a 2000 regulatory report culled from the voluminous discovery.

In that report, a physician, while discussing and analyzing an individual patient's medical history while on Accutane, states that Accutane "has been found to be causally associated with inflammatory bowel disease, including colitis." The record does not reflect the basis for that physician's comment. Nor does that statement suggest a consensus by other Roche physicians or employees about a causal connection between Accutane usage and IBD. Indeed, we do not know whether the statement represents anything more than one physician's understanding (or misunderstanding) of the relationship between Accutane and IBD. To be sure, that single statement is not clear and convincing evidence that Roche knew or should have known that the use of the word "associated" was inadequate.

Additionally, there is no evidence that Roche deliberately concealed or withheld any material information from the FDA or engaged in economically driven manipulation of the regulatory process. In fact, Roche's early postmarket monitoring led to the identification of IBD as a possible risk. At the urging of the FDA, Roche revised the initial warning language about IBD, removing the word "temporally" to more precisely align the warning with the evidence it had on hand regarding the potential permanency of IBD symptoms associated with Accutane.

Nor is there any evidence that Roche avoided necessary label changes for economic reasons. Roche's marketing personnel certainly expressed an interest in Accutane's financial success; it would have been surprising if it were otherwise. However, there is no evidence that Roche's financial interest in Accutane's success led it to withhold necessary IBD-related warnings. Cf. McDarby, 401 N.J. Super. at 69 (noting manufacturer's "strenuous, economically driven, opposition" to including cardiovascular risk in drug label). Roche was not averse to using causation language when appropriate. For example, Roche included label warnings that the use of Accutane posed "an extremely high risk" of causing birth defects and that "Accutane may cause depression."

Finally, the record shows that the FDA actively engaged in the postmarketing oversight of Accutane and proactively recommended strengthening warnings about IBD -- a recommendation followed by Roche. Whatever continuing concerns there may be about the FDA's postmarketing oversight capacity, there is no evidence in this record of shortcomings in the FDA's oversight of Accutane.

VII.

For the reasons expressed, we reverse the judgment of the Appellate Division in those cases in which it vacated the grant of summary judgment in favor of Roche and affirm its judgment in those cases in which it upheld the grant of summary judgment in favor of Roche. As a result, the 532 failure-to-warn cases brought by plaintiffs against Roche are dismissed.

CHIEF JUSTICE RABNER and JUSTICES LaVECCHIA, FERNANDEZ-VINA, SOLOMON, and TIMPONE join in JUSTICE ALBIN's opinion. JUSTICE PATTERSON did not participate.

All Citations

--- A.3d ----, 2018 WL 4761403

Footnotes

1 Because defendants moved for summary judgment, we consider the facts in the light most favorable to the non-moving party, plaintiffs. Brill v. Guardian Life Ins. Co. of Am., 142 N.J. 520, 540 (1995).

2 The physician label also cross-referenced IBD in the ADVERSE REACTIONS section:

> ADVERSE REACTIONS: .... The adverse reactions listed below reflect the experience from investigational studies of Accutane, and the postmarketing experience. The relationship of some of these events to Accutane therapy is unknown.
> ...
> *Gastrointestinal*: inflammatory bowel disease (see WARNINGS: Inflammatory Bowel Disease)
> ....

3 Birth defects and psychiatric side effects are specifically mentioned on the form, but IBD is not.

4 The warning for the Absorbica physician label includes, in pertinent part:

> Isotretinoin has been associated with inflammatory bowel disease (including regional ileitis) in patients without a prior history of intestinal disorders. In some instances, symptoms have been reported to persist after isotretinoin treatment has been stopped. Patients experiencing abdominal pain, rectal bleeding or severe diarrhea should discontinue Absorbica immediately [see *Adverse Reactions* (6.1)]
>
> ....
>
> Adverse Reactions
>
> ....
>
> The adverse reactions listed below reflect both clinical experience with Absorbica, and consider other adverse reactions that are known from clinical trials and the postmarketing surveillance with oral isotretinoin. The relationship of some of these events to isotretinoin therapy is unknown.
>
> ....
>
> Gastrointestinal: ... inflammatory bowel disease ....

5 A "side effect" is "[a]n action or effect of a drug other than that desired." Tabor's at 2153. A "contraindication" is "[a] symptom or circumstance that makes treatment with a drug or device unsafe or inappropriate." Id. at 553.

6 The trial court also conducted a state-by-state analysis as an alternative ruling. Under that approach, the court granted summary judgment in favor of Roche to plaintiffs who resided in thirteen jurisdictions other than New Jersey. In light of our ultimate disposition, a state-by-state review of the court's analysis is unnecessary.

7 Pursuant to MCL guidelines, the letter was directed to the Administrative Director of the Courts. See New Jersey Multicounty Litigation (Non-Asbestos) Resource Book 2 (4th ed. Nov. 2014) ("MCL Resource Book") (explaining that application for MCL designation is made to Supreme Court "through the Administrative Director").

8 In response to plaintiffs' cross-petition, Roche maintains that the Appellate Division correctly found that its warnings were adequate under the laws of eight states and that summary judgment was properly entered in its favor in the cases of those plaintiffs from those states.

9 Alabama, Arkansas, California, Colorado, Connecticut, Delaware, the District of Columbia, Florida, Georgia, Iowa, Idaho, Illinois, Indiana, Kansas, Kentucky, Louisiana, Maine, Maryland, Massachusetts, Minnesota, Mississippi, Missouri, Montana, Nebraska, Nevada, New Hampshire, New York, North Dakota, Ohio, Oklahoma, Oregon, Pennsylvania, Puerto Rico, Rhode Island, South Carolina, South Dakota, Tennessee, Texas, Utah, Vermont, Virginia, Washington, Wisconsin, and Wyoming.

10 Plaintiffs can overcome the presumption of adequacy in Texas by showing that a defendant "withheld from or misrepresented to" the FDA mandatory material information that was "relevant to the performance of the product" and "causally related to the claimant's injury." See Tex. Civ. Prac. & Rem. Code Ann. § 82.007(b)(1). However, unlike New Jersey, Texas does not apparently recognize "economically-driven manipulation of the post-market regulatory process," see McDarby, 401 N.J. Super. at 63, or clear and convincing evidence that a manufacturer knew or should have known in the postmarketing phase that the drug warning was inadequate, see infra Section V, as sufficient bases for overcoming the presumption of adequacy.

11 Indiana (Ind. Code § 34-20-5-1; Cansler v. Mills, 765 N.E.2d 698, 705 (Ind. Ct. App. 2002), disapproved of on other grounds by Schultz v. Ford Motor Co., 857 N.E.2d 977 (Ind. 2006)); Kansas (Kan. Stat. Ann. § 60-3304(a)); North Dakota (N.D. Cent. Code § 28-01.3-09); Oklahoma (Okla. Stat. tit. 76, § 57.2); Oregon (Or. Rev. Stat. § 30.900, .910; Chong v. STL Int'l, Inc., 152 F. Supp. 3d 1305, 1317 (D. Or. 2016)); Tennessee (Tenn. Code Ann. § 29-28-104; Goins v. Clorox Co., 926 F.2d 559, 562 (6th Cir. 1991)); Utah (Utah Code Ann. § 78B-6-703(2); Egbert v. Nissan N. Am., Inc., 156 P.3d 1058, 1062 (2007)); Wisconsin (Wis. Stat. §§ 895.047(3)(b), 903.01).

12 Arkansas (Ark. Code Ann. § 16-116-204, -205(a)); Connecticut (Conn. Gen. Stat. § 52-572q); Delaware (Lacy v. G.D. Searle & Co., 567 A.2d 398, 400 (Del. 1989)); the District of Columbia (Payne v. Soft Sheen Prods., Inc., 486 A.2d 712, 723 (D.C. 1985)); Florida (Thomas v. Bombardier Recreational Prods., Inc., 682 F. Supp. 2d 1297, 1300 (M.D. Fla. 2010)); Georgia (Weilbrenner v. Teva Pharm. USA, Inc., 696 F. Supp. 2d 1329, 1339 (M.D. Ga. 2010)); Idaho (Sliman v. Aluminum Co. of Am., 731 P.2d 1267, 1272 (Idaho 1986)); Illinois (Hernandez v. Schering Corp., 958 N.E.2d 447, 455 (Ill. App. Ct. 2011)); Iowa (Nationwide Agribus. Ins. Co. v. SMA Elevator Constr., Inc., 816 F. Supp. 2d 631, 654 (N.D. Iowa 2011)); Kentucky (Larkin v. Pfizer, Inc., 153 S.W.3d 758, 764-65 (Ky. 2004)); Maine (Doe v. Solvay Pharm., Inc., 350 F. Supp. 2d 257, 272-74 (D. Me. 2004)); Massachusetts (MacDonald v. Ortho Pharm. Corp., 475 N.E.2d 65, 70-71 (Mass. 1985)); Minnesota (Delude v. Johnson & Johnson, 726 F. Supp. 2d 1025, 1034 (D. Minn. 2010)); Missouri (Doe v. Alpha Therapeutic Corp., 3 S.W.3d 404, 419 (Mo. Ct. App. 1999)); Montana (Hill v. Squibb & Sons, E.R., 592 P.2d 1383, 1387-88 (Mont. 1979)); Nebraska (Freeman v. Hoffmann-La Roche, Inc., 618 N.W.2d 827, 841-42 (Neb. 2000)); Nevada (Allison v. Merck & Co., 878 P.2d 948, 960-61 (Nev. 1994)); New Hampshire (Brochu v. Ortho Pharm.

Corp., 642 F.2d 652, 657-58 (1st Cir. 1981)); Ohio (Seley v. G.D. Searle & Co., 423 N.E.2d 831, 836-37 (Ohio 1981)); Pennsylvania (Rowland v. Novartis Pharm. Corp., 34 F. Supp. 3d 556, 571-72 (W.D. Pa. 2014)); Puerto Rico (Guevara v. Dorsey Labs., Div. of Sandoz, Inc., 845 F.2d 364, 367 (1st Cir. 1988)); Rhode Island (Castrignano v. E.R. Squibb & Sons, Inc., 546 A.2d 775, 782-83 (R.I. 1988)); South Carolina (Allen v. Long Mfg. N.C., Inc., 505 S.E.2d 354, 357-58 (S.C. Ct. App. 1998)); South Dakota (McElhaney v. Eli Lilly & Co., 575 F. Supp. 228, 231-32 (D.S.D. 1983)); Vermont (Town of Bridport v. Sterling Clark Lurton Corp., 693 A.2d 701, 705-06 (Vt. 1997)); Washington (Laisure-Radke v. PAR Pharm., Inc., 426 F. Supp. 2d 1163, 1172 (W.D. Wash. 2006)); and Wyoming (Thom v. Bristol-Myers Squibb Co., 353 F.3d 848, 853-55 (10th Cir. 2003)).

13 See Louisiana (Stahl v. Novartis Pharm. Corp., 283 F.3d 254, 267 (5th Cir. 2002)); Virginia (Ball v. Takeda Pharm. Am., Inc., 963 F. Supp. 2d 497, 504 (E.D. Va. 2013)); Indiana (Tucker v. SmithKline Beecham Corp., 701 F. Supp. 2d 1040, 1066 (S.D. Ind. 2010)); Colorado (Caveny v. Ciba-Geigy Corp., 818 F. Supp. 1404, 1406 (D. Colo. 1992)); Alabama (Morguson v. 3M Co., 857 So. 2d 796, 801-02 (Ala. 2003)); California (Brown v. Superior Court, 751 P.2d 470, 477 (Cal. 1988)); Maryland (Nolan v. Dillon, 276 A.2d 36, 40-41 (Md. 1971)); Mississippi (Wyeth Labs., Inc. v. Fortenberry, 530 So. 2d 688, 691 (Miss. 1988)); New York (Martin v. Hacker, 628 N.E.2d 1308, 1312 (N.Y. 1993)).

We disagree with the Appellate Division's opinion that "it is enough in [Colorado, Indiana, Maryland, Mississippi, New York, and Virginia] that IBD was referenced" in Roche's label warnings to render them adequate.

14 Under the governmental-interest test, a court must "identify the governmental policies underlying the law of each state and how those policies are affected by each state's contacts to the litigation and to the parties." Veazey v. Doremus, 103 N.J. 244, 248 (1986).

15 See In re Bendectin Litig., 857 F.2d 290, 293-95, 304-05 (6th Cir. 1988) (applying single body of substantive law to nationwide product-liability litigation); In re "Agent Orange" Prod. Liab. Litig., 580 F. Supp. 690, 693, 700-06 (E.D.N.Y. 1984) ("[I]t is concluded that under the special circumstances of this litigation, all the transferor states would look to the same substantive law for the rule of decision on the critical substantive issues.").

16 In 1993, the American Law Institute (ALI) submitted to Congress for enactment a proposed choice-of-law rule for "mass-tort" actions transferred to federal court. American Law Institute, Complex Litigation Project, Proposed Final Draft (May 13, 1993). The proposed rule listed a number of factors that a court should consider "with the objective of applying, to the extent feasible, a single state's law to all similar tort claims being asserted against a defendant." Id. at § 6.01(a). The proposed rule was not enacted.

17 Either an Assignment Judge or an interested attorney may apply to this Court to have the case(s) classified as MCL. Id. at 2. If the Court classifies a case as MCL, it is assigned to a particular judge. Id. at 4. Currently, the nearly-twenty active MCLs in New Jersey are assigned to courts in three designated counties: Atlantic, Bergen, and Middlesex. New Jersey Courts, Multicounty Litigation -- Frequently Asked Questions, https://www.njcourts.gov/attorneys/mcl/mclfaq.html (last visited Aug. 17, 2018).

18 The Kessler & Vladeck article has been cited by state and federal courts for its insights regarding the FDA's approval process and postmarketing efforts. See, e.g., Wyeth, 555 U.S. 555, 579 n.12 (2009); Huck v. Wyeth, Inc., 850 N.W.2d 353, 397-98 (Iowa 2014); McDarby, 401 N.J. Super. at 57-58, 64-66. One of the authors of the article, David A. Kessler, is a former FDA Commissioner.

19 Premarket research has obvious limitations. Kessler & Vladeck at 470. According to the authors,

> [p]rior to FDA approval, drugs are tested on relatively small populations of patients, for durations rarely exceeding a year or two. Thus, pre-approval testing generally is incapable of detecting adverse effects that occur infrequently, have long latency periods, or affect subpopulations not included or adequately represented in the studies (for example, the elderly, ethnic minorities, and pregnant women).
>
> [Id. at 471, cited in Mut. Pharm. Co. v. Bartlett, 570 U.S. 472, 500 (2013).]

20 The CBE regulation identifies several other categories of changes "reflect[ing] newly acquired information" which the manufacturer (or corresponding party) may implement prior to approval by the FDA. 21 C.F.R. § 314.70(c).

21 The conduct in question occurred before the 2007 Amendments to the Food, Drug, and Cosmetic Act, during which the FDA "did not have the [statutory] authority to compel labeling changes, but instead had to negotiate changes with the drug's sponsor." McDarby, 401 N.J. Super. at 65 (alteration in original) (quoting Kessler & Vladeck at 466). As a result of the 2007 Amendments, the FDA now has enhanced postmarketing oversight powers. See Pub. L. No. 110-85, 121 Stat. 823. Those increased powers include the authority to require drug manufacturers to conduct postmarketing studies and clinical trials for approved drugs and products, 21 U.S.C. § 355(o)(3), and to mandate a labeling change it "deems appropriate to address ... new safety information," 21 U.S.C. § 355(o)(4)(E). However, as discussed below, there are still resource-related concerns about the FDA's capacity to fully carry out its postmarket responsibilities.

22 In particular, the GAO found that the FDA's database had inaccurate and incomplete data, in part due to delays in staff reviewing submissions. Id. at 23. The GAO estimated that the FDA failed to review in a timely manner more than half of the submissions associated with 1400 postmarket studies of drugs on the market. Id. at 23-24.

23 21 C.F.R. § 201.57 applies to prescription drug products for which an NDA or efficacy supplement was approved by the FDA between June 30, 2001 and June 30, 2006, was pending on June 30, 2006, or was submitted anytime on or after June 30, 2006. 21 C.F.R. § 201.56(b)(1). All other prescription drug products are subject to the requirements in 21 C.F.R. § 201.80. Ibid. Under § 201.80, manufacturers are required to revise the labeling if there is reasonable evidence of an association -- not a causal association -- of a serious hazard with the drug. 21 C.F.R. § 201.80(e).

24 Plaintiffs further cite the latter 1994 document as evidence that the use of Accutane was contraindicated in all patients with IBD or a family history of the disease. However, the document specifically indicates that the data regarding Accutane's association with IBD is "contradictory" and that there was not sufficient data to describe it as a contraindication. The document did note, however, that Accutane should be contraindicated for patients in the active phase of IBD. Significantly, the label warnings advised both physicians and patients that patients should discontinue Accutane use immediately if they experienced any IBD-related symptoms.

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