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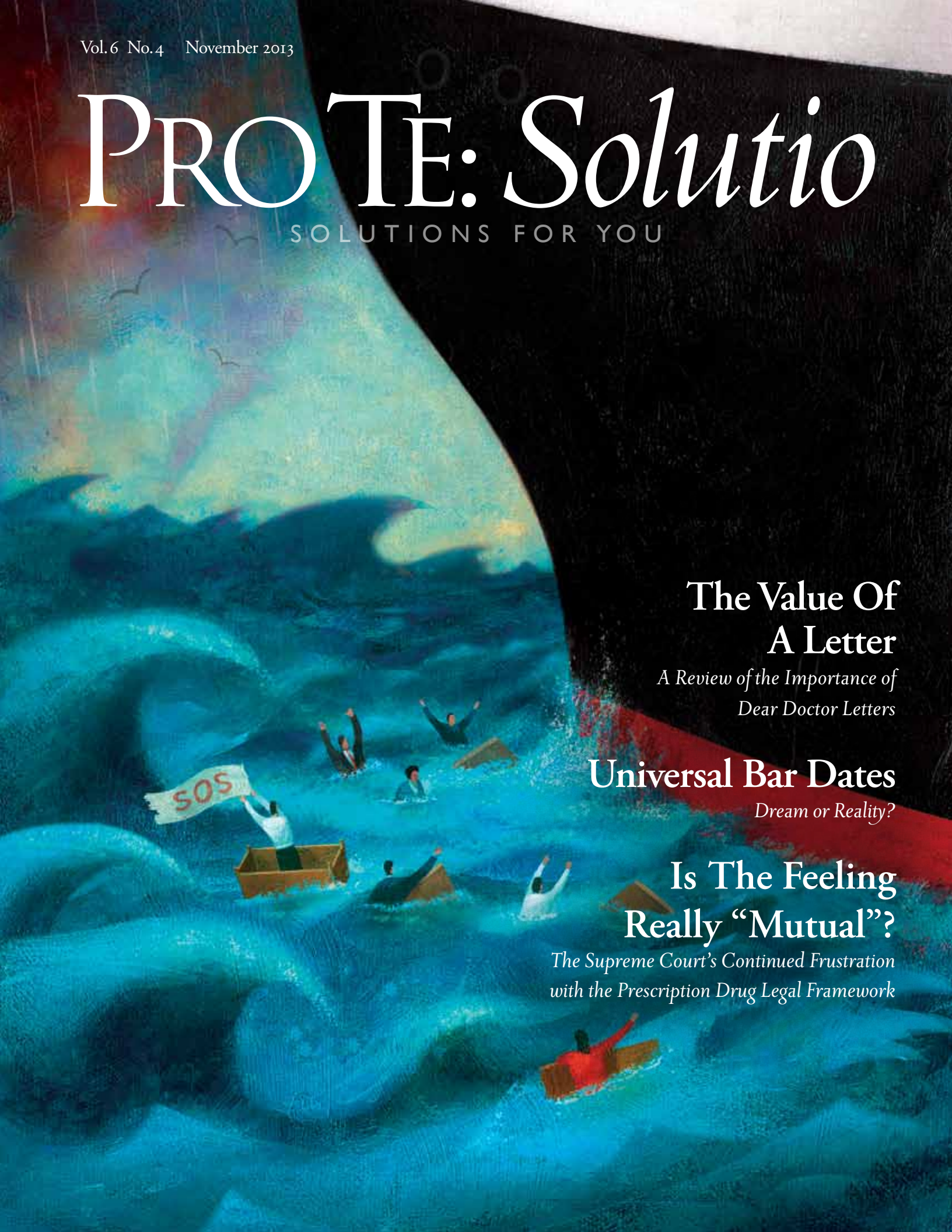
PRO TE: *Solutio*

SOLUTIONS FOR YOU



The Value Of A Letter

A Review of the Importance of Dear Doctor Letters

Universal Bar Dates

Dream or Reality?

Is The Feeling Really "Mutual"?

The Supreme Court's Continued Frustration with the Prescription Drug Legal Framework

Dear Client:

Sending new medical information about potential risks of your company's drug to medical providers is critical. But when should that letter go out? If you send it before FDA approval, you run the risk of the letter not being approved as is. However, if you wait for FDA approval, the letter may not go out for months. Either way, plaintiffs' counsel will criticize the timing of the letter. *The Value of a Letter: A Review of the Importance of Dear Doctor Letters* catches up with some recent case law on this issue.

Wouldn't it be nice if every lawsuit filed after a specific date regarding a certain drug or medical device was dismissed based on the statute of limitations? *Universal "Bar Dates" — Dream or Reality?* discusses how a lot of adverse publicity about your product may actually work to your advantage in having cases dismissed en masse.

A number of *Pro Te: Solutio* articles have examined the recent trio of United States Supreme Court preemption pharmaceutical cases. Now, the FDA is weighing in on this issue. *Is the Feeling Really "Mutual"? The Supreme Court's Continued Frustration with the Prescription Drug Legal Framework — and Forthcoming FDA Regulatory Action in Response to Mutual Pharmaceuticals v. Bartlett* continues our assessment of the latest developments as to preemption.

We hope you find this issue of *Pro Te: Solutio* helpful with the risk management and litigation issues you deal with every day.

Christy D. Jones
Co-Chair — Litigation

Charles F. Johnson
Co-Chair — Business and Corporate Healthcare

Pro Te: *Solutio*

Vol. 6 No. 4 November 2013

Sharing Solutions

It's human nature to share problems. But how often is someone willing to share solutions? Butler Snow wants to do just that — provide scenarios and the solutions that turned a client's anxiety into relief and even triumph. That's why we created this magazine, *Pro Te: Solutio*, which explores how real-life legal problems have been successfully solved.

That's also why we at Butler Snow redesigned and expanded our unique health-oriented industry group, now comprised of two major sections that handle business and litigation. The Pharmaceutical, Medical Device, and Healthcare Industry Group has more than 50 multi-disciplinary attorneys who provide creative solutions for the complex issues of the healthcare industry. This group includes product liability and commercial litigators; corporate, commercial, and transaction attorneys; labor and employment attorneys; intellectual property attorneys; and those experienced in government investigations.

Pro Te: Solutio is a quarterly magazine available only to the clients of Butler Snow. If you have questions or comments about its articles, you're invited to contact Christy Jones and Charles Johnson, as well as any of the attorneys listed on the last page of this publication.

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THE VALUE OF A LETTER:

A REVIEW OF THE IMPORTANCE OF DEAR DOCTOR LETTERS

Dear Colleagues and Friends,

With email, cell phones, text messages, and social media, writing letters has become a thing of the past. For drug manufacturers (and the lawyers who represent them), however, it is the very act of letter writing that may help avoid liability in a lawsuit regarding an alleged failure to warn. This letter/review highlights the importance of the form and, especially, the timeliness of Dear Doctor letters. So, before you chuck your letter writing skills (i.e., inside address, greeting, body, complimentary close, and signature), note the information below.

Requirements and Guidance for Dear Doctor Letters

According to the U.S. Food and Drug Administration (FDA), Dear Healthcare Professional letters (also known as Dear Doctor letters) are pieces of correspondence mailed from a pharmaceutical product manufacturer or distributor to physicians and other healthcare professionals to convey important product safety information.[1] The federal regulation that governs Dear Doctor letters, in part, provides:

> **21 C.F.R. § 200.5 – Mailing of important information about drugs.**
> Manufacturers and distributors of drugs and the Food and Drug Administration occasionally are required to mail important information about drugs to physicians and others responsible for patient care. In the public interest, such mail should be distinctive in appearance so that it will be promptly recognized and read. The Food and Drug Administration will make such mailings in accordance with the specifications set forth in this section. Manufacturers and distributors of drugs are asked to make such mailings as prescribed by this section and not to use the distinctive envelopes for ordinary mail.

The regulation goes on to set forth certain requirements dependent on whether the Dear Doctor letter is intended to convey new information about: 1) a significant hazard to health; 2) important changes in the package labeling; or 3) a correction in product advertising or labeling.[2] Additionally, the regulation specifies the proper form for Dear Doctor letters to include placement of the drug manufacturer's name and address, the font type and size, etc.[3] The regulation itself is concise, but the FDA also issued a guidance to assist industry and FDA staff to "improv[e] communication of important safety information" in Dear Doctor letters.[4]

Although the FDA's guidance contains suggestions and "should be viewed only as recommendations" instead of requirements, any pharmaceutical manufacturer that intends to send a Dear Doctor letter should become familiar with the FDA's guidance on the subject.[5] Moreover, the pharmaceutical manufacturer should actually work with the FDA to prepare the Dear Doctor letter prior to engaging in any mass mailing.[6] Indeed, the FDA actually "believes that effective communication of important new information in Dear Healthcare Provider letters can be best accomplished if FDA and the manufacturer work together" on such letters.[7] The guidance further provides that "FDA encourages manufacturers to consult with the appropriate review division in the development of a Dear Healthcare Provider letter to ensure that the letter clearly and accurately reflects both the manufacturer's and FDA's understanding of the issue and the action required to address the issue."[8] Working with the FDA on Dear Doctor letters provides an opportunity for the FDA to have input on the content of the letter, and manufacturers who do so may include a statement in the heading or in the body of the letter indicating that the FDA reviewed and agreed with the contents of the letter.[9] Most pharmaceutical manufacturers and lawyers understand that compliance with the FDA's guidance and requirements does not necessarily shield one from litigation, but consultation with the FDA is also particularly important to "avoid the need to send a corrective letter in the event that FDA determines […] that the content of the letter was somehow false or misleading."[10]

The Importance of a *Timely* Dear Doctor Letter

While the form and content of Dear Doctor letters are important, the *Tietz v. Abbott Laboratories, Inc.*, Illinois state court case indicates the importance of timely sending the letters.[11] The *Tietz* plaintiff alleged that Abbott, the manufacturer of a prescription immunosuppressant medication Humira®, failed to warn consumers or physicians that Humira could cause a rare infection known as histoplasmosis.[12] The *Tietz* plaintiff specifically alleged that his wife suffered from the rare infection as a result of using Humira, and physicians were unable to diagnose the condition for weeks due to Abbott's failure to warn.[13] Abbott submitted evidence that it had, in fact, mailed Dear Doctor letters advising of the rare infection in May 2010.[14] The *Tietz* plaintiff argued, however, that his wife had already been hospitalized for 10 days before Abbott distributed the letters.[15] Further, the *Tietz* plaintiff argued that the FDA had previously advised Abbott and other manufacturers — in September 2008 — to provide new information about the risks of the rare disease.[16] In other words, the *Tietz* plaintiff argued that Abbott's Dear Doctor letter advising of the risk was "too little, too late," and apparently the jury agreed, as it awarded a $2.2 million verdict.[17]

In the *Tietz* case, the manufacturer had mailed a Dear Doctor letter advising of the risk at issue but to no avail. In fact, the manufacturer submitted evidence that it worked with the FDA to secure approval of the contents of the letter (i.e., the manufacturer had complied with the FDA's guidance). The manufacturer's arguments were insufficient to overcome plaintiff's failure to warn allegation as the jury found that the Dear Doctor letter had not been sent in a timely manner. A cynical person may read the *Tietz* case and conclude that working with the FDA to mail a Dear Doctor letter lacks any value and is a complete waste of time. Any such way of thinking, however, seems to miss the point of the *Tietz* case. So, what is the point? The *Tietz* case seems to suggest that a Dear Doctor letter must be mailed within a timely period after a manufacturer learns of new safety information that should be shared with prescribing physicians and other healthcare providers. What remains unclear, however, is what period of time makes a Dear Doctor letter timely? Unfortunately, the answer is not in this letter, nor is it in the FDA's guidance, as the FDA only suggests "it is important to communicate new information *promptly* to healthcare practitioners involved in prescribing or dispensing a drug, or in care for patients who receive a drug."[18]

Other Cases re *Timeliness* of Dear Doctor Letters

Although the *Tietz* case and, more importantly, the FDA's guidance are silent on the time period that renders a Dear Doctor letter timely and prompt, a review of the case law reveals that the question is one for the jury. For example, in *Rutz v. Novartis Pharmaceuticals Corp.*, the *Rutz* plaintiff alleged that the defendant manufacturer of a cancer medication failed to warn about the risk of osteonecrosis of the jaw (ONJ) in a timely manner.[19] Specifically, the *Rutz* plaintiff alleged that the defendant manufacturer waited 10 months after receipt of the first ONJ-related adverse event to notify the FDA of its intent to revise the product labeling to reflect reports of ONJ with the use of its product.[20] Further, the *Rutz* plaintiff alleged that the defendant manufacturer waited 22 months before sending Dear Doctor letters to notify prescribing physicians of the label change.[21] The defendant manufacturer submitted evidence that it had received the first ONJ-related adverse event nearly six months after the *Rutz* plaintiff began using its product, and it voluntarily changed the product warnings to reflect the risk of ONJ once it had collected adequate data.[22] Plaintiff submitted, however, that the defendant manufacturer "knew about the risk of ONJ long before it amended its warning and sent the letters notifying doctors of the risk."[23] The court found that the issues of adequacy and timeliness of the defendant manufacturer's Dear Doctor letter and revised warnings were questions of fact for the jury.[24]

In *Winters and Baldwin v. Novartis Pharmaceuticals Corp.*, the *Baldwin* plaintiff also alleged that the defendant manufacturer of a cancer medication failed to warn about the risk of ONJ in a timely manner.[25] Specifically, the *Baldwin* plaintiff presented evidence that the defendant manufacturer "was slow to respond to an obvious prob-

lem and arguably tried to conceal or delay information concerning the risk of developing ONJ from the medical community and the public."[26] The *Baldwin* plaintiff began using the product at issue in July 2003; however, the defendant manufacturer had been notified of the risk of ONJ with the use of its product in June 2003 and instructed members of its sales force not to mention the risk as early as August 2003.[27] Although the defendant manufacturer changed the package insert to mention cases of ONJ in December 2003, it failed to send Dear Doctor letters until September 2004.[28] Further, by that time, the *Baldwin* plaintiff had been using the product at issue for 14 months and had lost two teeth.[29] The *Baldwin* plaintiff argued the "warnings were both insufficient and too late," and the jury agreed by returning a verdict for $225,000 on the failure to warn claim.[30]

A Medtronic multidistrict litigation (MDL) plaintiff made similar allegations against the manufacturer of implantable defibrillators for failure to warn in a timely manner.[31] Evidence was presented that the defendant manufacturer learned in early 2003 that its defibrillators had a defective battery that caused the products to lose charge in days instead of years.[32] The defendant manufacturer began receiving reports of premature battery depletion around February 2004, and it had received several reports by December 2004.[33] In February 2005, which was two years after first learning of the issue, the manufacturer mailed Dear Doctor letters advising of the risk of battery depletion and product failure.[34] The court found the evidence sufficient enough for a jury to determine whether the defendant manufacturer knew of the defect for a substantial period prior to advising of the defect.[35]

Conclusion

This letter serves as a friendly reminder of the value of Dear Doctor letters. In addition to providing valuable information to prescribers and other healthcare providers, Dear Doctor letters can help shield a manufacturer from failure to warn litigation. If case law is any indication, though, the timeliness of a Dear Doctor letter is as equally important as the contents of the letter. While there is no set amount of time to render a Dear Doctor letter timely, there is no time like the present to brush up on the case law and FDA's guidance and requirements for such letters to avoid a costly rewrite of the *Tietz* case.

Warmest regards,

Meta C. Danzey

M.D. (Meta Danzey)

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[1] Manual of Policies and Procedures 6020.10 "NDAs: 'Dear Health Care Professional' Letters," July 2003, at 2. <http://www.fda.gov/downloads/AboutFDA/CentersOffices/CDER/ManualofPoliciesProcedures/ucm082012.pdf>.
[2] 21 C.F.R. § 200.5.
[3] *Id.*
[4] FDA's Guidance for Industry and FDA Staff: Dear Health Care Provider Letters: Improving Communication of Important Safety Information, November 2010. (Referenced in subsequent notes herein as "Guidance.") <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM233769.pdf>.
[5] Guidance at 1.
[6] Per the FDA's Guidance, those intending to distribute Dear Doctor letters electronically should also consult the FDA's Guidance for Industry on Using Electronic Means to Distribute Certain Product Information. Guidance at 5. *See also* <http://www.fda.gov/RegulatoryInformation/Guidances/ucm125164.htm>.
[7] Guidance at 2.
[8] *Id.*
[9] Guidance at 5.
[10] Guidance at 2.
[11] *Milton Tietz et al. v. Abbott Laboratories, et al.*, No. 12-L-002715, Ill. Cir. Cook Co. (May 2013).
[12] See <http://www.lexisnexis.com/legalnewsroom/litigation/b/litigation-blog/archive/2013/05/10/illinois-jury-awards-2-2million-to-widower-in-1st-humira-infection-case-to-go-to-trial.aspx>.
[13] *Id.*
[14] *Id.*
[15] *Id.*
[16] *Id.*
[17] *Id.*
[18] Guidance at 2. Emphasis added.
[19] *Rutz v. Novartis Pharmaceuticals Corp.*, No. 12-CV-0026-MJR, 2012 U.S. Dist. LEXIS 177779 (S.D. Ill. Dec. 17, 2012).
[20] *Id.* at *15.
[21] *Id.*
[22] *Id.* at *12.
[23] *Id.* at *13.
[24] *Id.* at *15.
[25] *Winter and Baldwin v. Novartis Pharmaceuticals Corp.*, 882 F.Supp.2d 1113 (W.D. Mo. Aug. 3, 2012).
[26] *Id.* at 1118.
[27] *Id.*
[28] *Id.* at 1119.
[29] *Id.* at 1120.
[30] *Id.* at 1116, 1120.
[31] *In re Medtronic, Inc., Implantable Defibrillators Litigation*, 465 F.Supp.2d 886 (D. Minn. Nov. 28, 2006).
[32] *Id.* at 889.
[33] *Id.* at 890.
[34] *Id.*
[35] *Id.* at 897.

Written *by*
Meta Danzey

UNIVERSAL "BAR DATES"

DREAM OR REALITY?

Plaintiffs in all fifty states have brought multidistrict litigation (MDL) against your company over a drug it manufactures. The FDA approved a change to the product label over two years ago to warn of the potential association between use of the drug and the injuries at issue in the litigation. Your company sent Dear Doctor letters soon afterward to inform physicians of the label change. National and local media outlets featured the label change prominently in their news coverage for weeks, and advertisements by plaintiffs' law firms have blanketed television and print media for years. Meanwhile, suits alleging warning defects in the former product label — the one your company changed two years ago — continue to mount, even from jurisdictions with two-year statutes of limitations. All of these plaintiffs invoke the discovery rule, which generally tolls the running of the statute of limitations until the date the plaintiff knew, or in the exercise of reasonable diligence, should have known of her injury and its potential causal link to the defendant's product. But did the public events surrounding your company's drug put these plaintiffs on notice of their potential claims and thus trigger all of the relevant statutes of limitations to begin running by a universally applicable date?

During the past ten years, the concept of establishing universal bar dates has slowly but consistently gained acceptance among state and federal courts overseeing pharmaceutical multidistrict and consolidated litigations, with five courts establishing a universal bar date. No bright-line test has emerged for the appropriateness of a universal bar date. Rather, the courts have engaged in fact-intensive inquiries into whether there is a "last possible date" by which all plaintiffs should have known of their potential claims. Courts have considered many factors when establishing bar dates, including the existence of widespread publicity regarding the alleged side effects, Dear Doctor and Dear Patient letters, label changes, press releases, the publication of scientific studies and other medical literature, plaintiffs' attorney advertisements, and even FDA Advisory Panel votes.

1. IN RE DIET DRUGS MDL

In the *Diet Drugs* multidistrict litigation, the plaintiffs filed their claims more than five years after the diet drugs were withdrawn from the market but argued they could not have discovered that the drugs caused their injury within the statute of limitations period.[1] The court rejected this argument, noting the "pervasive" and "widespread publicity accompanying the withdrawal of the diet drugs from the market in September, 1997," including extensive local media coverage, "leading stories on major television network news programs, including *NBC Nightly News*, *CBS Evening News*, and *The Today Show*" and a front-page story in *USA Today*.[2] Moreover, the manufacturer, Wyeth, issued a press release, published full-page ads in leading newspapers, and issued a Dear Doctor letter, all advising patients and physicians of the potential association between use of the drugs and valvular heart disease.[3] Finally, the court pointed to the "comprehensive publicity campaign surrounding the nationwide class action Settlement Agreement with Wyeth" which lasted until March of 2000.[4] Based on these events, the court established a universal bar date coinciding with the end of the publicity campaign in March 2000, finding the campaign "put plaintiffs on inquiry notice that their alleged heart problems would be detectable through an echocardiogram."[5]

2. IN RE VIOXX MDL

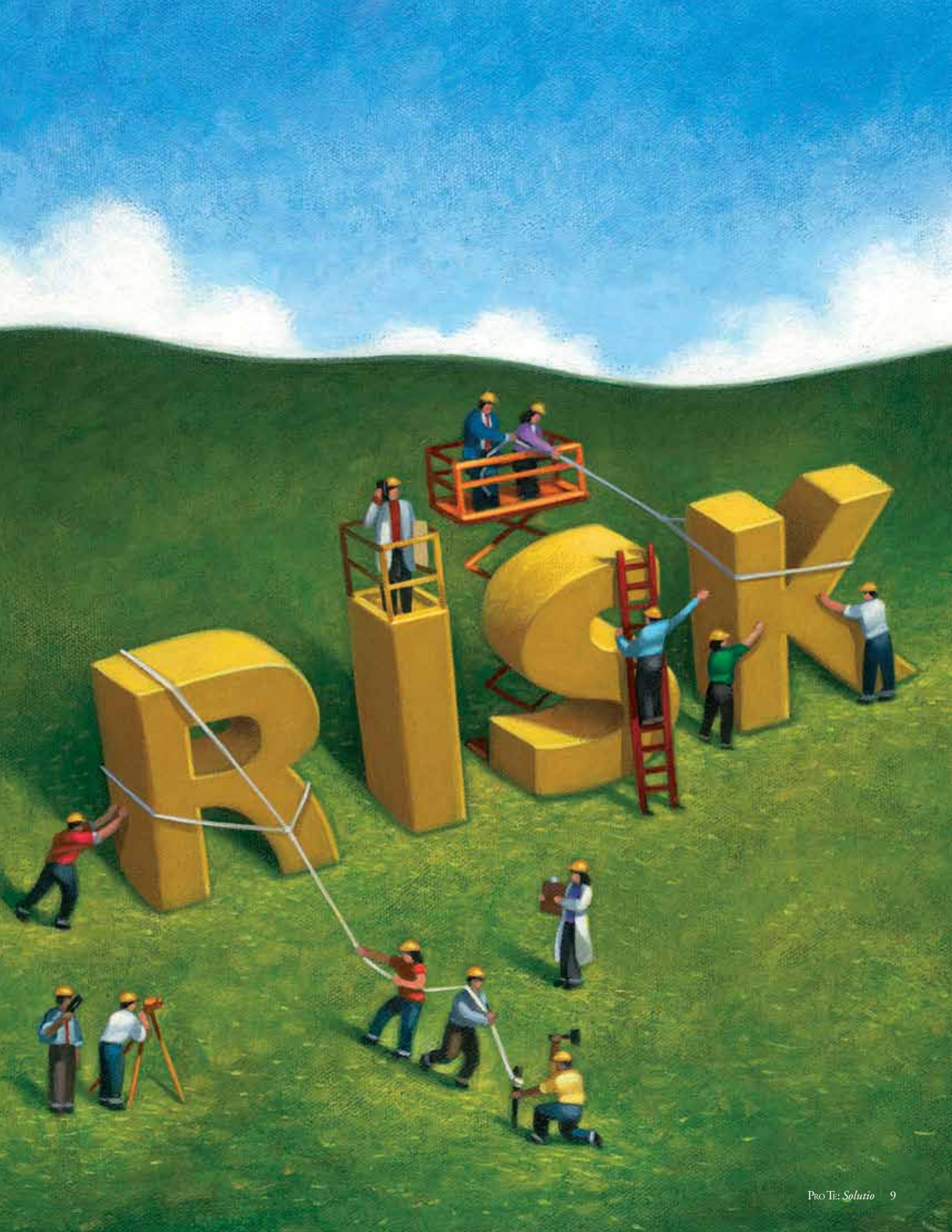
The *Vioxx* multidistrict litigation involved an "avalanche of media coverage" regarding the "largest and most-publicized prescription drug withdrawal in this country's history":

> On the morning of September 30, 2004, the national television network morning shows reported extensively on the withdrawal of Vioxx, including NBC's *The Today Show*, ABC's *Good Morning America*, CBS's *Early Show*, and CNN's *American Morning*. National coverage continued throughout the day with reports on National Public Radio and the networks' evening news broadcasts. The next day, October 1, 2004, saw more television coverage of the withdrawal and an onslaught of front-page stories in newspapers across the country.[6]

Merck argued that certain plaintiffs' tort claims were barred under "any conceivably applicable statute of limitations" because "at the very latest, the various limitations periods began to run on September 30, 2004, when Vioxx was withdrawn from the market."[7] Finding that this media coverage was "sufficient to put the plaintiffs on notice of a potential link between their alleged injuries and the use of Vioxx," the court entered summary judgment against the plaintiffs.[8] Whether plaintiffs had "actual knowledge" of the potential link between Vioxx and their alleged injuries was immaterial to the court's legal analysis.[9]

3. IN RE AVANDIA MDL

In the *Avandia* multidistrict litigation, GlaxoSmithKline ("GSK") sought to "establish a 'bar date,' i.e., the date by which any plaintiffs [could] be presumed as a matter of law to have been on notice of a possible link between Avandia and their injuries, and therefore to pursue any tort claims."[10] Several events occurring in 2007 had served to establish a potential link between use of Avandia and an increased risk of heart attack, beginning with a meta-analysis study which was published in the *New England Journal of Medicine* on May 21, 2007.[11] In response to the study's publication, the American College of Cardiology, the American Diabetes Association, and the American Heart Association issued a consensus statement expressing concern and advising patients taking the drug to speak with their physicians.[12] In July of 2007, the FDA convened an Advisory Committee meeting, which resulted in a 20–3 vote concluding that Avandia may increase cardiac ischemic risks.[13] The FDA required GSK to revise the label for Avandia, and a new black box warning regarding heart risk was approved on August 14, 2007.[14] From May through November 2007, GSK sent eight Dear Doctor letters to healthcare providers regarding studies of Avandia and cardiovascular health, as well as regulatory developments.[15] On June 1, 2007, GSK also published a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"Dear Avandia Patient" letter, defending the drug from "press coverage about the safety of Avandia."[16] The publication of the meta-analysis study, as well as the November 2007 label change, generated "substantial interest in the media" including lead stories in the national evening news and articles in national and local newspapers.[17]

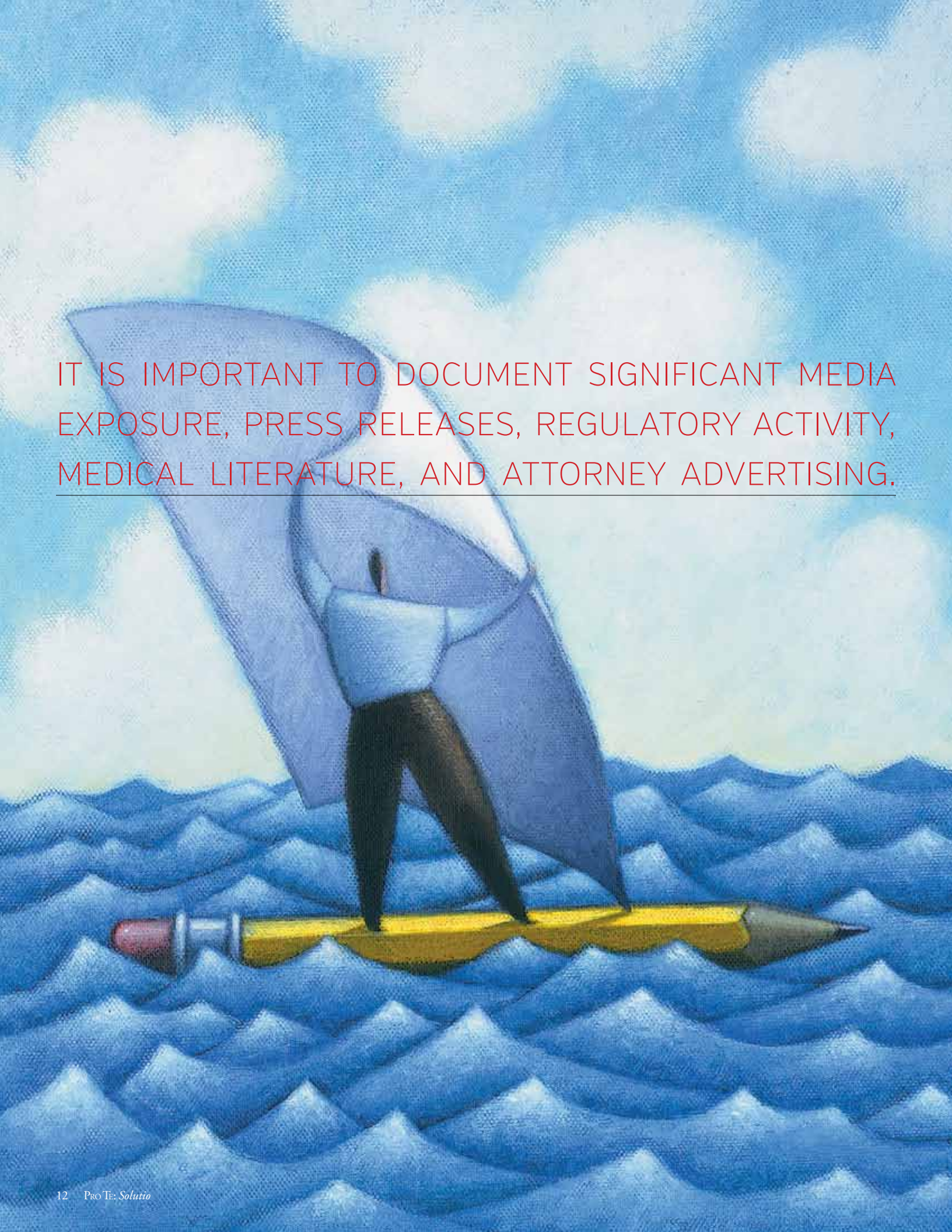
Based on the "cumulative effect" of the 2007 events and the "information available both to the general public and treating physicians throughout 2007," the court held that "a reasonable person who knew that he or she had suffered cardiovascular injury and had taken Avandia would have been put on notice by the end of 2007 to investigate a possible link between Avandia and the injury."[18] The court held that the statutes of limitations applicable to two plaintiffs' claims began to run by December 31, 2007, but noted that "the laws of certain states may have a different view of when a claim is tolled."[19]

4. IN RE ZYPREXA MDL

Unlike *Vioxx* and *Avandia*, the *Zyprexa* litigation did not involve extensive national and local media attention.[20] However, the manufacturer, Eli Lilly & Company ("Lilly"), revised the Zyprexa Package Insert on September 16, 2003, to include a warning to prescribing physicians about the risk to patients of weight gain and development of diabetes.[21] Lilly issued a press release the next day announcing the label change.[22] In November 2003, the American Diabetes Association, the American Psychiatric Association, the American College of Clinical Endocrinologists, and the North American Association for the Study of Obesity released a consensus statement finding that Zyprexa increased the risk of diabetes.[23] On March 1, 2004, Lilly sent a Dear Doctor letter informing physicians of the 2003 label change.[24]

The court found that the March 1, 2004, Dear Doctor letter would be considered the "latest possible date on which members of the medical community knew or should have known about Zyprexa's obesity and diabetes-related risks."[25] Applying the "learned intermediary" doctrine, the court imputed this knowledge to each of the individual plaintiffs, holding that March 1, 2004, was also the "latest possible date […] from which the statute of limitations may run as to any individual plaintiff."[26]

ESTABLISHING A UNIVERSAL BAR DATE CAN POTENTIALLY PRECLUDE A LARGE NUMBER OF CLAIMS WITH ONE DISPOSITIVE MOTION. IT MAY ALSO PREVENT A MASS TORT FROM BEING LITIGATED IN NEAR PERPETUITY.



IT IS IMPORTANT TO DOCUMENT SIGNIFICANT MEDIA EXPOSURE, PRESS RELEASES, REGULATORY ACTIVITY, MEDICAL LITERATURE, AND ATTORNEY ADVERTISING.

The Zyprexa MDL also involved claims alleging a causal link between the drug and pancreatitis.[27] On November 17, 2001, Lilly revised the "ADVERSE REACTIONS" section of the Patient Package Insert to include information regarding postmarketing reports of pancreatitis.[28] The court held the November 17, 2001, label change was the "date from which the statute runs as to pancreatitis," noting that the warning had been designed to alert consumers,[29] as opposed to the diabetes warning which had been "designed for prescribing doctors" and "did not mention weight gain or diabetes in the 'warning to patients' section.'"[30] Notably, the only other events cited by the court as potentially putting plaintiffs on notice of their claims were advertisements by plaintiffs' firms which ran from 2003 to 2007.[31] The November 17, 2001, bar date selected by the court predated these advertisements and was therefore based solely on the label change.

5. DELAWARE CONSOLIDATED SEROQUEL LITIGATION

In the Delaware consolidated Seroquel litigation, the Superior Court of Delaware analyzed that state's "time of discovery" exception to the running of the statute of limitations, which looks to when "someone from the scientific community found and revealed publicly a link between the physical condition and the exposure to the toxic substance."[32] Three of the plaintiffs were diagnosed with diabetes in 2004 but argued that they were not on notice of their claims until 2007 when they saw television advertisements aired by plaintiffs' law firms seeking potential plaintiffs for the Seroquel litigation.[33]

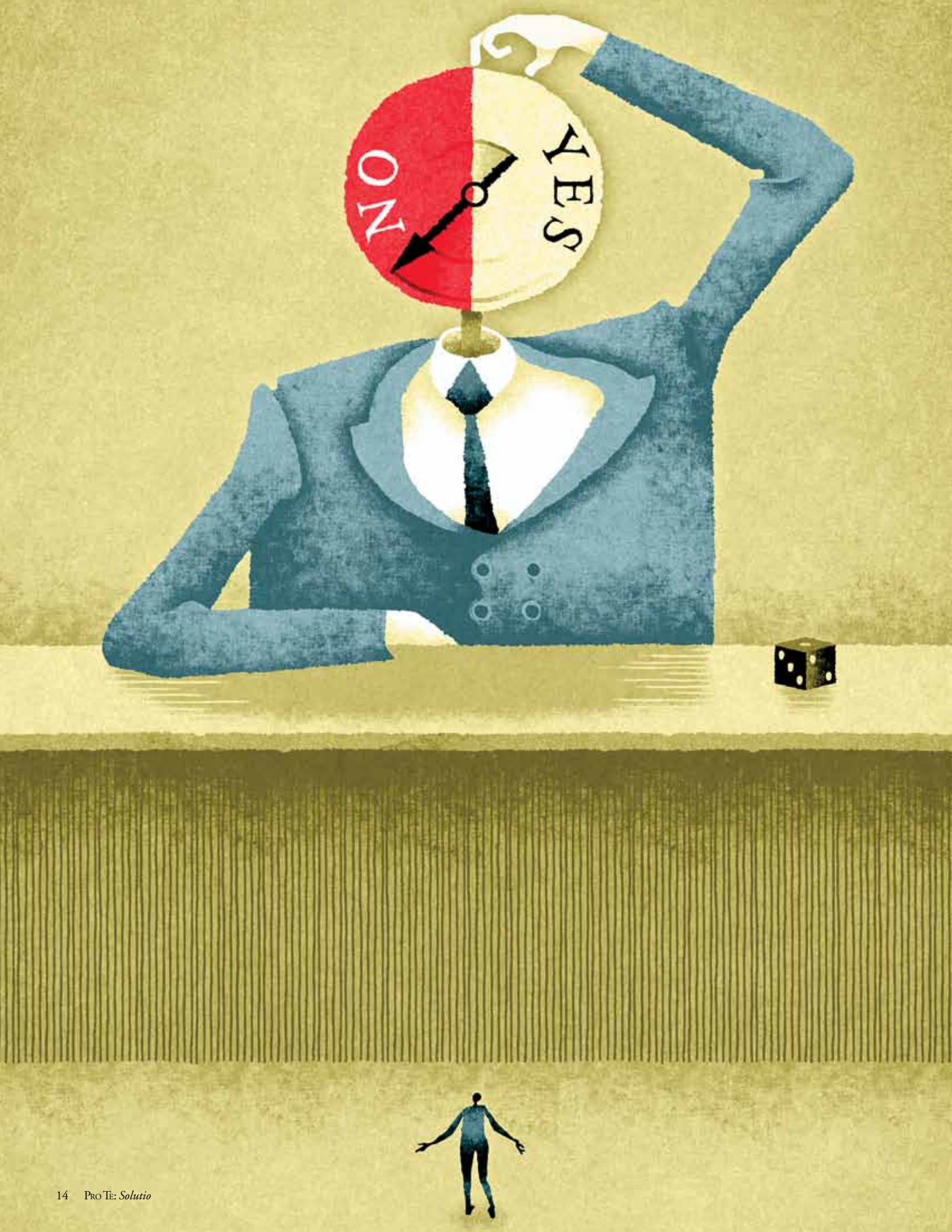
The court found that, as early as 2003, both medical and lay sources had published information regarding the possible link between Seroquel and diabetes.[34] Moreover, by January of 2004, the Seroquel label was changed to include a warning regarding the possible risk of diabetes.[35] The manufacturer, AstraZeneca, alerted the medical community to the new label in a Dear Doctor letter sent in January of 2004[36] and again in a second Dear Doctor letter sent in April of 2004. The court held that, under the applicable Delaware law, the latest possible date on which plaintiffs were on notice of their claims was January 30, 2004, the date of the first Dear Doctor letter.[37]

ESTABLISHING A UNIVERSAL BAR DATE

Establishing a universal bar date can potentially preclude a large number of claims with one dispositive motion. It may also prevent a mass tort from being litigated in near perpetuity. Because of these powerful qualities, counsel should consider possible bar dates early in the litigation and begin gathering facts and evidence to convince the court to adopt one of those dates. It is important to document significant media exposure, press releases, regulatory activity, medical literature, and attorney advertising. However, other events unique to the history of the drug should be considered as well, given the flexibility demonstrated by the courts. In most cases, counsel would be well advised to wait until the summary judgment stage to present the issue to the court, as all of the supporting cases have been decided on a full summary judgment record, and a loss on a Rule 12(b)(6) motion may predispose the court to disfavor the argument when it is renewed at the summary judgment stage. ■

[1] *Accadia v. Wyeth, In re Diet Drugs (Phentermine/Fenfluramine/Dexfenfluramine) Prods. Liab. Litig.*, 2004 U.S. Dist. LEXIS 26754, *3 (E.D. Pa. June 30, 2004).
[2] *Id.* at *11-22.
[3] *Id.* at *14-15.
[4] *Id.* at *15.
[5] *Id.* at *22.
[6] *In re Vioxx Prods. Liab. Litig.*, 522 F.Supp.2d 799, 803 (E.D. La. 2007).
[7] *Id.* at 804.
[8] *See Vioxx, supra*, 522 F.Supp.2d at 807-811 (applying the Pennsylvania, Illinois, and Puerto Rico statutes of limitations); *In re Vioxx Prods. Liab. Litig.*, 2007 U.S. Dist. LEXIS 83709, *7-8, 13 (E.D. La. Nov. 8, 2007) (applying the Kentucky and Tennessee statutes of limitations).
[9] *Vioxx, supra*, 2007 U.S. Dist. LEXIS 83709 at *7.
[10] *Faheem v. GlaxoSmithKline, LLC (In re Avandia Mktg., Sales Practices & Prods. Liab. Litig.)*, 2012 U.S. Dist. LEXIS 111272, *4 (E.D. Pa. Aug. 7, 2012).
[11] *Id.* at *11.
[12] *Id.* at *12.
[13] *Id.*
[14] *Id.*
[15] *Id.* at *13.
[16] *Id.*
[17] *Id.* at *14.
[18] *Id.* at *15-18.
[19] *Id.* at *19-20.
[20] *See e.g., Belcher v. Eli Lilly & Co. (In re Zyprexa Prods. Liab. Litig.)*, 2009 U.S. Dist. LEXIS 105431 (E.D.N.Y. Oct. 9, 2009) aff'd, 394 Fed. Appx. 821 (2d Cir. 2010) (unpublished).
[21] *Id.* at *98.
[22] *Id.* at *100.
[23] *Id.* at *101.
[24] *Id.* at *100.
[25] *Id.* at *105.
[26] *Id.* at *106-107.
[27] *See Ortenzio v. Eli Lilly & Co. (In re Zyprexa Prods. Liab. Litig.)*, 2009 U.S. Dist. LEXIS 47573, 68 (E.D.N.Y. June 1, 2009).
[28] *Id.* at *81.
[29] *Id.* at *81, *90.
[30] *See Belcher,* 2009 U.S. Dist. LEXIS 105431 at *98, *100; *see also Cunningham v. Eli Lilly & Co. (In re Zyprexa Prods. Liab. Litig.)*, 2010 U.S. Dist. LEXIS 49676, 14 (E.D.N.Y. May 19, 2010).
[31] *Cunningham, (In re Zyprexa)*, 2010 U.S. Dist. LEXIS 49676 at *35.
[32] *Burrell v. Astrazeneca LP*, C.A. No. 7C-01-412 (SER), 2010 Del. Super. LEXIS 393, *2 (Del. Super. Ct. Sept. 20, 2010).
[33] *Id.* at *3-5; *23-24.
[34] *Id.* at 25.
[35] *Id.*
[36] *Id.*
[37] *Id.*

Written by
Aaron Rice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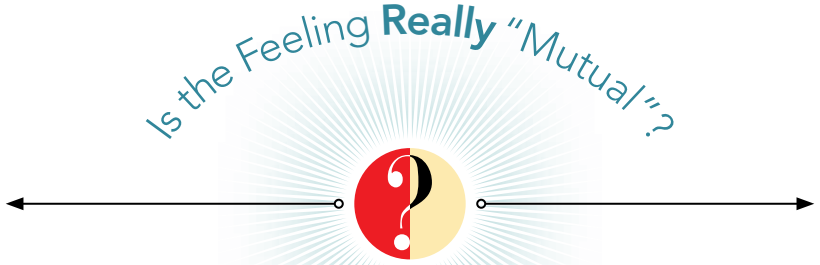


THE SUPREME COURT'S CONTINUED FRUSTRATION WITH THE PRESCRIPTION DRUG LEGAL FRAMEWORK — AND FORTHCOMING FDA REGULATORY ACTION IN RESPONSE TO *MUTUAL PHARMACEUTICALS V. BARTLETT*

I. Overview

The United States Supreme Court's now well-known trio of cases on implied preemption — *Wyeth v. Levine*,[1] *PLIVA v. Mensing*,[2] and *Mutual Pharmaceuticals v. Bartlett*[3] — has generated sweeping change in pharmaceutical litigation. Condensed to their most simplistic results (perhaps unfairly so), the scorecard can be summarized as follows:

- Implied conflict preemption for brand manufacturers? By and large, NO — unless the brand manufacturer can show clear evidence that the FDA considered, and rejected, proposed warnings on the same risks and injuries (*Wyeth v. Levine*);

- Implied conflict preemption for generic manufacturers based on a theory of failure to warn/adequacy of the warnings? Generally, YES — because generic manufacturers must ask FDA for permission (and get it) before changing a label beyond that authorized for the brand version (*PLIVA v. Mensing*); and

- Implied conflict preemption for generic manufacturers based on a theory of design defect? Generally, YES — under the rationale of *Mensing*, a generic manufacturer cannot unilaterally change the design of a product that was FDA-approved, and further, the manufacturer should not be forced to make a Hobson's choice of ceasing sales of the product altogether to avoid conflict (*Mutual Pharmaceuticals v. Bartlett*).

So we have what we have: three cases, with essentially two different results, that turn on one issue: whether the product in question is a brand or generic.

Other articles — including discussions in our very own *Pro Te: Solutio* — have considered how plaintiffs' firms are seeking to use the above cases as shields or swords. This article, by contrast, looks at an issue that the Supreme Court has raised in each of these three preemption cases: Congress's attention (or lack thereof) to the laws that have, according to the Supreme Court, directly resulted in seemingly disparate results, and the FDA's actions in response.

The Court's unabashed frustration at the prescription drug regulatory arena is perhaps best revealed in the following statement, penned by Justice Alito near the conclusion of the majority opinion in *Bartlett*:

> Suffice to say, the Court would welcome Congress' "explicit" resolution of the difficult pre-emption questions that arise in the prescription drug context. That issue has repeatedly vexed the Court — and produced widely divergent views — in recent years. […] In the absence of [such an] "explicit" expression of congressional intent, we are left to divine Congress' will from the duties the statute imposes.[4]

II. The FDA Response to Bartlett: Step 1

The above statement in *Bartlett* was issued on June 24, 2013. Less than two weeks later, FDA announced its intention to ultimately "create parity" for those plaintiffs who took generic products and found their state claims barred under *Mensing* and *Bartlett*. In early July 2013, the FDA took the first administrative step for a rule change by formally notifying the Office of Management and Budget (OMB) that it would propose new rules on this issue. That notice states[5]:

> **TITLE:** Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products
>
> **ABSTRACT:** This proposed rule would amend the regulations regarding new drug applications (NDAs), abbreviated new drug applications (ANDAs), and biologics license applications (BLAs) to revise and clarify procedures for changes to the labeling of an approved drug to reflect certain types of newly acquired information in advance of FDA's review of such change. The proposed rule would describe the process by which information regarding a "changes being effected" (CBE) labeling supplement submitted by an NDA or ANDA holder would be made publicly available during FDA's review of the labeling change. The proposed rule also would clarify requirements for the NDA holder for the reference listed drug and all ANDA holders to submit conforming labeling revisions after FDA has taken an action on the NDA and/or ANDA holder's CBE labeling supplement. These proposed revisions to FDA's regulations would create parity between NDA holders and ANDA holders with respect to submission of CBE labeling supplements.

The FDA has stated that "It is premature to cite what changes in the regulations might be," and that "[d]iscussions are under way."[6] More information was announced to be forthcoming in September 2013, but nothing has been released as of yet. The likely translation of the notice, however, is this: if promulgated, the rules would modify FDA regulations that define the circumstances under which generic manufacturers can change a label prior to formal FDA approval. Presumably, this would require generic manufacturers to change the label at the same time brand manufacturers do (i.e., before receiving formal FDA approval to make a label change when important new safety information is received about the drug). Stated colloquially, it could impose a "make the label safer first, get formal permission from FDA second" regime for generic manufacturers.

III. Let's Not Get Ahead of Ourselves: Lots of "Ifs," "Whens," and "Hows" Will Have to be Sorted Out

Even if the imposed rulemaking process proceeds as expected, the future of an actual change to the rules is hazy at best. The length of the rulemaking process and timing, questions about the validity of such measures, and the prospective relief such a rule change would effectuate (if at all) are important and contemporary concerns — which stakeholders will want to keep in mind as the process unfolds.

A THE RULEMAKING PROCESS WILL TAKE YEARS.

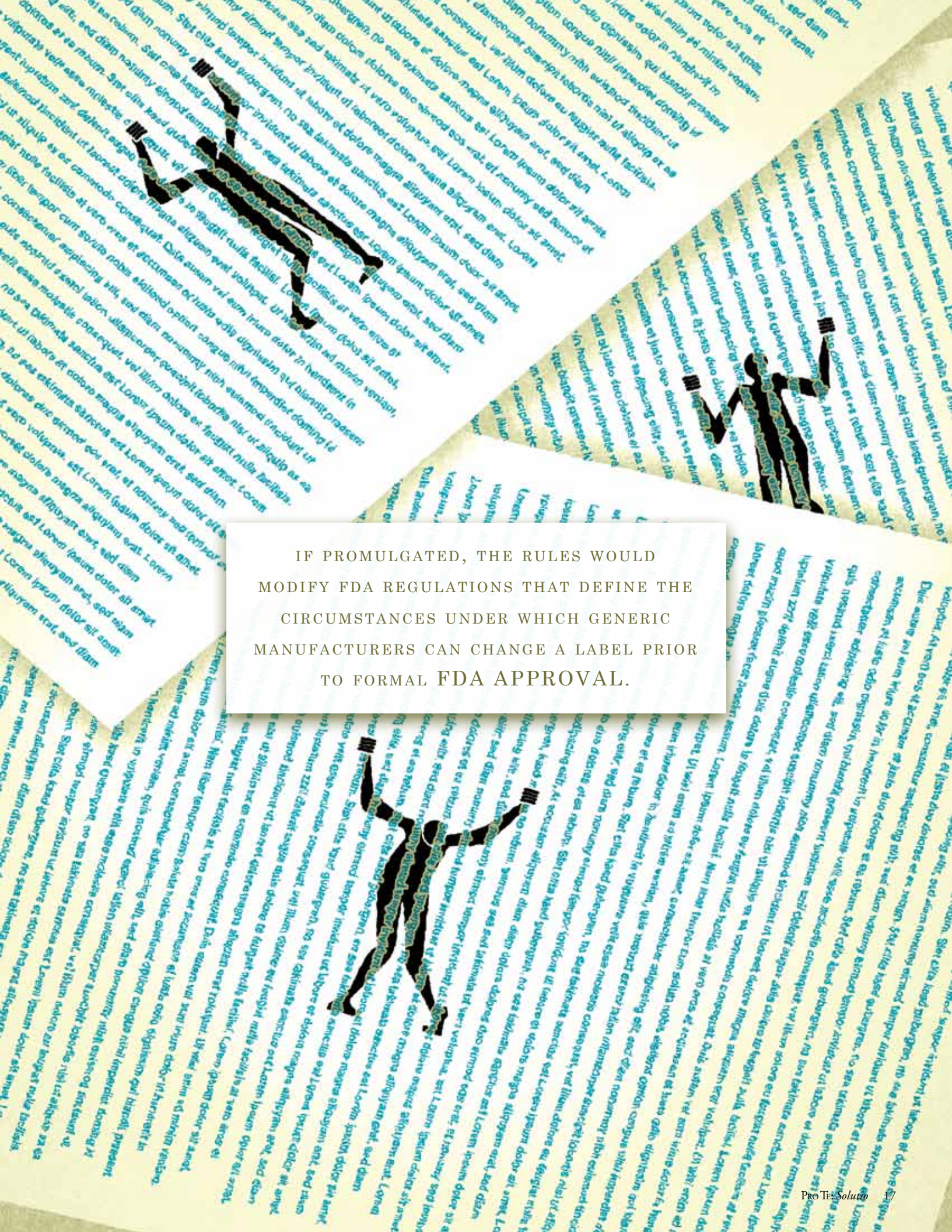
The rulemaking process is far from a quick run through a bureaucratic park. Years of wrangling are more likely.

As OMB explains, "[f]ederal regulations are created through a process known as 'rulemaking,' which is governed by the Administrative Procedure Act."[7] When a federal agency determines that regulatory action is needed, it develops and publishes a proposed rule in the *Federal Register* (the official daily publication for agency rules, proposed rules, and notices of federal agencies and organizations), solicits comments from the public on the proposal, and after the agency considers public feedback, it implements changes where appropriate and publishes a final rule, including its effective date, in the *Federal Register*. When an agency issues a "final rule," the agency must describe and respond to the public comments that were received.[8] As specific to the FDA, before a proposed or final rule is published in the *Federal Register*, it may be reviewed by "other parts" of the federal government, such as the Department of Health and Human Services (HHS), of which FDA is a part.[9]

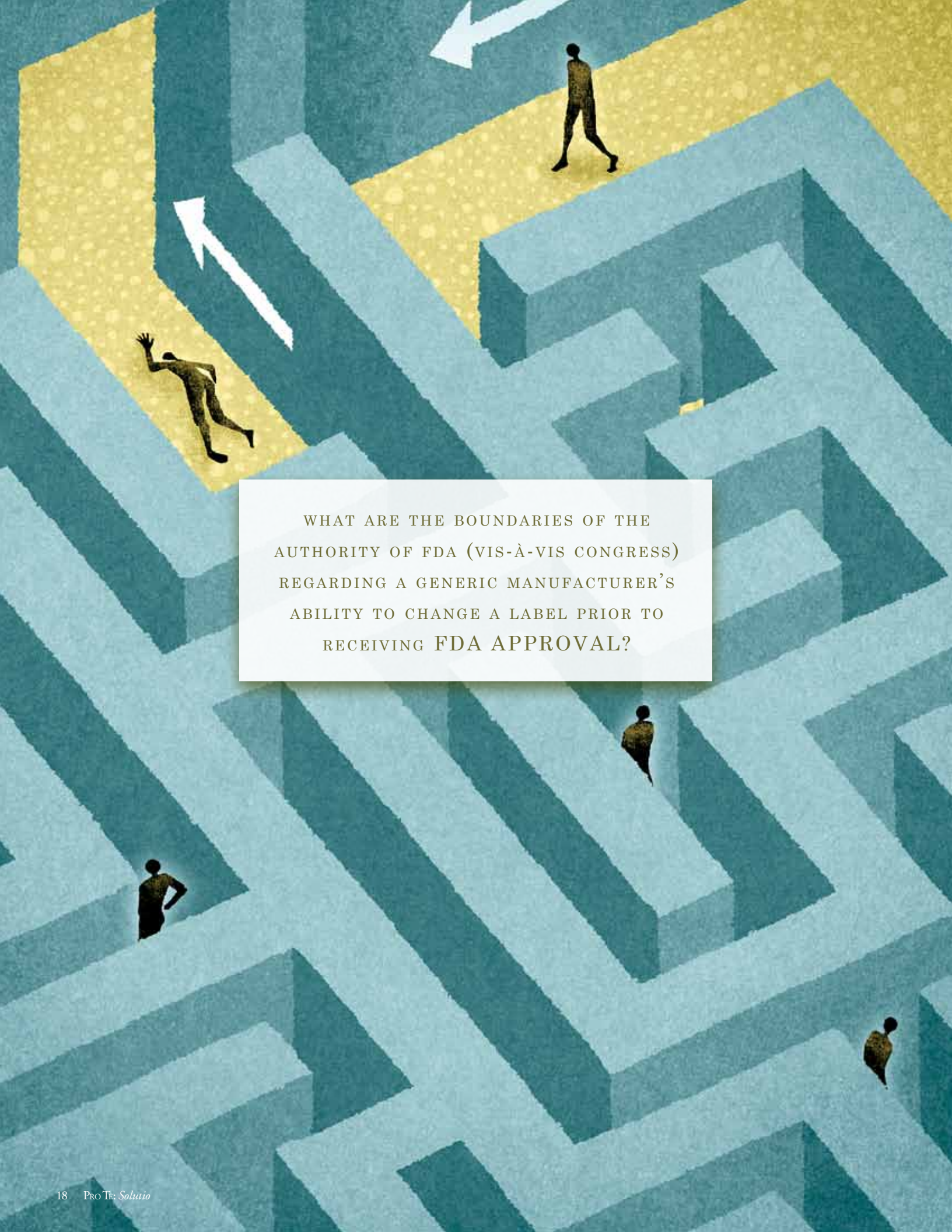
Even assuming the absence of any unusual federal government obstacles (think: sequestration, budget cuts), new proposed rules should not be expected anytime soon — or any time in the reasonably foreseeable future.[10]

B ANY RULE CHANGE WOULD BE PROSPECTIVE.

If and/or when new rules are promulgated, these changes will affect how FDA acts/enforces in the future — it will not change the validity of *Mensing* or *Bartlett*, both of which were (necessarily) evaluated under the regulatory scheme in place at their respective points in time. Indeed, the FDA's amicus brief in *Bartlett* — while advocating that the claims in *Bartlett* were preempted pursuant to current regulations and the holding in *Mensing* — nevertheless noted that "FDA is considering a regulatory change that would allow generic manufacturers, like brand-name manufacturers, to change their labeling in appropriate circumstances. If such a regulatory change is adopted, it could eliminate preemption of failure-to-warn claims against generic-drug manufacturers."[11] Any reach of the new rules will be prospective.



IF PROMULGATED, THE RULES WOULD MODIFY FDA REGULATIONS THAT DEFINE THE CIRCUMSTANCES UNDER WHICH GENERIC MANUFACTURERS CAN CHANGE A LABEL PRIOR TO FORMAL FDA APPROVAL.



WHAT ARE THE BOUNDARIES OF THE AUTHORITY OF FDA (VIS-À-VIS CONGRESS) REGARDING A GENERIC MANUFACTURER'S ABILITY TO CHANGE A LABEL PRIOR TO RECEIVING FDA APPROVAL?

C FDA's authority to make the proposed changes is not a slam dunk.

A final issue involves the validity of a change to the rules — specifically, whether FDA has the authority to do what it proposes to do through the rulemaking process, as opposed to the need for Congressional action.

According to OMB, "Congress enacts the legislation that mandates or authorizes agencies to issue regulations. Through the Administrative Procedure Act (APA) and other laws, Congress also establishes the procedures that govern agency rulemaking. Congress may use a variety of processes as part of its oversight of agency action, including holding hearings or informal meetings, issuing reports, or adopting legislation. In addition, Congress, through the Congressional Review Act (CRA) (5 U.S.C. Chapter 8), may review and choose to reject new regulations issued by federal agencies. The CRA requires federal agencies to submit all new final rules to both the House and Senate. After submission, Congress may begin a process to reconsider and vote to overturn the rule."[12]

The above explanation begs the question: what are the boundaries of the authority of FDA (*vis-à-vis* Congress) regarding a generic manufacturer's ability to change a label prior to receiving FDA approval? A comprehensive (or even sufficiently abbreviated) recitation of the full authority Congress has vested with FDA is far beyond this article. For these purposes, consider the statements contained in the United States' amicus brief in *Bartlett*: "Congress has vested FDA with the responsibility to determine when a new drug is 'safe' and 'effective' under the conditions of use stated in its labeling, so as to warrant the drug entering the interstate market."[13] Yet of extreme importance is that the "sameness in labeling" obligation for generic manufacturers is *statutory*,[14] and regulations must conform to the governing statute.

A detailed analysis of whether FDA would exceed the boundaries of its authorization in this rulemaking process is a topic left to legal scholars. Yet if FDA proceeds down the current path, consider that (a) its actions could be invalid if not based on a valid exercise of its authority, and/or (b) Congress could (if it so chose) overturn such rulemaking. If nothing else, this situation may result in a protracted administrative wrest for power.

It is notable that when Justice Alito commented in *Bartlett* that the Court would welcome resolution on the "difficult preemption questions that arise in the prescription drug context," the Court specifically said it would welcome "*Congress*' 'explicit' resolution" — so as to not have to "divine *Congress*' will from the duties the *statute* imposes" (emphasis added).[15] Perhaps one should not make too much of the Court calling on Congress as opposed to the *FDA* — in fact, Congress has not enacted any legislation since *Mensing*, which was more than two years ago — but maybe not. Perhaps *Congress* acting to resolve the lack of "parity" is precisely what the Court expects.

IV. Conclusion

The issuance of yet another generic implied preemption case in *Bartlett*, followed almost instantly by the FDA's announcement that it seeks to implement the rulemaking process to "create parity" in the generic versus brand labeling processes, has created a maelstrom of speculation of the continued validity of *Mensing* and *Bartlett*. Stakeholders should unquestionably be engaged in and educated about the rulemaking process. To that end, new information on the terms of the proposed rule should be soon forthcoming, a public comment period will follow, and advocates on every side of the issue should (and certainly will) be heavily involved. In the meantime, bear in mind that the feeling may not, in fact, be as "*Mutual*" as it appeared immediately post-*Bartlett*. Rule changes may well be coming. But no time soon. And not without a fight. ■

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[1] *Wyeth, Inc. v. Levine*, 555 U.S. 555 (2009).
[2] *PLIVA, Inc. v. Mensing*, -- U.S. --, 131 S. Ct. 2567 (U.S. 2011).
[3] *Mutual Pharm. Co. v. Bartlett*, -- U.S. --, 133 S. Ct. 2466, 2013 U.S. LEXIS 4702 (U.S. 2013).
[4] *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. at 2480.
[5] HHS/FDA. Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products. <http://www.reginfo.gov/public/servlet/ForwardServlet?SearchTarget=Agenda&textfield=0910-AG94>. *Last accessed* Sept. 22, 2013.
[6] Thomas, Katie, "F.D.A. Rule Could Open Generic Drug Makers to Suits," *New York Times*, July 3, 2013. *Available at* <http://www.nytimes.com/2013/07/04/business/fda-rule-could-open-generic-drug-makers-to-suits.html?_r=0>. *Last accessed* Sept. 22, 2013.
[7] Office of Information and Regulatory Affairs, *FAQs/Resources*, "Regulations and the Rulemaking Process," <http://www.reginfo.gov/public/jsp/Utilities/faq.jsp>. *Last visited* Sept. 22, 2013.
[8] Administrative Procedure Act (APA), 5 U.S.C. ch. 5. *See also* <http://www.reginfo.gov/public/jsp/Utilities/faq.jsp>. *Last visited* Sept. 22, 2013. *See also* <http://www.reginfo.gov/public/reginfo/Regmap/index.jsp>. *Last visited* Sept. 22, 2013.
[9] FDA explanation of rulemaking process: <http://www.fda.gov RegulatoryInformation/RulesRegulations/default.htm>. *Last visited* Sept. 22, 2013.
[10] This is certainly *not* to suggest that stakeholders should not be involved with the process; to the contrary, the system can only work if public comment is robust and interaction with FDA close.
[11] *Mut. Pharm. Co. v. Bartlett*, No. 12-142, Brief for United States as Amicus Curiae Supporting Petitioner, at fn. 2. *Available at* <http://www.scotusblog.com/case-files/cases/mutual-pharmaceutical-co-v-bartlett>. *Last accessed* Sept. 22, 2013.
[12] Office of Information and Regulatory Affairs, *FAQs/Resources*, "Regulations and the Rulemaking Process," <http://www.reginfo.gov/public/jsp/Utilities/faq.jsp>. *Last visited* Sept. 22, 2013.
[13] United States amicus brief, *supra*, at p. 24 (citing 21 U.S.C. § 355).
[14] 21 U.S.C. § 355. The "sameness" requirement for generic drugs is indeed statutory. As explained in *Bartlett*, 133 S. Ct. at 2471:

> First, the proposed generic drug must be chemically equivalent to the [**616] approved brand-name drug: it must have the same "active ingredient" or "active ingredients," "route of administration," "dosage form," and "strength" as its brand-name counterpart. 21 U. S. C. §§ 355(j)(2)(A)(ii) and (iii). Second, a proposed generic must be "bioequivalent" to an approved brand-name drug. § 355(j)(2)(A)(iv). That is, it must have the same "rate and extent of absorption" as the brand-name drug. § 355(j)(8)(B). Third, the generic drug manufacturer must show that "the labeling proposed for the new drug is the same as the labeling approved for the [approved brand-name] drug." § 355(j)(2)(A)(v).

[15] *Mut. Pharm. Co. v. Bartlett*, 133 S. Ct. at 2480.

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