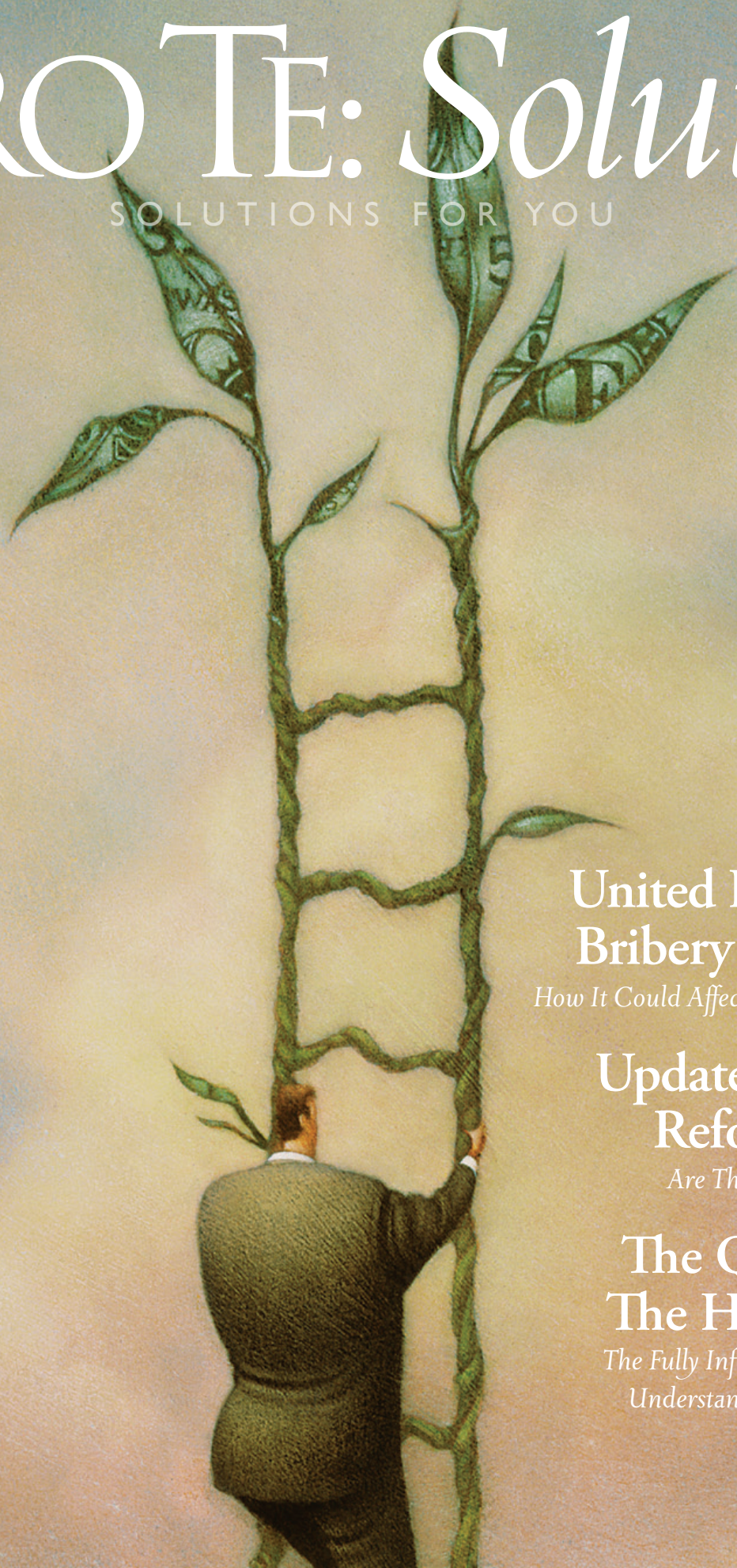


PRO TE: *Solutio*

SOLUTIONS FOR YOU



United Kingdom Bribery Act 2010

How It Could Affect U.S. Companies

Update On Tort Reform Caps

Are They Constitutional?

The Quest For The Holy Grail

*The Fully Informative, Yet Fully
Understandable, OTC Label*



DEAR CLIENTS:

At the heart of the pharmaceutical and medical device industry is a genuine desire to help people. But the complexities of the world in which the industry operates often complicate what seems to be such a simple and straightforward motivation.

Take, for instance, medical labeling. How can a company fill the need for clear, effective drug labeling that can be understood and followed by consumers? *The Quest for the Holy Grail: The Fully Informative, Yet Fully Understandable, OTC Label* discusses the complications of label production.

This issue's article *The United Kingdom Bribery Act 2010* further explores how the medical industry must operate with diligent attention to detail and forethought. While, the *Update on Tort Reform Caps: Are They Constitutional?* reviews current challenges to cap limitations that could indicate a ominous future for tort reform.

What could be simpler than wanting to protect and help children? The Pediatric Medical Device Safety and Improvement Act of 2007 requires that this special subpopulation be taken into consideration during medical device testing and research if a company is to receive FDA approval for a product. *Not Just for Adults Anymore* looks at how a company can plan ahead in order to meet the requirements of the act.

Though the medical device and pharmaceutical industry constantly faces innumerable challenges and complications, the reasons to struggle through them are simple and indeed highly motivating — helping save and improve the lives of others. We hope *Pro Te: Solutio* provides both clarification and encouragement for those working toward the ultimate benefit of us all.



CHRISTY D. JONES
*Chair — Pharmaceutical, Medical Device
and Healthcare Industry Department*



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PRO TE: *Solutio*

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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.

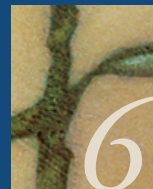
That's also why we at Butler Snow redesigned and expanded our unique health-oriented industry group, now comprised of two major sections that handle business and litigation. The Pharmaceutical, Medical Device, and Healthcare Industry Group has more than 50 multi-disciplinary attorneys who provide creative 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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WHAT YOU NEED TO KNOW



HOW IT COULD AFFECT U.S. COMPANIES

IF YOUR COMPANY IS BASED IN THE UNITED STATES and does business in any foreign market, you are likely familiar with the U.S. Foreign Corrupt Practices Act of 1977 (“FCPA”). The anti-bribery provisions of the FCPA generally prohibit any payments to foreign government officials for the purpose of obtaining or retaining business. Violations of the FCPA can result in criminal and civil penalties, including fines and imprisonment for individuals and substantial fines for corporate entities. Most U.S. companies doing business abroad have an understanding of the FCPA and have policies and procedures in place to prevent their employees and agents from committing bribery. However, the United Kingdom Parliament recently enacted the Bribery Act 2010, c. 23 (Eng.) (“UK Bribery Act” or “the Act”) that has the potential also to affect U.S. companies and their employees and agents.

OVERVIEW

In recent years, the UK government has been subject to a firestorm of criticism over its handling of investigations of alleged bribery of foreign officials by UK firms, particularly the controversial 2006 decision of then-Prime Minister Tony Blair's government to halt the Serious Fraud Office's investigation of BAE Systems' dealings with Saudi Arabia. The new UK Bribery Act, however, is one of the most restrictive and far-reaching anti-bribery laws in the world.

The UK Bribery Act creates four new offenses under UK law: two general bribery offenses (one related to bribing another person and the other related to accepting bribes), a discrete offense of bribing a foreign government official, and an offense related to the failure of a commercial organization to prevent bribery.

GIVING AND RECEIVING BRIBES

The first new offense covers offering, promising, or giving a financial or other advantage, or bribe, to another person intended to bring about improper performance of a relevant function or activity by that person. The second new offense deals with a person who requests, agrees to receive, or accepts an advantage for an improper performance of a relevant function or activity.

The UK Bribery Act defines a "relevant function or activity" extremely broadly, making it an offense to provide or receive bribes in connection with any public (i.e., governmental) function or virtually any business activity. Any person offering or accepting bribes in a *private business transaction* may be in violation of the UK Bribery Act. The reach of the Act is equally broad: The UK Bribery Act specifically includes in the definition of "relevant function or activity" activities taking place outside the UK and which need not have any connection with the UK.

BRIBING A FOREIGN PUBLIC OFFICIAL

Similar to the FCPA, the third new offense under the UK Bribery Act involves bribing a foreign public official with the intent of influencing that official for the



THE FINAL NEW OFFENSE OF THE UK BRIBERY ACT, THE FAILURE OF A COMMERCIAL ORGANIZATION TO PREVENT BRIBERY, WILL LIKELY BE OF MOST CONCERN TO U.S. COMPANIES.

UNDER THE ACT, A COMMERCIAL ORGANIZATION IS GUILTY OF AN OFFENSE IF A PERSON ASSOCIATED WITH THE ORGANIZATION BRIBES ANOTHER PERSON TO OBTAIN OR RETAIN BUSINESS.

purpose of obtaining or retaining business. But unlike the FCPA, the UK Bribery Act does not provide an exception for "facilitating" or "grease" payments for routine governmental actions, and any such facilitating payment, no matter how small, can be deemed an offense. The definition of "foreign public official" under the UK Bribery Act includes both foreign government officials and persons working for public international organizations.

JURISDICTION

The first three new offenses of the UK Bribery Act are implicated if any part of the act constituting the offense takes place anywhere within the UK. Additionally, the UK Bribery Act provides for jurisdiction over offenses committed outside the UK by UK citizens, UK nationals, UK corporate entities, and individuals ordinarily residing in the UK.

FAILURE OF A COMMERCIAL ORGANIZATION TO PREVENT BRIBERY

The final new offense of the UK Bribery Act, the failure of a commercial organization to prevent bribery, will likely be of most concern to U.S. companies. Under the Act,

a commercial organization is guilty of an offense if a person associated with the organization bribes another person to obtain or retain business. The Act provides that the offense covers any business or partnership formed under UK law *or any corporate body or partnership, wherever formed, which carries on business in any part of the UK, regardless of where the offense occurs*. As with the individual bribery offenses discussed earlier, this offense pertains to bribery in connection with either public functions or private business activity. A person will be deemed to be "associated" with a commercial organization if the person performs services for the organization, and this definition includes employees, agents, and subsidiaries.

The Act does provide an affirmative defense if the commercial organization can prove that it had in place "adequate procedures" designed to prevent associated persons from committing bribery offenses. The Act directs the UK Secretary of State to publish guidance regarding procedures commercial organizations may use to prevent associated persons from engaging in bribery offenses. The UK Secretary of State has advised Parliament that this guidance will be principles-based and will set out illustrative good practices rather than specific standards.

The fourth offense has the potential to increase the risk for U.S. companies doing business abroad. For example, under the terms of the UK Bribery Act, a U.S. company that does business in the UK will potentially be criminally liable if its agent operating in a third country bribes an official at a *private company* to obtain business with that company unless the U.S. company can prove that it had adequate procedures in place designed to prevent the prohibited activity.

PENALTIES

The penalties set forth in the UK Bribery Act are severe. Individuals guilty of any of the first three new offenses are subject to up to 10 years imprisonment and a fine, while corporate organizations guilty of the fourth new offense are subject to an unlimited fine.



THE UK BRIBERY ACT PROVIDES AN AFFIRMATIVE DEFENSE TO A COMMERCIAL ORGANIZATION IF THE ORGANIZATION CAN PROVE IT HAD IN PLACE ADEQUATE PROCEDURES DESIGNED TO PREVENT ASSOCIATED PERSONS FROM COMMITTING BRIBERY OFFENSES.

CONCLUSION

To protect themselves, U.S. companies doing business in the UK should do at least the following:

INTERNAL EVALUATION: A company should do an internal assessment of its level of exposure under the new law. Factors may include whether the type of business conducted by the company requires significant contact with government officials, the number of employees and agents of the company seeking to secure business in foreign countries, and the concentration of the company's business in countries where bribery may be an accepted part of the culture, particularly developing countries.

EDUCATION: Companies should immediately begin educating all employees about

the new offenses and potential severe penalties under the UK Bribery Act. Employees engaged with procuring business from foreign governments or foreign businesses should receive adequate education and training regarding the UK Bribery Act.

POLICIES AND PROCEDURES: The UK Bribery Act provides an affirmative defense to a commercial organization if the organization can prove it had in place adequate procedures designed to prevent associated persons from committing bribery offenses. Companies should review current anti-bribery policies and procedures and revise such policies

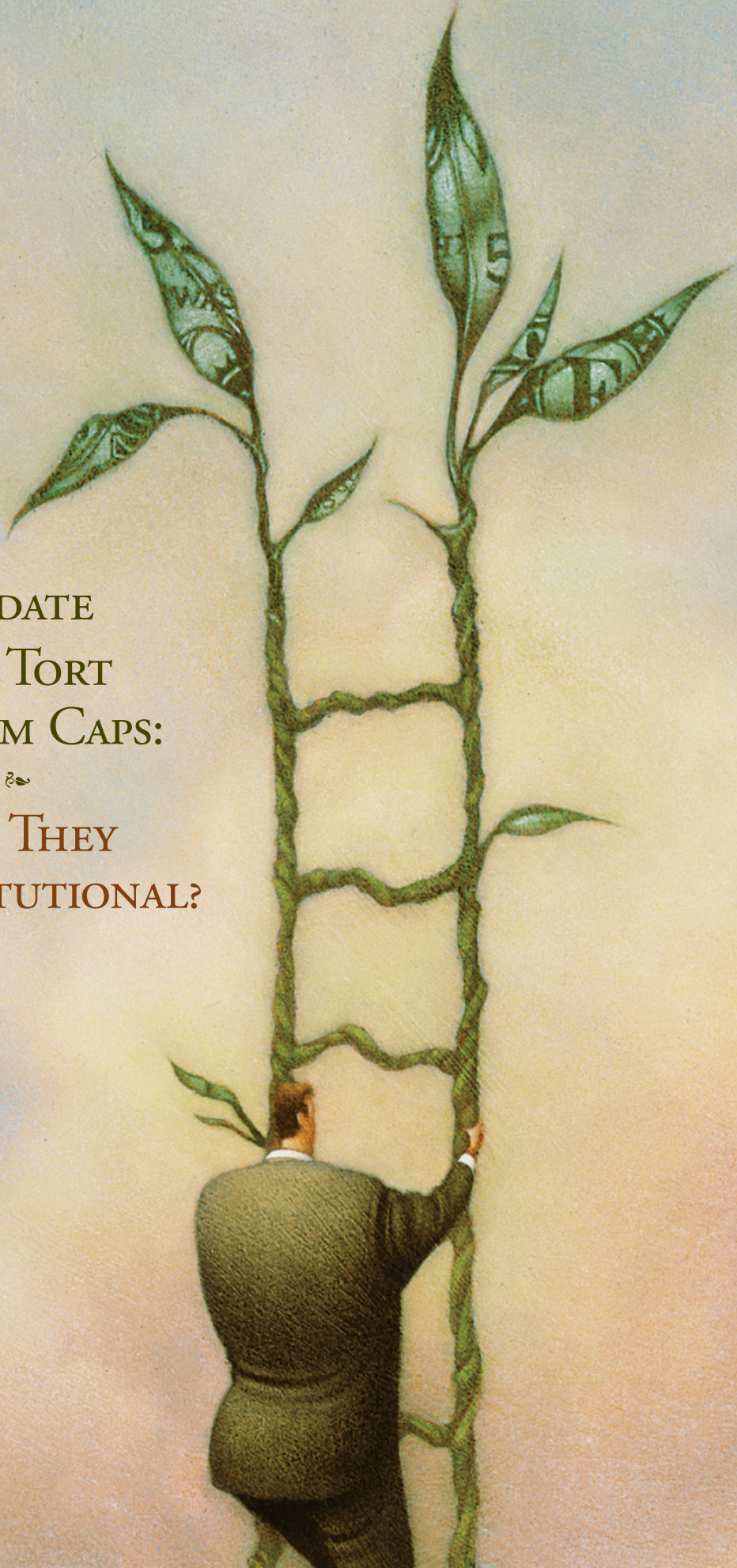
and procedures to ensure they are compliant with the UK Bribery Act.

COMPLIANCE AND ENFORCEMENT: The best policies and procedures are useless unless a company takes affirmative steps to ensure that its employees and agents are adhering to such policies and procedures. Companies should establish strong monitoring procedures directed toward discovering illegal bribery activity. Companies should also establish and enforce stringent penalties for bribery, including termination of any employee or agent engaged in illegal behavior.

WRITTEN by
JOEY DUDEK and
ELIZABETH SAXTON



UPDATE
ON TORT
REFORM CAPS:
☪
ARE THEY
CONSTITUTIONAL?



OUR OCTOBER 2008 edition of *Pro Te Solutio* featured the *Double-Quick, Inc. v. Lymas* case now pending in the Mississippi Supreme Court and represents the first challenge to Mississippi's statute that limits the amount of non-economic damages recoverable in tort suits to \$1 million.¹ The court heard oral argument in *Lymas* on June 8, 2010.² This update addresses the recent decisions handed down on the issue of the constitutionality of caps on damages as we await a ruling from the Mississippi Supreme Court on the issue.

In July 2009, a challenge was again made to Miss. Code Ann. 11-1-60 and its cap on damages in *Learmonth v. Sears Roebuck & Co.*, No. 4:06cv2252878, 2009 WL 2252878 (S.D. Miss. July 28, 2009). The court upheld the constitutionality of the statute. This decision has been appealed to the 5th Circuit and is still in the briefing stage.

Challenges to these limitations have been made in other states as well. On March 22, 2010, the Georgia Supreme Court, in a unanimous decision, ruled that the statutory cap on medical malpractice damages is unconstitutional in *Nestlehutt v. Atlanta Oculoplastic Surgery, P.C.*, 691 S.E.2d 218 (Ga. 2010). The statute at issue in *Nestlehutt* was OCGA §51-13-1, enacted in 2005. This section of Georgia's statutory code limits awards of non-economic damages in medical malpractice actions to \$350,000. After a jury award of \$900,000 in non-economic damages, the plaintiff moved to have the statute declared unconstitutional. The trial court granted the motion, refused to limit the award pursuant to OCGA §51-13-1, and found that the statute violates the Georgia Constitution by encroaching on the right to a jury trial, governmental separation of powers, and the right to equal protection.

The Georgia Supreme Court affirmed the trial court's ruling that the non-economic damages cap in OCGA §51-13-1 violates the right to a trial by jury. The court noted that the purpose of OCGA §51-13-1 was "to address what was classified as a crisis affecting the provision and quality of health-

care services in this state."³ The amount of damages sustained by a plaintiff is an issue of fact. The court stated that this has long been the law, and rulings establishing that damages are an issue of fact date back to 1935. Further, the court found that non-economic damages existed with even the very first claims of negligence that preceded the adoption of Georgia's constitution in 1798.⁴

In its analysis of the arguments in favor of the cap, the court refused to accept that cap limitations are analogous to remittitur statutes or statutes authorizing doubling or treble damages. The court distinguished the Legislature's ability to modify or abrogate common law and the inability of the Legis-



LIMITATION OF *non-economic* DAMAGES IN *personal injury* SUITS, AND *particularly medical malpractice* SUITS, ARE *vital parts* OF THE *tort reform efforts undertaken in many* U.S. JURISDICTIONS *in the early 2000s*. CURRENT *challenges* TO THE *constitutionality* OF THOSE CAPS MAY BE *ominous* HARBINGERS OF THE FUTURE OF *tort reform*.



lature to abrogate constitutional rights. The court held: "The very existence of caps, in any amount, is violative of the right to trial by jury."⁵ Of particular interest is that the court specifically considered and held that the ruling that OCGA §51-13-1 is unconstitutional applies retroactively.⁶

Three weeks before the ruling in *Nestlehutt* by the Georgia Supreme Court, Illinois' high court struck down its cap on non-economic damages in medical malpractice actions in *Lebron v. Gottlieb Memorial Hospital*, No. 105741, 2010 WL 375190 (Ill. Feb. 4, 2010). The *Lebron* Court held that the statutory cap violated the separation clause of Illinois Constitution (Ill. Const. 1970, art. II, §1). The result is not surprising given Illinois precedent. In 1997, the Illinois Supreme Court struck down the limita-

tion on non-economic damages in personal liability suits that had set a \$500,000 cap.⁷ The *Best* and *Lebron* courts relied specifically on the purpose of the separation of powers clauses which is "to ensure that the whole power of two or more branches of government shall not reside in the same hands" and to prohibit the legislature from enacting laws that unduly fringe upon the inherent powers of judges.⁸

Kansas also has a case before its Supreme Court challenging a limit of \$250,000 on non-economic damages in personal injury lawsuits.⁹ That court heard oral argument on October 29, 2009. The Kansas legislature enacted the statute in 1988. It was challenged in 1990, and the court, which at that time was a conservative court, upheld the limit on damages.¹⁰ The Kansas court has not issued a ruling.

Limitation of non-economic damages in personal injury suits, and particularly medical malpractice suits, are vital parts of the tort reform efforts undertaken in many U.S. jurisdictions in the early 2000s. Current challenges to the constitutionality of those caps may be ominous harbingers of the future of tort reform.

¹ *Double-Quick v. Lymas*, No. 2008-CA-01713-SCT (Miss. Sup. Ct.); see *Pro Te Solutio*, October 2008, Vol. 1 No. 4, available at <http://www.butlersnow.com/news/newsletters.htm>.

² Oral argument can be downloaded at http://mssc.wmlive.internapcdn.net/live_mssc_vitalstream_com-main-court-room.

³ *Nestlehutt*, 621 S.E.2d at 732.

⁴ *Nestlehutt*, 621 S.E.2d at 734.

⁵ *Nestlehutt*, 621 S.E.2d at 736.

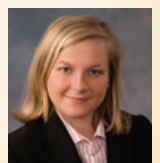
⁶ *Nestlehutt*, 621 S.E.2d at 739-40.

⁷ *Best v. Taylor Machine Works*, 689, NE2d 1057 (Ill. 1997).

⁸ *Best*, 689 NE2d at 1078.

⁹ See *Miller v. Johnson*, No. 99818, oral argument heard on October 29, 2009; see also KSA 60-19a02.

¹⁰ *Samsel v. Wheeler Transportation Servs., Inc.*, 789 P.2d 541 (Kan. 1990).



WRITTEN by ALYSON JONES

NOT JUST FOR
Adults
ANYMORE

NEW PEDIATRIC CONSIDERATIONS FOR PREMARKET APPROVAL OF MEDICAL DEVICES IN LIGHT OF IMPLEMENTATION OF THE PEDIATRIC MEDICAL DEVICE SAFETY AND IMPROVEMENT ACT OF 2007

On SEPTEMBER 27, 2007, President George W. Bush signed into law H.R. 3580, the Food and Drug Administration Amendments Act of 2007,¹ and in so doing, amended the Federal Food, Drug and Cosmetic Act (“the Act”). The law represented a significant addition to the Food and Drug Administration’s (“FDA”) authority. On April 1, 2010, the FDA promulgated a Direct Final Rule² implementing section 515A of the Act. Section 515A is also known as the Pediatric Medical Safety Device and Improvement Act of 2007.³

I. THE PEDIATRIC MEDICAL DEVICE SAFETY AND IMPROVEMENT ACT OF 2007

The Pediatric Medical Device Safety and Improvement Act of 2007 (“PMDSIA”) was introduced by Senator Chris Dodd on March 8, 2007.⁴ The purpose of the PMDSIA is to improve the process for the development of needed pediatric medical devices.⁵ According to Senator Dodd, the PMDSIA provides a comprehensive approach to ensuring that children are not left behind as cutting-edge research and revolutionary technologies for medical devices advance:

As the parent of two young children, it is essential that products used in children’s growing bodies, whether drugs or devices, are appropriately tested and designed specifically for their use . . . Because the pediatric market is so small and pediatric diseases relatively rare, there has been little incentive for medical device manufacturers to focus their attention on children. This legislation ensures that

*our nation’s children are receiving the best possible medical treatment and care at a critical time in their development.*⁶

A. REQUIREMENTS OF THE PMDSIA

The PMDSIA requires applicants who submit certain medical device applications under section 515A(a) of the Act to include the following “readily available” information:

- (1) a description of any pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure; and
- (2) the number of affected pediatric patients.⁷

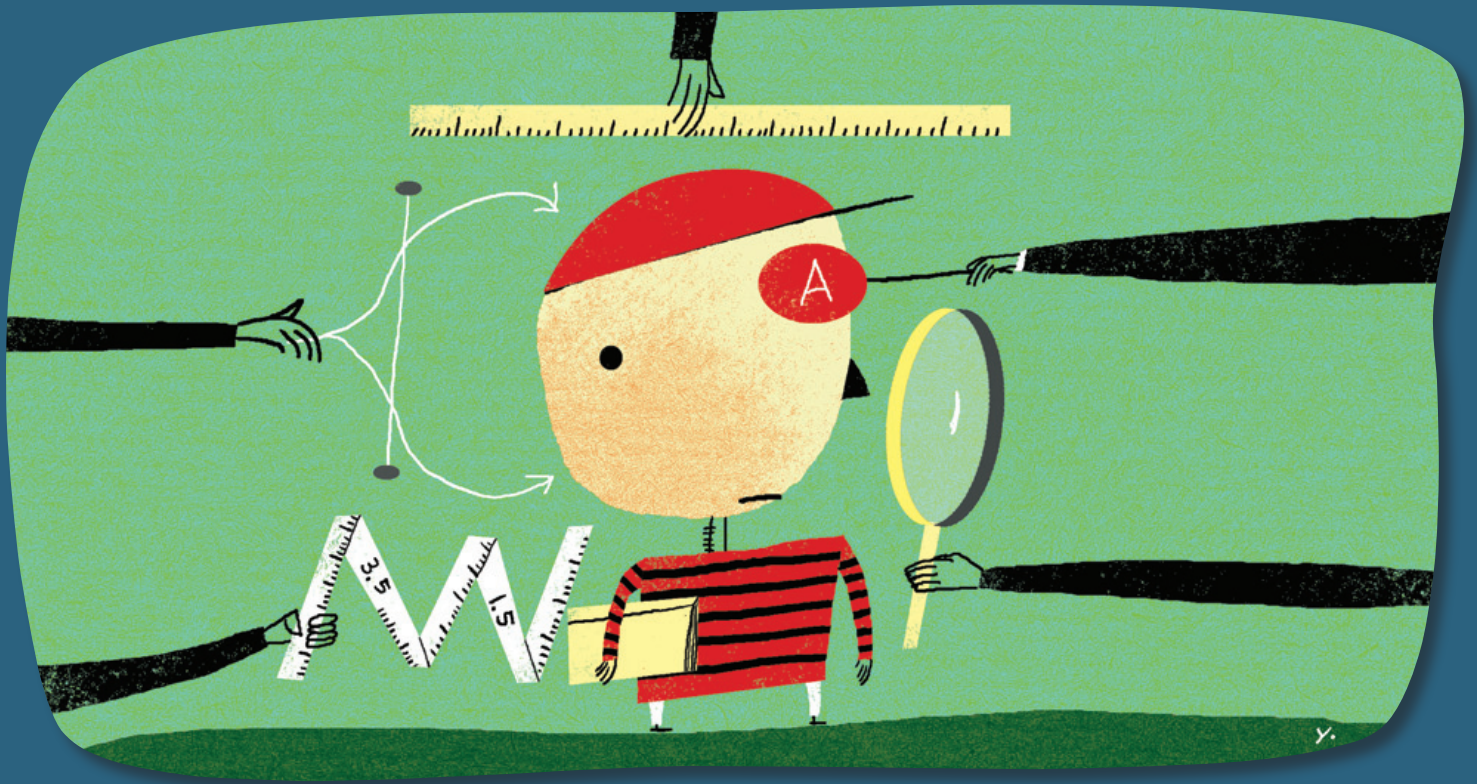
The age ranges for each of the populations included in the term “pediatric subpopulation” are as follows: 1) newborn or neonate: from birth to 1 month of age; 2) infant: greater than 1 month to 2 years of age; 3) child: greater than 2 to 12 years of age; and 4) adolescent: greater than 12 to 21 years

of age.⁸ The FDA has concluded that the term “pediatric patient” in section 515A of the Act refers to patients who are 21 years of age or younger at the time of diagnosis or treatment.⁹

The PMDSIA requirements apply to the following applications when submitted on or after the effective date of the rule:

- (1) any request for a humanitarian device exemption (“HDE”) submitted under section 520(m) of the Act (21 U.S.C.A. §360j(m));
- (2) any premarket approval application (“PMA”) or supplemental PMA submitted under section 515 of the Act (21 U.S.C.A. §360e); and
- (3) any product development protocol (“PDP”) submitted under section 515 of the Act (21 U.S.C.A. §360e).¹⁰

A PMA supplement applicant may incorporate by reference previously submitted information satisfying these requirements. The applicant must submit addi-



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tional information that has become readily available to the applicant since the previous submission.¹¹

The information submitted under the PMDSIA is designed to help the FDA track the following information that is required to be reported annually to Congress, in accordance with section 515A(a)(3) of the Act:

- (1) the number of approved devices for which there is a pediatric subpopulation that suffers from the disease or condition that the device is intended to treat, diagnose or cure;
- (2) the number of approved devices labeled for use in pediatric patients;
- (3) the number of approved devices exempted from a review fee pursuant to section 738(a)(2)(B)(v) of the Act (21 U.S.C.A. §379j(a)(2)(B)(v)); and
- (4) the review time for each device.¹²

According to Dr. Jeffrey Shuren, director of FDA's Center for Devices and Radiological Health, "[t]his requirement allows the agency to collect information that will help us better assess public health needs for medical devices that can be used for pediatric populations."¹³

In sum, the PMDSIA requires each applicant who submits an HDE, PMA, supplement to PMA, or PDP to: 1) describe, if "readily available," pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure; and 2) identify the number of affected pediatric patients.¹⁴

B. CONSEQUENCES OF NOT SUBMITTING "READILY AVAILABLE" INFORMATION

The FDA may withhold approval of the application if the applicant fails to submit the required pediatric subpopulation information. If an applicant lacks the requisite information enumerated in the PMDSIA, the FDA has certain protocols to address the deficiency, which are dependent upon the degree of the violations.¹⁵

1. FDA May Issue Conditional "Approvable" Letter

The FDA will contact an applicant in the normal course of the FDA review to inform

the applicant that the submission lacks the requisite information, and the FDA will ask the applicant to amend its application to provide the required information.¹⁶ If the application has no other deficiencies and otherwise meets applicable statutory and regulatory requirements for approval,



"Because the pediatric market is so small and pediatric diseases relatively rare, there has been little incentive for medical device manufacturers to focus their attention on children. This legislation ensures that our nation's children are receiving the best possible medical treatment and care at a critical time in their development."

— Senator Chris Dodd

but still lacks the information required by section 515(A)(a) (21 U.S.C.A. §360e(a) (1)-(2)), the FDA will issue an "approvable" letter informing the applicant that the FDA will approve the application once the requisite data has been provided to FDA.¹⁷

2. FDA May Issue "Not Approvable" or "Major Deficiency" Letter

If the application has other deficiencies or does not meet all applicable statutory and regulatory requirements for approval, the FDA will send a "not approvable" letter or "major deficiency" letter describing what the applicant must submit to the FDA before the FDA can approve the application.¹⁸ These letters may cite the absence of the mandatory pediatric subpopulation information in the section listing minor deficiencies.¹⁹

II. IMPLEMENTATION OF THE DIRECT FINAL RULE

The Direct Final Rule for the PMDSIA is effective August 16, 2010. Comments on the Direct Final Rule must have been received by June 1, 2010 (comments on information collection requirements), and June 15, 2010 (comments on Direct Final Rule).²⁰ If the FDA receives no timely significant adverse comments, the FDA will confirm the August 16, 2010, effective date of the Direct Final Rule within 30 days after the comment period ends.²¹

Because the FDA believes that the Direct Final Rule is noncontroversial, it does not anticipate receiving any significant adverse comments.²² In the event the FDA timely receives any significant adverse comment, though, the FDA will withdraw the Direct Final Rule in whole or in part within 30 days after the comment period ends.²³

A significant adverse comment is defined as "a comment that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without change."²⁴ In determining the significance of an adverse comment, the FDA will consider whether the comment raises an issue serious enough to warrant a substantive response in accordance with the Administrative Procedure Act ("APA").²⁵ Frivolous comments, insubstantial comments, or comments outside the scope of the rule will not be considered significant unless the comment states why the additional change makes the rule effective.²⁶ Moreover, the rule may be severed and parts of the rule that are not the subject of a significant adverse comment may be adopted.²⁷

The proposed amendments will not end, however, in the event of significant adverse comments. Consistent with the FDA's procedures on direct final rulemaking, the FDA, concurrent with the Direct Final Rule, also published a companion proposed rule that is identical in substance to the Direct Final Rule ("Proposed Rule").²⁸ The Proposed Rule provides the procedural framework to finalize the rule in the event that the Direct Final Rule is withdrawn because of

significant adverse comments.²⁹ The comment period for the Proposed Rule will run concurrently with the Direct Final Rule's comment period.³⁰ In that circumstance, any comments received will be considered comments on the proposed rule and will be considered in developing a final rule using the usual APA notice-and-comment procedures.³¹


III. RECOMMENDATIONS TO MINIMIZE THE POSSIBILITY OF APPROVAL DELAYS

Although there is a chance that the FDA could withdraw the Direct Final Rule and delay implementation of the Proposed Rule, the FDA clearly does not anticipate any significant adverse comments that would warrant either withdrawal or delay. That being the case, steps should be taken now to gather the requisite pediatric subpopulation data for any devices companies plan on submitting for approval under the HDE, PMA/ Supplemental PMA, or PDP processes. The necessary data may already be available from the underlying studies and research that have been done and may simply need to be put in the form required by FDA. If the data has not been tabulated, though, manufacturers should consider the most efficient and timely way to gather the data for purposes of submission. Because the FDA has not to date issued any guidance as to the scope of the term "readily available," manufacturers choosing to submit the device without the pediatric subpopulation data because the data may not be readily available could risk setting back the approval timeline for the device if the manufacturer's definition of "readily available" differs from that of the FDA. Clearly, companies should include tabulation of pediatric population data in the protocol for the development and manufacturing devices in the future so there will not be any snags at the approval process.

IV. CONCLUSION

On August 16, 2010, medical device manufacturers applying for FDA approval for their devices via: 1) a humanitarian device exemption; 2) premarket approval application; 3) supplemental premarket

approval application; or 4) product development protocol will likely have to include information pertaining to pediatric subpopulations that suffer from the disease or condition that the device is intended to treat, diagnose, or cure, as well as provide data pertaining to the number of affected



Companies that fail to include the requisite information or properly supplement risk rejection of their respective applications until the FDA receives the data. Companies should, therefore, preemptively identify and produce the requested pediatric subpopulation data for devices the companies intend to submit for approval.

pediatric patients. Although the FDA will allow applicants to incorporate by reference previously submitted information related to the referenced pediatric subpopulation, this information must be supplemented to include information that has become readily available to the applicant since the device's previous submission. Companies that fail to include the requisite information or properly supplement risk rejection of their respective applications until the FDA receives the data. Companies should, therefore, preemptively identify and produce the requested pediatric subpopulation data for devices the companies intend to submit for approval.

¹ Codified at 21 U.S.C.A. §§350f, 353b, 355-1, 355d, 355e, 360a, 360e-1, 360n, 360bbb-5, 360bbb-6, 379d-1, 379d-2, 379h-1, 379h-2, 379j-1, 379dd, 379dd-1, 379dd-2, 399a, 2101 to 2110, and 42 U.S.C.A. §247d-5a.

² FDA Direct Final Rule, *Medical Devices; Pediatric Uses of Devices; Requirement for Submission of Information on Pediatric Subpopulations that Suffer From a Disease or Condition That a Device Is Intended to Treat, Diagnose or Cure*, 75 Fed. Reg. 16347 (April 1, 2010).

³ 21 U.S.C.A. §360e-1.

⁴ Senate Bill 830, The Pediatric Medical Device Safety and Improvement Act of 2007.

⁵ *Id.*

⁶ <http://dodd.senate.gov/index.php?q=node/3802>.

⁷ 21 U.S.C.A. §360e(a)(1)-(2); see also 75 Fed. Reg. 16347 (April 1, 2010). The FDA does not define the term "readily available" in this context.

⁸ 21 U.S.C.A. §360j(m)(6)(E)(ii); see also, *Premarket Assessment of Pediatric Medical Devices* (May 14, 2004) at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089740.htm>.

⁹ 75 Fed. Reg. 16347 (April 1, 2010).

¹⁰ 21 U.S.C.A. §360e-1(b).

¹¹ 75 Fed. Reg. 16348 (April 1, 2010).

¹² 21 U.S.C.A. §360e-1(a) (3).

¹³ <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm206872.htm>.

¹⁴ *Id.*

¹⁵ For information concerning FDA interactive review process, see *Guidance for Industry and FDA Staff: Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements* at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm>.

¹⁶ 75 Fed. Reg. 16348 (April 1, 2010).

¹⁷ *Id.*

¹⁸ *Id.*

¹⁹ *Id.*

²⁰ 75 Fed. Reg. 16347 (April 1, 2010).

²¹ *Id.*

²² 75 Fed. Reg. 16366 (April 1, 2010).

²³ *Id.*

²⁴ 75 Fed. Reg. 16348 (April 1, 2010).

²⁵ *Id.*; see 5 U.S.C.A. §553 for relevant section from the Administrative Procedure Act.

²⁶ 75 Fed. Reg. 16348 (April 1, 2010).

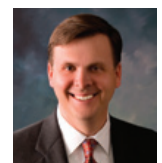
²⁷ *Id.*

²⁸ FDA Proposed Rule, *Medical Devices; Pediatric Uses of Devices; Requirement for Submission of Information on Pediatric Subpopulations that Suffer From a Disease or Condition That a Device Is Intended to Treat, Diagnose or Cure*, 75 Fed. Reg. 16365 (April 1, 2010).

²⁹ 75 Fed. Reg. 16366 (April 1, 2010).

³⁰ *Id.*

³¹ *Id.*; see 5 U.S.C.A. §552a et seq for relevant section from the Administrative Procedure Act.



WRITTEN by
MICHAEL HEWES



T H E
Quest
F O R T H E
Holy Grail

THE FULLY INFORMATIVE, YET FULLY UNDERSTANDABLE, OTC LABEL

I. INTRODUCTION

Wikipedia makes it sound simple:

The FDA requires that OTC products are labeled with an approved *Drug Facts* label to educate consumers about their medications. These labels comply to a standard format and are intended to be easy for typical consumers to understand.¹

Practical experience shows, though, that over-the-counter labeling is anything but simple: What information must be on the label? Should the label include additional information? Who qualifies as a “typical consumer?” How does one measure ease of comprehension? Those designing and seeking approval for an OTC label have to tackle not only these questions, but also many others implicit in the requirements of the Act, rules and regulations, as well as the many sub-issues each question generates.

The Federal Food, Drug, and Cosmetic

Act requires that a label be written “in such terms as to render it likely to be read and understood by the ordinary individual under customary conditions of purchase and use.”² Under the auspices of this and other mandates, the FDA has sought for decades to improve consumers’ understanding of OTC labels. Since the 1970s and before, the government has crafted rules and regulations with the intention of increasing comprehension and compliance. The elusive goal of designing an OTC label to achieve the optimal level of understanding remains a focus of the FDA. This article discusses the 2006 Nonprescription Drugs Advisory Committee (NDAC) meeting that addressed these OTC label issues and the 2009 Draft Guidance to Industry issued afterwards.

II. THE REGULATIONS

A. The Early Years

It is ironic that industry is to derive its guidance for crafting a pharmaceutical product’s label — at least in some part —

from the Federal Register, in the words of Dr. Eric Brass,³ “the single most unreadable thing in history.”⁴ Nevertheless, industry must navigate a labyrinth of governmental pronouncements when drafting an OTC label and subsequently seeking FDA approval.

In 1972, the FDA set out that the consumer should, “upon reading the label, [...] be able to determine the uses for the drug, any warning against use, and any other pertinent information which will allow him to use the drug adequately.”⁵ The first two “determinations” impact accurate consumer self-selection. The third — other information necessary for adequate drug use — is the obvious catch-all that impacts everything else.

Over time, the FDA attempted to provide industry additional guidance. For instance, in 1974, the agency pronounced that “the purpose of OTC medication is to permit consumers to engage in self-medication without medical or other professional supervision, or in any event with the least amount

of supervision feasible.”⁶ In essence, if consumers are to self-medicate safely without the input of a traditional learned intermediary such as a physician, then the label must function as a learned intermediary.⁷ Even then, the FDA recognized the limits of the OTC label:

[I]f labeling contains too many required statements, especially general statements of common sense, the impact of all warning statements on the label will be reduced. In addition, there is a space limitation on the number of statements that can appear on the labeling.⁸

B. Drug Facts

Twenty years later, in 1996, and still focusing on complexity, the FDA proposed a rule to provide “more simplified and understandable information” to consumers.⁹ The following year, the FDA noted once more that consumers were having difficulty understanding information contained in OTC labeling, and the agency proposed still another rule to improve comprehension by simplifying and standardizing labels.¹⁰ This 1997 proposed rule eventually became the 1999 Drug Facts regulation that governs OTC labels today.¹¹

One impetus for this renewed activity in the late 90s was studies indicating that consumers simply were not comprehending the information contained in OTC labels at levels acceptable to the FDA.¹² The agency described labels as “often printed in small type with a crowded layout and minimal white space.”¹³ As a result, it conducted two studies that looked at different formats and determined that OTC labels should “use [...] more concise and easy to understand language,”¹⁴ as well as uniform headings and format.

[R]esearch on reading behavior and document simplification shows that the use of less complex terminology, presented in shorter sentences with an organized or ‘chunked’ structure, is likely to improve consumer processing of the information [...].

Research also shows that consumers are more likely to engage in behavior that they believe they can successfully complete than in behavior that appears overwhelming [...] or that presents a ‘cognitive load,’ such as the task of reading densely worded consumer information [...].¹⁵

The FDA then set out specific templates for different pharmaceutical products, noting again that somehow all this important information must fit on the outside of the container.¹⁶ The story, though, did not end in 1999.

III. LABEL COMPREHENSION STUDIES

A. 2006 Nonprescription Drugs Advisory Committee Meeting

The focal topic of the 2006 NDAC meeting was the “design, analysis, and interpretation of consumer behavior studies used to support OTC switch applications.”¹⁷ Because a switch typically does not involve pharmacology as the main point of interest, the more important question is a behavioral one: “How will consumers use the drug in the OTC environment and ultimately, will consumer behavior lead to safe and effective use?”¹⁸ The answer requires more than intuition.

In general, as noted by FDA participant Dr. Andrea Leonard-Segal, three types of studies are used to attempt to predict consumer behavior in the OTC arena: label comprehension studies (LCS), self-selection studies (SSS), and actual use studies (AUS).¹⁹ The Committee discussed different aspects of each type, offered suggestions for conducting better studies, and posed questions that should be addressed in the future.

1. Self-Selection Studies

“The purpose of a self-selection study is to determine if the consumer can correctly decide whether or not the product is appropriate for him or her to use based on the label information.”²⁰ Thus, as the starting point, information required for accurate self-selection must appear on the Drug Facts label.²¹ It is not helpful if information criti-

cal to a self-selection decision is tucked away inside a package insert and unavailable at the point of purchase.²²

This kind of study may be conducted as a stand-alone endeavor, or as part of either an LCS or AUS.²³ One question arising with SSS is whether participants who incorrectly say the product is not right for them to use should be considered when determining the success of the study. After all, if the participant is not going to use the medicine, he or she will not be harmed by the medicine.²⁴ How these participants’ responses will be analyzed (e.g., counted as incorrect or simply disregarded) must be ironed out with the FDA beforehand as the responses could skew the numbers and result in a failed study.²⁵ Another issue to consider is whether “correct” self-selectors should answer additional questions to verify the accuracy of their decision — or whether the sponsor should bear the expense of independent verification.²⁶

A different issue arises with a subpopulation at particular risk if members incorrectly self-select. Because the risk is higher for this subpopulation, the FDA may consider setting a higher threshold for compliance than that for the general population. The question then becomes: “When should the majority who could benefit from access to an OTC drug be denied that access because of self-selection errors made by a subpopulation at risk from drug use?”²⁷

2. Label Comprehension Studies

LCS have two main purposes:

One is to test how the label communicates information to the consumer, and the other [...] is to test the ability of the consumer to apply label information in hypothetical settings in which the drug should or should not be used.²⁸

These studies typically allow the participant to have a copy of the label while answering questions either from a questionnaire or an interviewer.²⁹ They generally enroll about 300 subjects of normal literacy

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and 150 of low literacy.³⁰ Difficulties arise when the answers are “partly” correct (e.g., the correct answer is “stop use and ask a doctor,” but the participant responds with “call a doctor”).³¹ Agreement on how to categorize such answers beforehand could be critical in rating the success of the study.

LCS should be conducted only after the sponsor and the agency agree on the critical information. Otherwise, studies indicate that information simply will overwhelm people.³² As one participant put it, “Somebody has got to define what are the three things that every single person who takes this medicine must understand.”³³

3. Actual Use Studies

AUS mimic the OTC use of a product.³⁴

We sample consumers who we hope will represent the OTC population, people who are interested in the treatment, but who haven't been screened for medical suitability, and then finally, we essentially step back and let the consumer make the decisions about buying the drug, about using it, whether to buy it again, when to discontinue or stop [...].³⁵

This type of study can become quite difficult, depending on whether the medicine is indicated for short term or chronic use.³⁶ Analyzing compliance also is a tricky issue: What is the threshold for overuse, underuse, long-term adherence for chronic indications?³⁷

With respect to whether an actual use study “trumps” a comprehension study, the Committee consensus seemed to be that AUS are more important.³⁸ The point of the LCS, though, is that a “well-designed label comprehension program is in the sponsor's best interest to increase the likelihood of success of an actual use study.”³⁹

4. Miscellaneous Comments of the Committee

In addition to discussing these three types of consumer behavior studies, the Committee opined on a number of additional issues. Some of the ideas broached during this

meeting could have lasting consequences for industry—both as to the initial outlay that may be required to support a switch and the impact that implementation may have on litigation.

- Publish study results

Several participants questioned why the results of a sponsor's consumer behavior study should not be made public.⁴⁰ This idea of publication paralleled the oft-mentioned idea that consumer behavior studies have not been — but should be — an iterative process.⁴¹ The rationale for publication: If the good and not-so-good studies are made available, the information will be valuable as a learning tool. In other words, industry should be designing better and better studies by utilizing “good” concepts from earlier studies and discarding “bad” concepts⁴²:

[...] We have never had an iterative process that has carried us forward from one experience to another, so that each time we see a study we are comparing it to something that went before, and we have gradually improved our performance as we do this.⁴³

- Objectives set out beforehand

A common theme throughout the meeting was that the objectives of the study (i.e., what information was being evaluated) and the goal of the study (i.e., what percentage of comprehension will indicate “success”) need to be agreed upon with FDA prior to the study, and that there must be consequences if objectives and goals are unmet.⁴⁴ Inasmuch as the FDA is making the risk-benefit decision, one participant noted that there must be agreement on the “substantial risk”:

This means the sponsors and the agency have to agree explicitly and beforehand what the core issues are for the OTC switch for real risk.⁴⁵

Studies then are designed around that risk. The more substantial the risk, the higher the

level of necessary compliance.⁴⁶ In other words, there are no cookie-cutter study designs or set-in-stone benchmarks that apply to every switch, but each is dependent on the particulars of the medicine.⁴⁷

- Low literacy

Participants discussed at length the realities of literacy. As an initial matter, the *average* American reads at an 8th grade level but comprehends at a 6th grade level.⁴⁸ In other words, if consumers of low literacy are to be tested, the study must include subjects *below* those levels. One participant questioned whether labels even could be designed for lower literacy consumers.⁴⁹ Others questioned whether the target comprehension levels should be different for those of low literacy (e.g., 90% for average, but 70% for low).⁵⁰

- Other sources of information

One participant, after noting that reliance generally is placed almost exclusively on actual-use studies, suggested looking at other sources of information.⁵¹ For instance, information obtained from the prescription environment might be useful. Looking at patterns of use from other countries where the drug has been approved (even if the regulatory system requires behind-the-counter use) could provide insight. And, finally, a participant posited reviewing information from similar OTC products already on the market — post-marketing surveillance.⁵²

B. 2009 *Draft Guidance for Industry: Label Comprehension Studies for Nonprescription Drug Products*

With those comments from the NDAC meeting in mind, fast forward three years. The FDA's April 2009 Draft Guidance “is intended to provide recommendations to industry on conducting label comprehension studies.”⁵³ The Draft Guidance provides no recommendations for the other types of study discussed at the 2006 NDAC meeting: self-selection studies and actual-use studies. That omission is notable inasmuch as the FDA deemed it “important” to advise the reader that the data gleaned from

LCS is no predictor of actual consumer behavior.⁵⁴ In other words, consumer comprehension does not equate to consumer compliance. Despite this recognition, the FDA suggests that a sponsor conduct such LCS before conducting actual-use studies to determine whether “literate and low literate individuals can understand a drug product label.”⁵⁵

The Draft Guidance also sets out circumstances in which conducting LCS may not be a suggestion, but a requirement:

- Switches
- Substantive SNDAs, such as new indications
- New warnings
- Potential confusion over brand names and/or active ingredients
- Inclusion of a package insert⁵⁶

1. Study Design

As repeatedly stressed during the NDAC meeting, the Draft Guidance sets out that the study’s objectives must be established *before* the study begins. Primary communication objectives — information deemed most important to the safe and effective use of the product — should have a 90% or greater level of comprehension. These objectives can include understanding of indications, contraindications, or dose. Secondary communication objectives should have a target comprehension level of 80% or more. Self-selection may be tested as one of the communication objectives, or it could be tested in a separate study.

The Draft Guidance provides that the study “should include all subjects who could potentially use the drug product.”⁵⁷ Since the study participants will not ingest the medicine, exclusions should be rare and justified. In addition to testing comprehension in the general population, the study could be made more robust by targeting specific groups of particular interest as a result of indication (i.e., age) or contraindication (i.e., underlying contraindicated conditions). Finally, the Draft Guidance specifically notes that LCS should evaluate the comprehension of those individuals of low



literacy — below an 8th grade level of reading.⁵⁸ This point probably requires evaluating literacy levels at screening to ensure a sufficient enrollment of the population for statistical analysis.

2. Data Analysis

Just as the study’s objectives should be established *a priori*, so should the criteria for determining the success of the study.⁵⁹ In other words, the “success criteria should be related to the predefined target level of comprehension for the primary communication objectives.”⁶⁰ The Draft Guidance suggests utilizing a confidence interval of 95% (two-sided) where the lower limit for comprehension is above the 90% comprehension target level (or higher, depending on the design of the study). If the study has more than one primary communication objective, results for all should be evaluated.

3. Questionnaire

The Draft Guidance sets out that a sponsor should hire an expert when designing the study’s questionnaire⁶¹ and also lists other considerations:

- Drafting questions specifically to assess comprehension of primary communication objectives
- Utilizing simple, specific, non-compound and unambiguous questions
- Employing practical applications questions (e.g., John is 5 years old and weighs 40 pounds. How many teaspoons should he take?)

- Combining open-ended and close-ended types of questions (e.g., Mark has diabetes. Should he take the medicine?)
- Asking questions designed to elicit a narrative response (e.g., Why did you answer the previous question the way you did?)
- Recording verbatim responses, particularly for incorrect answers
- Avoiding leading or biasing questions, as well as the biasing ordering of questions
- Including “I don’t know” as a response, but excluding “Ask a doctor” as a response⁶²
- If self-selection is one of the primary communication objections, using questions to validate that selection at the end of the study (e.g., pointed questions about medical history)
- Pre-testing the questionnaire

4. Miscellaneous

The Draft Guidance suggests the use of comparator labels, either in different studies or within the same study⁶³ but notes that the “Drug Facts label format and content requirements should be used.”⁶⁴ LCS also should be open book tests. Because “customary conditions of purchase” usually do not require a consumer to memorize the label, study participants should have access to the label throughout the study. Finally, “[v]erbatim responses to all questions should be recorded.”⁶⁵

IV. CONCLUSION

The Draft Guidance appears to be only the tip of the iceberg compared to all of the matters discussed at the 2006 NDAC meeting. While one group suggested imposing additional requirements on industry, another group (or at least two members of the NDAC) admitted that they do not believe that labels matter when it comes to consumer behavior.⁶⁶ Two members, though, conceded one real area where labels do matter: litigation.⁶⁷

And some of the issues from the NDAC meeting and the Draft Guidance may be helpful to a sponsor subsequently embroiled in litigation. For instance, if the FDA sets

out what should be tested as a primary communication objective, a sponsor's not testing communication of some other language (e.g., an extremely rare adverse reaction) may be easier to justify to a jury. In other words, the FDA will have set out (perhaps in agreement with the sponsor) what it considers to be the "substantial risk" of the medication. Under the Draft Guidance, the sponsor will have successfully tested communication of that risk, and it will have an FDA-approved reason for why it did not test communication of other risks.

Nevertheless, despite decades of study and reams of regulations, the FDA continues to strive for better comprehension and compliance. And despite all the decades of work, there are only three takeaways. The first is the belief that "more research is needed."⁶⁸ The second is that "we have to recognize that no one label is ever going to be perfect for everybody."⁶⁹ And the third remains the same one iterated over several decades:

[T]he best way . . . to improve OTC labels [is] to find a way to say it clearly, standardize it, [and] don't say more than you need to.⁷⁰

¹ Wikipedia. "Over-the-counter drug." <http://en.wikipedia.org/wiki/Over-the-counter_drug>. Quoted as viewed June 29, 2010. Last accessed July 1, 2010.

² 21 U.S.C. 352(c).

³ M.D., Ph.D., Acting Chair, Nonprescription Drugs Advisory Committee.

⁴ Nonprescription Drugs Advisory Committee meeting, Sept. 25, 2006. Transcript available at <<http://www.fda.gov/ohrms/dockets/ac/06/transcripts/2006-4230t.pdf>>. ("NDAC Tr.").

⁵ 37 Fed. Reg. 9464 (May 1972).

⁶ 39 Fed. Reg. 19880 (June 1974).

⁷ NDAC Tr. at 74.

⁸ 40 Fed. Reg. 11717 (1975); *see also* NDAC Tr. at 15-16 (noting OTC products like cholesterol-lowering drugs and NSAIDs have more complex labeling that "populate the label to a magnificently cramped extent [...]. [A]t what point do we pack so much information into the label that people stop reading it [...]?""); *id.* at 353 (noting the speakers agreed that "listing all the side effects has no utility").

⁹ 61 Fed. Reg. 8450 (Mar. 1996).

¹⁰ 62 Fed. Reg. 9024 (Feb. 1997).

¹¹ 64 Fed. Reg. 13254 (Mar. 1999).

¹² *Id.*

¹³ *Id.* at 13277.

¹⁴ *Id.* at 13254.

¹⁵ *Id.* at 13255 (internal references omitted).

¹⁶ *Id.* at 13258.

¹⁷ NDAC Tr. at 10.

¹⁸ *Id.* at 73.

¹⁹ *Id.* at 14.

²⁰ *Id.* at 23.

²¹ *Id.* at 15.

²² *Id.* at 351 ("[...T]here is regulatory and philosophical consensus that the Drug Facts label must contain all the information that is required to make that initial self-selection material, and that other material is really supplementary.").

²³ *Id.* at 23.

²⁴ *Id.* at 24-25. The participant may be harmed, however, by not having the benefit of the drug (e.g., cholesterol-lowering drugs).

²⁵ *Id.* at 26, 27 (noting sponsors often do not provide information with respect to "incorrect" de-self selectors).

²⁶ *Id.* at 28-29 (noting verification can be "very difficult").

²⁷ *Id.* at 33.

²⁸ *Id.* at 17.

²⁹ *Id.* at 20.

³⁰ *Id.* at 23.

³¹ *Id.* at 22.

³² *Id.* at 70.

³³ *Id.*

³⁴ *Id.* at 30.

³⁵ *Id.* at 74.

³⁶ *Id.* at 31-32.

³⁷ *Id.* at 32-33.

³⁸ *Id.* at 342-43 ("I think I care more about the actual use because that is closer to how it is actually going to be started in terms of consumer use."); 343 ("I think actual use is much more informative in that result, and I think it does trump.").

³⁹ *Id.* at 344.

⁴⁰ *Id.* at 254, 264.

⁴¹ One participant opined that a distinct type of behavioral science — "methodological science of OTC switch" — should be created. *Id.* at 91-92.

⁴² *See id.* at 152.

⁴³ *Id.* at 169.

⁴⁴ *Id.* at 293-94 ("... [T]here is going to be a pre-specified threshold that is going to be in the protocol, in the statistical analysis plan, and it will be in the sponsor's best interest to reach prospective agreement with the agency as to what that threshold would be appropriate for that specific case."); 380 (noting Dr. D'Agostino "said 100 times today, [the study's threshold] has to be set out in advance *a priori* [...]").

⁴⁵ *Id.* at 78.

⁴⁶ *Id.* at 81.

⁴⁷ An exception for particular warning language could be switches within the same class that, for example, carry the same concerns of contraindication. It seems, however, that this matter already is addressed with class labeling.

⁴⁸ *Id.* at 372.

⁴⁹ *Id.* at 371. And if a label cannot be designed below these levels, is the FDA unfairly withholding medications that otherwise are safe and effective for the

average American?

⁵⁰ *Id.* at 374-75

⁵¹ *Id.* at 86.

⁵² *Id.* at 86-87, 93 ("analyzing the switches that have already taken place"). The sponsor, of course, was volunteered as the entity to bear the financial onus for such research. *Id.* One participant suggested a limited market approval and conducting Phase IV studies in that limited market. *Id.* at 94. At this juncture, however, the FDA does not have regulatory authority for a "limited market approval," although at least one FDA participant noted it was a "very good idea." *Id.* at 95.

⁵³ April 2009 Draft Guidance for Industry: *Label Comprehension Studies for Nonprescription Drug Products* ("Draft Guidance"), at 1.

⁵⁴ *Id.* at 1. Comparatively, during the NDAC meeting, Dr. Brass specifically noted that the studies are not "academic exercises" because they have as their goal the objective to "model and predict consumer behavior in the real marketplace." NDAC Tr. at 11. Apparently, that goal has yet to be reached.

⁵⁵ *Id.* at 1, 2.

⁵⁶ NDAC Tr. at 16 (noting consumer leaflets or package inserts can be a condition of approval and FDA "control[s] what is on the package insert").

⁵⁷ Draft Guidance at 5.

⁵⁸ *Id.* The FDA also suggested testing numeracy if label comprehension includes understanding numbers (weight-based dosing).

⁵⁹ *Id.* at 6.

⁶⁰ *Id.*

⁶¹ *Id.* at 7.

⁶² Dr. Doug Bierer, the CHPA representative, presented a somewhat contrary position. NDAC Tr. at 241 (suggesting "I would talk to my doctor" should not be an "incorrect" response).

⁶³ *Id.* at 8. *See also* NDAC Tr. at 148-151 (discussing comparison of labels and use of control groups).

⁶⁴ Draft Guidance at 9.

⁶⁵ *Id.*

⁶⁶ *Id.* at 177 (Dr. Alastair Wood, non-voting consultant: "[...] I don't believe labels work."); *id.* at 346 (Dr. Richard Neill, voting consultant: "[...] I believe [...] that labels don't matter much."). Of course, not everyone agreed. *See id.* at 39 (Dr. Ruth Parker, committee member: "I think everybody here would really agree that labels are necessary for drug safety.").

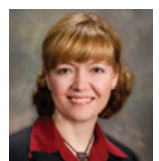
⁶⁷ *Id.* at 179 (Dr. Richard Neill, voting consultant: "I would mention that labels do work well at providing defensibility in court for sponsors and pharmacists and physicians and sometimes for patients."); *see also id.* at 180 (Dr. Wood agreeing and noting "that's why they are in small print and so long").

⁶⁸ *Id.* at 91.

⁶⁹ *Id.* at 98-99.

⁷⁰ *Id.* at 57. A fourth lesson to consider is that sponsors should be prepared for and attend future NDAC meetings focused on consumer behavior studies.

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