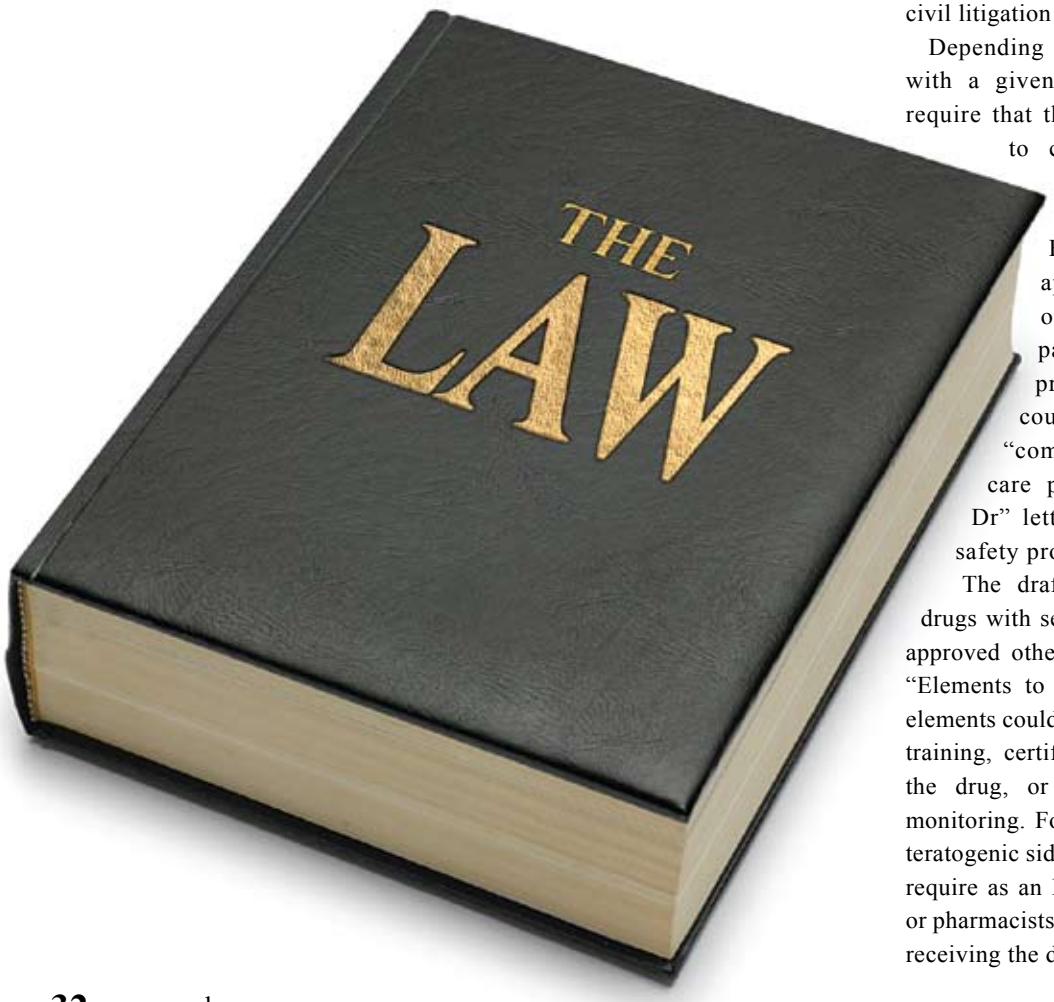
RISKY BUSINESS

Adam Moore and Devin Ross investigate the litigation implications of Risk Evaluation and Mitigation strategies.

Drug and biologic manufacturers have a new opportunity and challenge to confront in their risk management efforts. The FDA recently released its long-awaited draft guidance for the pharmaceutical industry on REMS (Risk Evaluation and Mitigation Strategies).[1] With this guidance and the REMS process come additional considerations for pharmaceutical products liability litigation. Senior management and in-house counsel would be wise to consider the potential effects the REMS process may have on their company's future litigation and to take steps to manage these concerns.



What are REMS

Under the Food and Drug Administration Amendments Act of 2007, the FDA can now require pharmaceutical companies to submit REMS prior to approval of certain drugs and biologics. REMS are required if the FDA determines that safety measures, in addition to drug labelling, are necessary "to ensure that the benefits of a drug outweigh its risks."[2] Once required, approved REMS are enforceable, and failure to comply with the provisions of an approved REMS can subject the manufacturer to fines in excess of $10 million. Equally important, REMS can have a significant impact on civil litigation as well.

Depending on the nature of the risk associated with a given drug or biologic, the FDA may require that the REMS contain various elements to communicate the drug's risks to health care professionals and the public. For some drugs, the FDA will merely require that the applicant provide medication guides or patient package inserts to educate patients regarding potential risks and proper usage. Additionally, the FDA could require the development of a "communication plan" targeted at health care providers including sending "Dear Dr" letters explaining risks and necessary safety protocols.

The draft guidance also explains that, for drugs with serious known risks that would not be approved otherwise, the FDA will require various "Elements to Assure Safe Use" (ETASU). These elements could include required health care provider training, certification of pharmacies that dispense the drug, or requiring patient registration and monitoring. For example, for a drug with potential teratogenic side effects (birth defects), the FDA may require as an ETASU that patients provide doctors or pharmacists with a negative pregnancy test before receiving the drug.

Balancing Concerns

Both the standard REMS and the more serious ETASU carry important litigation concerns. Much of a manufacturer's future litigation success depends on the nature of the warnings it provides. While product warnings should accurately describe the risks associated with the product, warnings that contain inappropriately strong language or that over-emphasize risks that are too remote will discourage the drug's use — even for those patients who may need it most. This is particularly true for ETASU because these heightened precautions may have the effect of limiting the drug's availability (for example, a requirement that a pharmacist takes a written test and is certified before dispensing the drug may limit patients' access in rural or low-population areas). Indeed, this important balancing of concerns must be taken as seriously during the REMS development process as it is in the labelling process.

Voluntary REMS as Double-Edged Sword

This FDA guidance introduces the somewhat new concept of *voluntary* REMS submissions, whose mere existence could have a significant effect on future litigation. The guidance states that "an applicant may voluntarily submit a proposed REMS without having been required to do so by the FDA." At first glance, this may look like a great opportunity to stave off future litigation, but it may turn out to be a double-edged sword. Before manufacturers quickly jump on board this new voluntary option, there are some catches to consider and manage.

- First, the guidance says that a manufacturer may voluntarily submit a proposed REMS "if the applicant believes an REMS would be necessary to ensure that the benefits of the drug outweigh its risks." As a result, such submissions may come with an unintended admission by the manufacturer that, without the proposed REMS, the drug's risks outweigh its benefits. Most states impose liability on manufacturers only when the product is "unreasonably dangerous" to the consumer. In states that have adopted the "risk/benefit" test, the product is unreasonably dangerous if the jury finds that its risks outweigh its benefits. Consequently, plaintiffs will argue that manufacturers who submitted a voluntary REMS have admitted that their product was "unreasonably dangerous."
- Second, the guidance clarifies that a voluntarily submitted REMS will not be approved "unless and until the FDA determines it is required." Thus, if the FDA finds the voluntarily submitted REMS was not required, it will not approve the REMS. This leaves the manufacturer in the difficult position of marketing its drug without an approved REMS despite the prior voluntary submission indicating the manufacturer's belief that REMS measures are necessary to make the product safe.

> TODAY'S CARELESS "CLICK" EASILY BECOMES TOMORROW'S "EXHIBIT A

Hence, the double-edged sword.

Manufacturers who do not submit a voluntary REMS will be cross-examined on that decision at trial. "Wasn't your company committed to doing everything in its power to ensure the safe use of its product?" Juries will be told that the company could have sent letters to doctors, provided a guide, or taken other safety measures to protect future users and chose not to. For those companies who do voluntarily submit the REMS, plaintiffs' attorneys will focus on the "admission" that the drug's risks, without the REMS, outweighed its benefits to the public — or on having placed a drug on the market without the FDA approving its REMS.

REMS Assessments and the Plaintiffs' Bar

As the pharmaceutical industry has learned over the years, plaintiffs' attorneys stand ready to pounce on any label changes a pharmaceutical company makes. This practice is likely to find its way into the world of REMS assessments as well. Just as the plaintiffs' bar monitors labelling changes — to take advantage of the opportunity to allege that a manufacturer either mislead patients or failed to adequately warn them of the drug's risks — changes to approved REMS are likely to invite litigation. In fact, changes to an approved REMS are potentially more serious than label modifications because plaintiffs will argue that they indicate that the FDA has determined that the risks of the drug in the market outweigh its benefits without the modification. In states where product liability is determined by a risk/benefit analysis, manufacturers required to add an REMS or to enhance an existing REMS are likely to find themselves in a difficult uphill battle.

For More Information

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Responsible Document Practices

As with the FDA approval process in general, the REMS process is likely to become a hotbed for so-called "bad documents" that can be taken out of context and used to the detriment of drug manufacturers. One cannot overstate the damaging effects that emails and internal written communications can have on future litigation. Today's careless "click" easily becomes tomorrow's "Exhibit A." As one plaintiff's attorney stated, when asked how he won a $253.5 million in a Vioxx trial: "The documents. The documents tell the truth."[3] Internal communications as well as those made with the FDA could easily resurface in litigation. Senior management and in-house counsel must take a pro-active approach to educating and training employees on responsible document creation practices.

It is not just careless emails that companies have to worry about. Scientific debate and self-critical documents can easily be distorted before the jury's eyes. A manufacturer's emphasis on responsible document creation throughout the REMS process can go a long way in protecting it in future litigation. While manufacturers should provide employees with opportunities to express and share their opinions on product design and effectiveness, any concerns must be addressed in a documented way, thus "closing the loop." Manufacturers should advise against creation of documents that vent frustrations, criticize the work of other team members, or contain speculation or personal opinion. Additionally, no document should ever be created that suggests the suppression of information or acquiescence in illegal conduct.

The REMS process also provides opportunities for creating "good documents." The process allows the manufacturer to expound on the positive aspects of its unique drug, while carefully characterizing the risk profile. This is a useful opportunity for a manufacturer to develop its positive story of the benefits of the drug to patients who are sick and suffering. The fact that this story is being formed outside of the courtroom only validates its use in future litigation. Additionally, a manufacturer's communications with the FDA throughout the process can establish the company's commitment to co-operation with the FDA and to the safe use of its product generally. However, presenting a history of co-operation in communicating with the FDA could be devastating at trial if the internal communications are inconsistent with that co-operation or raise issues that are not shared with the FDA. A "two-faced" company will not win favour with any jury.

Conclusion

If done correctly, and properly managed, the REMS process could become a positive factor in successful litigation down the road. Plaintiffs love to paint the picture of a company that knew the risks and intentionally failed to warn the public. The REMS process focuses on establishing the best way to inform and warn about a product's risks. Increasing these warnings through the REMS process will not only provide a stronger defence at trial, but may also lower the number of lawsuits against the company overall. One thing is clear, the REMS process will play a significant role in future litigation.

References

1. Food and Drug Administration, Guidance for Industry: Format and Content of Proposed Risk Evaluation and Mitigation Strategies (REMS), REMS Assessments, and Proposed REMS Modifications, released September 2009, www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM184128.pdf. [hereinafter Draft Guidance].
2. 21 U.S.C. § 355-1(a)(1) (2008).
3. Alex Berenson, "For Merck, Vioxx Paper Trail Won't Go Away," *N.Y. Times*, Aug. 21 (2005).