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Two Masters

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American government rests on the principle of distrust of government. Not only is power within the federal government checked and balanced. Power is divided between the federal government and the state governments. So what if a state law conflicts with a federal law? The Constitution says that the "Constitution, and the Laws of the United States . . . shall be the supreme Law of the Land; . . . any Thing in the . . . Laws of any State to the Contrary notwithstanding." Sometimes the conflict between federal and state law is obvious and the Supremacy Clause is easily applied. But sometimes . . .

Diana Levine received an intramuscular injection of Demerol for her migraine headache and of Phenergan—an antihistamine made by Wyeth—for her nausea.[1] She soon returned "complaining of 'intractable' migraines, 'terrible pain,' inability to 'bear light or sound,' sleeplessness, [and] hours-long spasms of 'retching' and 'vomiting.'" A physician's assistant gave her both drugs again, this time intravenously. The PA had a choice between "the 'IV-push' method, whereby the drug is injected directly into a patient's vein, or the 'IV-drip' method, whereby the drug is introduced into a saline solution in a hanging intravenous bag and slowly descends through a catheter inserted in a patient's vein."

Phenergan is corrosive and causes gangrene if it enters an artery. The danger is greater with IV push because the needle may penetrate an artery or the drug may escape "from the vein into surrounding tissue" (perivascular extravasation) and contact arterial blood. Phenergan's label had "at least six separate warnings" about this. The label said

> that "[t]he preferred parenteral route of administration is by deep intramuscular injection." If an intramuscular injection is ineffective, then "it is usually preferable to inject [Phenergan] through the tubing of an intravenous infusion set that is known to be functioning satisfactorily. Finally, if for whatever reason a medical professional chooses to use IV push, he or she is on notice that 'INADVERTENT INTRA-ARTERIAL INJECTION CAN RESULT IN GANGRENE OF THE AFFECTED EXTREMITY.'"

Intravenous injections are often given in the crook of the elbow (the antecubital fossa), but that is "a universally recognized high-risk area for inadvertent intra-arterial injections" because arteries there may be in unpredictable places. The *Lippincott Manual of Nursing Practice* warns, "in a red-text 'NURSING ALERT,' that the antecubital fossa is 'not recommended' for administering gangerous drugs, 'due to the potential for extravasation.'" And thus the Phenergan label said:

> Due to the close proximity of arteries and veins in the areas most commonly used for intravenous injection, extreme care should be exercised to avoid perivascular extravasation or inadvertent intra-arterial injection. Reports compatible with inadvertent intra-arterial injection of Phenergan Injection, usually in conjunction with other drugs intended for intravenous use, suggest that pain, severe chemical irritation, severe spasm of distal vessels, and resultant gangrene requiring amputation are likely under such circumstances.

Nevertheless, to help Levine "in a swift and timely way," the PA "pushed a double dose of the drug into an antecubital artery over . . . '[p]robably about three to four minutes,'" even though Levine complained of a burning sensation she later said was "'one of the most extreme pains that I've ever felt.'" Asked "why she ignored Phenergan's label and failed to stop" after Levine complained of burning pains, the PA "explained that it would have been 'just crazy' to 'worr[y] about an [intra-arterial] injection' under the circumstances." The PA also said "'[i]t never crossed my mind'" that an antecubital injection could hit an artery. It "'just wasn't something that I was aware of at the time.'"

As the Phenergan label had warned, gangrene set in, and Levine's forearm had to be amputated. She sued the doctor, the PA, and the health center for malpractice. Those claims were settled, and the doctor and the PA agreed to testify for Levine in a suit against Wyeth. That suit alleged that the Phenergan "labeling was defective because it failed to instruct clinicians to use the IV-drip method of intravenous administration instead of the higher risk IV-push method." And it alleged "that Phenergan is not reasonably safe for intravenous administration because the foreseeable risks of gangrene and loss of limb are great in relation to the drug's therapeutic benefits."

The jury "found that Wyeth was negligent, that Phenergan was a defective product as a result of inadequate warnings and instructions, and that no intervening cause had broken the causal connection between the product defects and the plaintiff's injury." It awarded $7.4 million in damages.

The federal Food, Drug, and Cosmetic Act requires a company seeking Food and Drug Administration approval of a new drug to propose a label describing the drug and its use. The FDA may approve the drug only if it is safe and effective for use as labeled. ("Label" is misleading. The label is a sheet or pamphlet that can run many pages. Its primary audience is medical personnel, not the user.)

So the FDA—a federal agency—had decided (repeatedly over half a century) that Phenergan was safe and effective as labeled. A state's courts had held Wyeth liable because the label's warnings were insufficient. The basic issue, as the Supreme Court's majority put it, was whether recognizing "Levine's state tort action creates an unacceptable 'obstacle to the accomplishment and execution of the full purposes and objectives of Congress' . . . because it substitutes a lay jury's decision about drug labeling for the expert judgment of the FDA."

Wyeth thought so. It said "the FDCA establishes both a floor and a ceiling for drug regulation: Once the FDA has approved a drug's label, a state law verdict may not deem the label inadequate . . . ." The majority, however, thought Congress had not intended the FDCA to preempt state action. "Congress enacted the FDCA to bolster consumer protection against harmful products." Congress "may have recognized that state law remedies further consumer protection by motivating manufacturers to produce safe and effective drugs and to give adequate warnings."

The dissent noted that the FDA itself had said that the FDCA sets "both a 'floor' and a 'ceiling,'" so that "FDA approval of labeling . . . preempts conflicting or contrary State law." The majority acknowledged that agencies "have a unique understanding of the statutes they administer." But the FDA's opinion was "entitled to no weight," partly because it "reverse[d] the FDA's own longstanding position without providing a reasoned explanation."

The legal argument in *Wyeth* was about Supremacy Clause jurisprudence and is too complex and technical to summarize here. But underlying the legal arguments were conflicting assumptions about regulating drugs.

First, the majority apparently assumed that the FDA's job is to protect consumers from harmful drugs. On this view, state restrictions on drugs promote the federal goal of preventing drugs from injuring consumers. The dissent, however, apparently assumed that the FDA can err in either direction—that consumers need protection from harmful drugs, but also that overprotection can deny consumers drugs that are, on balance, worth the risk.

Second, the majority evidently assumed that state-court decisions obliging manufacturers to add warnings to labels do little harm—that more information can only help. The dissent, however, said that the PA had "disregarded at least six separate warnings that are already on Phenergan's labeling, so respondent [Levine] would be hard pressed to prove that a seventh would have made a difference." The dissent also may have believed that there can be too much disclosure—that the longer and knottier the disclosure, the less likely it is to be read and the harder it is to decipher.

Third, the majority and the dissent may have thought differently about institutional competence. The majority emphasized the jury's role as the (nearly) dispositive finder of facts. The dissent said that "juries tend to focus on the risk of a particular product's design or warning label that arguably contributed to a particular plaintiff's injury, not on the overall benefits of that design or label." Juries only see people who have "already suffered a tragic accident," while "patients who reaped those benefits are not represented in court." The FDA, in contrast, can "consider the interests of all potential users of a drug."

Wyeth is like many judicial opinions of bioethical interest. It affects medical policy—here regulating drugs. Assumptions about medical policy influence judicial thinking. But the issue is not medical policy, the briefs and oral arguments barely address it, the judges have no particular understanding of it or particular competence to make it, and the case has precedential consequences in unrelated areas of law.

This haphazard way of making medical policy is comprehensible only if we recall the federal system of checks and balances. The Supreme Court isn't supposed to make medical policy; here it's supposed to decide who may make it. After *Wyeth*, states may demand more restrictive labeling requirements than the FDA has imposed. But Congress is free—should it wish to, should it overcome legislative obstacles, and should it secure the president's signature—to enact a statute preempting that authority.

Furthermore, if the FDA goes through a formal and burdensome process—instead of more casually asserting its opinion in the preamble of a regulation—it may be able to preempt that authority as well (unless the president or Congress objects or the courts find some legal defect with its work).

Meanwhile, the FDA has tried another tactic. Its press release says that the drug "first went on the market in 1956" and that the "FDA has reviewed the published literature and post-marketing adverse event reports." The FDA is not requiring that the label say that (as Levine had alleged) the drug "is not reasonably safe for intravenous administration." Rather, the FDA is requiring manufacturers to include "a boxed warning" that "will highlight the risk of serious tissue injury when this drug is administered incorrectly."

The FDA may thus have strengthened its warning, but it has affirmed its belief that IV administration should be permitted. Does *this* FDA ruling preempt contrary state law? Wyeth's counsel in *Wyeth* thinks so. But until the issue is litigated, we cannot know.

No wonder Justice Frankfurter once said that "[a] constitutional democracy like ours is perhaps the most difficult of man's social arrangements to manage successfully."

1. Unless otherwise noted, all facts and quotations are from one of the four opinions in *Wyeth v. Levine*, 129 S Ct 1187 (2009).