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IN THE WAKE OF *WYETH V. LEVINE*: Making the Case for FDA Preemption and Administrative Compensation

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Pharmaceuticals are subject to what are, in effect, two overlapping and often conflicting regimes for overseeing drug safety: mandatory regulation by the U.S. Food and Drug Administration and lawsuits seeking billions of dollars in damages in the common-law state tort system. This dual system is both irrational and destructive, particularly insofar as it discourages innovation, raises drug prices, and denies patients access to many medicines that are reasonably safe and effective.

To put an end to this dual regulatory regime, we recommend that Congress broadly preempt state tort lawsuits seeking to hold drugs and medical devices responsible for claimants' illnesses and injuries. Malpractice actions in state courts now available to plaintiffs would be unaffected by our proposal.

To deal with the consequences of serious and unforeseen drug side effects, we instead urge Congress to create a system modeled on the Vaccine Injury Compensation Program. Congress created VICP in 1986 in response to a wave of "junk science" litigation in the 1970s and 1980s that nearly destroyed the vaccine industry. VICP, while not without its own shortcomings, has since proven itself to be a scientifically credible mechanism for offering timely and fair compensation to the victims of rare vaccine side effects, while incurring much lower transaction costs than the tort system.

Initially the program should be funded by taxes levied on manufacturers on the basis of their market share. As the relative safety of their respective products emerged, manufacturers would be assessed taxes on the basis of their share of payments to successful claimants, which would be determined by the safety performance of the drugs they make.

Our argument rests on the conviction that the FDA's regulatory regime, while imperfect in many respects, is nonetheless better suited to weighing the benefits and risks of new medicines than state courts, which may consider only liability for harm to the particular plaintiffs before them. Far from ignoring the potential hazards of drugs under review, the FDA faces strong incentives to exercise excessive caution. The result is a system that promotes voluminous warnings on the labels of approved drugs and delays in approving or denying outright reasonably safe and effective medical innovations.

State tort litigation only exacerbates the effects of the FDA's biases and raises consumer prices. Moreover, many lawsuits allege that a drug manufacturer should have placed stronger warnings or even contraindications on a label, ignoring the fact that the FDA had explicitly considered the risk and then mitigated it by specifying the warning language to appear on the product label.

Unfortunately, both the U.S. Supreme Court and Congress have been moving in the wrong direction on the issue of FDA preemption:

- In its *Wyeth v. Levine* decision, handed down on March 4, 2009, the Supreme Court allowed a state court jury to substitute its judgment on a safety question for the FDA's. The side effect produced by the drug in question had been known to the FDA for almost thirty years, and the manufacturer, in FDA-approved language, had clearly disclosed the risk in six different locations on the label. The actual cause of the plaintiff's tragic injury was the treating physician's assistant's obliviousness to the label's plain warnings. In the aftermath of *Levine*, we are likely to see conflicting jury verdicts across the fifty states on the same issue or closely related ones. The result will be, so to speak, a race to the bottom, in which the most litigious jurisdictions will, in effect, set drug-labeling requirements for the nation as a whole.

- The day after the Supreme Court ruled in *Levine*, U.S. Representatives Frank Pallone (D-N.J.) and Henry Waxman (D-Calif.) introduced a bill called the Medical Device Safety Act that is intended to undo the Supreme Court's

2008 decision in *Riegel v. Medtronic*, which found that the plain language of the congressional act at issue was to preempt state tort lawsuits for injuries attributed to certain classes of medical devices.

We suggest that Congress should reject Pallone and Waxman's bill and instead clear the way for a sane, single and science-based system of safety review by broadly preempting state lawsuits concerning FDA-approved drugs and medical devices. Doing so would stop forum shopping and the filing of class actions that lump claimants with minor or no injuries together with a handful of legitimate claimants for the sole purpose of inflating attorneys' fees. A well-designed compensation program along the lines we suggest would offer as a substitute a mechanism for compensating the victims of unforeseen drug injuries, and it would do so without the uncertainty and expense of today's version of litigation. By limiting compensation to unforeseen injuries, the program we propose would also give companies a powerful incentive to rapidly update drug labels with new safety information and to invest further in both safety and effectiveness.

About the Authors

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Mr. Copland has published opinion columns in national, local, and online newspapers, including *The Wall Street Journal*, *The National Law Journal*, *Investor's Business Daily*, and *National Review Online*. He has testified before Congress and is a regular speaker and conference participant.

Prior to joining the Manhattan Institute, Mr. Copland was a management consultant with McKinsey and Company in New York. He earlier served as a law clerk for the Honorable Ralph K. Winter of the United States Court of Appeals for the Second Circuit. He has been a director of two privately held manufacturing companies since 1997.

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Mr. Howard has written on a wide variety of medical policy issues, including medical malpractice, FDA reform, and Medicare. He is often quoted on health-care issues and his columns have appeared in newspapers across the country, including the *New York Post*, *Dallas Morning News*, *Investor's Business Daily* and *WashingtonPost.com*. He is also a member of the Manhattan Institute's Project FDA, a committee of physician-scientists, economists, medical ethicists, and policy experts. Its purpose is to show how 21st-century technologies can help accelerate the drug-development and drug-approval process while maintaining drug safety.

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CONTENTS

In the Wake of *Wyeth v. Levine*: Making the Case for FDA Preemption and Administrative Compensation

James R. Copland & Paul Howard

INTRODUCTION

The U.S. Food and Drug Administration's oversight of prescription drugs, biologics, and medical devices has for decades been considered the global "gold standard," with most developed nations adopting the FDA's template when they oversee the development, testing, and marketing of new medical products.[1]

However, the agency's mandate of "protecting the public health by assuring the safety, efficacy, and security"[2] of biomedical products marketed for sale does not imply a guarantee of *absolute* safety. No medical device or product that is designed to alter the functioning of the human body is 100 percent safe under all circumstances for all patients; indeed, every medical product or procedure—from aspirin to open-heart surgery—carries with it the potential for severe and even fatal complications. Society tolerates the relatively rare risks of treatment only because of the greater and more certain pain and suffering inflicted by untreated illnesses.

Two questions naturally arise from this reality:[3] To what degree should society screen potential medical products, either to weed out those that are deemed unduly unsafe or to uncover new information about risks? And to what degree, if at all, should we compensate victims of adverse medical events?

Over the last fifty years, the United States has evolved a highly complex and mandatory process for prescreening the safety and efficacy of new drugs and devices, which we discuss in detail in this paper. Many criticisms of this process can be made[4], but one thing that is apparent is that the FDA is typically much more responsive to criticism that follows the discovery of previously unknown risks from new medical products than it is to arguments that too many medical innovations face delay or denial of market entry because of the agency's overcautiousness.

The overcautiousness of the FDA, along with its effect on medical innovation, is exacerbated by a compensation mechanism for medical injuries lodged in the state-based common-law tort system. Courts have come to rule not only on issues of negligence but on complex issues of causation and product labeling; as such, they constitute a second system of drug regulation. The lawsuits that they hear not only drive up the costs of products that in fact meet FDA safety regulations; they also discourage innovation in areas that are perceived to be litigation-prone.

Even if we concede that scientific experts may reasonably disagree with the FDA's regulatory decisions in individual instances, state courts and juries are poorly positioned to evaluate the *aggregate* effect of the FDA's regulatory regime on consumer welfare. In the course of litigation over FDA-approved medical devices and drugs, courts and juries take cognizance of only a single injured plaintiff and do not consider the competing risks and benefits that the FDA, in however flawed or constrained a fashion, must weigh for the *total* population of patients with a given illness—or for society as a whole.

Lawsuits launched in state courts also drive manufacturers, in hopes of deflecting lawsuits, to flood the agency with label warnings that may discourage patients from using beneficial medical products, and such lawsuits place additional political pressure on FDA officers to relabel or even withdraw products from the market on the basis of anecdotal evidence.[5] Making matters worse, much research suggests that compensating patients for their medical injuries through the tort system is extraordinarily expensive, time-consuming, and unpredictable.[6] Society's interest in promoting both medical innovation and the safety of medical products is clearly not best served by an ad hoc tort system that has a slim record of judiciously weighing scientific evidence.

Such critiques might be made of other kinds of product-liability lawsuits, but in this paper we limit our focus to FDA-regulated drugs and medical devices,[7] which constitute a substantial fraction of mass-tort litigation and affect the cost and delivery of health care, representing some 16 percent of the economy.[8] For a small subsection of this market—vaccines—Congress substantially replaced state tort lawsuits in 1986 with a science-based administrative compensation system, the Vaccine Injury Compensation Program. An administrative compensation system based on this successful model and applied to all drugs and medical devices would improve social welfare by accomplishing four goals:

1. Providing increased information on product safety through the routine surveillance of adverse events possibly caused by new medical products;

2. Promoting greater innovation in product safety;

3. Offering compensation in a fair, timely, and transparent manner for injuries resulting from serious, unforeseen drug side effects; and

4. Protecting manufacturers from unscientific and potentially ruinous lawsuits.

This paper offers an overview of:

- The current FDA regulatory regime
- The FDA's balancing of the risks and benefits of new drugs
- State product-liability law
- The normative case for preemption
- The vaccine example and our proposed administrative compensation system

Under the last item, parties injured by drugs approved by the FDA would be blocked from suing drug

manufacturers in state court, but they could still receive compensation for injuries so caused, provided the risk of suffering those injuries was not set out on an FDA-approved label accompanying the product. Compensation would be adjudicated by a specially dedicated administrative body operating independently of the FDA's other responsibilities.

FDA REGULATION OF DRUG DEVELOPMENT AND APPROVAL

The process of drug discovery and development is extraordinarily complex, time-consuming, and expensive—often involving hundreds of millions of dollars and over a decade of development time.[9] The industry estimates that only one out of every 10,000 compounds investigated for medical use will eventually receive FDA approval.[10] The rest will be tested and discarded because of safety or efficacy concerns.

Once a pharmaceutical or biotech company has identified a compound likely to inhibit or modify a targeted disease process, the drug will be subjected to substantial laboratory and animal testing—typically over the course of several years—to ensure that the compound has an acceptable safety profile and a significant impact on the intended target.

If the company is confident that the compound is a good candidate for human testing, it will approach the FDA with the results of its preclinical testing and request permission to begin clinical trials by submitting an Investigational New Drug (IND) application.

If the FDA approves the IND, clinical testing follows in three generally sequential phases. In Phase I testing, the drug candidate will be administered to (usually) healthy volunteers for ADME[11]-toxicity testing to see how the body absorbs, metabolizes, and excretes the compound and to note any side effects. Phase I testing is also typically intended to establish safe dosing limits.

For Phase II testing, relatively small numbers of patients (a few dozen) with the targeted disease will be given the drug to establish baseline efficacy (or lack thereof) and to add to the safety and dosing data already gathered.

If the two previous stages have been successful and do not provide evidence of side effects that would outweigh the potential benefits, companies will begin Phase III testing. Depending on the drug or indication, a Phase III trial involves assigning several hundred or thousand patients to a randomized controlled trial (RCT) in which some will receive the drug but others a placebo (sugar pill). In certain therapeutic areas, such as oncology, where it would be unethical to give a seriously ill person a substance known to be ineffective, patients will be offered the standard of care. For instance, in the testing of a new antibiotic for a severe bacteriological infection, some patients will randomly receive the new drug while others will receive an established treatment.

If the outcome of the Phase III trials is positive (that is, the company can ascribe positive outcomes to the drug and not to chance) at a statistical confidence level of 0.05 or less, the company will submit all its data on the drug, including its composition, manufacturing processes, and preclinical and clinical data, along with any reports of adverse events and the drug's proposed labeling indication, to the FDA in the form of a New Drug Application (NDA). It is not unusual for an NDA to include several hundred thousand pages of documentation.

BALANCING THE RISKS AND BENEFITS OF NEW DRUGS

No drug, device, or medical procedure is without risk. Indeed, any product that affects a patient's physiology is apt to have side effects—some serious, others less so—that the clinician and the patient must weigh against the risk of illness and death due to the underlying disease. In his testimony before Congress, former FDA deputy commissioner Scott Gottlieb, M.D., outlined the challenges that accompany all drug treatment:

> Every clinician who prescribes medicines has seen adverse drug reactions—the unintended

> and harmful effects of drugs. Human biology, after all, is conservative, meaning our bodies reuse a fairly small set of very similar molecular processes to get all of their jobs done.
>
> It follows that any drug that is active in blocking some molecular process in order to have its desired effect will also block the same molecular processes in other parts of the body, parts that could lead to an unwanted side effect. So there is no such thing as a completely safe drug.[12]

As a result, it has long been acknowledged that the FDA will tolerate serious drug-related toxicities associated with the treatment of serious and life-threatening ailments, particularly when there are few effective therapies available to patients, or when the drug under review represents a significant therapeutic advance over existing treatments. This is eminently rational: patients with serious illnesses are apt to have a much higher tolerance for risk than patients who suffer from more manageable or less life-threatening conditions.

Ideally, when a new drug or device is marketed, patients and physicians would have the guidance of a label that outlines all the individual risks and benefits of a medicine before use. In reality, given the limits of existing science and the enormous variation in human biology, no amount of premarket testing can uncover all potential side effects that may be associated with a new medicine. As noted previously, during development, prospective compounds will be tested on relatively small numbers of patients; if approved for sale, they may be used in hundreds of thousands or millions of patients. Additional premarket testing in larger clinical trials might uncover a greater number of side effects but would also delay patient access to valuable new therapies and, by adding to drug-development costs, increase drug prices or keep valuable drugs (for some indications) from being brought to market, if the chances were better than not that the added costs could not be recouped.

The FDA's effort to balance the conflicting values of speed and safety is complicated by the high visibility—and therefore the ensuing negative publicity—of two types of errors it may commit: "Type I" error, or approving a drug as reasonably safe that later turns out to be unsafe or ineffective; and "Type II" error, or withholding from the public a drug that is reasonably safe and effective.

The Type I error, insofar as it results in widely publicized deaths or serious injuries after a drug is approved for sale, is of greater public concern and consequently has the greater impact on agency oversight by Congress.[13] Exemplifying the Type I error is the history of thalidomide, a sedative that was widely marketed in Europe and Japan (but not the United States) to treat pregnancy-related nausea ("morning sickness") before it was discovered that it caused severe birth defects. The thalidomide tragedy led in 1962 to passage of the Kefauver Harris Amendment, which created what became the FDA's current drug-approval regime.

More recent examples of commercialized drugs being found to have side effects, such as Vioxx or Fen-Phen, fit neatly into a Type I narrative. Such Type I failures create the impression that the FDA has failed in its primary public obligation, which is to prevent unsafe drugs like thalidomide from reaching the market, and have led to the perception that there is a drug safety crisis, which has dominated debate over industry and FDA regulation for the last several years. According to this narrative, flaws in the FDA's approval and post-approval monitoring of new medicines justify a substantial role for private litigation in bringing adverse events to light and deterring negligent industry behavior. According to one often voiced critique:

> There are often important gaps in the ascertainment and reporting of adverse events associated with prescription drugs, and the balance of information presented to physicians about the risks and benefits of medications may understate the former and inflate the latter…. In this environment, litigation brought by government agencies and individual patients can help uncover previously unavailable data on adverse events, questionable practices by manufacturers, and flaws in drug regulatory systems.[14]

This argument is often repeated in the medical literature, but such analyses typically focus on only one side of the cost-benefit equation—risk—while failing to

consider information on benefits.[15] Indeed, since new indications cannot be added to drug labels without new clinical trials, dissemination of new information on benefits that may improve patient welfare lags behind less than fully scrutinized bad news, which travels through the media and dominates policy discussions. In addition, litigation typically heightens awareness of the potential risks of just one product, thus shifting market share to products that may have their own unknown risks. In any case, litigation does not collect post-market drug safety information systematically enough to be useful to regulators.

Perhaps the best demonstration of a bias in the treatment of risk/benefit information is the "black box" warning that the FDA added to SSRI antidepressants in 2003, after mixed data were gathered indicating that the drugs might cause a short-term increase in suicidal behavior, although reports submitted to the FDA on clinical trials revealed no suicides. Under considerable pressure from plaintiffs' attorneys and consumer groups, the FDA implemented its new label warning; predictably, the number of SSRI prescriptions fell. Shortly thereafter, adolescent suicides increased, following a decade-long decline, raising the question of whether the FDA's label warning may have caused more harm than good by scaring some physicians and families away from drug treatment for depression.[16]

There is also significant evidence, which we will discuss shortly, that the trial bar distorts, manufactures, or otherwise misrepresents evidence of drug injuries so as to increase aggregate damage awards and legal fees, which go up along with them.

In short, there is substantial evidence that the FDA faces powerful incentives to commit Type II errors—failing to approve a drug that is, in fact, mostly safe and effective and over-warning of the risks it might present.[17]

There are a few well-known instances, however, when societal pressures pushed the agency to address the problem of Type II errors. The most notable was the protests by AIDS activists during the late 1980s and early 1990s, when an AIDS diagnosis was effectively a death sentence. AIDS advocates argued that the FDA's lengthy and mandatory testing regime doomed thousands of AIDS patients to certain death. Offering them instead the possibility, however uncertain, of prolonging life through accelerated access to experimental therapies would have been preferable, these advocates argue.

Faced with the reality that AIDS patients were importing unapproved drugs from Europe and Mexico or traveling to foreign clinics to gain access to them, and under pressure from economists and policymakers who noted that the FDA was often excessively slow in weighing the evidence on many new drugs that were already available in Europe,[18] the FDA dropped its insistence on a sequential testing process and embraced a number of innovative programs, including "treatment" IND and "parallel track," which "allowed AIDS patients (and others) access to promising experimental drugs early in the development process, long before their safety and efficacy had been proved."[19]

In addition, Congress passed the Prescription Drug User Fee Act (PDUFA) of 1992, which "allowed the FDA to levy user fees [on] firms filing a New Drug Application or Biologic License Application, in exchange for guarantees on review times." The legislation has been renewed three times since then, in 1997, 2002, and 2007.[20]

In return for being given user fees with which to hire additional review staff, the FDA agreed to set a timetable for the "complete review" of 90 percent of submitted applications: ten months for a standard review; and six months for a priority review, if the product under review, in the FDA's judgment, offered a substantial improvement over existing therapies or was a treatment for currently unmet medical needs.

The implementation of the PDUFA regime also offered researchers an opportunity to perform a controlled experiment to answer the question of whether speeding up access to new medicines offered a net benefit or, rather, posed harm to patients—a key indicator of whether the FDA had been running an equal risk of committing Type I and Type II errors.

Research shows that accelerated review of submitted NDAs did not, in fact, harm patients. Researchers concluded that "by the most plausible measure,

[PDUFA] did not, in fact, have any effect on drug safety: neither the proportion of drugs eventually withdrawn (2–3 percent), nor the speed with which they were withdrawn, changed in any statistically significant way since the law's passage."[21]

In fact, researchers found that "the drugs approved and withdrawn since the law was enacted cost, at most, about 56,000 life-years in avoidable deaths." Conversely, "the calculation [of the benefits of added speed] implies that the act added 180,000–310,000 life-years—far more than the 56,000 life-years lost if, in fact, [PDUFA] was responsible for all of the mistakes of the drug review process."[22]

Due to the complexity of human biology, no premarket screening process can guarantee products to be without serious side effects. Second, the available data suggest that, if anything, the FDA is more prone to Type II errors than Type I errors. When state courts are allowed to second-guess the label warnings that the FDA requires for prescription drugs after it has explicitly ruled on such matters, we can expect companies to respond by reducing innovation, by raising prices, or by flooding the agency with new warning labels and contraindications in an attempt to forestall litigation, thus encouraging the FDA's existing tendency toward excessive caution in its regulation of pharmaceuticals.

PREEMPTION OF STATE PRODUCT-LIABILITY LAW

Under the Supremacy Clause of the U.S. Constitution, federal law supersedes state law.[23] A federal statute can preempt corresponding state laws either expressly or impliedly. However, in its landmark 1947 decision in *Rice v. Santa Fe Elevator Corp.*, the U.S. Supreme Court articulated a "presumption against preemption," unless preemption "was the clear and manifest purpose of Congress."[24]

Having just erected this apparent bulwark against preemption, the Court then proceeded to articulate multiple rationales for finding preemption of state law to be implied:

> Such a purpose may be evidenced in several ways. The scheme of federal regulation may be so pervasive as to make reasonable the inference that Congress left no room for the States to supplement it. Or the Act of Congress may touch a field in which the federal interest is so dominant that the federal system will be assumed to preclude enforcement of state laws on the same subject. Likewise, the object sought to be obtained by the federal law and the character of obligations imposed by it may reveal the same purpose. Or the state policy may produce a result inconsistent with the objective of the federal statute.[25]

The rationales spelled out in *Rice* are the basis of the three categories of implied preemption recognized by courts today:

1. *Conflict preemption*, that is, cases in which there exists "a clear inconsistency between what the federal government and the state government each allow or require";[26]

2. *Obstacle preemption*, that is, cases in which "the imposition of the state liability will *frustrate* the ends of the federal statute";[27] and

3. *Field preemption*, that is, cases "where the creation of a pervasive system of Federal regulation makes it reasonable to infer that Congress intended to disallow supplemental State law measures or where Congress legislates in an area where the Federal interest is so dominant that a Federal system can be presumed to displace State laws on the same subject."[28]

Whereas scholars such as Richard Epstein have argued for broad "field" preemption of state tort claims for FDA-regulated products,[29] the general rule, until this decade, rejected even the narrower claim that the FDA's extensive regulation of labeling preempted, on "conflict" or "obstacle" grounds, state tort "failure to warn" laws or rulings.[30] Over the last eight years, however, the FDA began to contest this interpretation. Beginning in 2000, it argued for both conflict and obstacle preemption in court briefs.[31] In 2006 the FDA

added the following language to its preamble: "FDA believes that under existing preemption principles, FDA approval of labeling under the [FDCA] . . . preempts conflicting or contrary State law."[32]

In the past two years, the U.S. Supreme Court has considered two major preemption cases involving drugs and medical devices. In the first, 2008's *Riegel v. Medtronic*, the Court considered the extent to which New York state common law could support claims that a medical device was defectively designed or that its label had failed to warn consumers, when the product in question was a "Class III" device that had gone through the FDA's full premarket approval process. *Riegel* was an express preemption case, because the Medical Devices Amendments to the FDCA, adopted in 1976, say that states may not "establish or continue in effect … any requirement … which is different from, or in addition to, any requirement applicable under [federal law] to the device."[33] Given such clear language, *Riegel* was by and large an easy case, and the Court determined, in an 8-to-1 decision, that the plaintiff's claims under state law of a design defect and failure to warn were expressly preempted.[34]

The Court's second major FDA-preemption case of the past year, *Wyeth v. Levine*, was more difficult. *Levine*, which the Court decided in March 2009, involved a drug rather than a medical device, placing the case outside the express preemption language of the Medical Devices Amendments. Because no preemption language exists in the 1938 FDCA, the Court had to determine whether the Vermont state common-law claims in the case were *impliedly* preempted by the FDCA's regulatory scheme.

As in most such cases, the facts in *Levine* are tragic. In 2000, Diana Levine, who played guitar professionally, had to have her arm amputated below the elbow after developing gangrene. The gangrene was caused when a physician's assistant at a Vermont clinic inadvertently injected the drug Phenergan (promethazine hydrochloride), made by Wyeth, into an artery, rather than a vein, of Levine's, using the intravenous-push ("IV-push") method in a second attempt to relieve the patient's nausea, a side effect of her severe migraine headache.

In marketing Phenergan, which was initially approved by the FDA in 1955, Wyeth warned of the risk of arterial exposure to the drug. As early as 1973, the manufacturer submitted a supplemental application to the FDA that warned of the risks of inadvertent arterial injection via IV-push administration. Subsequent Wyeth-initiated FDA reviews in 1979 and 1997 further strengthened Phenergan warnings and added more labeling detail about how medical administrators could minimize the risk of inadvertent arterial injection when performing an IV-push application of the drug.

The label adopted for Phenergan following the FDA's 1997 review contained four prominent notices of the risk of gangrene from arterial exposure, including:

> 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.

In addition, in two places, the label contained the following simple, bold, uppercase warning: ***INTRA-ARTERIAL INJECTION [CAN] RESULT IN GANGRENE OF THE AFFECTED EXTREMITY***.

Moreover, the label advised that "deep intramuscular injection" (IM) rather than intravenous injection was the generally preferred method of Phenergan administration. For cases in which an intravenous injection was necessary, the label stated that an intravenous drip (IV-drip) was the preferred method of drug delivery: "it is usually preferable to inject [Phenergan] through the tubing of an intravenous infusion set that is known to be functioning satisfactorily." The label also contained clear advice for minimizing risks associated with any intravenous administration: "When used intravenously, Phenergan Injection should be given in a concentration no greater than 25 mg per mL and at a rate not to exceed 25 mg per minute." And the label advised, "[i]n the event

that a patient complains of pain during intended intravenous injection of Phenergan Injection, the injection should be stopped immediately to provide for evaluation of possible arterial placement or perivascular extravasation." (Notably, the physician's assistant in *Levine* administered Phenergan as an IV-push, rather than an IV-drip, at twice the maximum dosage for intravenous injection specified on the label, and continued doing so despite Levine's complaints of severe pain.)[35]

Notwithstanding Wyeth's clear labeling of Phenergan's risks, and the treating physician's assistant's noncompliance with labeling specifications, the Supreme Court sustained Levine's multimillion-dollar jury award against Wyeth. In rejecting Wyeth's conflict-preemption claim, the majority opinion, written by Justice Stevens, relied on FDA regulations that permit companies "[t]o add or strengthen a contraindication, warning, precaution, or adverse reaction" or "[t]o add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product."[36]

The court acknowledged that the regulatory exception is intended to apply only to "*newly discovered risks* from the use of [a] drug."[37] The court noted, however, that the exception "is not limited to new data, but also encompasses 'new analyses of previously submitted data'."[38] The majority opinion went on to argue, implausibly, that Wyeth could have modified the label because it theoretically "could have analyzed the accumulating data,"[39] although there was no evidence that the company had actually done so. As Professor Epstein observed well before Stevens rendered his opinion:

> *Levine* presents a situation where the FDA gave explicit approval to the exact treatment, notwithstanding the precise side effect mentioned in the original warning. What would count as new information to render that explicit authorization obsolete? The mere occurrence of the identified side effect can't do it because it was warned of in advance. And in *Levine* the sketchy record reveals no evidence collected after the drug hit the market indicating a higher incidence of this failure (and perhaps others) that might call for a reevaluation of the risk/reward ratio for that procedure.[40]

In short, Justice Stevens's opinion rejected Wyeth's claim of conflict preemption by embracing a fanciful hypothetical in lieu of a considered analysis of the thirty-year evolution of the contents of Phenergan's actual label.

Justice Stevens' majority opinion also rejected Wyeth's claim of obstacle preemption, largely on the basis of an analysis of Congressional intent. In so doing, the Court missed the obvious point that the Food, Drug, and Cosmetic Act (FDCA), which was enacted in 1938, and its primary subsequent amendments, adopted in 1962, predated the very expansion of state product liability law that made Levine's lawsuit possible.[41] It was not until 1963, in the landmark California case *Greenman v. Yuba Power Products, Inc.*,[42] that Justice Traynor's doctrine of strict product liability became law; and not until *1965* that the Second Restatement of Torts launched modern failure-to-warn lawsuits by opining that "in order to prevent the product from being unreasonably dangerous, the seller may be required to give directions or warnings."[43]

What the dissenters in *Levine* correctly noted is that the attorneys presenting Levine's case before the jury argued that the Phenergan label "should not have allowed IV push" under *any* circumstances[44]—a direct challenge to the FDA's considered judgment that IV-push administration of the drug could be warranted and that the decision was best made by the treating physician. It is not hard to grasp how a lay jury, looking solely at the facts of this case, could have reached such a conclusion: Why, when the goal is merely to relieve migraine-induced nausea, assume the risk of losing a limb? There clearly are some situations, however, in which the FDA's decision to permit such an application would make sense. Because IV-push application of Phenergan injects the drug directly into a patient's bloodstream, it works more quickly than oral, suppository, or intramuscular-push application: three to five minutes for IV-push, versus twenty minutes for IM-push.[45]

In an emergency-room situation in which doctors must perform surgery quickly and a patient's vomiting

could severely compromise their ability to do so, time is of the essence, and the dramatically faster onset time of IV-push Phenergan application and the difficulty in setting up a slower IV-drip could spell the difference between life and death.[46] Owing in part to such considerations, the American College of Emergency Physicians coauthored an amicus brief to the Supreme Court for the defense in *Levine* arguing that "appropriate medical care is best determined by trained medical professionals."[47]

That other physicians' groups argued the contrary position is perhaps unsurprising, in view of the fact that liability not attached to manufacturers could fall upon treating doctors and hospitals. In *Riegel* and *Levine*, this point needs additional emphasis, for in both cases, the injuries sustained could plausibly be attributed to the error of the treating health-care worker. The balloon catheter device in *Riegel* was used on a patient who had a "diffusely diseased and heavily calcified" right coronal artery—a condition contraindicated on the FDA labeling.[48] Moreover, the device was approved only for a "rated burst pressure of eight atmospheres." Despite this, the doctor inflated the balloon to ten atmospheres, causing the balloon to burst.[49] Similarly in *Levine*, as noted previously, the treating physicians' assistant administered the Phenergan IV-push at twice the dosage that the FDA-approved label stated should be the maximum, and continued doing so after the patient complained of pain, again ignoring contrary label language.[50] In other words, in both cases, the injuries may well not have occurred had the FDA's actual label guidelines been followed. If, as in these cases, they had not been, a finding that claims against drug manufacturers are fully preempted need not amount to a denial of all recourse under state tort law for the injured claimants.[51]

THE NORMATIVE CASE FOR PREEMPTION

The Supreme Court's decision for the plaintiff in *Levine* may not keep the new Congress from amending the FDCA to preserve state common-law claims against drug and medical-device manufacturers. In response to *Riegel v. Medtronic*, last summer U.S. Representatives Frank Pallone (D-N.J.) and Henry Waxman (D-Calif.) introduced H.R. 6381, the so-called Medical Device Safety Act bill, which proposed adding the following language to the FDCA: "Nothing in this section shall be construed to modify or otherwise affect any action for damages or the liability of any person under the law of any State."[52] Pallone and Waxman reintroduced the legislation in the new Congress on the day after the Supreme Court decided *Wyeth v. Levine*.[53] For several reasons, such a change would be unwise.

As previously discussed, the FDA is already more likely to make Type II, rather than Type I, errors. The institutional pressures it faces tend to encourage overregulation, even though the evidence is strong that the number of lives saved through expedited drug approval under PDUFA, since the program's inception, has substantially exceeded the number of lives lost as the result of Type I errors.[54] The evidence thus gives the lie to arguments that tort litigation is a useful complement to FDA regulation, which should, in the view of preemption's opponents, be merely a "floor" above which states can impose additional duties. Given that on balance the FDA is more prone to Type II error, that tendency is only aggravated by the extra layer of review that civil courts provide, so the tort system generates a net social welfare loss.

In addition, in contrast to the FDA, which is charged with making cost-benefit trade-offs, civil juries not only are incapable of making them; they are actually forbidden to do so. A civil jury is charged merely with looking at the facts of the case before it, without considering the broader societal repercussions. Moreover, while the FDA makes *ex ante* decisions, juries ruling *ex post* are unavoidably subject to hindsight bias, which makes them more likely to assign liability than a neutral assessment of the facts would warrant.

The civil jury system is also poorly equipped to rule on complex scientific issues[55] or to weigh other kinds of trade-offs that the FDA must consider in its regulation and monitoring of medical products. As Philipson and Sun note:

> Damages in such cases are typically awarded by juries, who are not spending their own money. If juries are likely to award inefficiently

> high damages, then pharmaceutical firms will produce products that are inefficiently too safe, or may exit the market entirely as has been observed in the case of vaccine development…. In effect, product liability acts as mandatory product insurance for consumers.[56]

Even if most juries should reach a conclusion that comports with sound science and economics, an outlier jury could act otherwise—and impose a punitive damage award—thus impelling companies to take greater precautions. This "race-to-the-bottom" effect is exacerbated by the multistate, multijurisdictional nature of the American judicial system, which permits the phenomenon known as "forum shopping." Plaintiffs' lawyers, who routinely receive contingency fees of 33 percent or more,[57] have an incentive to maximize their recovery. Thus, attorneys will tend to move mass-tort cases into states and jurisdictions that are most likely to permit the consolidation of dubious claims with meritorious ones, and then to assign liability and give high damage awards.[58]

Exemplifying this problem is the multibillion-dollar Fen-Phen litigation, which *The American Lawyer* says "will long be remembered as a mass tort debacle." Although the evidence is clear that Fen-Phen caused serious heart-valve problems in a subset of users, after the drug was withdrawn from the market plaintiffs' attorneys launched cases that lumped thousands of minor or dubious claims in with a handful of severe injuries to inflate aggregate payments—and their fees. In 2004, cardiologists at Duke University reviewed hundreds of echocardiogram records alleging injuries caused by Fen-Phen; 70 percent, they concluded, should never have been approved for payment by trusts set up to handle the large number of claims. Even plaintiffs with records in the undeserving category suffered needless worry and consternation; in one case, "a patient whose condition was overstated for the sake of obtaining payment through the trust ended up having unnecessary heart valve replacement surgery."[59]

Furthermore, the laypeople who serve on juries, lacking the technical expertise of FDA scientists, have shown themselves susceptible to junk science and thus receptive to lawsuits that have their own expensive and dangerous side effects. For example, the morning-sickness drug Bendectin was used by as many as 25 percent of all expectant mothers in 1980, but by 1983, the manufacturer of Bendectin pulled the drug in the face of $18 million in annual legal bills—as against only $20 million in total sales. Though Bendectin is on the market around the world, it remains unavailable to pregnant women in the United States, despite more than thirty published studies—examining more than 130,000 patients—that have failed to find a link between the drug and birth defects. Since Bendectin was pulled from the market, the percentage of pregnant women hospitalized each year for morning sickness has doubled, but the incidence of birth defects has not declined.[60]

In addition to removing valuable drugs like Bendectin from the market and stifling research, the specter of drug litigation can adversely affect public health by changing doctor and patient behavior. In a 2003 Harris Interactive Poll, 43 percent of doctors said that they do not prescribe some drugs that are under threat of litigation for fear that they will be drawn into the suit, and 40 percent of pharmacists reported that patients refused to take medicines that were the subject of high-profile lawsuits—subjecting them to potentially serious though treatable disease. Parents are also refusing to have their children vaccinated in the face of thousands of lawsuits alleging (without any scientific evidence whatsoever) that vaccines cause autism. These children will be exposed to dangerous, perhaps even fatal, childhood illnesses.[61]

Such strong doctor and patient reactions to litigation highlight the risks of *overwarning*, one reason that the FDA maintains tight control over drug labeling decisions. Indeed, the brief in *Levine* authored by the Washington Legal Foundation and the American College of Emergency Physicians outlined specific cases in which overwarning led to inferior health outcomes: for example, the institution of new SSRI warnings was followed by a rise in teen suicides, and warnings about vaccines led to a decline in vaccination rates and then to an outbreak of measles.[62]

Critics of FDA preemption are concerned that even limited preemption would reduce the pressure on companies to produce safer products:

> Tort law assists patients who have been harmed by defective products, providing compensation…. [T]ort law deters industry negligence and deception and encourages disclosure and innovation to improve product safety. Common law failure-to-warn claims, for example, create incentives for companies to revise their labels in light of risks that were unknown at the time of approval or risks that are greater than originally thought.[63]

These critics, however, ignore the cost of Type II errors[64] and sidestep the tension that often exists between the incentives generated by common-law litigation and the FDA's own cost-benefit analysis. In many cases, as Tomas Philipson explains, the FDA's decision is binding—the company lacks the discretion to modify a label or product design. The result is a tort system that does little more than increase company costs, which are then, of course, passed along to consumers in the form of higher prices.[65] (In other cases, cost increases to drug manufacturers might deter innovation by raising the break-even point for revenue needed to support a product launch.)

Product liability's powerful price effect on medicines that do make it to market has been demonstrated powerfully by a pair of studies, authored by health economist Richard Manning, which looked at the effects of product-liability risk on the price of vaccines in the 1980s.[66] During that decade, some vaccines faced an onslaught of litigation, which ultimately led Congress to create an administrative compensation program that largely supplants the tort system (see below). While all vaccines' prices rose during the decade—doubling, on average—the two vaccines most subject to litigation rose much more dramatically: the price of the polio vaccine jumped sevenfold, while that of the diphtheria-pertussis-tetanus (DPT) vaccine rose to forty times its initial price.[67]

A BETTER CHOICE: ADMINISTRATIVE COMPENSATION

Although we argue that state tort liability does not enhance the safety of products already reviewed and approved by the FDA, we readily admit that ensuring the safety of products is not the sole normative function of the tort law, as we noted in the introduction. At its base, tort law is about compensating injured parties; and an aggressive preemption of state tort-law claims should perhaps entail the establishment of an alternative method for compensating those injured by unforeseen drug side effects, the Type I errors that are inevitable regardless of the quality of regulatory review. Significantly, state tort law provides compensation to some injured claimants but only through an adversarial process that exacts extraordinarily high transaction costs.[68] Furthermore, while some claimants win "jackpot" awards, others, equally deserving, go without compensation entirely.

As a better means of compensating injuries caused by unforeseen drug side effects, we propose that Congress supplement broad preemption with an administrative review process that more quickly, fairly, and cheaply provides redress to injured consumers. Such a process need not be created out of thin air, for a long-standing and successful program already exists for one class of pharmaceuticals—vaccines. It was established by Congress in the mid-1980s and is called the Vaccine Injury Compensation Program (VICP). A brief history would be instructive.

Vaccines are justly described as one of the greatest innovations of modern medicine. Prior to their invention and widespread use, human beings were largely defenseless against the ravages of smallpox, polio, and influenza epidemics. Survival guaranteed immunity to those lucky enough to weather the infection, but subsequent generations would inevitably succumb to fresh attacks.[69]

In the mid-1970s, a British research team claimed that it had scientific evidence that the pertussis (whooping cough) vaccine could cause permanent neurological damage in children. The study, although later discredited, panicked parents and sent immunization rates in England plummeting.[70] The U.S. media spread the claims, leading personal-injury lawyers to launch a wave of lawsuits against vaccine manufacturers. A series of high-value damage awards against manufacturers of the diphtheria-pertussis-tetanus and polio vaccines led

many companies to decide that the costs of staying in the market outweighed the benefits, and they exited the field—creating persistent vaccine shortages.[71]

Congress determined that since the societal benefits of vaccination are considerable—so considerable, in fact, that states require children in school or day care to be immunized—and the risks small, an administrative compensation program should be created for the protection of the small fraction of vaccine recipients harmed by vaccines. The program was also designed to protect the vaccine industry from destructive litigation and ensure a steady supply of new and innovative vaccine products. In 1986, Congress passed the National Childhood Vaccine Injury Act (NCVIA), which created the VICP.[72]

The program is relatively simple. The VICP is jointly administered by the Department of Health and Human Services and the Department of Justice, with attorneys from the DOJ representing HHS in proceedings before the court that hears vaccine claims, the U.S. Court of Federal Claims.[73] The VICP is designed as a no-fault program that covers all vaccines recommended by the Centers for Disease Control for routine administration to children. The program maintains a list of validated vaccine injuries on a "Table" that is updated as new evidence emerges, as well as an expert-witness program that provides the administrators with objective medical information.

If a covered vaccine is the alleged cause of the harm, claimants must file a claim with the VICP. Judicial remedies are available, but claimants must exhaust their administrative remedies before pursuing them.[74] Provided that the claim is a reasonable one and brought in "good faith," the VICP will cover attorneys' fees and any other evidentiary costs incurred by claimants, regardless of whether the claim is upheld.

Claimants can receive an award if they meet one of three tests: if an injury that is listed on the Table as being caused by vaccines occurred within an allotted time frame; if the vaccination significantly aggravated an existing condition; or if the claimant can prove that an injury (even if not listed on the Table) was directly caused by the vaccine. As noted previously, the VICP is a no-fault program, so claimants need not show any fault or negligence on the part of the manufacturer to recover. Moreover, for Table injuries, even causation questions require only minimal proof: claimants receive compensation automatically, as long as they can demonstrate that they were, in fact, injured and that their injury manifested itself in the listed time frame after a vaccination. Funding for the program is provided by an excise tax of 75 cents on every vaccine dose sold in the United States.

The NCVIA also established the Vaccine Adverse Event Reporting System (VAERS), created by the CDC and the FDA in 1990. This is a passive reporting system that allows the FDA and the CDC to monitor vaccines for possible new side effects, identify patient risk factors for side effects, and assess the safety of new vaccines down to the level of specific vaccine lots. According to the CDC, more than 30,000 VAERS reports are filed annually, with 10–15 percent classified as serious.[75]

The VAERS cannot, however, establish causation because the information collected is relatively incomplete. As information technology has improved, vaccine researchers have turned to "large linked databases" (LLDB), often held by insurers, to conduct tests of safety signals (indications of possible adverse events) that passive reporting systems like the VAERS have identified. Perhaps the leading vaccine LLDB is the Vaccine Safety Datalink (VSD), a program operated by the CDC and eight large managed-care organizations covering more than 6 million lives.[76] The VSD allows researchers to test safety hypotheses that have been generated elsewhere to determine whether the initial reports are epidemiologically credible.[77] In one recent example, after the VAERS received several reports of sudden deaths suggested to be linked to the cervical-cancer vaccine Gardasil, the VSD examined the records of 190,000 women and girls who had received at least one dose of the vaccine and found that there was in fact no association between the vaccine and such serious medical events as seizures, blood clots, and strokes.[78]

The VICP, while not perfect, has sustained a reputation for fair and timely compensation compared with that offered by the tort system. The Health Resources

and Services Administration reports that from 1990 to 2009, the VICP spent over $913 million on 1,086 compensated claims, indicating large awards for a relatively small number of children with serious injuries.[79] A 2005 federal government assessment of the program found that the vast majority of VICP outlays went directly to injured claimants; only 3 percent was spent on attorneys' fees and 11 percent on administrative costs. The assessment estimated that "transaction costs are reduced by as much as 56 percent in comparison to the tort system."[80]

While the VICP has played a substantial role in maintaining the health of the vaccine industry and offering compensation to injured claimants, it has also provided a test case for critics' claims that only the risk of exorbitant litigation provides companies with incentives to develop safer products. The record shows that the VICP has not in any way weakened market-based incentives the industry already has to improve safety further and otherwise innovate. Since the creation of the VICP, companies have continued to invest in the development of new and safer vaccine technologies such as subunit and conjugate vaccines; improved and modernized their vaccine manufacturing capacity; and brought valuable new vaccines to market. For instance, a safer acellular pertussis vaccine has replaced the whole-cell vaccine in the DTP formulation. Rotateq, a new vaccine for rotavirus, was licensed for sale after an earlier formulation was withdrawn out of safety concerns. Gardasil, the first vaccine proved to prevent cancer in humans, was licensed in 2006.

As long as vaccine manufacturers operate in a stable market that rewards innovation without the threat of destructive lawsuits based on flawed science and in a vaccine-reporting environment that quickly updates physicians, patients, and researchers on genuine adverse events, companies have powerful incentives to invest in new vaccine technologies. Indeed, companies can refer to the quality and safety of their products in pressing their case for higher reimbursements from public and private insurers.

Given the success of the VICP, the question naturally arises whether the program could and should serve as a template for administrative redress of injuries from all drugs and medical devices. We believe that the logic supporting the VICP can largely be extended to pharmaceuticals:

- Like vaccines, drugs as a group have enormous public health value.
- The testing, development, and marketing of both drugs and vaccines are extensively regulated by the FDA.
- Experts recognize that it is impossible to attain absolute safety and that patients benefit from drug innovation and price competition.

Given the parallels, as well as society's strong interest in spurring pharmaceutical innovation, policymakers should consider implementing an administrative compensation system for pharmaceuticals similar to the VICP.

Attributing adverse events to drugs, however, poses unique challenges. Since vaccines are given primarily to healthy individuals, it is usually possible to link a severe side effect to an administered vaccine and not an underlying health condition. Drugs, particularly those used to control chronic illnesses such as diabetes and heart disease, by contrast, are taken by individuals whose health is already substantially compromised, making it more difficult to say definitively that the root cause of an adverse event was drug treatment. Thus, policymakers would have to consider carefully the classes of individuals and injuries to be covered under any compensation program. If they did not, the program would overcompensate some individuals and thus discourage pharmaceutical companies from developing treatments for certain diseases.

While we do not undertake to prescribe such a program in detail here, we do think that an administrative compensation should possess the following features:

Field Preemption of Pharmaceutical Claims

Though we believe that the Supreme Court has erroneously limited conflict preemption in drug failure-

to-warn cases (see discussion of *Wyeth v. Levine*, above), an administrative compensation program for pharmaceuticals would be problematic—and perhaps worse than the status quo—unless coupled with *field* preemption for all drugs and devices. Were a substantial administrative remedy designed to operate alongside only narrow conflict or obstacle preemption rules, each case would face a separate trial-court factual determination. Some courts, of course, would find that state law had not been preempted, which would render the new alternative program merely an additional compensatory and regulatory scheme and reinforce the existing tendency toward Type II errors.[81] Even if courts regularly found that tort claims were preempted, the benefits of the administrative system would be substantially compromised by the significant expenses of responding to claims filed in court.[82] (Tellingly, the VICP itself has been subjected to end-run attacks by the plaintiffs' bar, particularly in the form of discredited claims that thimerosal, which the lawyers argued falls outside the VICP because it is a preservative rather than an actual vaccine,[83] is linked to autism.[84]) .

Limitation of Most Claims to Unforeseen Adverse Events

In some respects, vaccines are unlike other pharmaceuticals or medical devices. While vaccines generate clear positive externalities (i.e., unvaccinated individuals benefit from the vaccines others take), they also are subject to a "free rider" problem: the cost-free inclination of some individuals to avoid vaccination because they can enjoy the same protection as those who have been vaccinated, assuming almost everyone has done so and the disease is dormant.

The VICP tries to induce participation by those who might otherwise become free riders by promising to compensate them when they succumb to the rare adverse event. Since society as a whole benefits from the "herd immunity" conferred by vaccines, it seems logical and fair to compensate them even when their injures were foreseeable.

Many drugs, however, are designed to improve an individual's health without offering the broad positive externalities of vaccines. Thus, unless the medication in question was deemed essential to stopping the spread of a dangerous, communicable disease, the individuals taking it should *not* be compensated by an administrative review process for the side effects they suffered, assuming that the FDA knew of them and that they were described on the label.

A well-designed system limiting compensation to claims arising from injuries that were not anticipated by the FDA would have the salutary effect of encouraging drug manufacturers to disclose adverse events as they occurred during routine use. Such incentives would be reinforced if the administrative panel refused to compensate individuals harmed by side effects that manufacturers had voluntarily disclosed in reasonably clear language on drug labels before the FDA approved the final wording.[85]

Clearly Defined Causation and Injury Requirements

The VICP has quite low administrative costs because the inquiries it conducts need not consider questions of fault or negligence and because questions of injury and causation are relatively easy to resolve in the case of vaccines. As previously discussed, even a no-fault system for compensating individuals for the unforeseen side effects of pharmaceuticals would probably be more difficult and expensive to administer. Seriously ill or injured individuals will often develop additional ailments or injuries, with or without medical treatment. A drug's mere association with an adverse event—as, say, Vioxx usage is associated with heart problems—does not imply that it was the cause. Isolating a drug's impact from other confounding factors is difficult: Did Vioxx cause the heart attack, or was it chiefly or exclusively attributable to an individual's age, obesity, or lifetime of smoking?

Despite these difficulties, there is little reason to think that an administrative compensation system would be less adept at handling these questions than a lay jury, which in essence must weigh the same factors. Compared with the tort system, a good administrative system has the advantage of statistical precision and predictability. As with the VICP, various adverse

outcomes, once established with statistical confidence as having been drug-induced, would be added to a table of recoverable injuries. Individuals who took the drug before the adverse event or contraindication was listed on the label could make a claim for compensation. Those individuals would then have the burden of proving that the drug caused their injury, and the agency could consider the relative risk factors of the drug as well as various confounding factors in those individuals' medical history, such as age, weight, smoking, or preexisting conditions. Once a determination of injury was made, the agency would determine economic damages and the monetary value of noneconomic injury, with various injuries receiving fixed payouts according to schedules, as in workers' compensation systems. As with the VICP, administrative compensation decision makers should not be the same people as the FDA decision makers responsible for original drug approval and labeling, so as to avoid even the appearance of a conflict of interest.

System Funding

Although the VICP is funded by a simple tax on all vaccines, it might not be appropriate to extend such a funding mechanism to all drugs and devices, given their widely varying costs and benefits. Because an administrative compensation system beyond vaccines would apply to unforeseen, rather than known, side effects, system costs would most appropriately fall upon those manufacturers making the riskiest products. Such determinations would be difficult to make *ex ante*, almost by definition. Thus, drug and device taxes to fund the system should initially be allocated on the basis of market share. However, historical controls and improved data mining should eventually enable the program to "risk adjust" manufacturers' tax burdens on the basis of the size of the payouts to the users of their respective products, thereby encouraging manufacturers to pursue innovations in product design and delivery.

Independent Post-Market Drug Monitoring

Expansion of the FDA's ability to monitor drugs in a post-market environment—and more rapidly learn of unknown side effects or expand label indications on the basis of emerging benefit information—is a laudable goal in itself. As already outlined, the tort bar lacks the expertise, incentives, and infrastructure to explore the risks and benefits of new drugs in a credible way, and tort lawsuits tend on balance to compromise rather than complement the FDA's post-market surveillance.

The FDA Amendments Act of 2007 has already substantially strengthened the FDA's ability to identify and address safety-related issues in the post-market environment.[86] New agency powers include the ability to require manufacturers to make labeling changes and to require that companies implement additional controls or conduct studies of newly launched drugs through the use of a set of tools collectively known as Risk Evaluation and Management Strategy.[87]

A program like the VICP, by keeping extensive records of adverse drug events, would meaningfully supplement the FDA's new powers. The growing prevalence of information technology and sophisticated data-mining programs would enable regulators to quickly identify underlying trends that could then be subjected to further analysis and testing. As with the administrative compensation system, the post-market review process should be separate from the FDA decision makers responsible for original drug approval and labeling. Were the *ex post* reviewers the same individuals as the *ex ante* regulators, inevitably there would be individual and institutional incentives to ignore past mistakes. In addition, the post-market review process should be funded by a source other than the excise revenues that support the administrative compensation process, both to avoid the appearance of a conflict of interest and to ensure that the highest-quality science is used to study potential drug side effects and identify compensable individuals.

Remaining Tort-Law Remedies

Even though a well-constructed administrative compensation scheme would not offer a remedy to individuals affected by known side effects, they would retain the right to sue health-care providers for malpractice in the prescription of a contraindicated drug, or for the improper administration of a drug or device.

(As discussed, such remedies were available in both *Riegel* and *Levine*). These legal options are important forms of protection for unsophisticated consumers, who must rely on learned intermediaries.

A remaining question is what remedy might be available to individuals harmed by a drug or device as the result of a manufacturer's fraud on the FDA. Under the U.S. Supreme Court's *Buckman* decision,[88] "fraud-on-the-FDA" cases, being deemed to conflict with the FDA's rulemaking process, are preempted. In our view, *Buckman*'s holding is crucial to protecting the FDA's independence. Even if the FDA itself has determined that an applicant committed fraud, permitting fraud-on-the-FDA lawsuits as an exception to the broad field preemption that we are proposing would open the agency repeatedly to political pressure. To open the door to possible litigation, trial lawyers and their allies in Congress would inevitably press the agency to declare that a manufacturer had hoodwinked the agency. Preferably, the FDA would police fraud through normal channels, civil and criminal. Anyone injured in cases in which the FDA identified fraud should have recourse to the administrative compensation program. (In the event Congress decides to permit state-law tort cases to proceed in instances of fraud on the agency, it should do so only upon a formal FDA declaration.[89] Otherwise, the exception would swallow the rule by allowing even the feeblest suit to proceed, so long as it merely alleged that the agency had been defrauded.)

CONCLUSION

The FDA is far from perfect at protecting the public health. While the agency necessarily fails to identify some harmful side effects that have serious and often deadly consequences, it also creates serious and deadly social harms in rejecting, delaying, and overwarning about the drugs and devices that it considers for approval. There is both a theoretical and an empirical basis for believing that the agency has greater incentives to err on the side of caution, thus generating the latter, Type II errors and exacting a social cost that well exceeds that of previously undiscovered side effects—a calculus belied by the much more intense publicity and scrutiny that Type I mistakes often receive.

The imposition of state tort liability on top of the FDA regulatory process increases the perverse social effects of agency's Type II bias. Moreover, in many instances, state tort law directly contradicts the FDA's considered decisions. Product-liability directives can vary from state to state—indeed, from courtroom to courtroom—and jurors' decisions are impaired by a lack of expertise, hindsight bias, and rules that prohibit the very kind of social cost-benefit analysis that the FDA is obliged to employ. Rather than serving as a useful adjunct or complement to the FDA, state tort law in this field tends merely to retard innovation and raise consumer prices.

The FDA's overarching regulatory scheme argues for greater preemption of state common-law actions that conflict with FDA decisions than courts have yet recognized. Unfortunately, legislative forces are moving in precisely the opposite direction. Congress is considering legislation that would eliminate essentially all preemption of state tort actions concerning FDA-regulated drugs and devices, notwithstanding the U.S. Supreme Court's decision in *Wyeth v. Levine* limiting the scope of FDA preemption.

Preempting state tort claims does not preclude compensating individuals genuinely injured by unforeseen side effects. The successful Vaccine Injury Compensation Program offers a template from which Congress could construct a compensation program that offers a rapid and reliable remedy for adverse events inevitably caused by some pharmaceuticals. Even though inquiries into causation would be more complicated under an administrative program that included all pharmaceuticals, a workable system could be developed that would compensate drug injuries more quickly and fairly than the tort system. And, of equal importance, industry would retain powerful incentives to produce medical innovations of ever greater safety.

Endnotes

1. This is not to say that many agency procedures—from placebo-controlled trials in developing countries to terminal cancer patients' access to experimental drugs in the United States—are not subject to frequent criticism. For example, see Jonathan Kimmelman, Charles Weijer, and Eric M. Meslin, "Helsinki Discords: FDA, Ethics, and International Drug Trials," *The Lancet* 373, no. 9657 (January 3, 2009): 13–14; and Ronald L. Trowbridge and Steven Walker, "The FDA's Deadly Track Record," *Wall Street Journa*l, August 14, 2007.

2. See the FDA's Mission Statement at http://www.fda.gov/opacom/morechoices/mission.html.

3. The ancient Greeks recognized the dilemma facing physicians: they used the same word for medicine and poison, *pharmakon*.

4. See Tomas J. Philipson and Eric Sun, "Is the Food and Drug Administration Safe and Effective?," *Journal of Economic Perspectives* 22, no. 1 (winter 2008): 85: "Compared to many other regulatory agencies, relatively little research has been done by economists on the efficiency trade-offs involved with the FDA.… If a product application was supplied to the FDA with the scant amount of analysis that currently exists on the efficiency or performance of the policies of the agency itself, such an application would clearly be rejected on the basis of insufficient evidence."

5. Silicone breast implants were blamed for connective-tissue disease by trial lawyers and ultimately removed from the market, notwithstanding scientific evidence that showed "no association between implants and the connective tissue diseases and other disorders that were studied." Sherine E. Gabriel et al., "Risk of Connective-Tissue Diseases and Other Disorders after Breast Implantation," *New England Journal of Medicine* 330 (June 16, 1994): 1697-1702. SSRIs antidepressants received a severe "black box" label after high-profile lawsuits alleged that the drugs caused adolescents to commit suicide.

6. See, e.g., Troyen, A. Brennan, et al., "Incidence of Adverse Events and Negligence in Hospitalized Patients: Results of the Harvard Medical Practice Study I & II," *New England Journal of Medicine* 324 (1991): 370-84; Tillinghast-TowersPerrin, *U.S. Tort Costs: 2003 Update, Trends and Findings on the Cost of the U.S. Tort System* (2003): 17; Joseph N. Gitlin, et al., "Comparison of 'B' Readers' Interpretations of Chest Radiographs for Asbestos Related Changes," *Academic Radiology* 11(2004): 243; Alison Frankel, "The Fen-Phen Follies," *The American Lawyer*, March 1, 2005, available at http://www.law.com/jsp/article.jsp?id=1109597691121.

7. We do believe that serious critiques of state tort law can be made across the field of product liability (cf. the Federal Product Liability Fairness Act of 1998), but the statutory scheme of federal regulation varies widely across different economic sectors, thus affecting the case for preemption. Few economic activities are as heavily regulated by the federal government as are drugs and medical devices; and our view is that in light of the extensive regulation in this area, state common law should be broadly preempted by the Food, Drug, and Cosmetic Act, as are labor-management relations by the Labor Management Relations Act and employee pensions by the Employee Retirement Income Security Act.

8. Based on 2006 data from the Centers for Medicare & Medicaid Services (2008), available at http://www.cms.hhs.gov/ResearchGenInfo/, at Table III.7.

9. Joseph A. DiMasi, Ronald W. Hansen, and Henry G. Grabowski ("The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* 22 [2003]: 151–85) estimate a total pre-approval cost of over $800 million. Two of the same authors later estimated the total development cost of a biotechnology product at $1.2 billion. See Joseph A. DiMasi, Henry G. Grabowski "The Cost of Biopharmaceutical R&D: Is Biotech Different?," Managerial and Decision Economics 2007; 28 (4-5): 469-479. See also Benjamin Zycher, Joseph A. DiMasi, and Christopher-Paul Milne, "The Truth About Drug Innovation: Thirty-Five Summary Case Histories on Private Sector Contributions to Pharmaceutical Science," Manhattan Institute, Medical Progress Report no. 6 (June 2008), available at http://www.manhattan-institute.org/html/mpr_06.htm.

10. See http://www.phrma.org/innovation.

11. In pharmacology, ADME is an acronym for "absorption, distribution, metabolism, and excretion."

12. Testimony before the U.S. Senate Committee on Health, Education, Labor, and Pensions, March 1, 2005. Available at http://www.aei.org/publications/pubID.22055,filter.all/pub_detail.asp.

13. See John E. Calfee et al., "Supreme Court Amicus Brief Regarding *Wyeth v. Levin*e" (June 3, 2008): "Because the harmful side-effects of the drug may be highly visible, a Type I error can and often does lead to impassioned criticism of the agency. On the other hand, a Type II error—the failure to permit marketing of a drug that would in fact provide benefits in excess of harms—is typically known only to the relatively few persons who are intimately involved in developing the drug and are largely hidden from patients and the larger medical community." Available at www.aei.org/publication28133.

14. Aaron S. Kesselheim and Jerry Avorn, "The Role of Litigation in Defining Drug Risks," *JAMA* 297, no. 3 (January 17, 2007): 308–11, at 308.

15. See also Catherine D. DeAngelis and Phil B. Fontanarosa, "Prescription Drugs, Products Liability, and Preemption of Tort Litigation," *JAMA* 300, no. 16 (2008): 1939–41; and Lawrence O. Gostin, "The Deregulatory Effects of Preempting Tort Litigation: FDA Regulation of Medical Devices," *JAMA* 299, no. 19 (2008): 2313–16; Gregory D. Curfman, Stephen Morrissey, and Jeffrey M. Drazen, "Why Doctors Should Worry about Preemption," *New England Journal of Medicine* 358, no. 1 (July 3, 2008): 1–3. None of these authors provides any systematic or objective evidence that any aspect of the FDA's existing regulatory authoritiy has a *net* negative impact on patient health, or that litigation addresses the alleged deficiencies of the existing post-market drug-safety reporting system. Instead, they focus on specific instances of FDA approval or slow withdrawal of "unsafe" drugs.

16. Daniel J. DeNoon, "Did FDA Teen Suicide Warning Backfire?" WebMD Health News, September 13, 2007. Available at http://www.medicinenet.com/script/main/art.asp?articlekey=83878. See also Jens Ludwig, Dave E. Marcotte, and Karen Norberg, who analyzed data from twenty-six countries on the effects of SSRI sales on suicide mortality rates and conclude that "an increase in SSRI sales of one pill per capita (about a 12 percent increase over 2000 sales levels) is associated with a decline in suicide mortality of around 5 percent" ("Anti-Depressants and Suicide," NBER Working Paper 12906, February 2007, available at http://www.nber.org/papers/w12906).

17. Alternatively, even when a serious side effect is discovered in the post-market environment, it is not necessarily the case that the agency has committed a Type I error. Take the case of Vioxx: for many patients with severe

rheumatologic illness, Vioxx was a treatment that substantially increased quality of life. Vioxx's withdrawal in the face of litigation threats left these patients without a good alternative, or at least the choice to use the drug once they had given their informed consent. In many cases, better information—not market withdrawal—is in the best interest of patients. For some sense of the trade-offs facing patients and physicians, see Benjamin Brewer, "Doctor Struggles to Help Vioxx-Deprived Patients," *Wall Street Journal*, November 23, 2004. Available at http://www.collegejournal.com/article/SB110113543945680878.html.

18. See Sam Peltzman, *Regulation of Pharmaceutical Innovation: The 1962 Amendments* (American Enterprise Institute, 1974); William M. Wardell and Louis Lasagna, *Regulation and Drug Development* (American Enterprise Institute, 1975); and K. I. Kaitin and Jeffrey Brown, "A Drug Lag Update," *Drug Information Journal* 29 (1995): 361–73.

19. Fran Hawthorne, *Inside the FDA: The Business and Politics Behind the Drugs We Take and the Food We Eat* (Hoboken, N.J.: Wiley, 2005), p. 54.

20. Philipson and Sun, "Is the Food and Drug Administration Safe and Effective?."

21. T. Philipson, E. Berndt, A. Gottschalk, and M. Strobeck, "How Safe Is Too Safe?," *The Milken Review* 2 (2006): 38–46, at 44.

22. Ibid, p. 45.

23. Federal law is supreme, assuming that it is enacted pursuant to a constitutional grant of authority. See U.S. Const. art. VI, cl. 2 ("[T]he Laws of the United States [are] the supreme Law of the Land").

24. *Rice v. Santa Fe Elevator Corp.*, 331 U.S. 218, 230 (1947).

25. Ibid. (citations omitted).

26. Richard A. Epstein, "The Case for Field Preemption of State Laws in Drug Cases," *Northwestern University Law Review Colloquy* 54 (2008): 55.

27. Ibid.

28. Testimony of Randolph D. Moss, July 14, 1999, U.S. Senate Committee on Government Affairs.

29. See Richard A. Epstein, "Why the FDA Must Preempt Tort Litigation: A Critique of *Chevron* Deference and a Response to Richard Nagareda," *Journal of Tort Law* 1 (2006): 5.

30. See Katherine M. Glaser, "A Step Toward Preemption: The Effect of the FDA's 2006 Preamble," *Temple Law Review* 80 (2008): 877 & n. 62 (collecting cases).

31. See ibid. at 882–85 (citing Mark C. Levy and Gregory J. Wartman, "*Amicus Curiae* Efforts to Reform Product Liability at the Food and Drug Administration: FDA's Influence on Federal Preemption of Class III Medical

Devices and Pharmaceuticals," *Food and Drug Law Journal* 60, no. 4 [2005]: 495); see, e.g., Amicus Brief for the United States in Support of the Defendant-Appellee and Cross-Appellant, and in Favor of Reversal of the District Court's Order Denying Partial Summary Judgment to Defendant-Appellee and Cross-Appellant, Motus v. Pfizer, Inc., 358 F.3d 659 (9th Cir. 2002) (Nos. 02-55372, 02-55498), 2002 WL 32303084, at *17.

32. Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products, 71 Fed. Reg. 3922, 3934 (January 24, 2006) (codified at 21 C.F.R. pts. 201, 314, 601).

33. 21 U.S.C. §360k(a).

34. See *Riegel v. Medtronic, Inc.*, 128 S. Ct. 999 (2008).

35. See Wyeth's petitioner's brief (2008), at 20.

36. 21 C.F.R. § 314.70(c)(6)(iii)(A), (C). Some academic commentators have seized upon the codification of such language in the Food and Drug Administration Amendments Act of 2007 to argue against preemption of state-law claims. See, e.g., David A. Kessler & David C. Vladeck, "A Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims," *Georgetown Law Journal* 96 (2008): 461 (cited in *Wyeth v. Levine*, No. 06-1249, slip op. at 23 n. 12 (U.S. March 4, 2009)).

37. 47 Fed. Reg. 46,623.

38. See *Levine*, slip op. at 12 (citing 47 Fed. Reg. 49,604).

39. Ibid., at 13.

40. See Epstein, *supra* n. 26, at 59.

41. The majority opinion also relied on Congress's 1976 preemption language in the Medical Devices Amendments, 21 U. S. C. § 360k(a), as a rationale for its determination that Congress did not intend that the FDCA preempt state tort claims in cases like Levine's: "Its silence on the issue, coupled with its certain awareness of the prevalence of state tort litigation, is powerful evidence that Congress did not intend FDA oversight to be the exclusive means of ensuring drug safety and effectiveness." *Levine*, slip op. at 18. While the 1976 Medical Devices Amendments did post-date the expansion of state product liability, including failure-to-warn suits, there was nothing the court cited in its opinion to suggest that Congress considered *any* amendments to the broader FDCA apart from the special regulations it was enacting particularly for medical devices. Assuming that Congress deliberately failed to enact a broader substantive statutory revision in the course of enacting a more specific subordinate statute displays an extreme naïveté about the log-rolling processes involved in legislative action. See generally James M. Buchanan & Gordon Tullock, *The Calculus of Consent: Logical Foundations of Constitutional Democracy* 132-46 (Ann Arbor, Mich.: University of Michigan Press, 1962) (discussing majority voting and log-rolling). Cf. Antonin Scalia, *A Matter of Interpretation: Federal Courts and the Law* 32 (Princeton, N.J.: Princeton University Press, 1997) ("It is much more likely to produce a false or contrived legislative intent than a genuine one. The first and most obvious reason for this is that, with respect to 99.99 percent of the issues of construction reaching the courts, there *is* no legislative intent . . . .").

42. 377 P.2d 897 (Cal. 1963).

43. Restatement (Second) of Torts § 402A, comment j (1965). Comment j of the Restatements went on to state: "[W]here warning is given, the seller may reasonably assume that it will be read and heeded; and a product bearing such a warning, which is safe for use if it is followed, is not in defective condition, nor is it unreasonably dangerous."

44. *Levine v. Wyeth*, 944 A.2d 179, 182 (2006), *aff'd*, No. 06-1249 (March 4, 2009).

45. See http://www.adaweb.net/Portals/0/Paramedics/documents/promethazine.pdf.

46. We do not mean to suggest that IV-push application of Phenergan should be limited to emergency-room situations. In fact, nurses and other medical professionals regularly administer the drug through IV-push, according to label specifications, without error. Whether the decision to administer Phenergan in Levine's case was medically warranted is beyond the scope of this paper.

    We also emphasize that even if the FDA erred in permitting the IV-push method of administering Phenergan—or not limiting its use more explicitly—the case for preemption here is strong, as long as on balance the FDA gets it right more often than not and shows a bias in favor of Type II errors, as the evidence suggests. That is, even if *some* juries correctly second-guess the FDA in *some* cases, the systemic bias created by an additional layer of review will favor Type II error and lower social welfare.

47. See Washington Legal Foundation and American College of Emergency Physicians (2008), amicus curiae supporting petitioner in *Wyeth v. Levine*, at 2.

48. See *Riegel*, 128 S. Ct. at 1005.

49. Ibid.

50. See Wyeth's petitioner's brief (2008), at 20. Levine did sue her physician's assistant, her doctor, and the clinic for malpractice, prior to suing Wyeth. After that suit settled, the physician's assistant wrote Levine a letter admitting "responsibility" for the tragedy.

51. Even if no compensation were warranted, it is our position that the regulatory and compensatory questions should be addressed separately. State courts and juries have a natural interest in assuring that patients injured by pharmaceuticals or medical procedures have some compensation for serious injuries—and companies ("deep pockets") may appear to a jury to be the only source of ready compensation available, even when there is no negligence or malpractice involved.

52. H.R. 6381 § 2(a) (2008).

53. See Press Release, "Health Leaders Introduce Legislation Reversing Supreme Court's Medical Device Decision," March 5, 2009.

54. For simplicity's sake, in this paper, we adopt a straightforward utilitarian calculus, under which the substantially

higher cost of Type II errors caused by FDA regulation easily outweighs the cost of Type I errors permitted by the FDA. Some might instead prefer making a philosophical distinction between sins of commission and those of omission. Such niceties are not easily applied to this case, since a Type I or Type II error may be caused by either action or omission, depending on the identity of the referent actor: for a Type I error, the manufacturer acts but the FDA fails to act; for a Type II error, the FDA acts and prevents the manufacturer from acting.

55. Juries' weakness at handling scientific evidence exists in many product-liability cases, not merely those involving the FDA. Improving the use of scientific evidence in the courts has been the subject of multiple books; see, e.g., Peter W. Huber and Kenneth R. Foster, *Judging Science: Scientific Knowledge and the Federal Courts* (Cambridge, Mass.: MIT Press, 1997); Peter W. Huber, *Galileo's Revenge: Junk Science in the Courtroom* (Basic Books, 1991), and courts have labored to improve the evidence presented to juries; see, e.g., *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993).

56. Philipson and Sun, "Is the Food and Drug Administration Safe and Effective?," p. 99. The logic here is that consumers as a result pay higher prices for pharmaceutical products and bear the costs of forgone innovation.

57. See Lester Brickman, "Effective Hourly Rates of Contingency Fee Lawyers: Competing Data and Non-Competitive Fees," *Washington University Law Quarterly*, 81 (2003): 653.

58. See John H. Beisner & Jessica Davidson Miller, "They're Making a Federal Case Out of It . . . In State Court," *Manhattan Institute Civil Justice Report* No. 3 (2001).

59. *See* Frankel, supra n. 5.

60. There is currently no drug in the United States that is labeled specifically for treating pregnant women who have nausea. A variety of drugs are used off-label, and companies have no incentive to perform clinical studies on such uses or develop new drugs for this indication because of litigation risks.

61. In 2008, after vaccination rates declined, the U.S. experienced the largest measles outbreak since 1996. See CDC's MMWR report for August 22, 2008. Out of the 135 documented sufferers, 112 were unvaccinated or had unknown vaccination status, with over 66 percent of these unvaccinated on account of religious or "philosophical" exemptions. In Great Britain, vaccination rates plummeted after *The Lancet* published a study in 1998—long since discredited (see John Harlow, "MMR Row Doctor Andrew Wakefield Spreads Fear to US," *Sunday Times*, September 28, 2008)—linking the MMR vaccine to autism. On April 3, 2006, the *London Times* reported:

    > Immunisation rates [in Britain], eight years after the first scare over the combined measles, mumps and rubella (MMR) vaccine, are among the lowest in Western Europe. Fears that the triple jab could lead to autism caused take-up to fall from over 90 per cent in 1998 to less than 80 per cent two years ago. Currently, 81 per cent of children have the combined vaccine before they are two; many European countries achieve the 95 per cent coverage recommended by the World Health Organisation to prevent outbreaks.

    Available at http://www.timesonline.co.uk/tol/news/uk/health/article701459.ece.

62. See Washington Legal Foundation and American College of Emergency Physicians (2008), amicus curiae supporting petitioner in *Wyeth v. Levine*.

63. Gostin, "The Deregulatory Effects of Preempting Tort Litigation," p. 2315. See also Kessler & Vladeck, "A

Critical Examination of the FDA's Efforts to Preempt Failure-to-Warn Claims" (2008).

64. As we noted earlier, the FDA has strong incentives toward making Type II errors, and its regulation is likely to be overly burdensome as a result.

65. See Philipson and Sun, "Is the Food and Drug Administration Safe and Effective?," at 93 ("Given that the FDA's mandated level of [product safety] investment is binding, product liability in this case does not have additional deterrence effect beyond the FDA's regulations. However, product liability raises firms' costs and therefore product prices, since it requires firms to pay damages to consumers, and this increase in price for no corresponding gain in product safety reduces social welfare.").

66. See Richard L. Manning, "Changing Rules in Tort Law and the Market for Childhood Vaccines," *Journal of Law and Economics* 37 (1994): 273; idem, "Products Liability and Prescription Drug Prices in Canada and the United States," *Journal of Law and Economics* 40 (1997): 234.

67. See idem, "Changing Rules in Tort Law and the Market for Childhood Vaccines."

68. See, e.g., Tillinghast Towers Perrin, supra n. 5, at 17.

69. The historian Roy Porter describes this as the "era of epidemics":

> The immediate invasion of a town by smallpox or another infection was a fulminating epidemic and subsequent decimation. Population recovery would then get under way, only for survivors' heirs to be blitzed by the same or a different pestilence, and yet another, in tide upon tide… . With almost everybody slain or immune, the pestilence would withdraw … moving on to storm other virgin populations, like raiders seeking fresh spoils.

(*The Greatest Benefit to Mankind: A Medical History of Humanity* [New York: W. W. Norton, 1997], p. 23)

70. Paul A. Offit, *The Cutter Incident: How America's First Polio Vaccine Led to the Growing Vaccine Crisis* (New Haven, Conn.: Yale University Press, 2005).

71. Idem, "Why Are Pharmaceutical Companies Gradually Abandoning Vaccines?" *Health Affairs* 24, no. 3 (2005): 622–30.

72. National Childhood Vaccine Injury Act of 1986, 42 U.S.C. § 300aa-22:

> No vaccine manufacturer shall be liable in a civil action for damages arising from a vaccine-related injury or death associated with the administration of a vaccine after October 1, 1988, if the injury or death resulted from side effects that were unavoidable even though the vaccine was properly prepared and was accompanied by proper directions and warnings.

73. The Court of Federal Claims hears cases where citizens sue the federal government for monetary redress; the NCVIA gave the court jurisdiction over claims related to vaccine injuries. Placing the administrative compensation program under the Court of Federal Claims is significant because unlike general Article III courts, the Article I Court of Claims is not bound by Seventh Amendment jury trial requirements.

74. VICP claims are tried before special masters who exclusively adjudicate vaccine injuries. Rulings can be appealed

to the Court of Federal Claims, and to the United States Court of Appeals for the Federal Circuit. Once remedies have been exhausted, VICP claimants can opt out of the program and initiate a traditional tort lawsuit by filing a motion rejecting the judgment. Perhaps because VICP processing is expeditious and claimants in the system need not show fraud or negligence, such motions are uncommon: in the eight years following passage of the NCVIA, only seventy claimants out of 3,142 adjudicated in the system opted out. See Thomas F. Burke, *Lawyers, Lawsuits, and Legal Rights: The Battle over Litigation in American Society* (Berkeley, Cal.: University of California Press, 2002), at 163.

We note that an effective administrative compensation system for all drugs and medical devices could not have the liberal opt-out rules of the VICP because the inquiries will have to examine more complicated questions of causation, as we discuss below in more detail. Because Congress has the power to preempt tort litigation in this area in its entirety, it also can make our proposed administrative compensation system an exclusive remedy, subject to caveats that we discuss below.

75. See http://www.cdc.gov/vaccinesafety/vaers.

76. See http://www.cdc.gov/vaccinesafety/vsd.

77. R. T. Chen et al., "The Vaccine Safety Datalink: Immunization Research in Health Maintenance Organizations in the USA," *Bulletin of the World Health Organization* 78, no. 2 (2000): 186–94.

78. Aliza Marcus, "Merck's Gardasil Isn't Linked to Risks in U.S. Study," Bloomberg News, October 22, 2008. Available at http://www.bloomberg.com/apps/news?pid=20601124&refer=home&sid=aiu3HUxq2GEo. The FDA also reports:

    Concerns have been raised about reports of deaths occurring in individuals after receiving Gardasil. As of June 30, 2008, 20 deaths had been reported to VAERS. There was not a common pattern to the deaths that would suggest they were caused by the vaccine. In cases where autopsy, death certificate and medical records were available, the cause of death was explained by factors other than the vaccine.

79. Source: http://www.hrsa.gov/vaccinecompensation/statistics_report.htm.

80. See the detailed assessment of the program at http://www.whitehouse.gov/omb/expectmore/detail/10003807.2005.html.

81. See James R. Copland, "Tragic Solutions: The 9/11 Victim Compensation Fund, Historical Antecedents, and Lessons for Tort Reform," January 13, 2005, available at http://www.manhattan-institute.org/pdf/clpwp_01-13-05.pdf ("As the experience with no-fault auto insurance makes clear, 'add-on' programs of this type tend to perform woefully by allowing potential claimants to opt for the highest-returning option between two parallel systems.").

82. In the American legal system, plaintiffs' lawyers have an incentive to file low-probability claims, and defendants have an incentive to settle them. See Marie Gryphon, "Greater Justice, Lower Cost: How a 'Loser Pays' Rule Would Improve the American Legal System," *Manhattan Institute Civil Justice Report* No. 11 (2008): 4-7 (discussing viability of "nuisance suits" under an American Rule system).

83. On February 12, 2009, the Special Master at the U.S. Court of Federal Claims overseeing omnibus claims alleging that thimerosal or the MMR vaccine caused autism ruled in several test cases that the evidence against such claims was "overwhelming." See Cedillo v. Secretary of Health and Human Services Case No. 98-916V (ftp://autism.uscfc.uscourts.gov/autism/vaccine/Hastings-Cedillo.pdf).

84. See Jim Copland, "Liable to Infection Flu Vaccine in Short Supply Partly Because of Trial Lawyers and 'Tort Tax,'" *Dallas Morning News*, December 14, 2003.

85. Drug manufacturers are allowed to modify drug labels in the light of new or emerging safety information, pending final FDA approval.

86. The act can be read in its entirety online at http://frwebgate.access.gpo.gov/cgi-bin/getdoc.cgi?dbname=110_cong_public_laws&docid=f:publ085.110.

87. For a critical appraisal of the FDA Amendments Act, and whether it continues the overemphasis on Type II errors, see John E. Calfee, "Reform without Reason: What's Wrong with the FDA Amendments Act of 2007," September 26, 2007. Available at http://www.aei.org/publications/filter.all,pubID.26859/pub_detail.asp.

88. *Buckman Co. v. Plaintiffs' Legal Committee*, 531 U.S. 341 (2001).

89. See ibid. at 354–55 (Stevens, J., concurring) (arguing for permitting fraud-on-the-FDA suits "[i]f the FDA determines both that fraud has occurred and that such fraud requires the removal of a product from the market").

PROJECT FDA

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Utilizing 21st Century technologies to help develop better FDA regulations and a faster and safer drug and medical device pipeline

The time and costs required to bring new medical products to market is growing ever larger. Today, it may take more than a decade and hundreds of millions of dollars to bring a single new medical product innovation to the public from initial conception to FDA approval. The slow pace and high cost of development contributes to the cost of health care and delays patient access to potentially lifesaving innovations.

At the same time, the FDA is facing a crisis in confidence among consumers, media and policymakers, with some critics declaring the agency "broken"—unable to ensure that medical products offered for sale in the U.S. are reasonably safe and effective. Doctors and academic medical centers, too, face growing concerns about allegedly harmful interactions with industry during the development and marketing of medical products. The result is a growing call for sweeping new regulation of the industry at both the state and federal levels.

Advances in the molecular and genetic understanding of disease have the potential to make health care more predictive and preventive rather than empirical and reactive—thus improving patient outcomes and reducing health care costs. Unfortunately, in our zeal to reduce risks, regulate potential conflicts, and mandate transparency, we may reduce incentives for companies to develop and market improved products due to increased tort litigation; inhibit doctors from collaborating with companies in designing safer and more effective products; and slow the FDA's efforts to bring its oversight activities into conformity with the latest scientific and technical advances.

The membership of Project FDA includes practicing physician–scientists, economists, medical ethicists and policy experts. Committee members will examine the current framework and direction of federal and state regulation to ensure that the medical innovation pipeline remains robust and that all stakeholders—including industry, academic medical centers, and regulators—are taking advantage of appropriate opportunities to bring safer and more effective products to market utilizing 21st Century technologies.

Issues that Project FDA will address include:

- Improve the ability of the FDA to collaborate with outside organizations to develop regulatory standards that are adapted to the latest scientific findings on clinical trial design, biomarkers, diagnostics and disease modeling that have the potential to speed patient access to groundbreaking new therapies
- Implement regulatory preemption for FDA approved labeling from state "failure to warn lawsuits" so that the FDA can make a national judgment about appropriate drug labeling and drug warnings
- Create a science-based administrative compensation program for drugs similar to the one currently used for vaccine related injuries so that patients who are injured by serious but unforeseen side effects receive appropriate and timely compensation
- Promote cost-benefit analysis of existing FDA regulations as they affect the "speed v. safety" tradeoff in the development and regulatory review of new medicines to ensure that they promote overall social welfare
- Educate the public and policymakers on the value of innovation and the need for close working relationships between academic medical centers, industry, and regulators in the quest to translate basic science discoveries into new cures; this also includes examining the impact of conflict-of-interest regulations on FDA Advisory Committees as well as on the ability of academic researchers to partner with industry to develop new therapies
- Increase FDA funding for Critical Path Initiative and related activities, which have the potential to revolutionize drug development and drug safety

http://www.manhattan-institute.org/projectfda