

Liability and Compensation for Adverse Reactions to HIV Vaccines

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Liability for personal injuries related to vaccines has been a matter of intermittent controversy for a quarter of a century (191, 201). Some pharmaceutical and biotechnology companies have said that the possibility of being liable for adverse reactions to vaccines or drugs may deter them from developing or distributing new products that could help reduce the spread of disease or its toll on the population (32, 160, 162, 209).

Although there is little evidence to prove or disprove the effect of potential liability on vaccine development, research on vaccines has lagged behind other pharmaceutical research, and several bodies have considered limiting the liability of vaccine makers in the hope of encouraging the continued development and sale of important vaccines (82, 140). Some have recommended a no-fault compensation system to largely replace liability litigation involving adverse reactions to vaccines (95). Congress enacted the National Childhood Vaccine Injury Act in 1986 (42 U.S.C. 300aa-10 et seq.) to establish a no-fault compensation program for injuries resulting from pediatric vaccines and to limit vaccine manufacturer liability for such injuries (115). Congressman Fortney “Pete” Stark circulated a proposal for a similar bill to create a no-fault compensation program for injuries arising from the use of any future vaccine to prevent AIDS (170).

In spite of decades of debate and several changes in state and federal laws, the controversy over liability for vaccine injuries has never been put to rest. In part, this may be because whether or how liability affects vaccine development has not been, and perhaps cannot be, measured empirically to reach reliable answers. But the controversy also reflects fundamental differences of opinion regarding responsibility for goods of social importance and responsibility for injury. Should government or private industry

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be responsible for ensuring the production of products that benefit society by preventing disease? Who should be responsible for injuries resulting from such products? Reasonable people may answer such questions quite differently. Even if they temporarily agree on a practical solution to a specific problem, the underlying political and ideological differences resurface with each new product that promises social benefit. Today they appear in a new debate over whether liability may deter companies from developing and marketing new vaccines to prevent HIV infection or progression to AIDS.

This chapter examines whether alternative injury compensation systems may facilitate the development and marketing of new vaccines to prevent HIV infection or AIDS. The first section of this chapter summarizes the possible goals of compensating people who experience adverse reactions to HIV vaccines. The second section reviews several factors that may deter private companies from developing an HIV vaccine and the possible influence of potential liability. The third section reviews basic concepts of tort liability applicable to personal injury and how they might apply to an HIV vaccine. The final section of this chapter considers alternatives for compensating adverse reactions to HIV vaccines and how they might affect the goals of HIV vaccine development and equitable compensation for injuries.

RESPONSIBILITY FOR INJURY AND COMPENSATION

Compensation systems can be classified into four broad categories on the basis of their organizational structure and the mechanism for determining who is entitled to what kind of compensation for what injuries and from whom: tort liability systems, voluntary contractual arrangements, public and private insurance systems, and administrative

compensation programs. The choice of system depends upon the goals to be accomplished by compensation. A threshold decision, therefore, is the need for or desirability of compensating injuries. Obviously, if there is no need to compensate injuries, there is no need to establish a compensation system. This section describes the reasons most commonly put forth for compensating injuries.¹

REASONS FOR COMPENSATING INJURIES

Injuries give rise to both physical and financial losses, as well as emotional turmoil. The injured person inevitably bears the physical consequences. Financial losses, however, may be shifted to someone else by requiring that party to compensate the victim with money.² These are the only choices available with respect to financial losses: leave them where they lie (with the injured person), or transfer all or part to someone else. With every type of injury, therefore, the question arises whether the financial losses should be shifted to someone else, and, if so, to whom. Compensation for injury has been justified for economic, philosophical or ethical, and pragmatic or social policy reasons.

■ Economic Reasons

Economists and legal scholars have argued both for and against compensating the victims of injury to achieve economic efficiency (26, 51, 80, 104, 161). The general idea is to minimize the total social costs of injury or maximize net social utility, taking into consideration both the benefits of a product or activity and the injuries it produces. Although opinions vary on what should be the optimal model, none necessarily requires that the number of injuries themselves be minimized. For example, it may be cheaper to pay compensation

¹ This section draws heavily upon Mariner, 1994 (116).

² Compensation may also take the form of in-kind services provided to the injured person, but because these have a monetary value and are ordinarily paid for with money, they will not be separately discussed.

for injuries than to modify a product to prevent the injuries.

Many conceptions of economic efficiency are difficult to apply in practice. Models based on perfect competition may not take into account how buyers and sellers behave in an imperfect world. Not everyone necessarily agrees on what counts as a benefit or a cost, especially where benefits and injuries fall on quite different segments of the population.

It is frequently assumed that companies can internalize the costs of injuries (recoup compensation payments) by raising the prices of their products, thereby spreading the costs over a large population. Even if compensation costs cannot be fully recouped from sales, the loss experienced by the company is relatively small when compared with the loss an uncompensated individual would suffer. Compensation then serves to spread the costs more equitably.

When injuries are frequent or severe enough to require a company to pay substantial costs that threaten its continued viability, it is ordinarily believed to be more economically efficient for a company to make the product safer, if possible, or cease producing the product. Some commentators have argued that this is economically inefficient if the product produces a significant social benefit (79). In theory, such an imbalance should not occur because the product's price should reflect its social benefit.

Economic analyses of loss allocation have influenced thinking about the nature of compensation, but have rarely been decisive on the question of whether compensation should be paid at all.³

That question is more often answered with reference to moral arguments about who should bear responsibility for the consequences of injury.

■ Ethical Reasons

Injury compensation has long been justified as the moral duty of those who are responsible for causing injury. It is perhaps the most widely accepted basis for legal liability in tort (59). Principles of justice derived from the works of such diverse scholars as Kant, Bentham, and Locke support compensation for injury caused by an identifiable entity.

There is, however, room for debate on what counts as causing injury and the circumstances in which moral responsibility for injury, and therefore compensation, should be ascribed. Depending upon the circumstances, compensation may be:

1. morally required, so that not providing it is unjust;
2. morally desirable as an act of virtue, but not morally required; or
3. not morally required and possibly unjust.

Swazey and Glantz offer a useful paradigm to describe why society may apply different moral rules to different injuries (179). They argue that social conceptions of moral or ethical obligations to human research subjects may vary depending upon whether the subjects are seen as victims, heroes, or contractors.⁴ Victims are characterized as those who have been misused or injured without their consent⁵ (9). They may be especially vulnerable or targets of exploitation who have few

³ For example, Philipson and Posner apply economic theory to the AIDS epidemic and conclude that the federal government "has no, or even a negative, stake in the development of treatments, such as the drug AZT, that merely prolong the lives of persons [with HIV because AZT] may increase the total medical costs by extending the period during which infected persons demand and receive treatment (138)." Fortunately, such reasoning has not halted AIDS treatment research.

⁴ Their analysis is directed only to compensation for research injuries. It is pertinent to this discussion, however, because it describes generalizable theories and because the question whether human subjects in clinical trials of candidate HIV vaccines deserve compensation will necessarily have to be addressed first.

⁵ Well-known research examples include subjects in the Tuskegee Syphilis Study (88), the Willowbrook Hepatitis B Study (90), and, more recently, radiation experiments conducted under the sponsorship of the Department of Energy (162, 188, 209).

means to avoid the injury in question. Victims have a strong moral claim to compensation, especially where society has facilitated the research or benefited by the use of a product (42, 200).

Heroes, in contrast, are seen as willing volunteers who assume risks in order to accomplish a goal, ordinarily for someone else's sake (179). Since heroes are not supposed to seek any reward, there is no obligation to compensate them. At the same time, society may wish to reward them voluntarily for their heroic efforts.

Contractors are often seen as businessmen striking a bargain (179). As long as the bargaining process is fair, contractors may be entitled to no more than they bargained for, and may be seen as seeking an unfair advantage if they later demand more. Thus, for example, those who voluntarily buy a product without initially contracting for compensation may have little, if any, moral claim to it later.

This paradigm offers some insight into why some people may view entitlement to compensation for vaccine-related injuries so differently. Those who focus on principles of distributive justice view vaccine recipients as benefiting society by preventing disease transmission. In this view, injured recipients who are perceived as victims are morally entitled to compensation and not providing it would be unjust. Recipients who are perceived as heroes, such as subjects of research in clinical trials, have a lesser claim, but compensation is a morally desirable act of caring for those who benefited society.

In contrast, those who focus on respect for persons and autonomous choices may perceive vaccine recipients as contractors with no moral claim to compensation. In this view, the recipient has agreed to assume the risks of vaccination (and has received its benefits), and providing compensation would be wrong because it does not respect the subject's autonomous choice. This is the effect of informed consent in tort law. A person who has agreed to vaccination with knowledge of any attendant risks (including the possibility of unknown risks) is not entitled to compensation if a disclosed risk materializes to his injury. As long as the initial contract discloses the risk so that the re-

cipient can decide whether or not to accept it, the contract is fair. In moral discourse, society has, at best, a privilege to compensate such persons as an act of charity, and not doing so is not unjust.

The view based on autonomy can be criticized on two grounds. First, it may be wrong to believe that consent to assume the risks of vaccination necessarily includes consent to assume the financial costs of injury. Indeed, it may be unfair to ask anyone to assume such costs if the injury is severe. Second, as a practical matter, one may question whether the contract can be made on fair terms. The ideal of voluntary, understanding, informed consent is not always achieved in practice, especially in a research setting (10, 92).

We do not yet know whether people who take an HIV vaccine will appreciate the consequences of their decision. In particular, we do not know whether people would consent to waive compensation for injury because they are rarely given the option of compensation. Most research studies advise potential subjects that compensation is not available. People who take vaccines are rarely advised that their consent will be deemed to be an assumption of the risks of financial loss. Of course, people take many risks from driving automobiles to white water rafting for which no one else is financially responsible.

Tort law has taken a somewhat broader view of entitlement to compensation by basing it on responsibility for injury. In 1951, Glanville Williams identified four possible goals of tort law imposing liability for personal injury: 1) justice (imposing the cost of injury on the one who causes it); 2) compensation (replacing the victim's losses); 3) deterrence (creating disincentives for socially undesirable activity that could result in personal injury); and 4) appeasement (assuaging the victim's desire for vengeance through compensation) (210). Most discussions of tort liability goals have used the same or a similar formulation (59, 142). Although justice may provide tort law's primary moral justification, compensation and deterrence are its most commonly recognized functions.

Sunstein has noted that traditional principles of compensatory justice have found compensation

appropriate when: 1) “[t]he event that produced the injury is both discrete and unitary”; 2) “[t]he injury is sharply defined in time and in space”; 3) an identifiable defendant has clearly caused the harm suffered by an identifiable plaintiff; and 4) the harm is not attributable to some third party or to “society”⁶ (177). He argues that these criteria are not well suited to affording justifiable compensation where the relevant harm cannot be connected to a discrete event, where there is scientific uncertainty, where the risk is shared or collective, or where the defendant has an ambiguous relation to the harm, as in environmental hazards.⁷

Current tort law would not readily accommodate compensation for increased risks rather than actual injuries. This has obvious implications for injuries to those who are vaccinated because of possible uncertainties about the cause of some injuries and the degree to which any risk may have been avoidable. It suggests that there may be some circumstances in which compensation should be provided even if it would not be granted under tort principles.

■ Social Policy Reasons

Compensation for vaccine-related injury has been seen as a pragmatic solution to a social problem. That social problem is sometimes characterized as unfairness to those with vaccine-related injury who suffer significant financial losses as well as physical and emotional damage and who have no legal claim to compensation from others. Compensation may benefit society as a whole if injuries are deterred and injured persons are adequately provided for. More commonly, the problem is seen as a means to relieve vaccine producers from

an unfair burden of liability for injuries that should not be compensated or are compensated excessively through product liability claims. If compensation costs less than litigation, society, as well as manufacturers, may benefit by reducing litigation expenses. If liability deters the production of socially beneficial products, society may benefit from the availability of those products if they are produced.⁸

Compensation and liability appear to be linked in discussions of vaccine-related injuries because of a general sense that injured vaccine recipients deserve compensation, but that vaccine producers should not be responsible for paying compensation for *all* the injuries. Compensation can be justified on the ground that society benefits from reduction in disease and those who are willing to join the disease prevention effort should be compensated if injury results, perhaps even if the injuries were unforeseeable. This would grant compensation in many cases in which tort principles would deny compensation.

The fact that injury compensation can be justified, and is even desirable, however, does not answer the question of who should be responsible for compensating the injury. If compensation is to be provided beyond that currently permitted under tort principles, should the vaccine producer, government, or someone else be responsible?

SOCIAL GOALS OF ALLOCATING RESPONSIBILITY FOR INJURY

If compensation is warranted for all vaccine-related injuries that are not caused by negligence,⁹ the central questions are: who should provide the compensation, and how? Financial responsibility

⁶ One might add that compensation is generally precluded if the plaintiff has effectively consented to the injury by assuming the risk.

⁷ Many regulatory programs (environmental protection, occupational health and safety, and food and drug regulation) are intended to prevent or minimize social risks that may arise in the future, often to a class or group of people whose affected members cannot be identified in advance. Sunstein argues that these programs operate to provide a mechanism for deterring risks, but not for compensating actual injuries (177).

⁸ Where law mandates vaccination, as with pediatric vaccines, people have little opportunity to refuse to be vaccinated. The social benefit conferred by mandatory childhood immunization was one reason for creating the federal National Vaccine Injury Compensation Program in 1986.

⁹ Because negligence is a deviation from acceptable conduct, and is not an inherent vaccine risk, injuries resulting from the negligence of a vaccine producer or one who administers a vaccine are ordinarily believed to remain the responsibility of whoever caused the injury.

for adverse reactions to a future HIV vaccine may be structured to help achieve one or more of the following goals:

1. to assure the development of an effective vaccine to prevent HIV infection or AIDS;
2. to assure the marketing and distribution of an HIV vaccine;
3. to assure the marketing and distribution of an HIV vaccine at a reasonable cost to users;
4. to assure the use of HIV vaccine to prevent HIV infection or the development of AIDS;
5. to assure compensation to persons injured as a result of an HIV vaccine;
6. to minimize the total social costs of HIV vaccine development, marketing, and injuries; and
7. to minimize the total social costs of HIV infection, including prevention and transaction costs.

It should be noted that none of these goals can be achieved solely by assigning responsibility (or liability) for injuries. Rather, by assigning responsibility to different parties, society may encourage or discourage progress toward specific goals. The ways by which the allocation of responsibility affects progress towards each of these social goals is described below.

■ Development and Marketing

The first two goals—HIV vaccine development and marketing—might be achieved by assigning financial responsibility to government, the producer, or the injured person. The choice depends upon who is to develop and market vaccines and how responsibility for injury affects their decisions.

The federal government has both funded and conducted HIV vaccine research and might assume responsibility for product development, if not marketing. It is more likely, however, that the private sector, which has also conducted vaccine research, will pursue product development and marketing, as it has in the past. Responsibility for injury might encourage the type of vaccine desired

or it might discourage vaccine development entirely.

In theory, the key goal of responsibility for injury is deterrence: to provide an incentive to produce products of acceptable quality and to deter the production of products with avoidable risks. But the degree to which responsibility for injury actually promotes product safety and effectiveness is debatable and difficult to verify (20, 61, 178). Other mechanisms, such as the U.S. Food and Drug Administration (FDA), may achieve the goal equally well.

Currently, it is impossible to predict the degree to which either FDA regulation or potential responsibility for injury may affect an HIV vaccine's safety and effectiveness. Some would argue that, in the absence of such knowledge, responsibility should be retained. Others would argue that it should not because it may discourage producers from developing or marketing any vaccine. This assumes that producers who are otherwise willing and able to develop a vaccine would refuse to do it if they retained financial responsibility for adverse reactions. As discussed in the next section of this chapter, it may be impossible to confirm or refute that assumption, although HIV vaccines development has not been halted by the potential for liability.

■ Reasonable Vaccine Costs and Vaccine Use

The third and fourth goals of allocating responsibility for injury—offering vaccines at a reasonable price and assuring vaccine use—address the need for access to HIV vaccines. The obvious purpose of developing an HIV vaccine is to prevent HIV infection and stop the AIDS epidemic. A safe and effective vaccine must not only be produced, it must be used by those at risk for HIV infection. Unless an HIV vaccine is to be given away free to anyone who wishes it, the cost to vaccine purchasers, whether private individuals or government entities, must be affordable. If the cost of injuries drives the price of vaccine too high, it will not be

used.¹⁰ In that event, it may be cheaper (in theory) to rely on behavioral education to help prevent some modes of HIV transmission. Thus, if responsibility for injury causes producers to set an unaffordable price on vaccines, many people may not be able to obtain it.

On the other hand, if individual vaccine recipients must bear the financial burden of adverse reactions, then they may be unwilling to use the vaccine. Either result undermines the goal of vaccine distribution and use. One alternative for government is to limit the price at which vaccine is sold, either by negotiating government prices with producers or by legislation limiting prices. However, vaccine makers may be unwilling to produce a vaccine that is subject to such price limitations.¹¹

■ Compensation for Adverse Reactions

Responsibility for injury may be allocated so as to achieve the fifth social goal—to provide compensation to those injured in the most efficient, fairest or least costly manner. If the goal is to spend the fewest dollars on injuries, then the choice might be to leave injured people to pay for their injuries. This would avoid any administrative or transaction costs associated with transferring compensation to the injured, but not the burden on injured persons. This option has little appeal because the financial costs of injury are sometimes more than one person can bear. It also seems unfair to the individuals when society as a whole benefits from the vaccine's use. Moreover, if responsibility for injury has the effect of deterring injuries, then requiring compensation may reduce total costs by reducing the number of injuries. It may be more efficient to spread the cost of injuries across the population of vaccine users or the larger society by making government or vaccine producers financially responsible.

■ Minimizing Vaccine and Injury Costs

If responsibility for injury is to be allocated so as to provide compensation to injured people, then the responsible party may be selected so as to achieve the sixth social goal—to minimize the total social costs of vaccine development and marketing and the costs of injury. This takes into account the fact that injuries do impose costs on individuals, even though they may be less visible to society than the costs reflected in the price of products.

Often this goal is erroneously invoked by those who wish to achieve the narrower objective of minimizing the costs to one participant in an endeavor. For example, if only the costs to manufacturers were recognized, limiting liability and compensation would reduce manufacturers' costs. The remaining injury costs would not disappear, however; they would rest with injured people or government. If government wishes to minimize its own costs, then it would ordinarily impose financial responsibility on vaccine producers. However, if the price of vaccine rose higher than the cost to government of providing compensation, and government purchased a significant proportion of vaccine, government would incur much of the cost theoretically imposed on producers. The least costly option would depend upon whether government controlled the price of vaccine, either by regulation or negotiation.

■ Minimizing Total Social Costs of HIV Infection

The seventh goal of responsibility is to minimize the total social costs of HIV infection. In assessing the social costs and benefits of HIV vaccine development, production, and distribution, all of the social costs of HIV infection should be taken into account. Society is already paying a high price, in terms of human suffering as well as economic

¹⁰ Of course, this ignores the human cost of not preventing HIV transmission if the vaccine is not used. It also assumes that vaccination is voluntary.

¹¹ It may be difficult to achieve both the goals of affordability and production if production is to remain entirely with the private sector.

losses, for the persistence of HIV infection. Moreover, current efforts to prevent HIV transmission also impose social costs. The benefits to be gained by preventing additional disease are likely to outweigh the costs of vaccine development, marketing, and injury compensation. If so, then the question is how to allocate responsibility for injury in order to maximize those benefits and minimize those costs.

■ Conclusion:

Any system for assigning responsibility for injury that satisfies one goal may undermine another. For example, a system that minimized the costs of compensation to vaccine makers might encourage vaccine development, but also reduce incentives to limit potential safety risks, and result in more injuries. A system that provided generous compensation to all injured parties might achieve the goal of equitable compensation, but might be too expensive for many companies that society wishes to attract to vaccine development to achieve other goals. Government assumption of responsibility for compensation might conflict with other goals to minimize government expenditures or to fund other important programs. The amount of compensation may also affect the price of marketed vaccines. At some point, high prices may deter potential vaccine recipients from taking the vaccine. Systems that discourage either vaccine development or vaccination may work against the goal of preventing HIV transmission and disease.

Most important, any system that limits compensation to injuries from one specific cause, like

an HIV vaccine, raises questions of fairness to people with similar injuries caused by something else. A compensation system limited to persons with adverse reactions to an HIV vaccine invites the question why people living with HIV infection or AIDS (or any other illness or injury, for that matter) should not be compensated in the same manner.

POTENTIAL DETERRENTS TO HIV VACCINE DEVELOPMENT

As the first section of this chapter illustrates, who should bear responsibility for adverse reactions to HIV vaccines depends upon the goals of HIV vaccine development and compensation for injury and how responsibility for injury may affect vaccine producers' decisions about vaccine development. If society intends to rely on the private sector to develop and distribute an HIV vaccine, then private sector attitudes toward responsibility for injury must be considered. If private companies are unwilling or unable to distribute an HIV vaccine if they are charged with responsibility for injury, then arguments that they *should* have that responsibility will not suffice to produce a vaccine.¹² If, on the other hand, responsibility for injury has little impact on their decisions, then even elimination of responsibility for injury will not improve the prospects for private sector vaccine development.

This section examines the degree to which legal responsibility or liability for adverse reactions might affect private companies' decisions whether to develop and market an HIV vaccine.¹³ Unfortunately, there is no empirical evidence that of-

¹² If government were to produce or distribute the vaccine, such concerns would be unnecessary.

¹³ This examination is based on a literature review; an empirical study was beyond the scope of this report. The possible approaches to studying potential liability's effect on product development have inherent biases and limitations. These parallel the approaches to studying defensive medicine described in the Office of Technology Assessment's 1994 report *Defensive Medicine and Medical Malpractice* (1995), and have similar limitations. One approach is to ask vaccine companies why they did or did not develop specific vaccines. Such surveys may elicit biased responses. If respondents believe that the survey is intended to measure sensitivity to liability, they may exaggerate liability's role in their decision making in the hope of gaining added protection against liability in general. If liability is not mentioned, respondents may underplay its role in favor of emphasizing purely scientific or other reasons. An alternative approach is to compare the products developed, marketed and abandoned by companies with their exposure to liability. Such a study requires access to information concerning products not marketed as well as data on companies' liability experience which companies are generally unwilling to disclose.

fers a clear answer to the question. There are no epidemiologic studies of the effect of liability like those ordinarily required to prove vaccine risks. Inferences might be drawn from past behavior but are highly speculative because the reasons underlying decisions about research and marketing are not independently verifiable. The available evidence consists largely of anecdotes.¹⁴ Analyses of the effect of liability have been forced to rely on inferences from history and assumptions based on logic (and sometimes ideology).

Companies in private industry necessarily make choices about what business to pursue and what products to make. Because new biologic and pharmaceutical products require a substantial investment of both time and money, choices by companies in the pharmaceutical and biologic industry may have long-term consequences for their product line (194).

An initial fundamental decision is whether to invest in the production facilities and equipment, as well as human expertise, necessary to produce an HIV vaccine. Factors influencing such a decision include: whether the company already has (or has access to) adequate facilities that can be used or adapted for HIV vaccine purposes or financial resources to construct such facilities; whether existing or new facilities can be used or adapted to other purposes within the company's business if vaccine development is unsuccessful; whether the company has sufficient regulatory and clinical trials expertise, as well as financial resources, to pursue testing an investigational product in clinical trials with human subjects and applying for

FDA approval; whether the market for the product is likely to support a price that will cover the costs of development and marketing and still produce an acceptable profit; the likely length of patent protection that will preclude other companies from marketing a similar product and competing on price; and whether other potential investments and products are more likely to produce the same or higher profit (82, 121, 194).

It seems logical that potential liability for product-related injuries can influence decisions about whether to pursue developing a specific product. Whether that influence becomes significant depends on its relative weight compared with other factors, especially the scientific and technical feasibility of HIV vaccine development and its expected financial return compared with alternative investments.

■ Scientific and Technical Feasibility

The major obstacle to developing an HIV vaccine is HIV itself.¹⁵ Despite remarkable advances in scientific knowledge about HIV, too little is known about how to produce an immune response in human beings that would protect against infection or development of disease to be assured that an effective vaccine can be produced in the foreseeable future.¹⁶ For example, it remains unclear how to protect against multiple or mutating strains of HIV, how to prevent mucosal infection or infection through sexual contact in addition to infection through the blood stream, whether cell mediated immunity is required in addition to

¹⁴ Two Institute of Medicine committees attempted to evaluate existing evidence that certain adverse reactions were or were not caused by pediatric vaccines (85, 87, 174). They classified the evidence into 5 categories: 1) No evidence bearing on a causal relation; 2) The evidence is inadequate to accept or reject a causal relation; 3) The evidence favors rejection of a causal relation; 4) The evidence favors a causal relation; 5) The evidence establishes a causal relation (174). Applying their categories to the available evidence bearing on a causal relationship between liability for adverse reactions to vaccines and private industry's willingness to develop or distribute an HIV vaccine, one can at best conclude that the evidence is inadequate to accept or reject a causal relation.

¹⁵ The journal *Science* surveyed "more than 100 of the [vaccine] field's leading researchers, public health officials, and manufacturers" for their opinion on why vaccines have not been developed for many serious infectious diseases, especially those considered priorities by the Institute of Medicine (37). The 67 respondents reported that the "Scientific unknowns are the highest hurdles...but they also stressed that the field lacks strong leadership and funding to speed progress (37)."

¹⁶ For a description of current HIV vaccine research and development, see chapter 2.

humoral immunity (to free virus), and whether infection mediated by both cell-free and cell-associated virus can be prevented. Moreover, it is not known whether a vaccine that does not prevent initial infection by the virus could prevent the development of disease and reduce or prevent active HIV transmission to others. Promising research is beginning to answer such questions, but, historically, it has been especially difficult to develop vaccines to prevent viral infections—and HIV is an extraordinarily complex virus (99).

In April 1984, Secretary of Health, Education and Welfare Margaret Heckler optimistically announced that an HIV vaccine would be ready for testing in 1986 (151). A decade later, the scientific community may not be much closer to developing an effective vaccine, although it may better understand why. The difficulty of determining the precise mechanism by which the virus might be neutralized in human beings may discourage companies from mounting the research effort that is likely to be required to solve the problem.

Other technical considerations may affect vaccine development decisions. On the plus side, the technologies used to produce new recombinant vaccines may be adaptable to other promising products, like diagnostics (192). New recombinant vaccines can be produced in large quantities and, because they are usually stable for long periods, are generally less expensive to produce than other biologic products. At the same time, vaccines pose numerous technical challenges.¹⁷ Animal testing requires special facilities and money to maintain the animals. Finding a suitable adjuvant to enhance the immunogenicity of a candidate vaccine has already proved difficult. Candidate vaccines produced from laboratory adapted strains in cell lines may not protect against other HIV strains that infect human beings in the real world, that is, field isolates.

One way to increase the effectiveness of vaccination may be to combine two or more candidate

vaccines made by different companies. This requires the cooperation of different companies in a highly competitive industry. The difficulty of sharing technical information while protecting trade secrets and patents may make such joint ventures unattractive to some companies. Moreover, products that are developed in collaboration with governmental agencies, such as the National Institute of Allergy and Infectious Diseases (NIAID) or the National Cancer Institute (NCI), may give rise to disputes over patent ownership, such as that between Burroughs-Wellcome Co. and National Institutes of Health's (NIH's) licensee, Barr Laboratories, over Zidovudine (AZT) (55). Some companies prefer not to collaborate with the NIH because of the constraints imposed by its "reasonable price" requirements.

Another technical barrier is the need for dedicated product development facilities to produce vaccines. These must comply with FDA regulations specific to biologics, are estimated to cost as much as \$10 million to construct, and may have to be updated periodically (121). They also must include expensive ongoing production and quality control processes conforming to Current Good Manufacturing Practice (CGMP) to ensure the potency and purity of each batch of vaccine. The cost of conducting large field trials has also been cited as a major obstacle to vaccine development (121). Large research-based vaccine manufacturers have an advantage in these respects, since few small biotechnology companies have large production facilities or clinical field trial capabilities. Those that can get the financing may prefer to pursue products with a higher probability of success.

It is encouraging that almost thirty candidate HIV vaccines are currently being tested in Phase I and II clinical trials¹⁸ (207). According to public reports, most of these vaccines have been well tolerated and have produced few side effects so far, which supports predictions that they should be reasonably safe. Whether any of these candidate

¹⁷ For a further discussion of difficulties with vaccine development, see chapter 2.

¹⁸ For a description of current HIV vaccines in development, see chapter 2.

vaccines will prove to be effective enough to prevent HIV infection or disease progression in a significant proportion of human vaccine recipients remains to be seen. Indeed, the reported results are somewhat discouraging so far (34, 100).

Phase III trials, in which vaccine efficacy can be studied, remain in the proposal stage, with some companies and prospective study populations eager to begin large field trials with the candidate vaccines that have completed phases I and II trials (3, 133). In late 1993, NIAID expected to begin Phase III trials between 1994 and 1998, “as soon as promising candidates are available,” and awarded two contracts to administer feasibility studies and multi-site phase III trials both in the United States and abroad (122). On June 17, 1994, however, an NIAID advisory committee voted to delay phase III clinical trials of the two vaccine candidates that have proceeded the furthest in clinical testing (40, 125).¹⁹ Committee members were not convinced from prior test data that these candidate vaccines could prevent HIV infection in enough people to warrant their use in a large Phase III field trial. Ultimately, NIAID recommended proceeding with efficacy trials only if and when more compelling data could be produced. This is likely to delay such trials for one to three years (125).²⁰

Regardless of the merits of the specific vaccines at issue, the decision not to go forward with phase III trials in 1994 may send a discouraging signal about the difficulty of surmounting the scientific obstacles to developing a suitable vaccine.

Some AIDS researchers argue that it would be worthwhile to proceed with the candidates that have already been tested, even if they are not expected to prevent disease transmission or progression in most recipients. They point out that some lives could be saved even if the vaccines are effective in only 30 percent of recipients or if they reduce (while not eliminating) clinical disease or the virulence of the virus and its likelihood of transmission to others.²¹ This is of special concern in countries with rising rates of infection, such as Thailand, Uganda, and Zaire.²²

Others would prefer to concentrate on developing new vaccine candidates with greater promise of effectiveness. They argue that using the tested candidates for immediate Phase III field trials could delay or deter the development of a more effective vaccine. The logistics of organizing a large field trial, especially overseas, are formidable (although perhaps less expensive than in the U.S.), and it may be difficult to use the same population for more than one vaccine. The combined difficulty and expense of mounting such trials may deter some companies from launching a later trial if another vaccine has already been tested and approved.

Researchers at a November 1994 meeting on Advances in AIDS Vaccine Development sponsored by NIAID heard additional discouraging news (126). Newborn monkeys who received a promising prototype simian immunodeficiency (SIV) vaccine derived from live attenuated virus exhibited symptoms of SIV disease and one

¹⁹ Both candidates, one by Genentech, Inc., the other by Biocine Company, a joint venture of Chiron and CIBA-Geigy, are recombinant vaccines using gp120, an HIV-surface protein. For further discussion of these vaccines, see chapter 2.

²⁰ This does not mean that trials cannot go forward in other countries. The companies may try to persuade the World Health Organization or national governments that their vaccines deserve to be tested in phase III trials.

²¹ Such a vaccine could not be counted on to prevent HIV infection, so a recipient would still have to practice safe behaviors to avoid becoming infected, or, if infected, to avoid infecting others.

²² There may also be concern about imposing on private companies an obligation to provide any vaccine that is ultimately approved to the population of research subjects that were used to test it, a principle accepted by most, but not all, scholars of research ethics (110). Industry representatives have argued that this would mean giving the vaccine away free in foreign countries that cannot afford market prices or pay in hard currency. Their resistance persuaded the CIOMS not to include such a requirement in its 1993 International Ethical Guidelines for Biomedical Research Involving Human Subjects (42). For a discussion of the CIOMS Ethical Guidelines, see chapter 3.

monkey died. This may set back efforts to develop HIV vaccine using a similar model. In addition, eighteen human research subjects who received candidate HIV vaccines in clinical trials have become HIV infected despite having high titers of neutralizing anti-body (36). Although their infection may indicate only that the vaccine is ineffective or less than completely protective, the possibility that the vaccine might increase susceptibility to infection may be considered.²³ Some researchers worry that no vaccine that is currently in Phase II trials can achieve even very low levels of efficacy.

Current HIV vaccine research is both exciting and frustrating because so much has been learned yet progress toward an effective vaccine has been so slow. If a private company does not believe that research can identify an adequate vaccine candidate over the next decade, or if it does not have the resources to develop one, then it is not likely to pursue HIV vaccine development.

■ Market and Financial Factors

If scientific obstacles can be overcome and an HIV vaccine appears technically feasible, the major factor influencing vaccine development is its expected return on investment or profitability. Private industry must look to the potential market to predict the revenues it may yield in order to compare them to the predicted costs of development and marketing, and the potential profits from alternative investments.

The potential market for HIV vaccines is worldwide. However, from a company's perspective, the relevant market consists of paying purchasers. Potential HIV vaccine markets, then, include individual vaccine recipients who can pay for the vaccine either out-of-pocket or with insur-

ance and government agencies which purchase vaccine for distribution to individuals. The paying market may include health care workers, people with hemophilia, and people at risk for HIV infection (such as employed men who have sex with men). This parallels the market for hepatitis B vaccine (HBV) and exists primarily in the United States, Europe, Australia, and possibly Japan. It may also exist in the "carriage trade" in other countries (like Thailand, India, and Egypt). This market may be quite profitable, even though it includes fewer people than the market for other vaccines, like those against polio and influenza.

It is possible, however, that not everyone in this market would be willing to buy an HIV vaccine, perhaps because they mistakenly do not consider themselves at risk for HIV infection, because they prefer to avoid risk behaviors instead of being vaccinated, or because they fear adverse reactions (or acquiring HIV infection) from a vaccine. Some people may fear being labeled as "at risk" if they seek vaccination or being stigmatized as having HIV infection if they become seropositive as a result of vaccination. National or local laws requiring vaccination would maximize the use (and purchase) of HIV vaccines. HIV vaccination appears unlikely to be made mandatory for the entire population, at least in industrialized countries. It might be possible to generate legislative support for mandatory vaccination of certain populations at high risk of HIV infection, such as newborns born to HIV-positive women or certain health care workers. But even targeted mandates are likely to face opposition and may depend upon the perceived safety and effectiveness of the vaccine to be used.

The market may also be affected by the price of the vaccine. Some potential purchasers may be unwilling to pay more than a certain price for the

²³ For a discussion of possible HIV vaccine enhancement of susceptibility to HIV infection, see chapter 2.

vaccine unless it is covered by health insurance.²⁴ Physicians in the U.S. have traditionally placed little emphasis on preventive care, other than the required childhood immunizations, perhaps because they, in turn, are paid comparatively little for such services (105).

The United States may be the most profitable market for vaccines in the world. Many foreign markets are not attractive because they are highly regulated and vaccine prices are often limited, either by governments (which purchase drugs and vaccines for national health programs) or by competition with foreign vaccine makers (who may receive government subsidies). Many developing countries have severely limited budgets for vaccine purchases and are unable to pay in the hard currency demanded for transnational sales (147).²⁵ U.S. companies are reluctant to sell at a lower price abroad than in the United States for fear of charges of price-gouging in this country.²⁶ Thus, the United States offers the most attractive market for HIV vaccines made by United States companies.

Federal, state, county, and city government purchasers may provide a secure market for HIV vaccine. The volume of government purchases may be higher than the total population willing to pay for vaccination because the government may provide vaccine for those unable to pay or not covered by insurance. The population at risk for HIV

infection includes a disproportionate number of people who are uninsured for immunizations and who could not afford to pay for vaccination themselves. Government purchasers may not be willing to pay the price that private companies wish to charge for vaccine, however, especially if they purchase large volumes. There is precedent for governments demanding a lower-than-market price for vaccine. The federal government negotiates prices for pediatric vaccines that are significantly lower than “catalog” prices (121). It is also beginning to do the same for drugs,²⁷ which may make companies fearful that all governmental purchase prices may be regulated more strictly in the future (33).

At the same time, greater price regulation of drugs may make vaccines relatively less unattractive as compared with drugs, which historically and in general, have commanded significantly higher prices than vaccines. If government purchasers were unwilling to pay a high price for an HIV vaccine, companies might be unwilling to sell to them (172). However, it would be awkward for companies to sell a vaccine to private individuals and clinics or physicians while refusing to sell to government.

Vaccines suffer from the disadvantage of not being advertised to the public (as compared with over-the-counter drugs). This means that companies cannot build a market directly, but must rely

²⁴ Private health insurance policies in the U.S. rarely cover the cost of preventive vaccination. President Clinton’s proposed Health Security Act would have included childhood and certain other immunizations in its comprehensive benefit package that must be covered by all health insurers. (U.S. Congress, Senate, S. 1757, Health Security Act, Sec. 1128, (Washington, DC: U.S. Government Printing Office, 1993).) Immunization against HIV has not been included in health reform proposals, presumably because no vaccine is available.

²⁵ The price of some U.S. vaccines is higher than the per capita budget for health care in some developing countries (147).

²⁶ In 1982 Congressional hearings, a vaccine maker was chastised for charging the U.S. government a higher price than that for foreign countries. After the hearing, U.S. companies no longer bid for UNICEF or PAHO contracts to sell vaccines at low prices in the developing world.

²⁷ The Medicaid program receives rebates on outpatient drug prices from manufacturers (Social Security Act, s.1927), and certain Public Health Service grantees and certain disproportionate share hospitals receive discounts on outpatient drug purchases (Public Health Service Act, s.340B). Many private health insurers, health maintenance organizations, and large hospitals have negotiated new, lower prices for bulk purchases to reduce health care costs. President Clinton’s proposed Health Security Act would have encouraged negotiated price reductions and rebates on certain drugs purchased by Medicare. (U.S. Congress, Senate, S. 1757, Health Security Act, Sec. 1128, (Washington, DC: U.S. Government Printing Office, 1993).)

on physicians and health agencies to buy the product and use it with their patients.²⁸ In addition, vaccines do not create a loyal market of users (105). Unlike drugs that are used repeatedly for chronic diseases, vaccines are used only once or a limited number of times per person. A highly successful vaccine would eliminate its own market by eradicating the disease. Indeed, this is the goal for an HIV vaccine. On the other hand, if only one HIV vaccine is approved, a company is likely to hold a monopoly for many years and will not need to spend money persuading physicians to use it. Government agencies may be counted on to encourage vaccine use, and fear of AIDS may be sufficient incentive for many people.

The most profitable product for a private pharmaceutical company is a patented product that is the only available or effective means to treat or prevent a serious disease.²⁹ An HIV vaccine would surely qualify in this category. This monopoly position, coupled with strong demand for the product, often allows pricing at whatever the market will bear, (61, 194) as experience with AZT (12) and Clozaril demonstrated. Market potential is ordinarily assessed by comparison with other products that a company might pursue instead of HIV vaccines. Because so few products ever emerge from the research and regulatory pipeline with FDA approval, it makes economic sense to invest in the product with the highest profit potential.

An HIV vaccine is likely to have considerable appeal to companies that believe that market demand will be strong, the price will not be regulated, and users will pay the price. HIV vaccine development may appear unattractive to companies that perceive any of these factors to be absent.

■ Potential Liability for Adverse Reactions

HIV Vaccine Experience

The evidence that fear of liability has dissuaded companies from pursuing HIV vaccine development comes from reports of companies that withdrew, some only temporarily, from research. A review of these cases, however, reveals that other factors typically were present—a disappointing product, lack of financing, poor market predictions, internal corporate restructuring, or potential patent problems—that could account for the action.

Genentech

Genentech stopped research on a preventive HIV vaccine in 1986, citing liability concerns as one reason. Observers close to the company noted that the vaccine was set aside after it failed to protect chimpanzees against HIV infection and the vaccine-producing cell line was suspected of having retroviral particles. Genentech has since resumed research with a different recombinant vaccine, now in clinical trials, which it hopes to take to market.

In 1986, before Genentech dropped its first vaccine, California had enacted legislation limiting the liability of California makers of an AIDS vaccine, with support from Genentech (Calif. Health & Safety Code 5. 199.49). In 1988, the California Supreme Court issued an opinion endorsing immunity from strict liability for prescription drug makers, which is thought to be equally applicable to vaccine makers, (225) and California repealed its statutory protection against liability (Calif. Stats. 1988, ch. 1555, 5.3). The company also be-

²⁸ Recently, some pharmaceutical companies have begun advertising prescription drugs directly to consumers. It is possible that vaccines could be advertised directly to consumers in the future.

²⁹ It is not known whether any vaccine candidate would not qualify for patent protection.

came part of Hoffman-La Roche, a large Swiss pharmaceutical company, which may provide it with financial backing to pursue expensive vaccine development. Large companies with substantial assets, however, are often thought to be more vulnerable to liability claims than small companies with few assets because of their deeper pockets (61).

Finally, the company apparently clarified or resolved earlier scientific questions about vaccine production, safety and efficacy. Which, if any, of these factors persuaded the company to proceed with a new HIV vaccine is unknown outside the company. By mid-1994, Genentech and Biocine were prepared to test their candidate vaccines in the first U.S. phase III field trials. After the NIAID decided not to proceed in June 1994, the companies were reportedly disappointed, and ready to seek alternative ways to pursue the trials without NIAID support (40).

Oncogen

Oncogen, a subsidiary of Bristol-Meyers Squibb, stopped producing preventive vaccine (using live vaccinia virus as a vector to express recombinant gp 160) in 1992 before testing its efficacy in human subjects. A researcher reportedly attributed the decision to “fear of lawsuits from injured vaccine trial subjects” together with “other commercial negatives like a questionable market and patent snafus” (32). Others note that lack of data indicating potential efficacy prompted discontinuation.

Immune Response Corp

Immune Response Corp., co-founded by Jonas Salk, was also reported to delay testing its whole, killed-virus vaccine in uninfected subjects because of liability concerns, but other reports said the company was willing to go forward if the vaccine showed evidence of effectiveness (32).

The vaccine has been tested, without liability issues, in HIV-positive people as a therapeutic means to prevent disease progression to AIDS. Although the whole, killed-virus approach has shown promise, (124) it has raised safety concerns it might cause HIV infection if any of the virus survived processing. Recent tests of live attenuated SIV vaccine in newborn monkeys lend weight to such fears (126).

MicroGeneSys

MicroGeneSys reportedly refused to conduct trials of its vaccine to prevent HIV transmission from HIV-positive pregnant women to their newborns, unless the state legislature granted it immunity from liability (172). Lobbyists for MicroGeneSys argued that children born to HIV positive mothers, many of whom had used illegal drugs, are at high risk for medical problems which might be blamed on the vaccine. The company’s president reportedly claimed that a new law was needed to establish a parent’s right to consent to involving a fetus in research (169).³⁰ The company refused to conduct trials in Tennessee which offered no special protection against liability.

Connecticut, the company’s home state, enacted a statute in 1991 granting Connecticut manufacturers, research institutions, and researchers immunity from civil liability for personal injury to research subjects resulting from administration of any investigational AIDS vaccine (Conn. Gen. Stat. 19a-591-591, 1992c). The law, which offered no compensation to injured subjects, provides immunity from both strict liability and negligence in cases involving research subjects, but retains liability for gross negligence, and reckless, willful or wanton misconduct. At the same time, Connecticut provided substantial economic support to the company, which had no income-producing product and needed substantial capital to construct a plant to produce vaccine (17). MicroGeneSys insisted on conducting the

³⁰ It is questionable whether a company would be liable under existing common law for fetal injuries resulting from research to which the pregnant woman consented (31).

trial at Yale University only, rejecting other planned and proposed sites in Connecticut. After about a year, only two subjects were enrolled. The trial was then closed because it could not produce useful data.

Elsewhere, Genentech conducted trials of its vaccine to prevent maternal HIV transmission in the NIAID-supported sites around the country, although only California had statutory protection against manufacturer liability for injuries arising out of such trials. Preliminary results have not supported hopes for the vaccine effectiveness in pregnant women, and Genentech is dropping its therapeutic vaccine research to concentrate on preventive vaccines.

MicroGeneSys did not mention liability when it lobbied successfully for a \$20-million congressional appropriation to the Department of Defense (DOD) to finance trials of its vaccine for therapeutic use in HIV-positive adults. The appropriation, for a specific project proposed by an individual company outside the usual peer review channels, created considerable controversy, was opposed by DOD, NIH, and FDA, and was ultimately rescinded (38). NIH, FDA, and DOD preferred a trial comparing several candidate vaccines chosen by peer review.

The first vaccine to be approved for testing in human beings (in 1987), MicroGeneSys's product might not fare well against the more recent generation of candidate vaccines. MicroGeneSys's corporate partner, American Home Products, Wyeth-Ayerst Laboratories, which had financed the company and acquired worldwide marketing rights to the vaccine, terminated its agreement with MicroGeneSys and its involvement with the vaccine's development in January 1994 without comment (39).

Abbott

Another report involved Abbott Laboratories' human immunodeficiency virus immune globulin (HIVIG), which was intended to stop the transmission of HIV from HIV-positive mothers to their newborns. Not a preventive vaccine, HIVIG contains antibody against HIV derived from the plasma of HIV-positive people with strong immune responses to the virus. Researchers hoped it would reduce the viral load in pregnant women with HIV and prevent infection of their children, either before or during delivery. A large multicenter trial of HIVIG had been planned under the sponsorship of Abbott and the National Heart Lung and Blood Institute, the NIAID and the National Institute of Child Health and Human Development. After two years of planning, Abbott suddenly withdrew in 1992, citing liability concerns (41). Researchers could not recall earlier mentions of liability, even though high-level company representatives had met with them to plan the trials.

Some participants and observers believed that Abbott was seeking to get rid of its blood products division in a reorganization to improve profitability and used the trial as the excuse to do so. According to news reports, Abbott's interest in the trial dropped after the head of its transfusion medicine branch left the company. Abbott first objected to certifying that its costs and prices to government were properly computed, a standard NIH requirement that NIH finally waived (41). Then Abbott objected to patent rights arrangements. Finally, Abbott asked for indemnification against liability (citing the Swine Flu Program³¹ as precedent), which NIH could not provide without Congressional action. Other organizations that make immunoglobulin did not consider liability an ob-

³¹The Swine Flu Program, created by Congress in 1976 to encourage the development and marketing of a vaccine against a strain of swine flu which was expected that fall and winter, held manufacturers harmless from injuries arising from the swine flu vaccine, and permitted claims for vaccine-related injuries to be filed with the U.S. government. The program is discussed in more detail in the next section.

stacle.³² One AIDS organizer opined that Abbott was trying to manipulate activists and researchers to lobby Congress for liability protection (41). Abbott employees active in transfusion medicine later formed their own company and successfully bid to produce HIVIG for the multi-center trials, which finally began in 1993.

Summary

These examples fail to clarify the role of potential liability in HIV vaccine development. It is plausible that liability was a concern. It is also plausible that liability was not a serious consideration. In all cases, other factors could explain not pursuing an HIV vaccine, most commonly lack of evidence of effectiveness, but also inadequate financing, poor market predictions, corporate restructuring, and potential patent problems.

Garber argues that when a company says it is withdrawing a socially beneficial product from the market because of fear of liability, such statements should have credibility (61). But vaccines may be an exception. If the primary reason for withdrawal is financial—such as a desire to focus on products with much higher returns—a company may be loath to state publicly that it is foregoing a socially beneficial product in order to make more profit. The public is likely to find ordinary concern for profits less acceptable when the product it loses is greatly needed, and more likely to tolerate the loss if it seems beyond a company's control.

Moreover, from the company's perspective, there is always the possibility that Congress might take action to limit liability, which would decrease expenses. The only risk in attributing withdrawal to liability is that Congress might require the company to guarantee production or to sell at a low price in return for limiting liability. But Congress

has never imposed such a quid pro quo, so the risk is probably negligible.

Drugs Withdrawn from the Market

A look at drugs that have been the target of liability claims and whether they remained on the market may yield some clues as to whether potential liability is a serious threat to HIV vaccine development. Studies of product withdrawals recognize the impossibility of identifying the reasons for withdrawal in many cases (61, 178). It is often difficult to sort out whether producers acted out of concern for consumers, fear of regulatory action, actual regulatory action, disappointing financial returns, changing business opportunities, litigation experience, fear of liability, or some combination of these.

Relatively few drugs have been withdrawn after marketing.³³ Some undoubtedly were withdrawn or never marketed because risks materialized that made them too hazardous to use. Such withdrawals for safety reasons are sometimes attributed to liability. To be sure, a drug that turned out to be dangerous to use, especially if its benefits were limited, could be the subject of liability claims. As Bovbjerg notes, however, one must assume that “right-thinking” producers would withdraw a dangerous drug because they did not wish to subject consumers to its dangers, or their reputations to public wrath, not merely because of potential liability (21). To assume that liability is the sole cause of such withdrawal would mean that liability is the sole deterrent to marketing unsafe drugs.

Drugs that have been withdrawn from the market include Bendectin, DES (diethylstilbestrol), MER-29, Merital, Oraflex, Selacryn, Versed and Zomax. Bendectin and DES were the subject of mass tort claims in which thousands of claimants

³² Burroughs Wellcome Co. jointly sponsored trials of AZT in pregnant women to determine whether it would reduce HIV transmission. Preliminary results are encouraging.

³³ Most medical products that have been withdrawn have been medical devices rather than pharmaceuticals: the Dalkon Shield; Copper-7 and other IUDs; Bjork-Shiley Heart Valve; and silicon-gel breast implants (61, 178).

have filed suit amid substantial publicity. The last five drugs were not involved in extensive liability claims and are rarely mentioned in discussions of liability effects on product marketing. Garber suggests that perhaps the fact that other alternatives were available mitigated their withdrawal (61).

The few studies of product liability claims for medical products indicate that the claims are highly product-specific, with Bendectin accounting for the majority (194).³⁴ Bendectin, the drug to prevent morning sickness during pregnancy, is the best example of a drug that can be said with any confidence to have been withdrawn for liability reasons. There is little, if any, evidence that the drug causes serious side effects. The producer, Merrell Dow Pharmaceutical, has won all but a few of the litigated cases.³⁵ The FDA did not require withdrawal of the product, although warnings were strengthened (61, 105). Yet the cost of defending or settling the more than 2,000 suits that have been filed may not have been worth the effort or expense.³⁶

DES, a synthetic estrogen produced by several companies (including Abbott Laboratories, Eli Lilly & Co., Squibb Corp., and Upjohn Co.), is a more complicated example because it did cause cancer in the daughters of women who used the drug to prevent miscarriage. The FDA approved DES in 1941 and banned its use in 1971. Although many have decried its withdrawal (80) and no drugs to prevent miscarriage are being marketed now, no one suggests that withdrawal of DES itself is a great loss to society. One reason it has become a cautionary tale for liability seems to lie in the fact that the risk was latent, exposing several

companies to lawsuits a generation after the drug was used.

It may be that the possibility for mass tort litigation involving risks to a fetus unknown at the time of marketing is a special case which deters marketing certain drugs. Bendectin and DES were both intended for use by pregnant women who wanted to have a child. Drugs used for pregnancy are more susceptible to claims alleging serious permanent harm to children than other drugs (194). Until quite recently, few drugs prescribed for pregnant women were tested in pregnant women before marketing (118), so that their effects on the fetus were often unknown.

Several drugs with recognized serious side effects (such as Accutane, Clozaril, and Cytotec) remain on the market in spite of successful claims of liability. The FDA reportedly estimated that Accutane, Hoffman-La Roche's drug to treat severe cystic acne, had caused perhaps 1,300 birth defects by 1986 (61, 164). Hoffman-La Roche has provided special information kits to prevent the drug's use in pregnant women, but has not withdrawn the product, as might be expected if liability claims determined product availability.

Similarly, Sandoz's Clozaril (used to treat schizophrenia) has potentially fatal side effects in perhaps two percent of patients (139). It requires careful monitoring of white blood cell counts to avoid agranulocytosis. It is possible that the potential for liability is diluted by the physician's involvement in supervising the drug's use.³⁷ Still, contrary to conventional wisdom, the severity of the side effects has not been sufficient to deter

³⁴ Although claims involving pharmaceuticals and medical devices have risen since the 1960's, there is no information on whether the baseline level of claims was too high, too low, or about right, because the merits of such claims were not (and probably could not be) investigated.

³⁵ Bendectin was the subject of *Daubert v. Merrell Dow Pharmaceutical, Inc.*, 113 S.Ct. 2786 (1993), in which the U.S. Supreme Court held that the *Frye* rule for admitting scientific evidence in Federal court was superseded by the Federal Rules of Evidence, which permits the admission of "all relevant evidence" unless specifically excepted by the Rules (8).

³⁶ One commentator suggests that mothers who had used Bendectin may have viewed the company with suspicion because it had acquired other problem products, including Thalidomide, MER-29, DES, and Agent Orange (154).

³⁷ The limited potential for damages in the case of people with severe schizophrenia who are unable to work, even while using the drug, may also reduce the financial exposure for liability, although it is unclear what proportion of patients would fall into that category. Damages for the death of an individual are typically less than damages for permanent injury.

marketing. Cytotec would appear to have even greater potential for withdrawal because its benefits have less dramatic social value. The drug is used to prevent ulcers in patients who take non-steroidal anti-inflammatory drugs (like aspirin and ibuprofen) for arthritis, but can cause abnormal bleeding and miscarriage or abortion in pregnant patients (61, 139). G.D. Searle still markets Cytotec with strong warnings of the risks.

Another factor influencing product withdrawal may be the importance of the revenues it produces for a company. Prozac (an antidepressant) reportedly accounts for about 25 percent of Eli Lilly's drug sales, \$1 billion in the United States. Lawsuits have claimed that the drug causes suicide, violence, and even murder, but the validity of such claims is uncertain at best. The background rate of such behavior among users means that some cases may be misattributed to the drug but that it will also be difficult to prove causation. Such circumstances appear to be precisely the sort that would prompt a manufacturer's withdrawal of a drug for fear of unfounded liability claims. Indeed, they parallel Bendectin's claims experience (61). Nonetheless, Lilly is not expected to withdraw Prozac and is vigorously defending all claims against it. The generally favorable publicity it has received suggests that a significant proportion of the population wants the drug on the market (102).

Halcion, the most widely prescribed sleeping pill in the United States, has also been the subject of claims that it causes suicide and violence.³⁸ The Upjohn Co. is keeping the drug on the market—it has reportedly produced about \$2 billion in sales—although alternative medicines are available. The company recently brought a libel suit in England against the British Broadcasting Corpo-

ration and an expert witness who testified for plaintiffs and publicly criticized Upjohn (18).

In sum, it is difficult to generalize about the effect of liability concerns on marketing from these examples. In particular, they say nothing about products that were never marketed in the first place.³⁹ They do suggest, at a minimum, that whatever weight potential liability may have, it is balanced with other factors to predict the net social and financial returns that marketing a specific product may bring.

Different companies may give such factors different weights. Arguably, breakthrough drugs for diseases without any current cure, or drugs that offer a significant improvement over existing drugs, are more likely to be marketed (and remain on the market) than “me-too” drugs or those with only marginal additional benefits or fewer risks. Drugs that may harbor serious latent hazards, especially those that might become the subject of mass tort claims, might be considered more susceptible to withdrawal, before or after marketing; but all the drugs discussed fall into this category, yet not all were withdrawn.

Perhaps the higher financial returns from a large market can offset concerns about potential exposure to large numbers of claims. The severity of inherent risks may not be determinative, especially if the drug can produce substantial revenues. If the hazards can result from multiple causes, the probability of claims attributing injury to the drug is higher than when causation is clear, but the proportion of claims resulting in liability is lower.

Where the risks are known, some companies may feel they can protect themselves against inappropriate liability by ensuring that proper warn-

³⁸ One woman, criminally indicted for homicide for fatally shooting her mother after taking Halcion, Valium, and codeine, had the charges dropped on the grounds that she was intoxicated by the drug. She sued Upjohn for negligence and received an \$8 million settlement (18). A decision by the Supreme Court of Utah (255) held that makers of FDA-approved drugs were immune from strict liability for defective design.

³⁹ Thalidomide may be an example of a drug that is not being marketed now because of its potential to cause severe birth defects when used by pregnant women to relieve nausea (105). Merrell reportedly settled claims that the drug caused birth defects among residents in Canada and the United States (154). Although the FDA had not approved thalidomide, it was distributed for investigational use. It is currently being investigated as a therapy for patients with leprosy or AIDS wasting.

ings are given, as they have with Accutane, Clozaryl, and Cytotec.⁴⁰ Others may not. Where adverse reactions cannot reasonably be predicted, there is always the possibility that serious harm could materialize in the future and, with it, liability claims. Although lengthier and more sophisticated pre-market testing has probably lowered the risk of unforeseen adverse reactions, no drug is free from that risk.

Vaccines Withdrawn from the Market

Conventional wisdom has held that, whatever the reasons for withdrawing particular drugs from the market, vaccines have been withdrawn primarily because of fear of liability for adverse reactions (13, 61, 79, 80, 105). As with drugs, there can be many reasons for withdrawing a vaccine; the lack of empirical data makes it difficult to draw generalizable conclusions.

The two examples of vaccines that were withdrawn or delayed to market are the swine flu and DPT (diphtheria-pertussis-tetanus) vaccines. In 1976, makers of swine flu vaccine said they would not produce or market the vaccine unless the Federal government assumed liability for adverse reactions. Their insurers would not provide liability insurance covering such reactions. The vaccine was developed hurriedly in response to public health officials' fears of a new influenza epidemic like the one that killed tens of thousands of people in 1918 (129). Amid substantial publicity, then President Gerald Ford encouraged everyone in the country to be vaccinated. There was insufficient time to test the swine flu vaccine in the same manner that other non-influenza vaccines were tested

if the vaccine were to be available to vaccinate the entire American population by flu season. In response, Congress enacted the National Swine Flu Immunization Program, whereby the Federal government assumed legal liability for non-negligent adverse reactions to the vaccine (180).⁴¹

The lessons from swine flu are conflicting. On the one hand, vaccine makers could not get liability insurance for the vaccine,⁴² and fear of liability apparently stopped vaccine production. Congress took such fears seriously enough to pass protective legislation (56). In addition, Guillain-Barré syndrome, an unexpected serious adverse reaction resulting in paralysis, did materialize, and with it, about 4,000 claims against the government. This gives credence to liability fears.

On the other hand, the government paid out less than \$2 per dose of vaccine distributed in awards and settlements to claimants.⁴³ The government agreed to accept responsibility in any case in which the symptoms of Guillain-Barré syndrome appeared within ten weeks of vaccination (a generous assumption of causation that would probably not be accepted by any vaccine maker), so that it paid a larger proportion of claims than would have been paid had the cases been litigated under ordinary tort requirements.⁴⁴ In litigated cases involving Guillain-Barré syndrome appearing after ten weeks or other conditions, court decisions awarded compensation in only six reported cases (247, 260, 286, 305, 308, 315).

Swine flu probably represents a worst case scenario for vaccine liability. The legislation was enacted as a temporary measure and was not designed to resolve liability issues systematically

⁴⁰ The tobacco industry has succeeded in defeating claims of liability for the use of cigarettes largely by virtue of warnings.

⁴¹ The federal government assumed responsibility for defending all claims and had a right of abrogation against the manufacturer in cases in which the manufacturer's negligence caused injury, allowing the government to obtain payment from the manufacturer for awards in negligence. However, the government also provided \$230 million in liability insurance for vaccine manufacturers, thereby paying for its own indemnity.

⁴² Most vaccine makers now self-insure in whole or in part.

⁴³ Total awards and settlements were approximately \$76 million, excluding administrative costs.

⁴⁴ According to one court, the government agreed to liability in Guillain-Barré cases not only to provide compensation to those who could not prove negligence, but also because the syndrome was not mentioned as risk in the consent document (315).

(82). As the Institute of Medicine noted, the legislation “only changed the defendant” (82). Certainly Congress is not anxious to repeat the experience and would shy away from assuming liability for any new vaccine. At the same time, the total amount of awards may be manageable if the vaccine is appropriately priced. This suggests that the price at which a vaccine can be sold may determine how much room there is for liability payments.

Swine flu development also differed from the circumstances surrounding most other vaccines because of its necessarily hasty development and its immediate use in millions of people. Of course, the more deliberate pace of research possible with most vaccines does not ensure that all risks will be discovered before marketing. But the more a vaccine is studied, the more likely it is that adverse reactions will be discovered.

Wyeth Laboratories ceased DPT vaccine production in 1984, reportedly because of claims filed asserting adverse reactions to the pertussis component of DPT. It is entirely plausible that Wyeth could have decided that vaccine production would not be profitable enough to justify defending additional lawsuits. At the same time, Wyeth reportedly faced replacing its old vaccine production facilities if it were to continue selling the vaccine. If the company wanted to get out of the vaccine business, this would have been the time to do it, before it invested heavily in an expensive new plant. Wyeth did continue to produce the vaccine, but sold it to Lederle for distribution.

Also in 1984, Connaught Laboratories announced that it would stop producing DPT because it was having difficulty getting liability insurance at a reasonable price. The Centers for Disease Control and Prevention (CDC) recommended vaccinating only older children to conserve diminishing vaccine supplies. Connaught soon found acceptable insurance and continued to

produce DPT. In 1986, prices for childhood vaccines rose dramatically.

CURRENT VACCINE RESEARCH AND DEVELOPMENT

Companies have few business incentives to produce vaccines at all. The number of U.S. vaccine makers has declined since the early 1970s. At that time, many vaccines were “me-too” vaccines, produced much like generic products and sold in high volume at very low prices (121). In the mid-1970s, the FDA began to require evidence of effectiveness of vaccines as a condition for continued marketing. Many vaccine makers may have dropped out of the business rather than conduct the expensive clinical trials necessary to demonstrate their vaccines’ efficacy. The U.S. market for children’s vaccines may not be large enough to support several competitors. The percentage of research and development (R&D) expenditures devoted to biologics (as opposed to pharmaceuticals) in the industry declined from 4 percent in 1973 to 2.1 percent in 1983 (121).⁴⁵ During that period, sales of biologics represented between 2.7 and 3.6 percent of total sales, including pharmaceuticals, of members of the Pharmaceutical Manufacturers Association (since renamed the Pharmaceutical Research and Manufacturers Association). Between 1973 and 1980, R&D expenditures for biologics ranged unevenly (between 12.9 and 23.1 percent of sales of biologics alone). In 1981, that percentage was 9.2 (121).

In recent years, however, vaccine research and development has increased in the United States. A recent report by the Institute of Medicine concludes that “the worldwide vaccine industry appears to be entering a new era of activity and innovation” (121). Applications submitted to the FDA to study new biologics rose from 66 in 1980 to 558 in 1992 (212). Most have been for thera-

⁴⁵ Total research and development for both pharmaceuticals and biologics increased gradually from 12.57 percent in 1973 to 15.32 percent of total sales in 1983 (121). Total R&D for 1990 was 17.4 percent of total sales.

peutics, but Investigational New Drug applications for vaccines have been increasing since 1990 (67 in 1990, 81 in 1992). Some established pharmaceutical companies in the United States have begun new investments in vaccine research.⁴⁶ Several U.S. companies are joining with foreign firms to develop or license vaccines.

The past four years have seen the introduction of a dozen new vaccines, including a new acellular pertussis component of the combination vaccine (DTaP) with diphtheria and tetanus toxoids by Lederle-Praxis and Connaught Laboratories, several new *Haemophilus influenzae* type b (Hib) vaccines, Japanese encephalitis virus vaccine, and a new typhoid vaccine. Other new or improved vaccines, including one to prevent chicken pox, are in clinical trials or expected to be approved by the FDA in the near future. It is possible that the industry went through a shaking-out period in the 1980s and is being restructured to meet the new scientific challenges posed by infectious diseases more efficiently.

The growth in biotechnology companies may have helped this trend. Biotechnology researchers are likely to be an important source of innovative products in the next few years (77). More than 75 biotechnology companies around the world were conducting vaccine research and development in 1992. Small companies may be able to invest in risky products because they have less to lose in the event of catastrophe.

At the same time, the biotechnology industry may experience a shake-out in the near future, with many of the estimated 1,300 companies going out of business. Few small companies have any FDA-approved products on the market, and thus have no product revenue. Most companies re-

portedly do not have enough financing to operate for more than two years (67, 77). The investment community may be wary of investing further in companies that face a low probability of producing a commercial product within the next several years, especially after news reports of the failure of eight companies' pharmaceutical products in clinical trials in 1994 (47). Small firms that are short of operating capital may sell or license their product rights or the entire company. Most are expected to be acquired by large pharmaceutical companies, including foreign companies.⁴⁷

Other biotechnology companies may survive by concentrating on only one or two products, by licensing new products to large domestic or foreign companies, or by limiting themselves to one phase of product development and conducting joint ventures with other companies that specialize in clinical trials, manufacturing, or marketing (77). If the pharmaceutical industry scales back its investment in research and development, the biotechnology industry may fill the gap in research. Which companies will do so remains to be seen.

The modern vaccine industry looks more like the pharmaceutical industry and less like the earlier vaccine industry. The trend appears to be toward developing sophisticated products, often the result of recombinant DNA technology, that can be sold at prices approaching the higher prices of pharmaceuticals. Often the technology used influences the attractiveness of vaccine production. Technologies that can be used to produce other marketable products, such as diagnostic tests, are more likely to be pursued than technologies that have only one use. In view of the fact that only a small proportion of potential products are ultimately approved by the FDA and successfully

⁴⁶ For example, Merck & Co., Inc., maker of measles vaccine, created its Merck Vaccine Division in 1991, has invested in a new biotechnology facility in Pennsylvania, and has entered into joint or cooperative ventures with other companies, such as MedImmune. Lederle Laboratories, the target of DPT vaccine lawsuits, acquired Praxis Biologics, developer of a conjugate *Haemophilus influenzae* type b vaccine (Hib-CV). American Cyanamid made the resulting Lederle-Praxis Biologics a regular business unit in 1992, giving it greater corporate weight (121).

⁴⁷ For example, Ciba-Geigy, Ltd. of Switzerland is reported to have agreed to buy 49.9% of Chiron Corporation, a profitable independent company and provide it with new financial and technical assistance (57). Ciba-Geigy and Chiron are also partners in Biocine which developed a candidate HIV vaccine.

marketed, companies may be reluctant to gamble a large investment on a single long-shot vaccine.

The National Childhood Vaccine Injury Act of 1986⁴⁸ may also have encouraged vaccine research because it limits producers' liability to a predictable amount (paid as a tax on vaccine sales) and frees them from defending claims. As originally enacted, however, the Act did not apply to investigational or newly approved vaccines. It was to cover only vaccines that children were required by law to take. A 1993 amendment permits the Secretary of Health and Human Services to extend coverage to new vaccines that are recommended for children; Hib and HBV vaccines are expected to be added soon. Vaccine makers may anticipate that other vaccines will be added. Most of the recently approved vaccines had been under development before the act took effect in 1988. If it does further encourage research, then an even larger increase in vaccine development should be expected in the future.

Research initiatives for HIV vaccine development are also encouraging. At least twelve companies are actively engaged in HIV vaccine research and development, and others are developing adjuvants and other supporting products.⁴⁹ This exceeds the number of companies developing a vaccine for any other disease. Almost 30 candidate vaccines are now in clinical trials (207). The debate over phase III field trials centers on scientific issues whether any of the candidate vaccines that have been tested show sufficient promise of effectiveness to warrant large-scale testing in human beings. Potential liability for adverse reactions does not appear to be a factor in these debates. There is a possibility that subjects injured in a foreign field trial might try to sue a U.S. vaccine maker in the United States (173). But the rarity of injuries in clinical trials in general (140) and the even

greater rarity of claims arising out of such trials suggests that liability has not much influenced decision-making about whether to conduct field trials abroad.

■ Conclusion:

There is evidence that vaccine research and development is increasing and that a surprising number of companies are engaged in HIV vaccine research. Indeed, more companies are developing vaccines for HIV infection than for any other single disease. Potential liability may have concerned a few companies, but it has not prevented a strong research effort and appears unlikely to halt HIV vaccine development. The major stumbling blocks remain scientific. Even if new vaccine candidates show more promise than those currently in clinical trials, the likely market for an HIV vaccine is uncertain. Given the business disincentives to producing an HIV vaccine, the vigor of research is encouraging.

Decisions about HIV vaccine research and marketing are likely to vary from company to company and from product to product, as they have with other vaccines and drugs in the past. Fear of liability may influence a few companies' choice of vaccine type, so that they may avoid killed or live attenuated vaccines in favor of recombinant vaccines that are believed to pose little or no safety risk. If so, the array of possible vaccines could be limited to the more expensive recombinant types.

TORT LIABILITY FOR ADVERSE REACTIONS TO VACCINES

■ Overview of Product Liability

Like manufacturers of all products, vaccine makers are responsible under state law for personal injuries caused by their own negligence or by a de-

⁴⁸The National Childhood Vaccine Injury Act of 1986 is discussed below under Public Compensation Systems.

⁴⁹See chapter 2 for a discussion on the current state of HIV vaccine development.

fect in their products.⁵⁰ Tort law provides two categories of legal responsibility for personal injuries caused by products: negligence and strict liability (94).⁵¹

Negligence is conduct by the product maker that deviates from standards of acceptable conduct adhered to by the ordinary manufacturer of similar products and that results in harm to the product user. To succeed on a negligence claim, a plaintiff must prove that: 1) the manufacturer had a duty to the plaintiff, 2) the manufacturer breached that duty, 3) the plaintiff suffered an injury for which damages may be awarded by law, and 4) the injury was caused by the manufacturer's breach of duty (94).

Few cases for vaccine-related injury are brought in negligence alone. Before 1960, plaintiffs were generally unable to prove that a manufacturer had been negligent or that a vaccine had caused an injury (228, 295, 314). Strict liability developed in part because consumers were frequently unable to obtain the evidence that a manufacturer of consumer products had acted negligently.⁵² By the mid 1960s, when more vaccines were being marketed widely in the United States, the state had begun to adopt the doctrine of strict liability for injuries caused by defective products, so that plaintiffs were able to apply that theory to vaccines as well as other consumer products (13, 168).

The concept of strict liability generally applied in the United States is summarized in Section 402A of the Restatement (Second) of Torts and holds “[o]ne who sells any product in a defective condition unreasonably dangerous to the user or consumer or to his property [liable] for physical harm thereby caused to the ultimate user or consumer....” (4).⁵³ Thus, strict liability is said to focus on the condition of the product itself, while negligence focuses on the behavior of the manufacturer (206). Because the manufacturer's actions or knowledge are often at issue in deciding whether a product is defective, however, the strict liability concept has increasingly mimicked aspects of ordinary negligence (72).

These rules would also apply in some cases involving adverse reactions to U.S. products that occur in developing countries and are litigated in the United States (see box 4-1).

PRODUCT DEFECTS

Traditionally, product defects have been divided into three categories: 1) manufacturing flaws, 2) defects in product design, and 3) errors or omissions in directions and warnings accompanying the product. Least controversial are manufacturing flaws or errors in the manufacturing process.⁵⁴ These produce something other than the product intended by the manufacturer, since the manufac-

⁵⁰ Although state laws vary to some degree, the basic principles are sufficiently similar to permit generalization for purposes of this report. There is no general federal tort law, although supporters of tort reform have sought enactment of a federal law governing product liability for many years. For a description of the National Vaccine Injury Compensation Program, see discussion below.

⁵¹ Causes of action also exist for breach of express or implied warranty of fitness for a particular purpose, but because they are not based in tort law, tend to cover the same facts and duties as strict liability and are usually superseded by strict liability or negligence claims, they are not discussed herein.

⁵² Strict liability combines elements of traditional actions in negligence (which do not require privity of contract) and warranty (which do not require proof of negligence). Warranty claims were available only to those who had purchased a product directly from a seller and were therefore in contractual privity (51, 52).

⁵³ Section 402A also specifies that the seller is liable if engaged in the business of selling the product and “it is expected to and does reach the user or consumer without substantial change in the condition in which it is sold.” This rule “applies although (a) the seller has exercised all possible care in the preparation and sale of his product, and (b) the user or consumer has not bought the product from or entered into any contractual relation with the seller” (4).

⁵⁴ Liability for manufacturing errors dates back from the thirteenth century when those who supplied contaminated food were subject to criminal liability (4).

BOX 4-1: Liability for Adverse Reactions to HIV Vaccines in Developing Countries:
The Doctrine of *Forum Non Conveniens*

Although the NIH has postponed Phase III clinical efficacy trials of HIV vaccines in the United States, some U.S. pharmaceutical manufacturers have begun large-scale clinical trials of HIV vaccines in developing countries. These U.S. pharmaceutical manufacturers are thus exposed to liability for adverse reactions to HIV vaccines that occur among trial participants in developing countries.

Plaintiffs may seek to bring a legal proceeding to the place of manufacture if they believe there is an opportunity for a larger recovery. Foreign trial participants who are injured by HIV vaccines manufactured in the United States may prefer to bring suit in U.S. courts, because U.S. product liability law is considered more favorable to plaintiffs than product liability laws of most developing countries. For instance, U.S. law allows plaintiffs to hire attorneys on a contingency fee basis, so that the plaintiff's attorney is not paid unless there is a recovery. U.S. law allows for the award of punitive damages in product liability cases, whereas the laws of many developing countries do not. And unlike most countries, U.S. law permits jury trials in product liability cases; awards by juries have the reputation of being more generous.

The legal doctrine of *forum non conveniens*, however, substantially limits the ability of foreign plaintiffs to bring suit in U.S. courts. One of the original intents of this doctrine was to prevent "forum shopping" by plaintiffs, but the doctrine has increasingly been used as a means for "reverse" forum shopping by defendants who wish to dismiss cases brought by foreign plaintiffs in U.S. courts. In analyzing whether to grant a *forum non conveniens* motion, courts consider a three-part test. The court first determines whether an appropriate alternative forum exists where the plaintiff can receive redress (usually the home country of the plaintiff, or the place where the injury occurred). In determining whether there is another suitable forum, the court is not to consider which forum would be more or less favorable to either of the parties.¹

If the court finds that an acceptable alternative forum exists, then it determines whether the greater "convenience" of the alternative forum would warrant dismissal. In determining whether it is more appropriate to bring the suit in an alternative forum, the court is to balance the various public and private interests in the location of the suit.

In considering *forum non conveniens* motions, courts have emphasized the administrative burden of the case on U.S. courts. This concern was important in the court's decision to grant a *forum non conveniens* motion to dismiss in *In re Union Carbide Corporation*, (268), which followed an explosion at a chemical plant in Bhopal, India, with a large number of deaths and injuries. U.S. lawyers who were representing a number of injured individuals and their families in a tort action against Union Carbide sought to try the case in a United States Federal court. The court decided that India's legal system could provide an adequate forum. The court also decided that India's courts were the most appropriate forum, considering the location of the witnesses, the evidence, and the documentation for this case. The court weighed the public and private interests involved, and, in dismissing the case, placed the greatest emphasis on administrative concerns. The court reasoned that "the American interests are relatively minor. Indeed, a longer trial . would unduly burden an already burdened court, involve both injury and hardship and heavy expense." *Ibid.*

(continued)

¹In *Piper Aircraft Co. v. Reyno*, (287) the Supreme Court held that the doctrine of *forum non conveniens* applied despite the possibility that the plaintiff may face less favorable product liability laws in foreign courts. The court reasoned that U.S. courts, with their strict liability theory, potential choice of fifty jurisdictions, availability of jury trials, contingent attorney's fees, and rules allowing extensive discovery, are especially attractive to foreign plaintiffs, further congesting crowded U.S. dockets.

**BOX 4-1: Liability for Adverse Reactions to HIV Vaccines in Developing Countries:
The Doctrine of *Forum Non Conveniens* (Cont'd.)**

The doctrine of *forum non convenient* has been raised in a number of cases involving injuries from U.S. pharmaceutical products marketed abroad.² In some cases, especially involving injuries that may also have occurred to a large number of other persons as well, courts have granted *forum non conveniens* motions to dismiss the case. In *Dowling v. Hyland Therapeutics*, (237), the plaintiff, an Irish hemophiliac, brought suit in a Federal court in New York City against the U.S. manufacturer of HIV-infected blood clotting factor that he received. The blood product was manufactured in the United States, and the blood product was administered to the plaintiff in Ireland. The court dismissed the case, reasoning that “[t]he public interest in AIDS prevention is equally important in New York as in Ireland. However, in all other respects, the public interest clearly favors trial in Ireland. Irish law would apply since Dowling received treatment, allegedly contracted HIV, and at all times resided in Ireland.” *ibid.*³

However, in other cases involving individual injuries that were unlikely to have occurred to many others, courts have permitted foreigners injured by U.S. drugs and vaccines to bring their case into U.S. courts, See, e.g., *Cadenstope v. Merck*, (227); *Chan Tse Ming v. Cordis Corp.*, (230); *Corrigan v. Bjork Shiley Corp.*, (233); *Haddad v. Richardson-Merrell, Inc.* (256); *Hodson v. A./-f. Robins Co., Inc.*, (261)

Given that the U.S. judicial system is overburdened, courts are expected to continue to use the doctrine of *forum non conveniens* to limit access of foreign plaintiffs to U.S. courts.

SOURCE: R.E. Stein, Blicher & Stein, Washington, DC, “Selected Issues of AIDS Vaccine Liability,” unpublished contractor report prepared for the Office of Technology Assessment, U.S. Congress, Washington, DC, Sept. 30, 1994

² All of the cases cited here involve drugs that have been approved and marketed. To date, there are no cases where a foreign plaintiff has been permitted to sue in the United States for injuries that occurred during a foreign trial of a U.S.-manufactured drug or vaccine.

³ See also *De Melo v. Lederle Laboratories*, (236) (Eighth Circuit Court of Appeals upheld the dismissal by a federal district court of a lawsuit brought by a Brazilian woman permanently blinded in Brazil by a drug manufactured in the United States. While the U.S. labeling for the drug warned of permanent blindness, the Brazilian labeling warned only of temporary blindness).

turing process failed to conform to the manufacturer’s own specifications, and are generally limited to particular units or batches of the product. Examples include adulterated or contaminated products and products in which a toxic element was not removed or rendered harmless by the manufacturing or quality control process. Claims based on manufacturing defects in vaccines are extremely rare, probably because such defects themselves are so rare.⁵⁵

Defects in design are problems with the product specifications themselves, not an isolated manufacturing error. A design is defective if the product could have been developed so as to reduce its inherent danger to the user without significantly decreasing its effectiveness. Whether a design is defective depends upon a manufacturer’s behavior in its research and testing activities and the state of scientific knowledge at the time of product development. Thus, although liability for design

⁵⁵ The so-called Cutter incident occurred when the manufacturing process for the Salk killed-virus polio vaccine failed to “kill” particles of live polio virus, the vaccine was used in a mass immunization program, and almost 100 people developed poliomyelitis (15). More than 60 lawsuits were filed. Plaintiffs in the lead case (250) ultimately won their action on the theory that the manufacturer had breached its implied warranty (302). Most of the remaining lawsuits were settled thereafter.

defects is theoretically part of strict liability, it is understood to apply in essentially the same way as liability for negligence. Few cases claiming that vaccines were defectively designed were brought until the 1980s (117).⁵⁶ More recently, several courts have rejected such claims and granted vaccine manufacturers effective immunity from strict liability for design defects, absent fraudulent conduct.

The vast majority of litigated claims involving vaccines are based on warning defects.⁵⁷ These are of two types: 1) a failure to provide warnings of risks inherent in the use of the product (failure to warn),⁵⁸ and 2) providing directions and warnings that fail to adequately describe product risks (inadequate warning). A defect in the warning is independent of any flaw in the product itself. A properly produced vaccine that is not accompanied by adequate warnings of possible side effects is a product that is defective *as marketed*.

■ Liability for Defectively Designed Vaccines

Most vaccine manufacturers and some commentators argue that drug and vaccine makers should be exempt from liability for defectively designed products (as long as they meet FDA requirements for approval) because of the benefits their products confer (159). Others argue that no exception should be made because not all drugs provide a significant social benefit and, because consumers are especially vulnerable to undetectable risks in pharmaceutical and biological products, their makers should be held to at least the same stan-

dards as manufacturers of ordinary consumer goods (211).

Courts have upheld both positions, although the trend appears to be against holding drug and vaccine makers liable for design defects (156). Almost all courts base their reasoning on Comment k to Section 402A of the *Restatement (Second) of Torts* (American Law Institute, 1977):⁵⁹

Unavoidably Unsafe Products. There are some products which, in the present state of human knowledge, are quite incapable of being made safe for their intended and ordinary use. These are especially common in the field of drugs. An outstanding example is the vaccine for the Pasteur treatment of rabies, which not uncommonly leads to very serious and damaging consequences when it is injected. Since the disease itself invariably leads to a dreadful death, both the marketing and use of the vaccine are fully justified, notwithstanding the unavoidably high degree of risk which they involve. Such a product, properly prepared, and accompanied by proper direction and warning, is not defective, nor is it unreasonably dangerous. The same is true of many other drugs, vaccines, and the like, many of which for this very reason cannot be legally sold except to physicians, or under the prescription of a physician. It is also true of many new or experimental drugs as to which, because of lack of time and opportunity for sufficient medical experience, there can be no assurance of safety, or perhaps even the purity of ingredients, but such experience as there is justifies the marketing and use of the drug notwithstanding a medically recognizable risk. The seller of such products, again with a qualifica-

⁵⁶ In 1985, a California Court of Appeals found only one case (224) in which strict liability had been applied to a prescription drug (oral contraceptives in that case) (273). No case involving vaccines was identified. The facts in *Brochu* may have permitted the plaintiff to recover in negligence without resorting to strict liability.

⁵⁷ Plaintiffs often bring claims in strict liability for both defects in design and warning defects, as well as claims in negligence, to ensure that their claim is not dismissed for failure to correct cause of action.

⁵⁸ This type of warning includes the failure to provide directions for the proper use of a product whose operation is not apparent to a consumer, but such directions are not relevant to the use of vaccines.

⁵⁹ The American Law Institute (ALI) prepares treatises that summarize several fields of law. Its *Restatement (Second) of Torts* is widely considered by the legal profession to be the most authoritative statement of tort law in the country. Most states have adopted its provisions, albeit not uniformly, and some states have interpreted its technical requirements slightly differently. In 1993, the ALI began preparing a new (third) restatement of the law which will include an updated volume on products liability (5).

tion that they are properly prepared and marketed, and proper warning is given, when the situation calls for it, is not to be held to strict liability for unfortunate consequences attending their use, merely because he has undertaken to supply the public with an apparently useful and desirable product, attended with a known but apparently reasonable risk.

Comment k describes an exception to strict liability in the case of products that are “unavoidably unsafe.” It was reportedly drafted in response to an unsuccessful proposal that all prescription drugs be exempt from Section 402A. The proposal was defeated, but Dean Prosser included language indicating that at least some drugs and vaccines should be exempt from strict liability for harms that could not be avoided if the product were to serve its beneficial purpose (132).

Most courts have refused to grant a blanket exemption for all drugs or vaccines (224, 229, 242, 251, 258, 273, 282, 284, 296, 300, 301, 303, 312, 318, 319). Instead they would exempt only those drugs and vaccines that are unavoidably unsafe, on a case by case basis.

However, other courts have held that makers of FDA-approved prescription drugs are entirely exempt from strict liability for defective drug design, regardless of the drug in question, because of the public interest in drug availability (255, 270, 277).⁶⁰ The California Supreme Court did so in 1988 in a case involving diethylstil bestrol (DES), even though the court doubted that DES could not have been redesigned to reduce its risks or replaced with a safer drug (225).

The American Law Institute is preparing a revised version of its *Restatement of Torts*, which

will include a volume on products liability that is expected to become available in 1995. The September 1994 draft of the chapter on liability for defective products includes provisions specifically delineating and limiting the liability of pharmaceutical and biologics manufacturers for personal injuries caused by their products (5). In particular, the draft abandons the use of the term strict liability and instead sets slightly different standards for “liability” in tort for harm caused by a product defect, depending on whether the defect is a manufacturing error, a design defect, or a warning defect. This characterization does not significantly alter existing law with respect to manufacturing errors and warning defects; it does describe a more stringent standard of proof for design defects, however. If these provisions are accepted by the Institute, they may further support the trend against holding manufacturers strictly liable for alleged design defects in prescription drugs and vaccines. Whether the states adopt all the Institute’s revisions remains to be seen.

Where defective design is a permissible basis for liability under current law, the plaintiff must prove that the product is defective because its risks render it unreasonably dangerous. The product’s benefit or utility is balanced against the risks it poses. This requires proving that, on the basis of scientific knowledge known or available at the time the product was marketed, the manufacturer knew or should have known that the risks could have been avoided or reduced without jeopardizing the product’s effectiveness and losing its benefit.⁶¹ Several courts have described the factors that should be considered in this calculus in differ-

⁶⁰ This does not necessarily preclude liability for claims of negligent design.

⁶¹ A few courts have applied a “consumer expectations” test, which required the plaintiff to prove only that the product was more dangerous than would be contemplated by an ordinary consumer possessing knowledge common in the community. This test appears to have been applied little outside the area of ordinary consumer products like automobiles and has little, if any, application to product liability claims involving drugs or vaccines (225). The consumer expectation test was used in the first formulation of a modern strict liability standard in *Greenman v. Yuba Power Products, Inc.*, (253), and its predecessor, *Escola v. Coca Cola Bottling Co. of Fresno*, (239) (Traynor, J., concurring). Both cases involved ordinary consumer products (a power tool in *Greenman*, a Coca Cola bottle in *Escola*), not drugs or vaccines. The consumer expectations test is also suggested in Comment g (to Section 402A), which defines a “defective condition” as “a condition not contemplated by the ultimate consumer, which will be unreasonably dangerous to him.” Comment j also notes that Section 402A liability applies “where the product is...in a condition not contemplated by the ultimate consumer.”

ent terms, sometimes creating uncertainty as to the precise evidence needed to prove or disprove a claim.⁶² Often, the plaintiff must show that a safer alternative design was feasible and would have achieved at least the same benefits. Nonetheless, in all its formulations, the risk-utility test embodies fundamentally the same concept.

The proposed revision of the Restatement of Torts, if adopted, would further narrow the grounds for liability for design defects in prescription drugs, including vaccines, and devices. It would provide that a drug is not reasonably safe due to defective design only if its foreseeable risks of harm are “sufficiently great in relation to its foreseeable therapeutic benefits so that no reasonable health care provider . . . would prescribe the drug . . . for any class of patients” (5). This would limit liability for design defects to drugs that do not provide any benefit to any group of patients. If a reasonable, informed health care provider would prescribe the drug to his or her patients, then the drug would not be deemed to have a design defect and no liability would attach. The effect of this restatement appears to be to reduce the grounds for liability for design defect. It may simply reflect the practical results in reported cases, however, since products whose benefits outweigh their risks are used by reasonable providers and are not found to have design defects.

Because a design defect case turns on a manufacturer’s knowledge and conduct, most courts have found that the cause of action is effectively one of negligence (225). Manufacturers are held to the knowledge of an expert in the field of drug or vaccine production. They have a duty to

keep up with advances in scientific knowledge and to conform to ethical drug industry standards in research, development, and marketing (242, 255).

In the 1980s, there was some concern that manufacturers could be held liable for failing to eliminate a product risk that was unknown or unknowable at the time the product was developed and marketed (146, 158). The 1982 New Jersey case that sparked such concerns, *Beshada v. Johns-Manville Products Corp.*, however, was largely overruled in 1984 (242).⁶³ The Supreme Court of California concluded that drug manufacturers are not liable for hazards not foreseeable at the time of sale (225).

As a practical matter, no drug or vaccine manufacturer has been found liable for selling a product with risks that were unknowable when marketed. A few cases have upheld jury or court decisions that Quadrigen (a vaccine combining DPT and polio vaccine marketed between 1959 and 1962) was defective because the preservative used or combination of vaccines created a known risk of harm and resulted in more adverse reactions than using the separate vaccines (284, 311).

The requirement that the risk be one that the manufacturer knew or should have known on the basis of scientific knowledge at the time the product was produced creates a defense to liability based on the state of the art or the state of science.⁶⁴ This is essentially a negligence defense because it relies on industry standards, not on subsequently detected product risks.

Design defect claims are claims that a different (safer and at least as effective) product should

⁶² These variations can add complexity to litigation, primarily for national companies that defend cases in several states.

⁶³ *Beshada v. Johns-Manville Products Corp.*, (223) involved asbestos, and *Feldman v. Lederle Laboratories*, (242), a failure to warn case, limited imputing knowledge of product hazards to asbestos cases. Other courts have not made any exception for asbestos, but require a showing that all manufacturers knew or should have known of the hazard to impose liability for failure to warn of a product’s dangers. (*Anderson v. Owens Corning Fiberglass Corp.*, (220)) But, in cases involving baby oil and asbestos, one court interpreted Washington’s tort reform statute to permit liability for design defects and failure to warn of unforeseen risks. (*Ayers v. Johnson & Johnson Baby Products Co.*, (221); *Falk v. Keene Corp.*, (241)).

⁶⁴ Some courts consider it an affirmative defense, requiring the manufacturer to carry the burden of proving the unavoidable nature of the risks and the fact that the benefits outweighed the risks at the time of distribution. (*Castrignano v. E.R. Squibb & Sons, Inc.*, (229); *Schackil v. Lederele Laboratories*, (297); *Taggart v. Richards Medical Company, Inc.*, (309); *Toner v. Lederle Laboratories*, (312)).

have replaced the product that was sold. Some drug manufacturers have argued that all claims of liability are preempted by Federal law because product specifications may not be altered without FDA approval. Ordinarily, FDA regulation of particular products or classes of products does not bar states from imposing additional requirements or providing state law remedies in tort (259).

The vast majority of courts have followed this principle with respect to vaccines (214, 242, 244, 251, 276, 280, 297, 300, 312, 319).⁶⁵

The fact that the FDA has approved one vaccine design does not mean that other vaccine designs might not be safer or more effective. However, FDA approval has often provided persuasive evidence that an approved vaccine was not defective. The Federal National Childhood Vaccine Injury Act does preempt manufacturer liability for failure to directly warn consumers but does not foreclose other state tort actions (*Abbott v. American Cyanamid Co.*, 844 F.2d 1108 (4th Cir.), cert. denied, 488 U.S. 908 (1988)).⁶⁶

In summary, although concerns about design defect litigation surfaced in the 1980s, there are no reported decisions after 1969 upholding liability for a defectively designed vaccine.⁶⁷ The majority of states permit a cause of action claiming defective design of a particular vaccine. Such claims are not generally preempted by federal law, and compliance with FDA requirements is not a legally conclusive defense. Nonetheless, plaintiffs have not been able to sustain a claim that a vaccine was defectively designed.

■ Liability for Errors and Omissions in Warnings

In view of the impossibility of creating a risk-free vaccine, tort law imposes an obligation on the manufacturer to warn of inherent risk. The history of vaccine warning defects litigation parallels the history of litigation involving informed consent to medical care. The two differ, however, in *whom* must be warned: a vaccine manufacturer ordinarily has a duty only to warn the physician prescribing its vaccine, not the person taking the vaccine; a physician has a duty to inform the patient of any vaccine risks.

In the 1960s, the majority of medical consent cases involved a failure to warn a patient of the risk of undergoing a specific medical procedure (53). Physicians failed to mention even the inherent possibility of death or paralysis, often because they believed that the patients would refuse the therapy if advised of the risk (91).

Courts uniformly found that the patients' right of self-determination entitled them to accept or refuse any treatment, even if their choices were foolish, as long as they were competent to make medical decisions (226, 231, 281, 293). In order to exercise that right, patients needed information that only physicians could provide, so the law imposed a duty of disclosure upon physicians that required them to tell patients not only the benefits of alternative treatments but also their material risks. Similarly, the first vaccine cases involved the absence of warnings of the risk of contracting poliomyelitis from the oral polio vaccine (235, 290).

⁶⁵ The proposed revision of the *Restatement* also continues this rule (5). But see *Hurley v. Lederle Laboratories*, (264), finding that the Food, Drug and Cosmetic Act and the Public Health Service Act preempted state claims as to the FDA's determination of the proper wording of a warning, provided that the manufacturer has not withheld any relevant information from the FDA.

⁶⁶ The Medical Devices Act (21 U.S.C. 360g et seq.) expressly preempts state laws affecting most medical devices. Two federal courts have found the statute's language precludes strict liability actions under state tort law for medical devices that require premarket FDA approval (274); *Stamps v. Collagen Corp.*, (306) Other courts have reached different results depending upon the device's classification and requirements for premarket approval (58, 275, 278, 279, 304).

⁶⁷ Design defect causes of action have been used primarily against commercial products, such as asbestos, consumer products, and medical devices, such as the Dalkon Shield, the Copper-7 IUD, the Bjork-Shiley heart valve, and silicon-gel breast implants (61).

A failure to warn can be prevented by providing a warning. But, as the next generation of informed consent cases showed, some warnings failed to mention material risks. Similarly, more recent vaccine cases have turned on the adequacy of the warning given. However, like informed consent cases, the majority of reported cases have been decided in favor of the defendant manufacturer or physician (238, 270, 289, 299).⁶⁸ This is primarily because vaccine makers have been exempted from the general duty of manufacturers to provide warnings directly to consumers.⁶⁹

The exception, known as “the learned intermediary rule,” holds that a manufacturer of prescription drugs or vaccines need only warn the prescribing physician, not the patient who receives the product (248, 255, 269, 310, 313). Courts have generally limited the manufacturer’s duty to warn consumers directly to those circumstances in which a vaccine is given *without* the intervention of a “learned intermediary,” generally a physician who makes a medical judgment that the vaccine is appropriate for an individual patient (63, 144).⁷⁰

Thus, a vaccine manufacturer’s duty to warn consumers directly applies only in mass immunization or routine public health programs where physicians are not making “individualized medical judgments” (235, 264, 286, 290). It has been applied to two vaccinations given in a private physician’s office, where the physician testified that he acted like a public clinic employee, dispensing vaccine without evaluating individual recipients (249, 294). Two of these cases appear to have given rise to the fear in the 1970’s and 1980’s that manufacturers would have to warn all vaccine recipients directly (235, 290). Recent cases, however, have reiterated that a vaccine manufacturer’s

duty to warn is limited to the prescribing or dispensing physician alone because patients cannot obtain vaccines except from a physician or medical clinic (258, 285, 288, 292, 301, 307, 322).

To succeed on a claim of inadequate warning, the plaintiff must prove that an adequate warning to the physician would have prevented the injury. This entails proving that the warning would have persuaded the physician not to give the vaccine to the patient, as well as proving that the injury would not have occurred if the vaccine had not been given (246, 307, 310, 321).

Physicians and other providers do have an independent obligation to warn patients of vaccine risks as part of their duty to obtain informed consent to any vaccination, regardless of the manufacturer’s action. Aside from patients with immunosuppression or allergies, however, it is often impossible to predict whether an individual patient is at risk of experiencing an adverse reaction to a vaccine, at least the first time it is given. Therefore, it is questionable whether an individualized medical evaluation would affect a physician’s recommendation about vaccination in most cases, and several cases have been decided against plaintiffs on the ground that the warning did not or would not alter the physician’s decision.

The National Childhood Vaccine Injury Act barred any cause of action for a manufacturer’s failure to directly warn a recipient (or a recipient’s parent or guardian) about the risks of any childhood vaccine covered by the compensation program. It also created a rebuttable presumption that warnings approved by FDA are adequate (42 U.S.C. 300aa-22(b), (c)). At the same time, the act required the Secretary of Health and Human Services to develop new written materials to provide

⁶⁸ Although the academic literature contains numerous articles debating the merits of the doctrine of informed consent to medical care, the number of cases actually claiming lack of informed consent remains very small and few such claims succeed.

⁶⁹ Section 402A of the *Restatement* imposes liability for inadequate warnings by sellers even if they do not sell directly to consumers. The duty was imposed on the manufacturer because it, not the retail seller, controlled the condition of the product, assuming it had not been altered after it left the manufacturer’s hands. The proposed revision of the *Restatement* retains this general rule and the exception for prescription drugs. (5)

⁷⁰ A few cases have found that a nurse acted as a learned intermediary (*Rohrburgh v. Wyeth Laboratories, Inc.*, (292); *Walker v. Merck & Co.*, (317) (*Mazur v. Merck & Co., Inc.*, (276)). but others disagree on the grounds that nurses do not ordinarily make medical judgments.

parents with information about the benefits and risks of each childhood vaccine. Earlier, the CDC, which buys about half the domestic supply of pediatric vaccines, had prepared “Important Information Sheets” to serve as warnings, and the CDC played a primary role in drafting the materials required by the act.

Before the act took effect, most childhood vaccine manufacturers had required the CDC to assume responsibility for providing such warnings or alternatively to have a learned intermediary dispense the vaccine as a contractual condition of the sale of vaccines. One federal court of appeals recently held that a vaccine maker fulfilled its duty to warn by such a contract with the CDC, regardless of whether or not the warning actually reached the recipient (276). More recently, the Supreme Court of Nevada reached the opposite conclusion where the vaccine was distributed by a county health district with information sheets prepared by the CDC (219). The court found that the manufacturer cannot be relieved of ultimate responsibility for an inadequate warning where it knew that the contractor used warnings that omitted risk information the manufacturer had provided with the vaccine.

Liability based on inadequate warnings has been criticized on the ground that it is too difficult to describe vaccine risks in terms that patients can understand.⁷¹ The legal doctrine does not require that patients understand the information included in the warning, although it is obviously better if they do. Instead, most courts require only that the risks be disclosed in ordinary language that is understandable by a reasonable lay person (226, 231). Because the learned intermediary rule applies in most vaccine cases, however, warnings

are directed not to patients, but to physicians, who are presumed competent to understand technical information and its implications.

A few cases have found specific warnings inadequate because they failed to apprise physicians of the vaccine’s known risks (240, 311). In most cases, warnings have been found adequate in that they disclosed all reasonably known risks (238, 270, 273, 288, 299). As with all cases alleging design defects, the state of scientific knowledge determines whether a risk should be disclosed (225, 242, 243, 255), and FDA approval of labeling information is often persuasive evidence of the adequacy of a warning (242, 296).

Most lawsuits claiming injury from vaccines allege several bases for liability, including defective design, inadequate warning, and negligence in manufacture, design, or risk disclosure. Because, except for manufacturing defects, strict liability requires proof similar to that required to prove liability for negligence, the specific cause of action may be less important than the possibility of any liability.⁷² This means that where a vaccine maker is exempted from liability on one basis (such as design defects), it may be subject to claims of liability on other grounds. Specifically, the number of claims against vaccine makers may not be effectively reduced unless manufacturers are exempted not only from strict liability but also from liability for negligence.⁷³

■ Practical Problems with Litigation

Even if the principles of product liability law are sensible in theory, there can be practical problems with product liability litigation. The lengthy and cumbersome process of discovery, trial, and sometimes appeal is a perennial subject of legiti-

⁷¹ Similar concerns about the difficulty of describing risks have arisen with respect to informed consent to other medical procedures and informed consent to experimentation with human subjects. Sometimes such concerns mask a reluctance to disclose the risk at all or professionals’ discomfort with revealing uncertainty about risks (91). Recently, radiation experiments conducted in the 1950s have been denounced primarily because the human subjects of the experiments (including residents at schools for the mentally retarded and terminally ill patients) were not necessarily told that they were to be part of an experiment or any risks that it might entail (11, 75).

⁷² The cases finding a defective vaccine were based on an implied warranty of merchantability (284, 311).

⁷³ For further discussions about HIV vaccines and product liability see Rosenfeld, 1991 (149); Smith, 1992 (168); Arnold, 1991 (13).

mate complaint. This is true whether the basis for suit is strict liability or negligence. Determining whether a particular injury to an individual was caused by a particular vaccine and whether the risk could have been avoided is a complex, time-consuming, and expensive process for both sides of a dispute. Even if it is decided that the plaintiff should be compensated, determining the amount of damages has become a similarly complex matter. Although alternative dispute resolution procedures can be somewhat cheaper and faster than courtroom litigation, they do not eliminate the need to prepare a case. Thus, the very process of dispute resolution can discourage both the pursuit and defense of claims, as well as the thoughtful application of the law.

Studies of tort claims indicate that ten percent or less of claims are tried in court (46, 69, 73). The rest are withdrawn or settled before trial, with roughly half resulting in some payment to the plaintiff, although in lower amounts than average trial awards. This means that defendants have to deal with many more claims than wind up in court. There is no publicly available data showing whether similar figures apply to cases involving vaccines. If court awards influence settlements, as they are believed to do, then the low proportion of court decisions favoring plaintiffs may suggest that a lower-than-average proportion of claims are settled with payment to a plaintiff in vaccine cases.⁷⁴

It may not be the number of claims, but the possibility of an expensive mistake that worries vaccine makers. One kind of mistake is when a jury makes an error of fact, reaching a verdict that is not supported by credible evidence. In principle, such a mistake can be remedied on appeal, although additional time and expense can turn even successful appeals into pyrrhic victories. Some factual mistakes are inevitable in any dispute resolution system, whether or not it employs litigation.

Variations in each party's ability to produce credible evidence and present its case mean that some cases that ought to be won are lost and others that ought to be lost are won. Ideally, dispute resolution methods should be designed to minimize both types of errors but the ideal is not likely to be achievable without substantial additional expense.

A second type of problem is more difficult to avoid. These are mistakes arising out of the uncertainty of scientific knowledge that must be used to identify and categorize the possible risks and benefits of drugs and vaccines. If the essence of a defective design is the availability of knowledge indicating an unreasonable danger, at least in light of expected benefits, then information indicating that a drug might produce an adverse reaction is potential evidence of a design defect or a risk that should have been disclosed. It is, however, only *potential* evidence because it is a matter of knowledgeable interpretation whether and how the risk might materialize, and whether the possibility is sufficiently credible to warrant further investigation. A manufacturer might reasonably determine that the problem was a "fluke." But in a later lawsuit, the plaintiff might conclude that the manufacturer ignored an important potential risk. In some cases, it is impossible to know whether a drug or vaccine caused a particular injury in an individual or even whether it was capable of causing such an injury. In those cases, there may be no way to know whether a mistake was made, whatever the outcome might be.

If the law is not properly applied, then the process, not the law, stands indicted. But if the law cannot be properly applied at all in some circumstances, then it cannot serve its purpose. Unfortunately, there is no good information to determine what proportion of cases have been decided correctly or incorrectly, or what proportion cannot be decided correctly for lack of scientific

⁷⁴ Most reported court opinions that make final decisions in a case have dismissed a plaintiff's complaint or granted judgment for the defendant manufacturer (225, 255, 270, 271, 285, 288). However, few reported decisions contain final dispositions of a case. Most determine whether a plaintiff is entitled to go to trial. The outcome of any such trial or settlement in lieu of trial remains unreported.

knowledge (60, 153). Thus, we do not know whether litigation is producing good or bad decisions.

These types of uncertainties can give rise to fears of unwarranted liability on the part of vaccine makers. They can be compounded by fears of high damage awards, including punitive damages. Most punitive damages awards are in cases of intentional torts (like assault), unfair business practices, or fraud or bad faith in contracts.⁷⁵ Because liability for personal injury is rarely based on intentional or fraudulent conduct, but on negligence or strict liability, there should be little occasion for punitive damages.

The few studies that have been done have concluded that punitive damages are rarely awarded in personal injury actions and, where inappropriately awarded, are ordinarily reduced or reversed on appeal (45, 135, 185). The only known punitive damage award in a vaccine case was reversed on appeal and the vaccine maker found immune from liability (270). Punitive damages do not appear to be a significant factor in product liability (104).⁷⁶ In product liability cases, they are more likely to be awarded in cases involving defective automobiles or other consumer products than drugs or vaccines. Uncertainty surrounding inappropriate damage awards applies to almost all types of litigation.⁷⁷ Whether litigation itself is a necessary form of dispute resolution depends upon the feasibility of alternatives.

POTENTIAL LIABILITY FOR ADVERSE REACTIONS TO HIV VACCINES

Vaccines are ordinarily subject to liability for negligence, manufacturing defects, defects in design, and inadequate warnings of risks. However, liability is rarely found in specific cases. Why, then, is the perception of excessive liability for adverse reactions to vaccines so prevalent?

■ Vaccine Susceptibility to Liability Claims

Fear of liability may arise from several factors that distinguish vaccines from pharmaceuticals and other biologics and that may encourage people to pursue tort claims. Prophylactic vaccines are taken by healthy people to prevent disease. This means that adverse reactions are more noticeable and may be perceived as less tolerable than adverse reactions to a drug that a person takes to relieve the symptoms of illness. Vaccines may also be taken by sufficiently large numbers of people to permit the occurrence of a rare side effect that might not materialize in a smaller group.⁷⁸ When a healthy person who takes a vaccine suffers an illness or injury, there may be a natural desire to find a cause beyond random accident or one's own behavior. These factors are likely to encourage attributing the injury to the vaccine, correctly or incorrectly, especially when there has been no other change in the person's circumstances.

⁷⁵ The U.S. Supreme Court upheld a state punitive damage law as against a challenge that it was an unconstitutional violation of due process in *Pacific Mutual Life Insurance Company v. Haslip* (283). In their brief amicus curiae, the Pharmaceutical Manufacturers Association and the American Medical Association cited two instances in which punitive damages had been awarded with respect to drugs (an oral contraceptive and Coumadin) (136).

⁷⁶ Plaintiffs may include *claims* for punitive damages in their complaints, but they are rarely awarded. Similarly, the amount a plaintiff may claim for compensatory damages often bears little relationship to the amount, if any, actually awarded or collected. There is some evidence that, in cases in which compensatory damages are awarded, the amount of damages correlates with the severity of the injury (46).

⁷⁷ Physicians and scientists may empathize with vaccine makers' fear of liability in light of the widespread fear of medical malpractice litigation among medical practitioners. In both instances, the actual risk of being sued (and of losing a lawsuit) appears to be significantly lower than is believed by those who might be the target of a lawsuit (25, 109, 182).

⁷⁸ Of course, some drugs (like Valium and aspirin) are taken by millions of people.

When adverse reactions are suffered by children, the financial consequences can be severe. In cases of serious permanent injury, inability to work and the need for expensive rehabilitative or custodial care over a lifetime generate substantial costs that may not be covered by private or public insurance. A lawsuit for substantial damages may be the only source of payment for needed services. This may account for relatively more concern about potential liability for adverse reactions to vaccines administered to children than for those given to adults. Of course, the potential for large damages also exists with most drugs used by children and pregnant women.⁷⁹

Latent hazards that may not have been detectable before marketing may materialize ten or twenty years after a vaccine (or drug) is used. There is a greater chance of discovering such hazards when vaccines are used in children and young adults with longer subsequent life spans than those expected for older adults.

Thus, even if tort principles make it difficult for a plaintiff to win a lawsuit, there may be more claims brought with respect to vaccines than with respect to ordinary drugs.

■ Potential Adverse Reactions to HIV Vaccines

The risks of HIV vaccines most commonly mentioned are: 1) low levels of effectiveness (so that not every vaccine recipient is protected); 2) enhanced susceptibility to HIV infection (increased risk of acquiring infection upon exposure); 3) more rapid than normal (enhanced) progression of disease if HIV infection is acquired; 4) the development of cancer many years after vaccination;

and 5) direct vaccine-induced HIV infection from inadequately attenuated or inactivated virus in vaccines made from killed or attenuated HIV. In addition, HIV vaccination may result in social harms.

Low Levels of Effectiveness

There has been speculation among researchers that some candidate HIV vaccines now in clinical trials may ultimately prove effective in less than half of the vaccinated population.⁸⁰ If the vaccinated population is at risk for HIV infection, as anticipated, then some proportion may become infected after taking a vaccine of limited efficacy, even if the vaccine is not defective. Claims based on low levels (or lack) of effectiveness have not been brought against existing vaccines. The likelihood of success of a claim of lack of effectiveness of an HIV vaccine is speculative, but probably small as long as those who take the vaccine are warned of its limited efficacy and advised to take precautions against exposure to HIV infection.

A claim based on defective design would have to demonstrate either that a more effective vaccine was feasible or that the level of efficacy was so low that the vaccine should not have been marketed at all.⁸¹ Given the difficulties of finding a vaccine that works at all, and the need for a vaccine to prevent any additional HIV infection, neither requirement would be easy to meet. The more likely basis for a claim would be inadequate warning of the vaccine's limited effectiveness and the need for the recipient to take appropriate precautions. Ordinarily, a plaintiff would have to prove that any warning to the physician was inadequate and that an adequate warning would have caused the phy-

⁷⁹ This has fueled fears of large claims for contraceptive products and drugs used by pregnant women (31). The number of successful claims, however, appears to be smaller than the perception (44).

⁸⁰ For a discussion of effectiveness of current vaccines in development, see chapter 2.

⁸¹ The latter theory raised the possibility of a claim against the FDA for approving a vaccine in violation of its own standards of safety and effectiveness, although it would be difficult to prove that the level of effectiveness was too low in light of the need for a preventive vaccine. The United States Supreme Court has found that, under the Federal Tort Claims Act, the FDA may be subject to suit if it fails to follow its own governing statute and regulations, unless it is performing a discretionary function (222, 266). In the absence of any statutory or regulatory requirement for any minimum level of effectiveness, the balancing of risks and benefits in the approval of a new HIV vaccine is likely to be treated as a discretionary function which is exempt from challenge.

sician either not to recommend the vaccine or to warn the plaintiff more strongly against risk behaviors (119). If physicians are properly warned of a vaccine's limited effectiveness, the plaintiff would have no cause of action against the manufacturer. Rather, any claim would be against the physician for lack of informed consent.

In addition, a plaintiff would have to prove that he or she failed to take appropriate precautions against infection *solely* because of the inadequate warning. If the infection were acquired through sexual contact, the plaintiff would have to prove that he or she would have abstained from sex or used barrier protection in most, if not all, relationships. If the transmission occurred through intravenous (IV) drug use, it may be especially hard to prove that the plaintiff would have abstained or used precautions, like sterile needles.⁸² Alternatively, a plaintiff would have to prove that he or she would not have taken the vaccine had an adequate warning been given, and that *not* taking the vaccine would have prevented infection. Both alternatives would entail proving the somewhat implausible: continuous use of precautions against infection or complete avoidance of exposure to HIV infection.

Enhanced Susceptibility to Infection or Disease Progression

Some researchers have theorized that candidate vaccines might have the potential to increase one's susceptibility to infection with HIV or other organisms (24). Others have speculated that a vaccine might increase the rate of disease progression in people who become infected with HIV in spite of vaccination.⁸³ Both hypotheses raise the possibility of a claim for defective design if they are not investigated, or a claim for inadequate warning if they are not disclosed. Such a claim would face

the same difficulties as a vaccine with low levels of effectiveness, discussed above. In addition, a plaintiff would have to prove that the manufacturer knew or should have known that the vaccine was capable of causing the reaction. The strongest case against a manufacturer would be one in which the vaccine was demonstrated to cause the susceptibility in controlled clinical trials. This suggests that such hypotheses should be studied, at least to attempt to determine whether they are realistic concerns or merely theoretical.⁸⁴ Potential liability may provide an incentive to vaccine makers to invest in additional vaccine research, which may both clarify the vaccine's safety profile and increase the eventual cost of development. In this respect, however, HIV vaccines do not differ from other vaccines or drugs.

Development of Cancer

There has been speculation that, because HIV is a retrovirus, an HIV vaccine might cause cancer many years after vaccination.⁸⁵ The likelihood of a claim for vaccine-induced cancer is also similar to the claims for other potential adverse reactions. It differs primarily in the length of time it may take for the reaction to be discovered. This means that, in the absence of feasible studies that could predict the risk, if any, of cancer, neither manufacturers nor vaccine recipients would know whether the vaccine posed any such risk for perhaps two decades. Although a manufacturer is not liable for injuries caused by unforeseeable dangers in its products, there may be some question as to whether a manufacturer adequately investigated a suggested risk. Given the need for an HIV vaccine, however, it seems unlikely that a manufacturer would be held responsible for distributing a vaccine with a risk that could not be verified at the time it was released.

⁸² As a practical matter, juries may have little sympathy for habitual drug users.

⁸³ For a discussion of vaccine-induced enhancement of disease susceptibility, see chapter 2.

⁸⁴ Since some subjects who received investigational preventive vaccines have become infected, there is renewed attention to examining whether the vaccine simply failed to prevent HIV infection or might have enhanced the risk of infection upon exposure.

⁸⁵ The potential of an HIV vaccine to cause cancer is discussed in chapter 2.

Vaccine-Induced HIV Infection

Non-recombinant vaccines that use killed, inactivated, or attenuated virus have been reported to hold some promise (124). Concern about such vaccines arises from the possibility, albeit remote, that the manufacturing process might inadvertently fail to remove or render harmless part of the virus that could actively infect a person, or that an attenuated virus could revert to an infectious state.⁸⁶ Reports of newborn monkeys that became ill after inoculation with a live attenuated virus vaccine to prevent SIV may increase such concerns. A person who became infected with HIV from such a vaccine would have a claim against the manufacturer for injury caused by a manufacturing error.

It is unlikely that a claim for design defect would be possible, except in the unlikely event that the manufacturer knew or should have known that its manufacturing process could not render the virus incapable of infection. Although claims of vaccine manufacturing errors have been rare in the past, the consequences of a batch of vaccine accidentally escaping inactivation are sufficiently serious to make this type of vaccine unappealing to many vaccine makers. Thus, potential liability for manufacturing errors may discourage companies from developing this type of vaccine, and provide relatively greater incentive to pursue recombinant vaccines. At the same time, companies may not wish to pursue a type of vaccine that might produce HIV infection, regardless of exposure to liability, especially if they believe that they cannot eliminate the risk of manufacturing error.

Social Harms

HIV vaccines may pose risks of social harm that are not ordinarily linked with other vaccines or drugs. People who receive HIV vaccines will test positive on screening tests, making them especially vulnerable to denials of health or life insurance,⁸⁷ permission to travel abroad,⁸⁸ loss of employment or housing,⁸⁹ segregation in institutions, or rejection by family and friends (2) (98, 114).⁹⁰ People institutionalized in prisons or mental health facilities may be segregated or victimized. Other forms of discrimination and stigmatization are also possible. The possibilities remain largely unexamined.

An HIV vaccine may produce an antibody reaction that may be difficult to distinguish from a positive test for HIV infection, so that vaccine recipients may be mistakenly believed to be HIV positive. But vaccine recipients (and subjects in vaccine clinical trials) may be targeted for discrimination on the assumption that they are members of a risk group, regardless of whether they are shown to have HIV infection. Moreover, most such harms result from lawful conduct for which the vaccine recipient would have no legal recourse. Although job loss might violate the Americans with Disabilities Act (42 U.S.C. 12101 et seq.), most other forms of discrimination would not, and no law prevents family members, lovers, and friends from abandoning someone stigmatized as at risk for HIV infection.

Although such risks should be made clear to anyone who takes a vaccine, there is no precedent

⁸⁶ The potential for whole killed virus or attenuated virus vaccines to cause infection is discussed in chapter 2.

⁸⁷ Many health, life, and disability carriers now require an HIV test for individual coverage or extended coverage (173).

⁸⁸ The Department of State lists 45 countries that have restrictions on entry of HIV-infected individuals to their countries and require HIV tests of all or some people entering their countries (202).

⁸⁹ The U.S. armed forces, the Department of State, Job Corps and some other employers either require or urge employees to have HIV tests as a conditions of employment.

⁹⁰ These social harms are discussed in further detail in chapter 3.

for holding a vaccine maker liable for their occurrence, and it is unlikely that a claim would be successful on such grounds. Manufacturers are not responsible for the bigotry of others. Product liability is intended to impose responsibility for physical injury caused by defective products, not personal insults resulting from discriminatory actions. There does not appear to be any basis for counting social harm as either a manufacturing defect or a design defect.

It might be possible to claim that an adequate warning *should* include the risk of social harms.⁹¹ A successful cause of action would require the plaintiff to prove that he or she would not have been identified as at risk for HIV infection but for the vaccination. But, ordinarily it would be the act of vaccination, not the vaccine itself, that confers any stigma. Moreover, it is unlikely that a vaccine maker would be responsible for specifying social risks, since such risks are not necessarily within the realm of expertise of vaccine manufacturing. Physicians who administer HIV vaccines may be the more likely target for any claims that a vaccine recipient was not adequately warned about possible discrimination.

■ Different Uses of Vaccines

The same principles of liability apply to manufacturers of all vaccines, regardless of whether they are preventive (intended to prevent) or therapeutic (intended to treat or cure infection or disease), and regardless of whether the vaccines are experimental (investigational) or approved and licensed. The likelihood of adverse reactions and liability claims occurring may differ, however, depending upon the way in which a vaccine is used.

Preventive HIV Vaccines

Preventive HIV vaccines have most of the factors that make vaccines more susceptible to liability claims than drugs. They are intended for use by healthy individuals who may be sensitive to the

appearance of adverse reactions. At the same time, HIV vaccines are likely to be given to people at risk for HIV infection for the foreseeable future. Several risk groups are also at risk for other diseases, such as Hepatitis B and other blood-borne and sexually transmitted diseases. It may be difficult to distinguish some symptoms or illnesses from other causes from adverse reactions to vaccination, at least until sufficient years of experience with the vaccine have produced reliable data identifying vaccine-related risks.

Uncertainty about the cause of illnesses following vaccination may encourage vaccinees to attribute injuries to the vaccine and seek legal redress against manufacturers. On the other hand, the difficulty of demonstrating that the vaccine caused the injury is likely to discourage or defeat product liability claims. In other words, the very uncertainty that may increase the likelihood of lawsuits also decreases the probability of plaintiffs' success on the claims.

The characteristics of the populations that use an HIV vaccine may influence the potential for liability. Most people at risk of HIV infection are young adults with a relatively long life expectancy. Potential damages for permanent injury arising from vaccination could be substantial, although less than those for young children. A growing proportion of people at risk, however, are IV drug users, many of whom are not working and may not be able to claim lost income as damages. However, if the majority of people who actually take an HIV vaccine are middle-class workers, then permanent injury that deprives them of the ability to work will give rise to potential damages for lost income, as well as medical expenses. If HIV vaccines are given to newborns and young children, the potential damages increase proportionately with life expectancy. Pregnant women who are HIV-positive and take a vaccine to prevent transmission to their children can expect very limited damages because of their preexisting condition and shorter life expectancy.

⁹¹ Ethical principles would certainly require such warning in careful counseling sessions, but ethical principles go beyond legal duties. For a discussion of ethical duties to warn about adverse reactions to HIV vaccines, see chapter 3.

The number of vaccinations may also affect potential liability. If an HIV vaccine's effectiveness is limited over time and requires several doses and booster vaccinations, there are more opportunities per vaccinee for adverse reactions and for injuries following vaccination to be attributed to the vaccine. The costs involved may be balanced to some degree by the increased sales generated by a multiple dose vaccine.

In summary, the potential for liability arising from the use of an approved HIV vaccine appears to be similar to what might be expected from any new vaccine intended for use by adults. Although the possible damages from a successful lawsuit may be large in the case of a permanently disabled young adult or child, the probability of a successful lawsuit appears to be quite low. Although an HIV vaccine might carry unknown latent risks that portend a DES-like future, that possibility probably exists for every new drug and vaccine marketed. HIV vaccines are not unique in this respect. Currently, the most likely basis for liability claims is an inadequate warning of low levels of effectiveness or limited protection against HIV infection. Yet it would be very difficult for anyone who became HIV positive to prove that his or her infection was caused by either the vaccine or an inadequate warning of the vaccine's limited protection. Physicians are likely to be more vulnerable to such claims than vaccine makers.

Investigational HIV Vaccines

The potential for liability for adverse reactions to investigational preventive HIV vaccines is less than that for marketed vaccines. The legal grounds for liability are the same for both investigational and approved vaccines. But the nature of investigational vaccines and clinical trials reduces both the likelihood of claims and the probability of successful claims in practice.

It is generally understood that the purpose of clinical trials is to determine how safe and effec-

tive an experimental vaccine may be and whether unpredictable adverse reactions may occur. There are more protections for subjects in clinical trials than for patients in ordinary medical care settings. Federal regulations governing both federally funded research with human subjects and research intended for submission to the FDA require that subjects' informed consent be in writing in a document approved by an institutional review board (21 U.S.C. Parts 50 and 56). Regardless of the merits of the document itself, prospective subjects are likely to be made aware that they will be part of a research experiment and that the vaccine has not been approved by the FDA. The subject's consent has the legal effect of making the subject assume responsibility for any disclosed risks that materialize. Since most informed consent documents note that not all risks can be predicted and unknown adverse reactions might occur, there is little basis for a claim that the subject was not properly warned.

Historically, there have been no cases of product liability claims involving research, probably because there has been a very low incidence of observed or reported injury among research subjects (27, 118, 200).⁹² Rare adverse reactions may not materialize in a small cohort of research subjects and side effects may be reversed or minimized promptly where the subjects are being monitored by research investigators. Design defect claims are also minimized, if not precluded entirely, by the fact that the trial is being conducted to find out whether the vaccine works and whether it has dangerous side effects. Not until such trials are concluded and a risk is discovered or confirmed is there any significant basis for claiming that the vaccine was defectively designed.

It is possible that a vaccine might be too dangerous to test in human subjects at all. But this could only be inferred from prior laboratory research which should be reviewed by the FDA and an institutional review board. Those bodies serve

⁹² There have been several cases in which people were not told they were being used as human subjects in a research study or that the research could produce serious harm (9, 188, 265, 183).

as a safeguard against proceeding with unjustifiable research and, although imperfect, they ordinarily should prevent unreasonably dangerous research from going forward.

The most likely risk of a preventive vaccine trial is that a research subject may believe that the vaccine is effective to prevent HIV infection, fail to take precautions, and become infected. (In a blinded, randomized trial, the subjects are not told whether they have received the investigational vaccine or a placebo, although they can find out by getting tested, even if they are asked not to do so.) As with marketed vaccines, the subject might claim that he or she was not adequately cautioned against risk behaviors, but would probably find that especially difficult to prove in a research setting. The written informed consent document would provide evidence that the information was given. Such documents have proved sufficient to defeat claims of lack of informed consent by patients in medical settings (320). The best solution to such a problem is to prevent it, by making clear the uncertainty about the candidate vaccine before a subject agrees to participate in the trial.

Another potential, but probably remote, risk is that use of an early candidate vaccine would preclude a subject from participating in a later investigational study of a newer vaccine, perhaps one that proved to be more effective. Again, the most likely basis for a claim would be lack of informed consent, with results similar to those described above. It may be more difficult to explain the nature of this type of risk unless there is some laboratory basis for predicting the effectiveness of vaccines that have not yet been fully developed.

Finally, subjects who experience some of the social risks of participating in a vaccine trial may claim lack of informed consent to such risks. Merely volunteering for a vaccine trial can expose the subject to discrimination. Research subjects may be more vulnerable to social harms than the recipient of a marketed vaccine, because participation in a vaccine trial may be discovered more easily than receipt of a vaccine from a private physician or public clinic. As with physiologic reactions, the precise social risks that may befall a vaccine recipient may not be predictable in advance.

Indeed, vaccine trials may gather as much information about such risks as they do about vaccine safety and effectiveness. Thus, the risk of liability again depends upon the clarity with which the risk of social harm is presented, and the responsibility for warning prospective research subjects would lie with the investigators rather than the vaccine manufacturers.

Therapeutic HIV Vaccines

Therapeutic HIV vaccines that are used to treat people already infected with HIV are comparable to drugs. The special concerns surrounding the use of preventive vaccines do not apply. Patients and research subjects who take therapeutic vaccines may be willing to accept accompanying risks in order to receive any benefit the therapeutic vaccine might afford, as they have with drugs like Zidovudine, ddI, ddC, and d4T. Adverse reactions to the vaccine may be especially difficult to distinguish from other symptoms related to HIV infection and opportunistic infections and illnesses. Moreover, the potential for damages is quite limited because of the perceived limited life expectancy of people with AIDS. Perhaps this is why there have been no reports of fear of liability for adverse reactions to therapeutic vaccines. Even companies that reported fear of liability for their preventive vaccines actively pursued clinical trials of their therapeutic candidate vaccines without mentioning liability as a concern.

■ Conclusion

Preventive vaccines may be more susceptible to claims of liability than most drugs and biologics, primarily because they are ordinarily used in large numbers of healthy people. Their extensive use can permit even rare adverse reactions to materialize and people who expected vaccines to prevent disease may be less tolerant of such reactions than sick patients. As with drugs, the majority of claims have been directed against only a few vaccines. Despite the increased probability of claims, the proportion of reported cases that impose liability on the vaccine maker is very small. There is no publicly available evidence on the number or result of claims that were withdrawn or settled be-

fore a court decision. Thus, although the probability of *claims* of liability may be relatively high, the probability of actual *liability* is relatively low.

The main causes of action against a vaccine maker are claims of a defectively designed vaccine and an inadequate warning of vaccine risks. Plaintiffs have not succeeded on a claim of defective design, probably because of the improbability of demonstrating that a safer, equally effective vaccine could have replaced a vaccine approved by the FDA.⁹³ Few courts have found a vaccine maker liable for an inadequate warning of risks. More extensive and sophisticated warning statements may have improved vaccine makers' protection against such claims. In addition, a vaccine maker's duty to warn is ordinarily limited to the prescribing physician, who bears responsibility for disclosing vaccine risks to patients. Thus, physicians may now be more vulnerable to claims (of lack of informed consent) than vaccine makers.

The probability of future claims of adverse reactions to an HIV vaccine is impossible to predict because it depends upon what, if any, adverse reactions occur and whether they could be plausibly attributed to the vaccine. The probability of courts imposing liability in the case of an HIV vaccine appears to be about the same or lower than in the case of existing vaccines. This is primarily because of the difficulty of demonstrating that an adverse reaction was caused by the vaccine. Also important is the possibility that the most predictable risk of vaccination is discrimination against the person vaccinated for which manufacturers are not likely to be responsible.

Fear of liability for adverse reactions to vaccines may have been based on a perception in the 1970s and early 1980s that courts were expanding the grounds for liability. That expansion appears

to have halted and, although there is no guarantee that it could not recur, there is no reason to assume that it will.⁹⁴ More important, it is difficult to argue that the principles of product liability are unfair in theory. Rather, the major concern lies with the time, expense and uncertainty of the litigation process and the fear that the law will not be applied correctly, so that a vaccine maker is mistakenly held liable where it should not be.

Since liability itself is so rarely imposed, fear of liability may be more accurately described as fear of having to litigate at all. This is understandable, but not limited to cases involving HIV vaccines. Therefore, there appears to be little, if any, basis for claiming that HIV vaccines present a special or increased risk of liability. This does not mean that an alternative means of allocating responsibility for injury and compensation is not warranted for other reasons. It does mean that any alternative that is intended to remedy tort litigation's inefficiencies would have application beyond HIV vaccines.

ALTERNATIVE COMPENSATION POLICY OPTIONS

People who are injured as a result of vaccination with an HIV vaccine could receive compensation in a variety of ways. Currently, their only option, apart from private health and disability insurance, is likely to be a product liability claim against the vaccine maker, or a claim of professional negligence (medical malpractice) against the physician or other health care provider who vaccinated the individual, if the circumstances support a legal cause of action⁹⁵

This section summarizes several major policy options for compensating HIV vaccine-related injury—reforms in tort liability, voluntary contrac-

⁹³ The only reported decisions (in 1969) finding a vaccine (QuadriGen) defective were based on warranty, not tort law (284, 311). Whether any vaccine maker has settled any claims with payment to the plaintiff on this basis is unknown.

⁹⁴ If the revised version of the *Restatement of Torts* volume on product liability is accepted, the grounds for liability for design defects will be narrower than current legal principles in states that permit the cause of the action at all (5).

⁹⁵ Some recourse may be available with respect to California vaccines under a California statute, described below.

tual arrangements, government-financed insurance systems, and public no-fault compensation programs—and their advantages and disadvantages.⁹⁶ It also considers several alternative approaches to encouraging HIV vaccine development that focus on overcoming financial and scientific difficulties. Which option is best depends upon the goals to be achieved by compensation and how alternative approaches affect the achievement of other important goals like prevention of disease, deterrence of injury, and the just distribution of resources.

TORT LIABILITY REFORM

Tort liability functions as a compensation system by imposing legal responsibility for compensating certain specified injuries. It is also justified as a means of retributive justice or risk deterrence (51, 59, 210). Whether or not it serves adequately as a deterrent to risk, it is widely criticized as either ineffective or inefficient in providing equitable compensation. The tort system does not provide compensation to all victims of injury. In theory, compensation is allowed only in cases in which a plaintiff can prove another party's legal responsibility for an injury. In practice, many people who might have a valid cause of action in tort do not file a claim or receive compensation, and others who may not have a legitimate claim may pursue a cause of action and receive compensation (69, 74, 109).

The most common criticisms are that tort litigation is unreasonably time-consuming and expensive and often unpredictable or inconsistent, with some plaintiffs seeming to receive undeserved windfalls and others receiving nothing in spite of a legitimate claim (82, 131). Even those who do not support specific tort reform proposals often voice these criticisms (156).

Others argue that product liability principles make manufacturers responsible for injuries that are unavoidable (80, 158, 203). Sometimes the objection is that the law itself grants plaintiffs a

cause of action where, it is argued, it should not be permitted, such as for an injury caused by a design defect. More often, perhaps, the objection is that, in practice, judges and juries apply the law incorrectly, so that a defendant is mistakenly found liable. Of course, judges and juries make mistakes that operate in favor of, as well as against, defendants. But it is the prospect of mistaken liability, not mistaken absence of liability, that most often gives rise to calls for tort reform.

Almost all tort reform proposals seek to limit the liability of potential defendants. Limitations on liability, however, are cost control measures, not compensation mechanisms. Such limitations are ordinarily intended to decrease the number of people who seek and obtain compensation through litigation or the amount of compensation they receive. Such proposals may be justifiable if the goal is to save defendants money and if providing compensation to those who would not qualify under the reformed system is not relevant or desirable. If other goals are important, however, the specific limitations must be analyzed to see whether there is good reason to restrict compensation to a smaller population.

■ Reforms Granting Immunity from Strict Liability

Some vaccine manufacturers and legal commentators have argued that manufacturers should not be held strictly liable for a defectively designed vaccine. Several jurisdictions have, by court decision, already granted manufacturers immunity from strict liability for all vaccines (and drugs) (225, 255, 270, 277). The trend in other jurisdictions, while not granting complete immunity from liability, is for courts to reject claims for drug and vaccine design defects on a case-by-case basis, generally because the product is not found to be defective or the claimed defect was not avoidable (156).

One may draw conflicting conclusions from this trend. One is that the courts that have rejected

⁹⁶ Similar policy options have been reviewed by several groups (82, 95, 191, 201).

strict liability claims are applying the law correctly and as intended to sort out good products from bad ones, and good products are not being found defective. Another is that the courts have applied the law incorrectly, and companies are not being held liable for defective products. Finally, it could be argued that if most reported cases are being found correctly in favor of the defendant, then liability is not needed; drug and vaccine makers should be granted complete immunity from all strict liability, at least for defective design. This assumes that tort law has no deterrent effect. While everyone hopes that no drug or vaccine could ever be defective, it is probably an unrealistic assumption.

The argument for exempting all vaccines from strict liability is basically an argument that drugs and vaccines are special or differ from other products in significant ways that warrant protecting their producers from responsibility for injuries.⁹⁷ The California Supreme Court, for example, distinguished between drugs and ordinary consumer products on the grounds that the latter are used to “make work easier or to provide pleasure, while the . . . former . . . may be necessary to alleviate pain and suffering or to sustain life” (225). Of course, not all drugs have such valuable purposes,⁹⁸ and many ordinary consumer products provide important benefits.⁹⁹ If drugs and vaccines deserve immunity from strict liability, then they must be distinguished from other products on more precise grounds. In the absence of any such distinction, this argument requires exempting not just drugs and vaccines, but all equally beneficial products from strict liability. The alternative is to exempt only those particular drugs and vaccines, as well as other products, that confer special benefits on humankind. This is the kind of risk-benefit

analysis adopted by courts that require case-by-case evaluation of strict liability claims.

A second argument for exempting drugs and vaccines from strict liability (again, excluding manufacturing errors) is that federal regulations provide sufficient incentives to ensure safe and effective products. One reason for the adoption of strict liability was to deter manufacturers from marketing products that are unsafe. Here, the fact that most, if not all, drugs and vaccines are intended to prevent or alleviate suffering is not advanced as a reason to dispense with liability. The importance of drugs and vaccines does not explain why their manufacturers should not be deterred from marketing unsafe products. Rather, drugs and vaccines differ from ordinary consumer products because they cannot be marketed without FDA approval based on substantial evidence of safety and effectiveness.

Federal regulation is said to serve the deterrence function of tort liability, so that liability is superfluous and unnecessarily costly. This is a practical argument with considerable basis in fact. Although FDA approval has not generally been sufficient to preempt a claim, it has often provided convincing evidence to reject a claim that a product could have been made safer. Thus, even if it is appropriate to permit strict liability claims against specific drugs or vaccines, few can be successful where the manufacturer has complied with FDA testing requirements and the product remains approved. If FDA requirements for approval are diluted or its standards for evaluating the safety and effectiveness of vaccines are reduced in order to speed up the availability of an HIV vaccine, the argument loses some of its force. Expedited review by the FDA thus may undermine reliance on regulatory standards. In any event, in reviewing new

⁹⁷ This would leave manufacturers responsible for product injuries that, in theory at least, they could not prevent, while exempting them from liability for errors in design that, again in theory, could have been corrected. In practice, the argument is advanced selectively to seek immunity from liability for design defects and inadequate warnings, not from liability for manufacturing errors.

⁹⁸ Aspirin is intended to relieve pain, but its importance to the public may diminish when it is used to relieve a slight headache.

⁹⁹ Automatic electrical current shut-off devices or furnaces to heat homes, for example, provide important safety benefits and relief from suffering.

drugs and vaccines for approval, the FDA does not explicitly examine whether they might be made safer.

■ Reforms Limiting Liability

Where liability should not be removed entirely, numerous reform proposals are intended to reduce the number (frequency) of claims made, the number of claims in which a plaintiff can succeed (awards), or the amount of compensation payable to a successful plaintiff. Other reforms are intended to expedite the litigation process or make it more accurate or less expensive. A growing number of studies have begun to evaluate tort reforms adopted by the states, primarily those directed to reducing medical malpractice insurance premiums by reducing malpractice litigation (20, 185, 186).¹⁰⁰ In many cases, the generalizability of research results has been hampered by limitations on the data available and variations in study design (193). The studies show that reforms have had somewhat mixed results to date. Few reforms have had a significant effect on the price of insurance, the frequency of claims, or the amount of awards.

A limitation or cap on the amount of damages that can be awarded to a successful plaintiff has been the most effective type of reform to date. As might be expected, caps have been found to reduce the average amount of awards in successful cases in several studies (193). But they have not been found to affect the frequency of claims consistently (46, 213), perhaps because they apply to only a small proportion of claims made. Caps have been enacted to limit either non-economic damages (pain and suffering) or total damages (including incurred medical expenses and lost income).

Different studies have reached different conclusions with respect to the effect of different

types of caps. One study of reforms and malpractice insurance premiums found that premiums were reduced most successfully by a cap on total damages (213). This is consistent with conventional wisdom that insurers are best able to set premiums when they have a fixed ceiling on future expenditures. Caps on total damages, however, have been criticized as disadvantaging the most severely injured plaintiffs with the largest losses. One study found that an increased proportion of awards granted the maximum amount after a damage cap was enacted (66).

Limitations on the amount of plaintiffs' attorneys' fees, usually by placing a ceiling on the percentage of an award that can be paid as a contingency fee, are intended to limit claims made by discouraging attorneys from accepting cases, and to increase the proportion of the award that the plaintiff can keep.¹⁰¹ Danzon found such contingency fee limits had no effect on the number of malpractice claims made or the amount paid per claim (46), while another study found that they increased the amount paid per claim (213). Fee limits may have little effect where they are about the same as the prevailing customary percentage of awards.

Shortening the statute of limitations (the time within which a claim must be filed) to bar claims submitted long after an injury occurs also produced mixed results, with several studies finding no significant effect (193). Shorter statutes of limitations may encourage claims to be filed earlier (193).

Pretrial screening panels are intended to screen out nonmeritorious claims, expedite settlement, and reduce the costs of litigation. They have been difficult to evaluate because panel types vary from state to state and voluntary panels are not used frequently. Studies have found both increased pay-

¹⁰⁰ The Robert Wood Johnson Foundation and the Agency for Health Care Policy and Research, for example, support ongoing studies, of medical malpractice and the US General Accounting Office has conducted several studies (184). The Office of Technology Assessment summarized much of the published research in a 1993 report (193).

¹⁰¹ There has been little interest in limiting the amount of defendants' attorneys' fees, presumably because they do not affect plaintiffs' decisions to make claims. Legal defense costs do contribute to total litigation expenses.

ments for successful claims using mandatory panels (213), and decreased payments per claim using voluntary panels (193). Another study found that panels had no effect on the probability that a plaintiff would be awarded payment (166). Some may increase costs by adding another layer of procedure. One study found that panels were associated with reduced malpractice insurance premiums for obstetrics/gynecology but not for general surgery or general practice (213).

Collateral source offsets are intended to reduce the amount of awards and, indirectly, the number of claims, by prohibiting plaintiffs from collecting payment for insured losses, such as medical expenses.¹⁰² Again, study results are mixed, with two studies finding no significant effect on the frequency of claims in the case of mandatory offsets, one finding a significant reduction in claim frequency when discretionary offsets were included, and both finding a significant reduction in amount of payment in successful cases (46, 213).

Requiring the losing party to pay the successful party's attorneys' fees and costs also has had little demonstrable effect on claim frequency, payment per claim, or premium prices. This may be explained by the fact that this type of reform has generally been limited to rare cases in which a court finds the claim to be frivolous or fraudulent, and few cases have been found to fall into that category (193).

In summary, tort reforms intended to reduce claims and payments have had spotty success to date. Most types of reform adopted in the past are unlikely to make a dramatic difference in the frequency of future claims. Since most such reforms are intended to reduce litigation and the amount paid to plaintiffs, without improving the probability of "correct" results, they do little to make com-

penation more equitable. Studies of product liability claims have not yet been able to determine whether the distribution of claims and payments comports with actual legal responsibility for injury (60). Thus, there has been no way to determine whether the number of claims and number and amount of awards are "correct." In the absence of any baseline knowledge of how many claims and awards would be warranted in an error-free system, it is impossible to know whether there are currently too many, too few, or about the right number of claims and awards (153).

■ Reforms Favoring Compensation

Four different types of tort reform may address the goal of equitable compensation. The first is to change the substantive law governing compensatory damages to make them more consistent across plaintiffs with similar injuries. This might be accomplished by a schedule of injuries, ranked by severity, loss of function, or other criteria, each with an assigned dollar value or range of values. The amounts of compensation could be determined by calculating appropriate medical expenses for each injury and adding expected lost income or expenses for continuing care. It may be difficult to reach agreement on what values should be used in each category. For example, should lost income be calculated by reference to the individual's own income (which awards more to those with higher incomes, as is done now), or should the same rate, such as average non-farm wages, be applied to everyone? How, if at all, should the amounts be adjusted for inflation or geographic area? Such technical problems should not be minimized.¹⁰³ In addition, there is the question of whether the amount of awards can be set at a level that is sufficiently high to meet the reasonable

¹⁰² A health or disability insurer may require the insured/plaintiff to reimburse it for health care and other expenses paid by the insurer if the insured receives compensation covering such expenses.

¹⁰³ Officials in the Division of Vaccine Injury Compensation note that children with neurological injuries have such different needs that it may be impossible to establish a schedule that would be fair to all. However, it may be possible to schedule non-economic damages more easily (20).

needs of injured people, but still affordable by those who have to pay.¹⁰⁴

If such problems are surmountable, a schedule would offer some measure of consistency in compensation for the same type of injury. The schedule could be enacted by state legislatures, although a regulatory agency might be delegated responsibility for updating the award amounts periodically. Alternatively, courts could adopt the schedule to guide jury deliberations.

One advantage of scheduling compensation is that it makes defendants' exposure more predictable, and probably more insurable. Some counsel for vaccine makers have noted that it is not routine litigation, but the possibility of one multimillion dollar judgment that makes their employers nervous. If potential or maximum awards could be estimated on the basis of a schedule, they could more easily be accounted for in pricing. Of course, this does not eliminate the need for predicting the number of possible claims in the future; but that is true for all products.

A second type of reform is alternative dispute resolution, which is intended to expedite settlements in litigated cases and reduce expenditures. Although such procedures hold some promise for speeding up the resolution of disputes, they do not alter the law governing the cases they resolve. Their advantage is that they can be used with almost any type of dispute, regardless of how compensation is calculated. They may also produce more consistent decisions, especially if they are inexpensive enough to be used by more potential claimants and defendants.

A third type of reform would expand potential plaintiffs' opportunities to recover compensation; for example, by granting them a cause of action in instances that tort law currently forbids or by easing standards of proof for existing causes of action. This option would be unattractive to defendants. It is directly contrary to the current trend

among courts to limit defendants' liability (50). Some countries in the European Union, however, are moving in the opposite direction from the United States, toward strict liability for product injuries, in their harmonization of laws effort (175). Some countries may not allow a "state of the art" defense, called developmental risk, but would make companies liable for risks that were not discovered or foreseen. The justification appears to be that drugs and vaccines are too important to people's health to permit anything less than the most stringent safeguards against product risks. Japan is considering replacing negligence with strict liability for defective products, although opposition has reduced the likelihood of reform (43).

Some Northern European countries have patient compensation funds to assist those with adverse reactions to drugs and vaccines (23, 165). Others have compensation funds specific to adverse reactions to vaccines recommended for children (112). These countries have a longer tradition of government provision of social assistance to their residents than the United States. Their relatively more extensive programs of health and disability insurance leave injured people with fewer unreimbursed expenses, so there may be less need for other sources of compensation than in the United States.

A fourth type of reform would encourage more people to bring claims under existing law. Several studies have found that only a small proportion of people who are injured as the result of another's negligence actually file tort claims, and an even smaller proportion (perhaps half of those who file claims) eventually recover any compensation (46, 69, 74). The Harvard Medical Practice Study, for example, estimated that about 28 percent of all adverse events experienced by hospitalized patients in New York in 1984 were attributable to medical negligence (one percent of all patients discharged)

¹⁰⁴ The workers compensation system has been criticized for offering too little compensation, and this has been thought to encourage product liability claims as an alternative source of compensation, as in the litigation involving asbestos.

(109). Yet for every eight negligently injured patients, only one patient filed any claim of medical malpractice.¹⁰⁵ Tort reform designed to provide equitable compensation would encourage more, not fewer claims, as well as more accurate claims determination.

■ Summary

If the goal of reform is to minimize costs to government and vaccine makers, then tort reforms limiting the liability of vaccine makers would be the best choice. It does have disadvantages, however. Most important, it is difficult to justify withdrawing a legal remedy from one class of injured people (those with adverse reactions to HIV vaccines) while it is preserved for other classes. In the past, when liability has been limited, those injured have sometimes been provided an alternative compensation system, such as workers compensation or the National Vaccine Injury Compensation Program. Other reforms, such as most of those intended to limit medical malpractice liability, have not included any alternative compensation system.

As a practical matter, however, even granting vaccine makers immunity from strict liability for design defects may not change the litigation climate significantly. Such claims are effectively litigated like negligence claims and would not be eliminated without granting vaccine makers immunity from liability for their own negligence.¹⁰⁶ Protection against liability, whether in strict liability or negligence, for design defects would not foreclose claims for inadequate warnings of prod-

uct risks.¹⁰⁷ Elimination of product liability may result in shifting claims that would have been brought against vaccine makers to physicians and clinics that administer vaccines.¹⁰⁸ Such actions would probably be limited to claims of lack of informed consent, which may be difficult to prove. Nonetheless, physicians are not likely to welcome becoming a more visible target of complaints.

Tort reforms limiting liability are not likely to improve compensation for injured persons or make it more equitable. If the goal is to provide compensation within the tort arena to a larger proportion of people with injuries, then mechanisms to increase the number who file claims are needed.

Few reforms have the potential to correct the most pressing problems of tort litigation—its time and expense, and the possibility of inconsistent results. Of course, those problems are not unique to litigation involving vaccines. If tort reform is considered for vaccine-related injuries, it may have to be considered for all other types of injuries. This raises the question whether a Federal tort law should preempt state tort law. Although the advantages and disadvantages of such a change are beyond the scope of this paper, they should be studied if tort reform is thought to be an otherwise desirable option for HIV vaccines.

VOLUNTARY CONTRACTUAL ARRANGEMENTS

Private companies are free to reduce the time and expense of resolving claims by voluntarily agreeing to provide compensation without the necessity of litigation or legislation. The voluntary contract

¹⁰⁵ Patients who filed claims were not necessarily among those that the study identified as negligently injured (109). It is not known whether such cases involved negligence that was outside the scope of the study (such as outpatient incidents or incidents in years not studied) or whether such cases did not involve negligence at all, or both.

¹⁰⁶ See “Tort Liability for Adverse Reactions to Vaccines,” above. Connecticut enacted a statute limiting HIV vaccine makers and researchers’ liability for product defects and ordinarily negligence to encourage testing candidate HIV vaccines in human subjects.

¹⁰⁷ The revised *Restatement of Torts* on product liability, if adopted, may effectively eliminate most causes of action for design defects in the case of prescription drugs and vaccines (See “Tort Liability for Adverse Reactions to Vaccines,” above). One justification for reducing the scope of liability for design defects is to permit physicians to decide whether to use a specific vaccine. Warnings then become an important source of information about the vaccine’s risks and benefits that affect the decision whether to recommend the vaccine (5).

¹⁰⁸ For manufacturers that are owned by foreign companies, some part of any financial savings to the manufacturer is likely to accrue to the foreign owner.

model, such as that developed by Professor Jeffrey O'Connell and used by some schools with respect to football injuries, encourages such private agreements (130). A variant has been introduced in Congress, but never passed, in the Moore-Gephardt bill (99th Cong., 1st Sess., 1985). Applied to HIV vaccine use, it would have a vaccine maker or administrator contractually agree, at the time of vaccination, to promptly pay the vaccine recipient compensation for medical care and other specified financial losses in the event of an adverse reaction to the vaccine. Ordinarily, the vaccine maker or physician would agree to make an offer of compensation within a specified period of time, perhaps two to six months, following notification of injury. If the recipient agreed to accept the offer, he or she would ordinarily waive any right to pursue a tort claim. If a qualifying offer were refused, the recipient would forfeit certain tort remedies or be entitled to limited damages.

The advantage to the injured person is that a reasonable amount of compensation could be provided promptly following injury. The vaccine maker could limit its payments to actual out-of-pocket expenses (compensation for pain and suffering and for insured expenses is generally excluded) and incur few transaction costs, thereby improving the predictability and limiting the amount of liability expenses.

By itself, the contract approach does not affect tort law, and could be used voluntarily with or without tort reform. It could also be required by state or Federal legislation. A contract could be offered voluntarily by any vaccine maker, or any physician or clinic that administers vaccinations. It may be most attractive to companies that believe that they are likely to receive a substantial number of claims that would be successful under existing tort law. Companies that expect few such claims probably have little incentive to assume a voluntary burden of compensation, unless the contract can effectively limit claims to cases in which the company would have legal liability for the injury.

The contract model may work reasonably well in circumstances in which the payor and payee

agree to the arrangement before any injury occurs and where causation is relatively easy to establish. It may be attractive to physicians who administer vaccines to their patients and to investigators who give investigational vaccines to subjects in clinical trials. Physicians and researchers are better able to monitor adverse reactions among people who take vaccines, although it may be difficult to identify the cause of many adverse reactions, especially when the vaccine is investigational.

Vaccine makers have no personal relationship to those who take their vaccines. It is doubtful that a standard form contract offered by a vaccine maker prior to vaccination would work as well. Vaccine recipients may reject the contract as self-serving on the part of the vaccine maker, or they might agree to it on the mistaken assumption that it was required in order to receive the vaccine. The utility of the contract depends upon whether vaccine makers could produce a realistic offer in a limited amount of time. Deciding whether to offer compensation requires investigating the merits of a claim that a vaccine caused injury, a complex undertaking. This process is similar to that used in deciding whether to settle a tort claim. The most salient obstacle to using the contract approach with a new HIV vaccine would be the difficulty in determining whether the vaccine caused the injury and, therefore, whether an offer should be made.

Some hospitals have adopted similar compensation programs for injuries resulting from medical research, although there are few reports of their use. Whether this is attributable to lack of knowledge of the availability of compensation or lack of injuries or both is not known. Where the program is voluntary, compensation is not assured to all injured persons. Those institutions and companies that do adopt a program may have different policies that produce inconsistent results.

GOVERNMENT-FUNDED INSURANCE ARRANGEMENTS

Government-financed insurance programs could fund compensation for injuries, with or without any change in tort law, in several ways.

■ Government-Funded Excess Insurance

If the only problem with relying on tort compensation were its cost, and that cost dissuaded vaccine makers from pursuing vaccine development, then one alternative would be to shift at least some costs to government by having government assume the obligation for liability costs in excess of a fixed amount. A state or the Federal government could purchase excess insurance or reinsurance policies or use government funds to pay excess amounts out of general or special revenues. Such a program could be adopted whether or not tort liability were altered. If government wished to change the number and amount or distribution of its payments, however, it could modify tort law either to increase or decrease the number or amount of awards to claimants. In the absence of any change in the way damages awards are calculated, it would not affect the possibility of inconsistent awards for similar injuries. Although individual states could adopt a reinsurance or excess insurance program, consistency could not be achieved unless all states adopted a substantially similar system.

The primary disadvantage of creating such a program for HIV vaccine injuries is that it may be impossible to predict the amount of excess insurance needed until there have been many years of experience with the vaccine. It is unlikely that the federal (or any state) government would commit to expenditures with no ceiling. It will also be especially difficult to determine the amount at which liability costs to vaccine makers should be deemed excessive. That question involves complex social policy decisions about the degree to which government and private industry should be responsible for HIV vaccine-related injuries, as well as the fairness of liability determinations.

Other more practical questions would have to be resolved. For example, should such costs be limited to awards to plaintiffs, or should they also include the costs of defending claims? If defense costs are included, how would they be verified? Would companies be willing to allow government to audit their records? Should government accept cost certification as sufficient proof of expendi-

tures? Such questions are not insoluble. A more sensitive question is whether an excess insurance program would set a precedent for government reinsurance of liability expenses for other tort claims, from medical malpractice to automobile injuries.

■ Government-Funded Disability Benefits

Vaccine-related injuries could be compensated through a state or Federal disability insurance program that covers only adverse reactions to HIV vaccines or one that covers many or all injuries. For example, the Social Security program could be amended to specifically include coverage of injuries resulting from HIV vaccines. A more general expansion of disability insurance to cover injuries regardless of cause would be more in keeping with the purpose of Social Security, however, which bases eligibility on disability and age and already covers AIDS-related disabilities.

The only compensation mechanism that avoids serious questions of horizontal justice is a program that compensates all injuries regardless of their cause. This is because every program that provides compensation only for injuries from one cause requires a justification why those injuries deserve special compensation when injuries from other causes do not. The need for financial assistance is not a sufficient reason to provide compensation to some injured persons but not others with similar needs. The desire to encourage the production of important products by protecting them from liability is also not a sufficient justification when the makers of equally important products are not similarly protected. The cost and inefficiency of the tort system is not a sufficient reason to replace it with a special compensation program for only some people but not others. Other reasons specific to injuries from one cause are required to justify a special compensation system for those injuries. Although justifications may exist, they are often complex and difficult to identify.

Other countries, like Germany, have had general disability insurance programs in place for decades. The New Zealand Accidental Injury pro-

gram provides compensation for injuries from almost all causes (62). The Commission established to study accidental injuries concluded that limiting the program to injuries from particular causes was both illogical and unfair and recommended universal coverage as the only defensible approach (1).

In the United States, a federal general disability insurance program may be more feasible if future health care reform achieves universal coverage of health insurance. Health insurance takes care of one significant cost of injuries. The remaining expenses are those needed to replace lost income to pay for living expenses and, in cases of permanent disability, rehabilitation or long-term care. These latter expenses can be paid for with disability benefits funded by insurance or general revenues.

Establishing such a program would require answering many of the questions raised for a cause-based compensation program, such as the seriousness of injuries covered, how much and what type of compensation would be available, and whether those responsible for certain injuries should contribute to financing the system.¹⁰⁹ The cost of such a program may require new government revenues, although it could be financed in part by taxes on products and services that caused injury. The existence of a compensation program may encourage a larger proportion of injured people to seek compensation. Because the costs of disability for the entire national population are relatively consistent over time, unlike the costs of injuries from specific products, they are likely to be more predictable than the cost of compensating injuries caused by new HIV vaccines. Moreover, a general disability insurance system would avoid the administrative expenses of resolving disputes over causation. There would be no need for separate administrative programs for injuries from different causes, each with its own fixed costs.

A general disability benefits program could exist with or without tort liability. A program that provided only compensation, however, could not purport to serve any deterrence function. If deterring unsafe products and services continued to be an important social goal, additional mechanisms would be needed, such as regulation of products and services, or requiring providers of products and services to help finance the program in accordance with the proportion of injuries attributed to their products.

PUBLIC COMPENSATION SYSTEMS

Federal and state governments have created several publicly administered injury compensation programs. Examples include state workers compensation programs, Virginia's Birth-Related Neurological Injury Compensation Act (Va. Code Ann. 38.2-5001 et seq.), Florida's Birth-Related Neurological Injury Compensation Act (Fla. Stat. 766.301 et seq.), the Federal National Vaccine Injury Compensation Program (42 U.S.C. 300aa-10 et seq.), the Federal Black Lung Benefits Act (30 U.S.C. 901 et seq.), and, most recently, the Radiation Exposure Compensation Act (42 U.S.C. 2210 et seq.).

Most such compensation programs are limited to specific injuries from specific causes (cause-based), but provide compensation on a no-fault basis. As long as the injury is demonstrated to result from the specified cause, compensation can be granted without the need to prove negligence or other traditional legal responsibility for the injury.

No-fault compensation systems have advantages over tort litigation. The most salient is that a larger proportion of injured people are entitled to compensation. There are ordinarily no defendants, so that parties that might otherwise be liable for injury need not participate in the claims deter-

¹⁰⁹ See Elements of a Compensation Program, below.

mination process or pay compensation.¹¹⁰ The costs of administering the compensation system can be less than the total costs of litigation so that a larger proportion of funds go to injured people. Costs are ordinarily spread over a large population or society as a whole, rather than falling on individual companies or organizations. Compensation can be funded from different sources to achieve different goals. General tax revenues can be used where the program benefits society. Special taxes on entities that create the risk (such as employers in workers compensation, or vaccine makers in the National Vaccine Injury Compensation Program) can be used to link the benefits and risks of specific products or actions.

No-fault compensation systems have two main disadvantages. A cause-based system must satisfy the requirements of horizontal justice by justifying different or special treatment for one class of people or injuries. The more compensation programs that exist for specific causes, the more difficult it becomes to defend excluding other injuries from a no-fault system. This can be seen in the tendency to call for a special compensation program to remedy social problems.¹¹¹

No-fault systems (whether or not cause-based) may also generate more, rather than less, cost, either in compensation awards or administrative expenses. Because no-fault systems compensate more people than would receive compensation (or even file a claim) in tort law, a system's cost depends upon who is eligible for compensation and the level of compensation awarded.¹¹² Per-capita compensation at the level of average tort awards would generate higher costs. Very low levels of

compensation may be inadequate or unfair and generate dissatisfaction, as seen in some worker compensation programs. In the absence of reliable estimates of the number of compensable injuries, it is difficult to predict system costs.

Most important, no cause-based system can avoid disputes over the cause of injuries. Determining causation is often difficult and time-consuming, especially where the scientific and medical evidence is uncertain or conflicting (115).¹¹³ Yet no-fault systems are often recommended in order to provide needed compensation in circumstances where causation is unclear or controversial. Thus, the same complexities that make litigation frustrating and expensive are often necessarily part of no-fault compensation proceedings.

Health care reform proposals debated in the 103rd Congress included provisions affecting compensation and liability for adverse reactions to HIV vaccines (see box 4-2).

■ The National Vaccine Injury Compensation Program

The National Vaccine Injury Compensation Program (42 U.S.C. 300aa-10 et seq.) was enacted in 1986 as part of the National Childhood Vaccine Injury Act in response to concerns that vaccine makers would not continue to produce childhood vaccines or to develop new ones if the pressure of liability for adverse reactions were not abated and the need for financial assistance to families whose children suffered permanent injury or death following vaccination (115). In August, 1992, Con-

¹¹⁰ Most systems provide that the compensation program is subrogated to the rights of the claimant so that it may seek reimbursement for compensation paid from anyone who is legally liable for the injury. This is most often provided with respect to injuries caused by negligence.

¹¹¹ In 1986, Congressman Edward Markey called for compensating human subjects in radiation experiments sponsored by the Department of Energy's predecessors (190). Recent publicity has renewed interest in the proposal.

¹¹² The Harvard Medical Practice Study estimated that a compensation system for medical malpractice in New York State could be financed for approximately the same amount as current malpractice insurance premiums if it limited compensation to serious permanent injury or death, and excluded injuries lasting less than six months and medical expenses covered by Medicaid (70).

¹¹³ For example, in workers compensation cases, it is generally far more difficult to determine the cause of a worker's chronic disease than the cause of a traumatic injury.

BOX 4-2: Health Care Reform and HIV Vaccines

Health care reform proposals that were debated in the 103rd Congress and ultimately defeated would have had implications on compensation for adverse reactions to HIV vaccines. Each of the proposals, to the extent that they expanded access to health insurance coverage, would have better ensured access to medical care for HIV vaccine trial participants. However, none of the proposals addressed needs for long-term care

President Clinton's Health Security Act provided for coverage for investigative medical treatments.¹ Decisions about which investigative medical treatments to cover, however, were left to the discretion of the individual health plans. In addition, coverage only applied to investigative treatments that are qualifying, meaning that investigational treatment has been given as part of an approved clinical trial, and that another treatment would have been provided as routine care if the participant were not receiving the Investigational treatment. Approved clinical trials were those sponsored by government agencies such as the National Institutes of Health, the Food and Drug Administration, the Department of Veterans Affairs, the Department of Defense, or a qualified nongovernmental research entity or a peer reviewed and approved program

Other proposals that were presented to Congress did not specifically address these issues. The "single payor" approach (Wellstone) would provide universal coverage for medical care, including medical care for adverse reactions to HIV vaccines.² The plan did not detail whether the costs of experimental therapies would be covered under the plan.

HIV vaccine liability would also have been affected by health reform proposals that included provisions reforming medical malpractice liability. Clinton's Health Security Act included provisions reforming medical malpractice and strict liability for injuries from pharmaceuticals, including vaccines (Health Security Act, sees 5501 *et seq.*) However, the Act left in place current product liability rules for injuries from pharmaceuticals due to negligence.

SOURCE: R.E. Stem, Blicher & Stem, Washington, DC, "Selected Issues of AIDS Vaccine Liability," unpublished contractor report prepared for the Office of Technology Assessment, U S Congress, Washington, DC, Sept. 30, 1994

¹U.S. Congress, Senate, S. 1757, *Health Security Act, Sec. 1128* (Washington, DC U S Government Printing Office, 1993).

²U.S. Congress, Senate, S. 491, *American Health Security Act of 1993* (Washington, DC: U.S. Government Printing Office, 1993).

gressman Fortney "Pete" Stark introduced the National Vaccine Development and Compensation Act, patterned after the National Childhood Injury Compensation Act, which would create a compensation program for injuries occurring in the development and marketing of an HIV vaccine (170). Because the National Childhood Vaccine Injury Act has been suggested as a model for compensating injuries following future vaccination with HIV vaccines, (Stark) it is described in some detail here.

The program, which took effect October 1, 1988, provides compensation on a "no-fault" basis for injuries resulting from vaccines to prevent poliomyelitis, diphtheria, pertussis (whooping cough), tetanus, measles, mumps, and rubella. These were the vaccinations then ordinarily required in all states to permit children to enter school or day care.¹⁴ The program is a "no-fault" system because it does not condition eligibility for compensation on any party's legal liability for the

¹⁴The Act was amended in 1993 to permit coverage of vaccines recommended by the CDC for routine administration to children. (42 U.S.C. 300aa- 14(e))

injury. Claimants (called petitioners) are entitled to compensation if they demonstrate either that the injury is listed in a statutory Vaccine Injury Table or that the injury was actually caused by a covered vaccine, and also meet other eligibility requirements.¹¹⁵ There is no requirement that the vaccine be shown to have been defective or negligently administered or warnings inadequate. Neither vaccine makers nor health care providers are parties to the proceedings.

The program has been lauded for reducing tort claims against vaccine makers. This is undoubtedly because the act postpones and effectively precludes most lawsuits in two ways. First, it forbids tort claims against vaccine makers unless a petitioner has filed a claim with the Program. Only if a petitioner rejects the Program's decision may he or she commence a lawsuit.¹¹⁶ The likelihood of succeeding in court on a claim that has been rejected by the program is probably too small to encourage petitioners to proceed. Only if a petitioner has a very strong claim and believes that a court would award much more than the program would a lawsuit be worth the effort.

Second, the act also bars liability on the part of vaccine manufacturers for failure to issue a direct warning of risks to the petitioner (42 U.S.C. 300aa-22(c)). However, most courts have reached the same result by finding that the manufacturer

has no duty to warn the vaccine recipient. This leaves petitioners with a possible claim that the manufacturer's warning to the prescribing physician was inadequate, but the act provides that the warning shall be presumed adequate if the vaccine maker complied with all FDA requirements (42 U.S.C. 300aa-22(b)(2)). This represents a nominal change in the law; however, few cases have found FDA-approved labeling to be inadequate. Although petitioners may prefer the compensation system to litigation, in effect, they have little alternative. It should not be surprising that there are few liability claims against manufacturers for adverse reactions to the covered vaccines.

Parents or guardians of injured children¹¹⁷ file petitions for compensation with the United States Court of Federal Claims (formerly the United States Claims Court) in Washington, DC. A special master in the Court's Office of Special Masters¹¹⁸ reviews the petition and makes two determinations: whether the petitioner is eligible for compensation and, if so, how much compensation is to be awarded. The Secretary of Health and Human Services is named Respondent in the proceedings. The Department's Division of Vaccine Injury Compensation¹¹⁹ reviews petitions and offers its opinion on whether the injury was in fact caused by a vaccine. Compensation may be denied if the Special Master determines that, on the

¹¹⁵ Petitioners have the burden of proving entitlement to compensation. The vaccine must have been received in the United States or as a U.S. government employee or dependent overseas; the injury must last more than 6 months and result in more than \$1000 in unreimbursable expenses, or death; the petition must be filed within a specified time period; and the petitioner must not have collected an award or settlement for the injury.

¹¹⁶ Petitioners with retrospective claims who have recovered compensation in an earlier lawsuit are not eligible for the program. Those who had commenced a lawsuit before the Program took effect were not permitted to file a petition unless their lawsuit was suspended pending the Program's determination. A recent decision by the federal court of appeals for the First Circuit, however, held that the husband and daughter of a woman who received compensation from the Program (for contact polio) were entitled to commence a tort action for their own loss of the woman's consortium, because the husband and daughter were not eligible for compensation from the Program (54, 298). The Court of Federal Claims has also held that a prior tort recovery by a parent for her own losses did not bar a petition on behalf of the child for compensation from the program (215).

¹¹⁷ Eligibility is not limited to children, and specifically includes polio contracted from someone who was vaccinated with OPV.

¹¹⁸ There are currently seven Special Masters who work exclusively for the program.

¹¹⁹ The division is part of the Bureau of Health Professions, Health Resources and Services Administration, U.S. Department of Health and Human Services.

basis of a preponderance of the evidence, the injury was not the result of the vaccine in question.¹²⁰

There are actually two programs, one for vaccinations that occurred before October 1, 1988 (retrospective cases), and another for vaccinations on or after October 1, 1988 (prospective cases). All petitions for retrospective cases had to be filed by January 31, 1991. Compensation for permanent injury in retrospective cases is limited to unreimbursed medical and rehabilitation expenses incurred after judgment; past expenses are not covered.¹²¹ Awards in retrospective cases are paid from general revenues appropriated by Congress. Until 1993, appropriations were \$80 million per year; for FY 1993, they were \$110 million and are authorized to continue at that level for future years.

Prospective cases may be filed within three years after the injury materializes,¹²² and have no limit on the amount of compensation payable, except that compensation for death is fixed at \$250,000 as in retrospective cases, and non-economic compensation may not exceed \$250,000.¹²³ Awards are paid from a trust fund financed by excise taxes on sales of the covered vaccines.¹²⁴ The fund had approximately \$700 million in unallocated, unawarded funds as of March 30, 1994.

Like most compensation systems in the United States, the program is cause-based. Only injuries or deaths caused or aggravated by a covered vaccine are compensable. Congress sought to avoid litigation-like disputes over causation by providing a list of medical conditions that are statutorily presumed to be caused by a covered vaccine in a Vaccine Injury Table, shown in table 4-1 (42 U.S.C. 300aa-15). The table lists conditions, such as anaphylaxis and residual seizure disorder, and the time period following vaccination within which the injury must have occurred to be presumptively compensable. However, in the majority of cases, causation has been disputed.

Many disputes, especially those involving the pertussis component of DPT,¹²⁵ were disagreements over whether a child actually experienced a condition listed in the table 4-1. These included disputes over whether the medical evidence demonstrated an injury covered in the table or whether factors unrelated to vaccination caused the injury. In addition, there were disagreements about whether a death resulted from a qualifying injury. The table did not eliminate difficult, time-consuming disputes over eligibility for compensation.

¹²⁰ Determinations may be made with or without a hearing including petitioners, their attorneys and witnesses, and medical reviewers from the Division of Vaccine Injury Compensation, which is represented by attorneys from the Department of Justice. The majority of cases to date have involved hearings, either in person or by telephone conference call.

¹²¹ In the case of death, compensation is fixed at \$250,000. A maximum of \$30,000 may be awarded for the combined cost of lost income, pain and suffering, and attorneys' fees and costs.

¹²² In the case of death, the period is two years after the date of death, but not later than four years after the initial injury.

¹²³ Compensation for injury may include past and future medical expenses and rehabilitative and custodial care (to the extent not paid for by insurance, other than Medicaid), lost income, pain and suffering (up to \$250,000), and reasonable attorneys' fees and costs.

¹²⁴ The excise taxes per dose of vaccine currently in effect are: DPT- \$4.56; MMR (measles-mumps-rubella)- \$4.44; polio- \$0.29; and DT (diphtheria-tetanus)- \$0.06.

¹²⁵ Which, if any, adverse reactions to the pertussis component result in permanent neurological damage or death has been at the center of controversy for decades (85). Parents of children who suffered serious injuries or death following DPT vaccination were instrumental in initially advocating a compensation Program. (They also pressed for the adverse reaction monitoring Program and efforts to improve the safety of vaccines, which were provided for in companion legislation creating the National Vaccine Program. That Program, however, may soon be phased out). Not surprisingly, pertussis is the cited vaccine in the majority of petitions filed with the Program. But the Program has not settled the scientific controversy over the cause of many adverse reactions; nor was it designed to do so. The Secretary of Health and Human Services proposed revising the Vaccine Injury Table to add, modify, and remove several conditions presumed to result from rubella and pertussis vaccines. After publication of a follow-up study of the National Childhood Encephalopathy Study (111, 120) and the Institute of Medicine's analysis of the new data (87), however, the Secretary postponed action on the regulations in order to allow time for additional public comment. (59 Fed. Reg. 13916, Mar. 24, 1994).

TABLE 4-1: Vaccine Injury Table, National Vaccine Injury Compensation Program

Illness, disability, injury, or condition covered and time period for first symptom or manifestation of onset or of significant aggravation after vaccine administration, by vaccine.

Diphtheria-tetanus-pertussis (DPT); pertussis; DTP/polio combination; or any other vaccine containing whole cell pertussis bacteria, extracted or partial cell bacteria, or specific pertussis antigen(s)

- Anaphylaxis or anaphylactic shock, within 24 hours
- Encephalopathy (or encephalitis), within 24 hours
- Shock-collapse or hypotonic-hyporesponsive collapse, within 3 days
- Residual seizure disorder in accordance with subsection (b)(2), within 3 days
- Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability injury, or condition arose within the time period prescribed

Measles, mumps, rubella, or any vaccine containing the foregoing as a component; DT; Td; or texan us toxoid

- Anaphylaxis or anaphylactic shock, within 24 hours
- Encephalopathy (or encephalitis), within 15 days for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component, within 3 days for DT, Td, or tetanus toxoid
- Residual seizure disorder in accordance with subsection (b)(2), within 15 days for mumps, rubella, measles, or any vaccine containing any of the foregoing as a component, within 3 days for DT, Td, or tetanus toxoid
- Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability, injury, or condition arose within the time period prescribed

Polio vaccines (other than inactivated polio vaccine)

- Paralytic polio: in a nonimmunodeficient recipient, within 30 days, in an immunodeficient recipient, within 6 months, in a vaccine-associated community case, no time limit
- Any acute complication or sequela (including death) of an illness, ability, injury, or condition referred to above which illness, disability injury, or condition arose within the time period prescribed

Inactivated polio vaccine

- Anaphylaxis or anaphylactic shock
- Any acute complication or sequela (including death) of an illness, disability, injury, or condition referred to above which illness, disability injury, or condition arose within the time period prescribed

SOURCE :42 U.S.C. 300aa-14(1)(a).

In its early years, the program suffered from inadequate funding and had difficulty developing an efficient mode of operating (115). The statute has been amended almost every year to correct technical problems. Now, however, the Program appears to be functioning relatively smoothly (198) and has been reauthorized as a permanent program.

As of September 7, 1994, the Program had received 4,069 petitions for retrospective injuries and 574 petitions for prospective injuries (table 4-2). Since retrospective petitions cover any injury or death resulting from a vaccination before 1988, they may indicate the number of adverse

reactions that were believed by parents to be vaccine-related for each covered vaccine since it was first introduced, beginning with IPV (injected polio vaccine) in the mid- 1950s. The number of petitions exceeds the number of lawsuits involving DPT brought against vaccine makers during the same period reported to the CDC. Some petitioners who did not file lawsuits may have believed that they did not have a cause of action in tort law. Others may not have been aware of the possibility that their children injuries might be connected to vaccination until publicity about the program reached them.

TABLE 4-2: Number of Petitions Filed (as of Sept. 7, 1994), National Vaccine Injury Compensation Program

Fiscal year	Vaccination before October 1988	Vaccination after October 1988	Total
1988	24	0	24
1989	146	1	147
1990	3,060	31	3,091
1991	839 ^a	19	958
1992	0 ^b	91	191
1993	0	37	137
1994	0	95	95
Totals	4,069	574	4,643

^aAn additional 26 petitions filed were not accepted as timely filings.

^bThe deadline for filing retrospective petitions was Jan. 31, 1991. No retrospective petitions may be filed after that date.

SOURCE: Division of Vaccine Injury Compensation U S Department of Health and Human Services, 1994.

About 45 percent of the retrospective petitions filed between October 1, 1988 (when the Program became effective) and January 31, 1991 (the deadline for filing retrospective claims) had been finally decided by the United States Court of Federal Claims by September 7, 1994 (table 4-3). Of these, only 32 percent were determined to be entitled to compensation.¹²⁶ Payments totaling \$417.2 million have been made to petitioners in about two-thirds (67 percent) of the adjudicated cases.¹²⁷ In fiscal year 1992, many awards could not be paid on a timely basis because the revenues appropriated to fund them were not sufficient. The average award in a retrospective case involving permanent injury is about \$1 million, although awards in 1994 average \$750,749.¹²⁸

Prospective petitions are more representative of the number and type of claims that could be

made annually on an ongoing basis. An average of 96 prospective petitions per year were filed during the six-year period 1989 through 1994 (table 4-2). More than a third (38 percent) of the 574 prospective petitions have been decided (table 4-4). Of decided cases, 44 percent have been determined to be compensable. Awards (including attorneys' fees in noncompensable cases) have been paid out to petitioners in 145 (67 percent) of the 217 adjudicated cases for a total of \$53.8 million (table 4-5).¹²⁹ Awards for permanent injury are highly variable, but tend to exceed awards in retrospective cases because the children are younger and are eligible for past as well as future losses, and higher lost wages and pain and suffering awards.¹³⁰ The trust fund for prospective awards has always had a surplus. If prospective petitions continue to be filed and compensation awarded at the same rate

¹²⁶ This contrasts with the Program's experience during its first two years of operation (1989 and 1990), in which 73 percent of retrospective claims were awarded compensation. Since the majority of the retrospective claims were filed in late 1990 and January 1991, the earlier claims may have involved different or stronger facts.

¹²⁷ Award amounts also include "reasonable attorneys' fees" for petitioners' attorneys, which may be awarded in cases brought in good faith even if the petitioner is determined to not be eligible for compensation.

¹²⁸ Awards in the case of death are limited to \$250,000. About 12 percent of all petitions filed have involved death. Awards in cases of permanent injury have ranged from \$120 to \$4,000,000 (Division of Vaccine Injury Compensation).

¹²⁹ A, Institute of Medicine informal survey in 1984 found that the four responding vaccine makers had paid a total of about \$2 million for all liability claims closed or settled in the previous ten years and an additional \$1.8 million in defense costs (82). Even adjusting for inflation, the Program appears to provide substantially more compensation than did tort litigation.

¹³⁰ As of March 1, 1994, 51 percent of awards (34 out of 67) were for the death of a vaccine recipient, totaling \$8.6 million. Awards for injuries totaled \$32.8 million for 33 cases, or just under \$1 million per compensable claim.

**TABLE 4-3: Results of Adjudicated Claims (as of September 7, 1994),
National Vaccine Injury Compensation Program For Vaccines Before October 1988**

Fiscal year	Award granted # (%)	Claim denied # (%)	Claim dismissed # ^(o/o)	Total
1989	9 (41)	0	13 (59)	22
1990	98 (79)	10 (8)	16 (13)	124
1991	132 (29)	65 (14)	256 (56)	453
1992	135 (29)	51 (11)	280 (60)	466
1993	102 (21)	63 (13)	316 (66)	481
1994	102 (36)	36 (13)	147 (52)	285
Totals	578 (32)	225 (12)	1,028 (56)	1,831

SOURCE: Division of Vaccine Injury Compensation, U S Department of Health and Human Services, 1994

as they have been during the last six years, the trust fund will continue to accumulate surplus funds. This would suggest that the surtax on vaccines is set at too high a level and could be reduced.¹³¹

The program's major advantages are the relative speed with which it can make decisions (compared with litigation) and the fact that it compensates a much larger proportion of children than would receive any recovery otherwise. The Program's ability to make speedy decisions was hampered by an unexpected influx of retrospective petitions in late 1990 and January 1991, as well as by funding disruptions; many retrospective cases have taken years to resolve. Prospective cases have generally been decided within the statutory period of 14 months.

Administrative costs appear reasonable for the services rendered. The Court of Federal Claims and its Office of Special Masters, the Division of Vaccine Injury Compensation, and the Vaccine Injury Claims Division of the Department of Justice have received a total of between \$4.5 and \$9 mil-

lion annually in appropriations to pay for staff and resources.¹³²

Although the program was not originally intended to be a model for replacing tort liability with no-fault compensation, it has been suggested as one for HIV vaccine-related injury. Congressman Stark circulated a proposal for legislation to create a no-fault compensation program for such injuries patterned after the legislation creating the program (170). The major technical difficulty with developing a compensation program for HIV vaccines lies in determining what types of injuries should be deemed compensable before sufficient experience with a vaccine permits causation to be reasonably determined.¹³³

It may not be necessary to create another independent compensation system. HIV vaccines might be added to the vaccines covered by the existing program. The statute now provides for covering new vaccines when they are recommended for routine administration to children. In the near future, the Secretary of Health and Human Ser-

¹³¹ It may also suggest that the estimates for liability, which were higher than the surtax amounts, were too high. The Public Health Service is contemplating recommending changing the amount of the excise tax to generate only about \$60 million per year, which should be adequate to fund prospective awards.

¹³² Over the five-year period 1989-1993, \$7.5 million per year would total \$37.5 million to decide 1,768 cases yielding total awards of \$424.6 million. This represents about 8% of total awards plus administrative costs. In the future, a smaller number of petitions are likely to be filed and decided.

¹³³ Another important technical difficulty with the proposal involved the manufacturer's bond, the mechanism used to provide indemnity during the clinical trials stage. Some manufacturers objected that a bond would be difficult for a small company to raise. In addition, some manufacturers did not want their bond to be used to pay for adverse reactions attributable to other companies' vaccine candidates (173).

**TABLE 4-4: Results of Adjudicated Claims (as of September 7, 1994),
National Vaccine Injury Compensation Program For Vaccinations After October 1988**

Fiscal year	Award granted # (%)	Claim denied # <small>(o/o)</small>	Claim dismissed # <small>(o/o)</small>	Total
1989	0 (0)	0	0 (0)	0
1990	2 (67)	0 (0)	1 (33)	3
1991	10 (37)	4 (15)	13 (48)	27
1992	28 (42)	6 (9)	33 (49)	67
1993	22 (35)	10 (16)	30 (48)	62
1994	33 (57)	7 (12)	18 (31)	58
Totals	95 (44)	27 (12)	95 (44)	217

SOURCE: Division of Vaccine Injury Compensation, U S Department of Health and Human Services, 1994

vices is likely to recommend adding Hepatitis B vaccine and hemophilus influenza type b vaccine to the list of covered vaccines. These additions would be consistent with the purpose of covering vaccines that are recommended, if not required, for children. It is unlikely that an HIV vaccine would be required for children or adults, although it might be recommended for people at high risk of HIV infection, including newborns whose mothers are HIV positive. Adding HIV vaccines to the program would represent a larger break with the original purpose of the program than adding vaccines recommended for children. It raises the question why other vaccines taken primarily by adults should not be covered.

Beyond the program itself, attention to the larger question of horizontal justice may require asking why injuries from other causes should not be covered. If the most anticipated adverse reaction to an HIV vaccine is HIV infection, covering adverse reactions to HIV vaccines would treat people differently depending upon how they became infected. People who became infected as a result of vaccination would be eligible for special compensation, but those who became infected in other ways would not. This is true for any cause-based compensation program, of course, but it may be particularly sensitive in view of the limited resources often available to people living with HIV infection and AIDS.

■ State Compensation Programs

Two states, California and Connecticut, have adopted special measures pertaining to HIV vaccines that are described briefly below. In addition, Virginia and Florida have operated compensation programs for birth-related injuries that may suggest some lessons for the creation of cause-based compensation programs.

California

In 1986, California created the AIDS Vaccine Victims Compensation Fund as a source of future no-fault compensation (Cal. Health & Safety Code, Ch. 1.14, s. 199.50). The program is limited to people who suffer personal injury caused by an HIV vaccine that is developed by a California company and approved by the FDA or the state. It does not cover research-related injuries or injuries resulting from vaccines from non-California companies. Compensation (for medical expenses, lost earnings, and up to \$550,000 in non-economic damages) is to be awarded by the California Board of Control out of funds collected from a surcharge on future HIV vaccine sales. Claimants remain free to pursue any tort claim they may have for the injury, but the state is entitled to recoup any damages that duplicate a program award. Since no vaccine has yet been approved for marketing, the program has not become operational. The authorizing legislation is relatively general, leaving details to be worked out by a task force.

**TABLE 4-5: Awards Paid to Petitioners (as of September 7, 1994),
National Vaccine Injury Compensation Program**

For Vaccinations Before October 1988		
Fiscal year	Number	Amount (\$millions)
1990	91	\$71.9
1991	149	75.4
1992	215	84.5
1993	390	110.4
1994	396	75.0
Subtotals	1,241	\$417.2
For Vaccinations After October 1988		
Fiscal year	Number	Amount (\$millions)
1990	0	0
1991	14	\$4.2
1992	33	13.1
1993	40	15.0
1994	58	21.5
Subtotals	145	53.8
Totals	1,386	\$471.0

SOURCE: Division of Vaccine Injury Compensation, U S Department of Health and Human Services, 1994

The AIDS Vaccine Victims Compensation Fund was part of legislation that was intended to remove three obstacles to AIDS vaccine development identified by California vaccine companies to the legislature: the high cost of testing investigational vaccines, an uncertain market, and strict liability for adverse reactions to vaccines. The legislation provides for grants to California vaccine makers for research and testing investigational vaccines and guaranteed state purchases of up to 500,000 units of an approved vaccine (at up to \$20 per dose if fewer than 500,000 doses are sold within three years after FDA approval) (Calif. Health & Safety Code, s.199.45-51, 199.55-60). The state has provided almost \$2 million dollars in research grants to two California companies. Under the statute, grants are to be repaid from sales of an approved HIV vaccine; California is also to receive royalties from such sales after the grant is re-

paid, with the royalty to be negotiated at the time of the grant award. In the absence of any licensed HIV vaccine, the state has not had to appropriate any funds to fulfill its purchase commitment. Because the statute gives the state discretion to choose among competing vaccines on the basis of their safety, effectiveness, and cost, it is not clear whether the guaranteed purchase is sufficiently precise to offer manufacturers a reliable market.

The 1986 legislation also limited the liability of manufacturers, in effect, to liability for negligence. In 1988, the California Supreme Court issued its decision in *Brown v. Superior Court* (225) which effectively precluded strict liability based on design defects caused by FDA-approved prescription drugs. The decision, which is considered to apply to FDA-approved vaccines as well as drugs, provided more protection against liability than the legislation, and the provisions limiting li-

ability were repealed the same year (Calif. Statutes 1988, ch. 1555 s.3).¹³⁴

California had already adopted a limited compensation program for severe adverse reactions to mandatory childhood vaccines in 1977 (Calif. Health & Safety Code, s. 429.35-.36, 1977; (112)). That program, however, provided compensation only for medical and institutional care up to a maximum of \$25,000. California's Medical and other programs for disabled children were expected to provide other assistance. Children with severe injuries requiring extensive medical care could seek compensation from the fund in addition to pursuing any tort remedy they might have against a vaccine manufacturer. The legislation provided immunity from liability for physicians and others who administered the required vaccines. Perhaps because of its narrow scope, the program has received only a handful of claims. It was created in the aftermath of the swine flu program in the hope of encouraging continued vaccine development and marketing, but it was not considered an adequate model for the later AIDS Vaccine Victims Compensation Fund or the National Vaccine Injury Compensation Program, and has had little, if any, influence on vaccine development or compensation policy.

Connecticut

Connecticut adopted a statute protecting manufacturers, research institutions and researchers from liability for personal injury resulting from the administration of any HIV vaccine to a research subject (Conn. Gen. Stat. ss. 19a-591-591b) (172). The law exempts those involved in

clinical trials of an HIV vaccine from all liability, including liability for negligence, unless the person provided false information to the FDA in connection with an Investigational New Drug application, or caused injury by gross negligence or reckless, willful or wanton misconduct. It was enacted after MicroGeneSys said it would not test its vaccine to prevent maternal-fetal HIV transmission in HIV-positive pregnant women. The trial was closed when it failed to enroll enough subjects to permit conclusions about the effect of vaccination to be drawn. MicroGeneSys is no longer pursuing those trials.

Virginia

The Virginia Birth-Related Neurological Injury Compensation Act (Va. Code Ann. 38.2-5001 et seq.) was enacted in 1987 in an attempt to reduce the cost of medical malpractice insurance on the theory that tort claims against obstetricians for birth-related injuries were driving up the price of insurance, limiting available coverage, and threatening the availability of obstetric services. It protects participating physicians from tort liability for medical malpractice for specific, narrowly defined birth-related injuries to newborns, and offers compensation in very restricted circumstances.

The Virginia program is limited to severe neurological injuries to a newborn that are caused by a physician who participated in the program and which render the infant "permanently in need of assistance in *all* activities of daily living." (Va. Code Ann. s. 38.2-5001 (emphasis added)).¹³⁵ Given the narrow definition, it should not be surprising that the program had received only ten

¹³⁴ In 1992, California enacted a law limiting the liability of HIV vaccine manufacturers, research institutions, and researchers participating in clinical trials of vaccines intended to prevent HIV transmission from a pregnant woman to her baby. (Calif. Health & Safety Code, s. 199.89) Liability is expressly limited as in the *Brown* decision. The law does not preclude liability for negligence, gross negligence, or reckless, willful or wanton misconduct, or for providing false information to the FDA.

¹³⁵ Birth-related neurological injury was redefined in 1990 as "injury to the brain or spinal cord of an infant caused by the deprivation of oxygen or mechanical injury occurring in the course of labor, delivery or resuscitation in the immediate post-delivery period in a hospital which renders the infant permanently motorically disabled and (i) developmentally disabled or (ii) for infants sufficiently developed to be cognitively evaluated, cognitively disabled. In order to constitute a 'birth-related neurological injury' ..., such disability shall cause the infant to be permanently in need of assistance in all activities of daily living. This definition shall apply to live births only and shall not include disability or death caused by genetic or congenital abnormality, degenerative neurological disease, or maternal substance abuse." Va. Code Ann. s. 38.2-5001.

claims by mid-1994,¹³⁶ although the Virginia State Medical Society had predicted at least 40 claims per year (118). Of these claims, seven were awarded compensation, two were denied and one was pending in August 1994.¹³⁷

Claims against participating physicians and hospitals must be brought to the program exclusively. Physicians are protected against liability for the injuries covered by the program (Va. Code Ann. 38.2-508). The Virginia Worker Compensation Commission makes decisions on claims. Physicians (primarily obstetricians) and hospitals elect to participate in the program and pay an annual assessment. Assessments on non-participating physicians have been suspended because of surplus revenues in the compensation fund.

Florida

The Florida Birth-Related Neurological Injury Compensation Act (Fla. Stat. 766.301 et seq.) was modeled after the Virginia program. It has received more claims, presumably because it defines a compensable injury slightly more broadly.¹³⁸ The Neurological Injury Compensation Association (NICA) had received 108 claims through fiscal year 1993.¹³⁹ Of these claims, 31 received an award, 42 were denied as noncompensable by a judge (of which 4 were on appeal), and 22 were denied by the NICA and pending judicial determination. Total awards, which are paid throughout the child's lifetime as expenses as incurred, are estimated to be about \$73 million, with about \$5 million having been paid out.

It is not known whether either the Virginia or the Florida program has had any effect on malpractice claims or insurance rates for obstetricians in those states. In its recent report on defensive

medicine, the Office of Technology Assessment speculated that the "subset of injuries is so small and the link between these injuries and physician practices so unclear, removing personal liability for the specified birth-related injuries probably has very little impact on defensive medicine and . . . impact on malpractice premiums is unclear" (195). No study has documented increased access to obstetrical care, one of the goals of the Virginia and Florida statutes.

ELEMENTS OF A NO-FAULT COMPENSATION PROGRAM

If a no-fault compensation program for HIV vaccine-related injuries is desirable, it can be constructed in different ways to suit different purposes. If the choices made are already part of an ongoing program, HIV vaccine-related injuries might be added to that program. The following pages summarize key elements of a no-fault compensation program and how they might be adapted to adverse reactions to HIV vaccines.

■ Eligibility

The first question to be decided is who should be eligible for compensation. Should the program be limited to United States citizens or residents, or should anyone who receives an HIV vaccine be eligible? In the National Vaccine Injury Compensation Program, people who are employed by the Federal government, such as diplomats and military personnel and their dependents, are covered if they receive a U.S.-made vaccine abroad, like all individuals who receive a vaccine in the United States. Should the program cover foreign citizens residing in their own countries who receive vaccine made by a U.S. manufacturer? Obviously, the

¹³⁶ Eleanor Pyles, Virginia Office of Birth-Related Compensation Claims, Richmond, VA personal communication, Aug. 8, 1994.

¹³⁷ Ibid.

¹³⁸ " 'Birth-related neurological injury' means injury to the brain or spinal cord of a live infant weighing at least 2,500 grams at birth caused by oxygen deprivation or mechanical injury occurring in the course of labor, delivery, or resuscitation in the immediate post-delivery period in a hospital, which renders the infant permanently and substantially mentally and physically impaired. This definition shall apply to live births only and shall not include disability or death caused by genetic or congenital abnormality." (Fla. Stat. 766.302(2)). Florida's definition does not require that an infant require assistance in *all* activities of daily living.

¹³⁹ NICA claims office, Tallahassee, FL personal communication, Aug. 8, 1994.

broader the eligible population, the more expensive the program. But if the program is to encourage HIV vaccine development for overseas use, as in Africa and Asia, it may wish to include foreign vaccinees, although potential liability claims from foreign vaccinees does not appear to threaten vaccine development. A different question may arise as to what counts as a U.S. vaccine if the company that makes it is owned or controlled by a foreign company.

It is customary to fix a time within which claims must be filed (a statute of limitations). Ordinarily, this would be several years after an injury manifests itself. If adverse reactions to HIV vaccines are not expected to occur for many years after vaccination and if they are difficult to identify, the first claims might not be expected for many years after the program begins.

Programs have often distinguished between investigational and marketed products, reserving compensation to those injured as a result of a marketed product. If a compensation program is to encourage research, as well as provide compensation, it may wish to cover injuries to research subjects. However, research-related injuries raise special questions in most of the categories discussed below.

The National Vaccine Injury Compensation Program was originally justified because it covered childhood vaccines required by law. An HIV vaccine is not likely to be required for any specific population, at least not in the near future. If a compensation program covers vaccines that are recommended or voluntary, then it may set a precedent for expanding the program to cover all recommended or voluntary vaccines.

■ Compensable Injuries

The question of what injuries to cover may be the most difficult and the least capable of resolution before an HIV vaccine acquires several years of experience. Three threshold questions could be answered sooner, however. The first is whether all injuries should be covered, regardless of seriousness, or whether there should be a minimum level of severity, defined in either physical or financial

terms. If the compensation program is to make compensation more equitable, then, arguably, even transient injuries should be covered. After all, the less serious the injury, the less likely it is to be compensated in the tort system. If resources for compensation are limited, however, it may be necessary to restrict compensable injuries to those for which people are unlikely to be able to pay themselves. This could be done by specifying the particular injuries, by requiring injuries to be permanent or last more than six months, for example, by covering only uninsured or unreimbursed expenses, or by requiring that the injury cost more than a minimum amount in medical expenses or lost earnings or both. The particular choice might be balanced with the amount of compensation payable. More injuries could be compensated if the amount of compensation per injury were limited. It should be recognized, however, that if insured expenses are not covered, those costs remain with the health or accident insurer.

The second threshold question is whether to include HIV infection as a compensable injury. The possibility that vaccine recipients might become infected as a result of vaccination (because of enhanced susceptibility to infection, limited efficacy of the vaccine, or a manufacturing defect) poses an initial difficulty. If it is impossible to determine whether a person's HIV infection resulted from a vaccine or from other causes, it might be impractical to include HIV infection as a compensable injury. In many cases, it is likely to be quite difficult to attribute HIV infection to lack of vaccine efficacy rather than risk behavior. On the other hand, if HIV infection is the most common injury among vaccine recipients, then a compensation program that excludes HIV infection will compensate very few people.

A third question is whether social harms, such as discrimination in housing, employment, insurance, and personal relationships, should count as compensable injuries. Although compensation systems have traditionally been limited to cases involving physical injury for which someone could be legally liable, social harms, including lawful discrimination, may injure many HIV vac-

cine recipients. Social harm also serves to distinguish HIV vaccines from other vaccines. It may be difficult to determine whether discrimination resulted from taking an HIV vaccine or from other factors. At the same time, the cost of compensating lost earnings, housing, insurance, and even personal relationships, may be no higher than compensating similar losses resulting from permanent physical injuries.

Finally, injuries do not always appear in a single episode. Thus, it will be necessary to determine whether adverse reactions that aggravate or worsen existing health conditions should be compensable. Some adverse reactions result in death, although death may not be immediate. It may be impossible to determine whether death resulted from another compensable injury until more is known about adverse reactions to HIV vaccines.

■ Causation

If a compensation program is limited to injuries that are caused by an HIV vaccine, then causation must be determined. In the absence of a list of compensable injuries (and no complete list will be available immediately) and for injuries that do not appear on such a list, a procedure for deciding causation in individual cases is needed. Like tort law, most compensation programs place the burden of proving causation on the injured person. As a practical matter, however, the injured person is the least likely to be able to find the evidence needed to prove causation. The same factors that make a list of compensable injuries impossible may preclude proving causation. Some presumptions could be used to overcome this difficulty, such as presuming causation for any injury that cannot be explained by credible scientific or medical evidence as caused by something other than the vaccine. Alternatively, a reduced amount of compensation might be provided in some circumstances in which causation cannot be established.

The standard of proof, applicable to all requirements for compensation, affects decision making about causation in particular. Most programs use the preponderance of the evidence standard,

which may be the standard most favorable to claimants. More stringent standards, like clear and convincing evidence, may be too difficult to meet, at least for many years. The standard of beyond a reasonable doubt, ordinarily reserved for criminal prosecutions and, in some states, for civil commitment, seems inappropriate and probably would be met very rarely whether one was trying to prove or disprove causation.

The type of evidence that should be admissible to prove or disprove causation may create problems. How much weight should be given to the opinion of individual treating physicians? Should epidemiological studies be admitted and, if so, how might they inform individual cases? Should the testimony of the injured person be sufficient to prove causation or must it be corroborated? What type of evidence should be required, permitted, and excluded to prove causation of social harms?

■ Compensation Benefits

The type and amount of compensation available affect both the program's attractiveness to potential claimants and its overall cost. If claimants retain the option to file lawsuits as an alternative to using the compensation program, then awards may have to be reasonably comparable to those available after litigation in order to attract claimants away from court. Of course, other program features, such as expeditious decisions, may offer sufficient attractions, but they may not be fully operational in the early years of a program.

Compensation may be provided for several types of losses. Medical expenses are the most common. These may include hospital and physician expenses, rehabilitative expenses, special education, vocational training, behavioral therapy, case management, residential and custodial care, medical and special equipment, adaptive construction to refit a home, and travel expenses related to obtaining care. It is difficult to justify limiting most of these expenses, especially those paid out of pocket. Many compensation programs do not compensate expenses that are paid for by

health or accident insurance.¹⁴⁰ Whether such reimbursed expenses should be compensated depends upon who should bear the ultimate loss, the compensation program or the health or accident insurer. If it is appropriate for the health insurer to bear the loss, then the program might enroll the injured person in a health insurance program (if not already enrolled) rather than attempt to estimate and compensate future medical expenses.

If any health care reform succeeded in providing universal health insurance coverage, then a compensation program that did not cover insured expenses would be able to minimize payments in this category. It should be noted, however, that no health reform proposal contemplates covering long term care for permanent disabilities, so that the compensation program might be expected to do so.

Compensation for lost earnings is intended to enable an injured person to pay daily living expenses. Lost earnings can be calculated on the basis of an individual's actual losses, which pays high income people more than low wage earners, or on the basis of a standard formula independent of actual income. The use of actual losses is consistent with tort litigation practice but generally fails to compensate those who have no earnings, especially women with children who are not in the paid workforce. Standard formulas have been used in the case of young disabled children who will never be able to work, and could be applied to others.

In the case of death, many compensation systems pay a fixed dollar benefit in lieu of other forms of compensation. The size of the benefit varies with the nature of the program, although it is ordinarily less than the amount payable in the case of permanent injury which is intended to provide for living expenses. If the benefit were intended to replace the earnings that would have supported the decedent's family, however, it might be calculated

in the same manner as lost earnings. If an injured person who has received compensation for the injury later dies, a death benefit could be paid or not, depending upon the purpose of the payment.

Compensation for social harms could be limited to actual losses, such as lost earnings, medical expenses that would have been covered by lost health insurance (or the amount of a more expensive policy, if obtainable), the increased cost of housing, and similar expenses. Additional amounts to compensate for any damage to one's reputation might also be considered, although these could be included in non-economic damages.

Noneconomic damages are intended to provide some compensation for the pain and suffering occasioned by injury. In tort practice, such compensation is often used to pay attorneys' fees in contingency fee arrangements, so that a plaintiff can at least be reimbursed for out-of-pocket expenses (although some fees can exceed the amount of noneconomic damages). If attorneys' fees are separately compensated, there may be less financial need for non-economic damages. But there may be reasons to compensate for pain and suffering, especially in cases of permanent injury and if the program intends to compete with litigation. Programs like the National Vaccine Injury Compensation Program limit noneconomic damages to a maximum amount, presumably to control at least one program cost.

It is also possible to provide fixed-dollar benefit payments in lieu of itemized compensation for losses and expenses, as does the Radiation Exposure Compensation Act (42 U.S.C. 2210 et seq.) and the United Kingdom's Vaccine Damage Payments Act (Current Law Statutes Anno. 1979, Ch.17). Fixing awards at a uniform amount obviously simplifies decision making and reduces administrative costs, but it does not purport to compensate for actual individual losses.

¹⁴⁰Currently, some health insurance plans cover treatment for adverse reactions from investigative treatments. Other insurance plans, however, do not cover ordinary and necessary care that is required as a result of participating in an experimental activity such as a vaccine trial, reasoning that the care would not have been required but for the experimental procedure (173).

If claimants are permitted to be represented by attorneys, then the program will have to pay something toward their attorneys' fees, at least in the case of those who cannot afford to hire an attorney. Attorneys may be seen as necessary by claimants who are unfamiliar with the system and unprepared to prove causation. It may be cheaper to grant attorneys' fees to all claimants than to implement an income or means test to determine who can and cannot afford to pay themselves. The amount payable for attorneys' fees affects the willingness of attorneys to represent claimants. The amount can be determined on a case-by-case basis by the decisionmaker. Although this requires additional administrative time, there is precedent for determining what is reasonable. Alternatively, a fee schedule could be used if one could be developed that was sufficiently flexible to account for variations in the type of cases expected under the program.

■ Mode of Payment

Traditionally, payments have been made in lump sums which require predicting future losses and reducing them to a present value. More recently, periodic payments have been used to spread out payments, reduce immediate costs, and minimize the chance that the recipient will use or invest the whole amount unwisely and be left indigent. An alternative is for the compensation program to purchase an annuity or pension that provides periodic income to cover anticipated expenses. This approach is generally less expensive than periodic payments because the premiums are often less than the total payouts. If annuities are used and the injured person later dies, a decision will have to be made concerning who—the program or the injured person's survivors—should be entitled to any death benefit. As noted above, an alternative to making payments for medical expenses would be to purchase health or long term care insurance for the injured person, which would function in much the same way as annuities, although future premiums would not necessarily be fixed at the time of purchase.

■ Decisionmaking Authority

A compensation program can be organized and operated in many different ways. The most important administrative decisions are who has the authority to make decisions about claimant eligibility and awards, and how it is exercised. In the administrative agency model, such as Social Security, the authority to make decisions is vested with an administrative agency. Proceedings are often informal and recourse is limited. An independent agency or review board can perform the same functions, as do some worker compensation commissions. This may be preferred when there is a reason to avoid linking compensation decisions to a particular government agency.

Alternatively, decisionmaking authority can be exercised by one or more federal or state courts. Federal courts created under Article III of the U.S. Constitution require a "case or controversy" as a condition of jurisdiction, so that the decision making process may have to have both a claimant and a respondent or defendant, increasing the likelihood of creating a litigation-like atmosphere. An Article I court, like the U.S. Court of Federal Claims that hears National Vaccine Injury Compensation cases, does not necessarily require an identified defendant; the federal government is identified as the respondent and is presumed to be the target of a claim for payment. Special masters, like those who decide cases in the National Vaccine Injury Compensation Program, could be used to expedite decision making in proceedings that are less formal than court hearings. With respect to HIV vaccine related injuries, the simplest means of creating a compensation program may be to add HIV vaccines to the list of vaccines covered by the National Vaccine Injury Compensation Program.

The degree of discretion granted to decision makers can affect the efficiency of the program. The more specific the legislation governing the program, the less freedom decision makers have. Specificity is often used to prevent arbitrariness. But it may also require frequent amendments to the legislation to adjust to unanticipated problems or changing conditions. If the administering

agency has the confidence of those who participate in the program, it might be granted the authority to make regulations governing many administrative procedures in order to reduce the rigidity that detailed legislation can produce.

Many compensation programs specify time limits for deciding claims in order to promote expeditious decisionmaking. Speed and informality may be a program's main advantages over litigation. Realistic time limits depend upon the complexity of the decisions to be made. More time is required to establish causation where there is scientific uncertainty than where there is clear evidence. More time is required to prove what is needed to compensate an individual when compensation is calculated on the basis of actual losses than when it is computed according to a schedule. If time limits are imposed, then the program should specify the consequences of exceeding a time limit, such as automatic payment or denial of compensation. Both alternatives can create incentives to delay dispute resolution and can operate unfairly in circumstances of unavoidable delay.

Not everyone will agree with the decisions of a compensation program. Should determinations of eligibility and compensation be appealable? Administrative programs ordinarily have an internal review mechanism, with appeals possible in at least some cases to the courts. The availability and extent of appeals may take into account the amount of compensation permitted by the program and whether claimants have the option of taking their case to court instead of the compensation program.

■ Relationship to Tort Law

A compensation program can be an exclusive source of compensation or an optional alternative to tort litigation. If the program's major goal is to eliminate tort litigation, then exclusivity may be preferred. If the program intends to make compensation more equitable and also retain any deterrent effect, then making the program optional may be preferable. The program could still be

made a required "first resort" that must be used before proceeding in tort.

Many compensation programs have a right of subrogation that grants to the program any rights that a successful claimant might have against a third party who would be legally liable for the claimant's injuries. The program is then entitled to sue the third party for reimbursement of the compensation paid to the claimant. This both replenishes the program's funds for awards (although the cost of litigation may increase other expenditures) and shifts the cost of compensation (but not administration) to the responsible party. This is useful where it is beneficial to retain the link between responsibility for injury and financial loss. As a practical matter, however, proving that a third party is liable is difficult in vaccine cases, and is likely to be especially difficult in HIV vaccine cases, so the opportunities for subrogation may be limited.

■ Conditions on Program Operation

When the effects of a new program are uncertain, the authorizing legislation sometimes limits its period of operation with a sunset clause. If at the end of the time period the program is operating successfully, it may be reauthorized; if not, it may expire without doing further damage. Continued authorization may be contingent on the occurrence of certain conditions, such as the initial or continued marketing of an HIV vaccine or pricing. For example, the program might be continued only if an acceptable vaccine remains on the market and its price does not exceed a specified amount, or only if vaccines are sold to government at below-market prices for distribution to indigent persons.

If the costs of the program are not reasonably predictable when it begins operation, the continuation of the program may be made conditional on the availability of funds for either administration or compensation or both. A program that risks termination, however, may be unable to attract sufficient support to achieve its goals.

■ Financing

A compensation program may be financed by society as a whole, by those who produce, sell or administer the vaccines that result in injury, or by those who purchase or benefit from the vaccines. Compensation may be funded from the same or different sources as administrative expenses. Financing by society generally means government funding from general tax revenues. The feasibility of such funding may depend upon budget limitations. If the program wishes to incorporate an element of risk deterrence, then it may prefer to have those who produce vaccines fund the program. This can be done by levying a tax on each dose of vaccine sold or distributed or by assessing vaccine makers according to the awards paid that involve their vaccines. In this way, vaccine makers retain some financial responsibility for the injuries caused by their vaccines, but are relieved of the burden of litigation. Of course, some or all of the assessments or taxes will be passed on to vaccine purchasers as part of the vaccine price. Where government buys significant quantities of the vaccine, government will bear a significant share of the ultimate cost of the compensation program.

■ Supplements to Compensation Programs

Compensation programs deal only with compensating injuries. They do not prevent injuries. Thus, if a no-fault compensation system supplants all or part of tort liability, other mechanisms must be in place to prevent or deter avoidable risks.

ALTERNATIVE INCENTIVES FOR HIV VACCINE DEVELOPMENT

Compensation programs deal with the consequences of vaccine use after a vaccine is developed. By themselves, they cannot guarantee that any vaccine is developed. Thus, if HIV vaccines are insufficiently attractive to private industry for

reasons of the difficulty and expense of research or an unrewarding market, other initiatives will be necessary to encourage vaccine development (100).

An Institute of Medicine committee, formed to study ways to foster U.S. industry participation in vaccine development for the Children's Vaccine Initiative, concluded that the most significant disincentives to producing new and better vaccines primarily for use in the developing world were the cost of research and clinical trials and the expected limitations on the price at which vaccines could be sold (121).¹⁴¹

The Committee recommended that the federal government create a National Vaccine Authority to support new vaccine product development (121). This type of initiative could be used to foster research and development of HIV vaccines. A National Vaccine Authority or similar entity could provide grants to private industry to develop HIV vaccines. It could also reduce the risks and costs to industry by establishing product development programs, production facilities to make investigational vaccines for clinical trials, and assistance in complying with FDA regulations. In addition, the authority might arrange procurement contracts to create a guaranteed market for approved vaccines. Estimates of the annual operating costs of a National Vaccine Authority (\$55 to \$75 million) for all vaccines, including HIV vaccines, are about the same as estimates of annual future compensation awards for the National Vaccine Injury Compensation Program (about \$60 million).

California created a research assistance program to provide grants to California vaccine makers to test candidate HIV vaccines in clinical trials.¹⁴² In order to ensure a market, the state also agreed to purchase a minimum number of doses of an approved HIV vaccine from a California HIV vaccine maker and to subsidize the price of vaccines to guarantee a price of \$20 per dose. Establishing a purchase price before a vaccine has even

¹⁴¹ The author served as a member of that committee.

¹⁴² See State Compensation Programs above.

TABLE 4-6: Incentives to HIV Vaccine Research and Development

Mechanisms for Increased collaboration and Information sharing among vaccine researchers to increase productivity and expedite research.

Simplification of collaborative arrangements between government and industry researchers.

Expanded access to preclinical nonhuman animal models for testing investigational vaccines.

- Tax deductions or credits for Investments in vaccine development,
- Expedited review by the FDA of applications for vaccine licenses.
- International harmonization of national vaccine licensing standards.
- Expanded patent protection for approved vaccines.
- Guaranteed purchases of vaccine supplies by government,
- National coordination of vaccine research and distribution policies.

SOURCE: Office of Technology Assessment, 1995

been tested in field trials is difficult. A future licensed HIV vaccine might be sold at a more than \$20 per dose, and vaccine companies may be unable or unwilling to agree to any specific price before a vaccine is approved. Nonetheless, such efforts are examples of policy innovations that might be considered, with appropriate modifications, at the national level.

Other actions, such as those listed in Table 4-6, may facilitate scientific research or encourage HIV vaccine development. Although beyond the scope of this report, they target specific points in the vaccine research and development process and are likely to have a more direct effect on HIV vaccine development than future compensation programs.

■ Conclusion

The initiatives supporting vaccine research and development recognize that neither limitations on liability nor compensation for injury can produce new HIV vaccines. It is not clear that a new compensation program is needed to abate fears of liability on the part of most companies engaged in HIV vaccine research. A compensation program cannot guarantee that important research will be done, that new products will be brought to market, or that any new products will be affordable to those who need them.

This is not to suggest that a compensation system should not be considered. But a compensation program can and should be adopted on its own

merits. Society might feel an ethical obligation to compensate those who take an HIV vaccine in an effort to abate the epidemic. Even if society does not feel an ethical obligation itself, it might conclude that compensation is nonetheless desirable as a means of rewarding those who suffer adverse reactions in an effort to prevent the continuing spread of HIV infection and the tragic toll of AIDS. The reasons for providing compensation, however, should be carefully considered in light of their application to other types of injuries.

It will be especially important to consider why people who have adverse reactions to a vaccine to prevent HIV infection or progression to AIDS should receive special compensation when people who have adverse reactions to drugs like Zidovudine, ddI and ddC, do not. Special compensation for HIV-negative people may give the appearance of social indifference to the needs of people living with HIV infection. A public debate about the justification for compensating specific injuries may offer a valuable opportunity to reconsider the ways in which responsibility for injuries and illnesses of all kinds should be allocated.

CHAPTER 4 REFERENCES

1. Accident Compensation Corporation, *Unintentional Injury: New Zealand's Accident Compensation Scheme* (Wellington, New Zealand: Accident Compensation Corporation, 1988).

2. AIDS Action Foundation, *HIV Preventive Vaccines: Social, Ethical, and Political Considerations for Domestic Efficacy Trials*, Report of a Working Group Convened by the AIDS Action Foundation (Washington, DC, July 1994).
3. Altman, L.K., "After Setback, First Large AIDS Vaccine Trials Are Planned," *New York Times*, p.C3, Nov. 29, 1994.
4. American Law Institute, *Restatement (Second) of Torts* (Philadelphia, PA: 1977).
5. American Law Institute, *Restatement of the Law of Torts: Product Liability*, Council Draft 2 (Philadelphia, PA: Sept. 2, 1994).
6. American Law Institute's Reporters' Study on Enterprise Responsibility for Personal Injury, *San Diego Law Review* 30:371-404, 1993.
7. Anders, G., "Vital Statistics: Disputed Cost of Creating a Drug," *Wall Street Journal*, p.B1, Nov. 9, 1993.
8. Annas, G.J., "Scientific Evidence in the Courtroom: The Death of the *Frye* Rule," *New England Journal of Medicine* 330: 1018-21, 1994.
9. Annas, G.J., and Grodin, M.A., *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation* (New York, NY: Oxford University Press, 1992).
10. Appelbaum, P.S., et al., "False Hopes and Best Data: Consent to Research and the Therapeutic Misconception," *Hastings Center Report* 17:20-24, April 1987.
11. Armstrong, D., and Allen, S., "Task Force Hits Radiation Tests at State Schools," *The Boston Globe* pp. 1,15, Apr. 15, 1994.
12. Arno, P.S., and Feiden, K.L., *Against the Odds: The Story of AIDS Drug Development, Politics & Profit* (New York, NY: Harper-Collins, 1992).
13. Arnold, A.J., "Developing, Testing, and Marketing an AIDS Vaccine: Legal Concerns for Manufacturers," *University of Pennsylvania Law Review* 139:1077-1121, 1991.
14. Baier, K. "Moral and Legal Responsibility," *Medical Innovation and Bad Outcomes: Legal, Social, and Ethical Responses*, M. Siegler (ed.) (Ann Arbor, MI: Health Administration Press, 1987).
15. Baynes, T.E., "Liability for Vaccine Related Injuries: Public Health Considerations and Some Reflections on the Swine Flu Experience," *St. Louis University Law Journal* 21:44-75, 1977.
16. Bergen, R.P., "Insurance Coverage for Clinical Investigation," *Journal of the American Medical Association* 201:305-306, 1967.
17. Bixby, L., and Spencer-Molloy, F., "The Struggle for Money to Fuel a Research Mission," *The Hartford Courant*, p. A1, Feb. 8, 1993.
18. Blum, A., "Halcion Stirs Litigation Storm," *National Law Journal*, A1, A23, Apr. 11, 1994.
19. Boston Consulting Group, Inc., "The Changing Environment for U.S. Pharmaceuticals: The Role of Pharmaceutical Companies in a Systems Approach to Health Care," monograph sponsored by Pfizer Inc. (Boston, MA: April 1993).
20. Bovbjerg, R.R., "Legislation on Medical Malpractice: Further Developments and a Preliminary Report Card," *University of California, Davis Law Review* 22:499-556, 1989.
21. Bovbjerg, R.R., "Problems and Solutions in Medical Malpractice: Comments on Chapters Six and Seven," *The Liability Maze: The Impact of Liability Law on Safety and Innovation*, P.W., Huber and Litan R.E. (eds.)(Washington, DC: The Brookings Institution, 1991).
22. Bovbjerg, R.R., et al., "Valuing Life and Limb in Tort: Scheduling 'Pain and Suffering'," *Northwestern Law Review* 83:908-976, 1989.
23. Braham, D., "No Fault Compensation Finnish Style," *The Lancet* 733-36, Sept. 24, 1988.

24. Burke, D.S., "Human HIV Vaccine Trials: Does Antibody-Dependent Enhancement Pose a Genuine Risk?" *Perspectives in Biology and Medicine* 35:511-530, 1992.
25. Burstin, H.R., et al., "Do the Poor Sue More? A Case-Control Study of Malpractice Claims and Socioeconomic Status," *Journal of the American Medical Association* 270: 1697-1701, 1993.
26. Calabresi, G., *The Cost of Accidents: A Legal and Economic Analysis* (New Haven, CT: Yale University Press, 1970).
27. Cardon, P.V., et al., "Injuries to Research Subjects: A Survey of Investigators," *New England Journal of Medicine* 295:650-654, 1976.
28. Carley, W.M., "Fatal Flaws, Artificial Heart Valves That Fail Are Linked to Falsified Records," *Wall Street Journal*, p. A1, Nov. 7, 1991.
29. Chase, M., "Multiple Mutating HIV Strains Stymie Researchers Seeking a Vaccine for AIDS," *Wall Street Journal*, p. B1, May 26, 1992.
30. Chesebro, K., "Galileo's Retort: Peter Huber's Junk Scholarship," *American University Law Review* 42:1637-1726, 1993.
31. Clayton, E.W., "Liability Exposure When Offspring Are Injured Because of Their Parents' Participation in Clinical Trials," *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, A.C. Mastroianni, et al. (eds.) (Washington, D.C.: National Academy Press, 1994).
32. Cohen, J., "Is Liability Slowing AIDS Vaccines?" *Science* 256:168-170, 1992.
33. Cohen, J., "Childhood Vaccines: The R&D Factor," *Science* 259:1528-1529, 1993.
34. Cohen, J., "Jitters Jeopardize AIDS Vaccine Trials," *Science* 262:980-981, 1993.
35. Cohen, J., "AIDS Vaccines: Are Researchers Racing Toward Success, Or Crawling?" *Science* 265:1373-75, 1994.
36. Cohen, J., "AIDS Vaccines: Will Media Reports KO Upcoming Real-Life Trials?" *Science* 264:1660, 1994.
37. Cohen, J., "Bumps on the Vaccine Road," *Science* 265:1371-73, 1994.
38. Cohen, J., "Peer Review Triumphs Over Lobbying," *Science* 263:463, 1994.
39. Cohen, J., "The HIV Vaccine Paradox," *Science* 264:1072-74, 1994.
40. Cohen, J., "U.S. Panel Votes to Delay Real-World Vaccine Trials," *Science* 264:1839, 1994.
41. Cotton, P., "Infants, Science May Lose as Liability Is Blamed for Company Pullout from HIV Prevention Trial," *Journal of the American Medical Association* 268:1987, 1991-1992, 1992.
42. Council for International Organizations of Medical Sciences, *International Ethical Guidelines for Biomedical Research Involving Human Subjects* (Geneva, Switzerland: World Health Organization, 1993).
43. Danaher, E.A., "Products Liability Overhaul: Strict Liability Is Coming to Japan," *The National Law Journal*, pp. 25, 28-29, Feb. 7, 1994.
44. Daniels, S., and Andrews, L., "The Shadow of the Law: Jury Decisions in Obstetrics and Gynecology Cases," *Medical Liability and the Delivery of Obstetrical Care*, Institute of Medicine (Washington, DC: National Academy Press, 1989).
45. Daniels, S., and Martin, J., "Myth and Reality in Punitive Damages," *Minnesota Law Review* 75:1-64, 1990.
46. Danzon, P., *Medical Malpractice: Theory, Practice, and Public Policy* (Cambridge, MA: Harvard University Press, 1985).
47. Dickinson, S.L.J., "Clinical Trial Reversals Forcing Biotech Firms to Refine Strategy," *The Scientist* 8:1, 6-7, 1994.
48. DiMasi, J.A., et al., "New Drug Development in the United States, 1963-90," *Clinical Pharmacology and Therapeutics* 50:471-86, 1991.
49. Dungworth, T., *Product Liability and the Business Sector: Litigation Trends in Federal Courts* (Santa Monica, CA: RAND Institute for Civil Justice, 1987).

50. Eisenberg, T., and Henderson, J.A., "Inside the Quiet Revolution in Products Liability," *UCLA Law Review* 39:731-810, 1992.
51. Englard, I., "The System Builders: A Critical Appraisal of Modern American Tort Theory," *Journal of Legal Studies* 9:27-69, 1980.
52. Epstein, R., "A Theory of Strict Liability," *Journal of Legal Studies* 2:151-204, 1973.
53. Faden, R.R., and Beauchamp, T.L., *A History and Theory of Informed Consent* (New York, NY: Oxford University Press, 1986).
54. Felsenthal, Edward, "Vaccine Injury Claims," *Wall Street Journal*, p. B5, Mar. 29, 1994.
55. Fersko, R.S., and Connolly, M.J., "AIDS Effort Sparks Patent Concerns," *New Jersey Law Journal* July 12, 1993.
56. Fineberg, H.V., and Nustadt, R.E., *The Epidemic That Never Was: Policy Making and the Swine Flu Scare* (New York, NY: Vintage Books, 1983).
57. Fisher, L.M., "Ciba-Geigy Deal with Chiron Set," *New York Times*, pp. D1, D6, Nov. 22, 1994.
58. Flannery, E.F., and Greenberg, S.N., "Liability Exposure for Exclusion and Inclusion of Women as Subjects in Clinical Studies," *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, vol. 2., Report of the Committee on the Ethical and Legal Issues Relating to the Inclusion of Women in Clinical Studies, Institute of Medicine, A.C. Mastroianni, et al. (eds.) (Washington, DC: National Academy Press, 1994).
59. Fletcher, G.P., "Fairness and Utility in Tort Theory," *Harvard Law Review* 85:537-573, 1972.
60. Galanter, M., "Reading the Landscape of Disputes: What We Know and Don't Know (and Think We Know) About Our Allegedly Contentious and Litigious Society," *UCLA Law Review* 31:4-71, 1983.
61. Garber, S., *Product Liability and the Economics of Pharmaceuticals and Medical Devices*, R-4285-ICJ (Santa Monica, CA: RAND Institute for Civil Justice, 1993).
62. Gellhorn, W., "Medical Malpractice Litigation (U.S.) Medical Mishap Compensation (N.Z.)," *Cornell Law Review* 73:170-211, 1988.
63. Gilhooley, M., "Learned Intermediaries, Prescription Drugs, and Patient Information," *St. Louis University Law Journal* 30: 633-702, 1986.
64. Grabowski, H.G., and Vernon, J.M., *The Regulation of Pharmaceuticals: Balancing the Benefits and Risks* (Washington, DC: American Enterprise Institute, 1983).
65. Grodin, M.A., and Glantz, L.H. (eds.), *Children as Research Subjects: Science, Ethics and Law* (New York, NY: Oxford University Press, 1994).
66. Groufein, W.P., and Kinney, E.D., "Controlling Large Malpractice Claims: The Unexpected Impact of Damage Caps," *Journal of Health Politics, Policy and Law* 16:441-464, 1991.
67. Hamilton, J., "Biotech: An Industry Crowded with Players Faces an Ugly Reckoning," *Business Week* 84-88,90,92, Sept. 24, 1994.
68. Hansen, R.W., "The Pharmaceutical Development Process: Estimates of Development Costs and Times and the Effects of Proposed Regulatory Changes," *Issues in Pharmaceutical Economics*, R. I. Chien, (ed.) (Lexington, MA: Lexington Books, 1979).
69. Harris, D., et al., *Compensation and Support for Illness and Injury* (New York, NY: Oxford University Press, 1984).
70. Harvard Medical Practice Study, *Patients, Doctors, and Lawyers: Medical Injury, Malpractice Litigation, and Patient Compensation in New York*, The Report of the Harvard Medical Malpractice Study to the State of New York, 1990.
71. Henderson, J.A., Jr., and Eisenberg, T., "The Quiet Revolution in Products Liability: An Empirical Study of Legal Change," *UCLA Law Review* 37:479-553, 1990.
72. Henderson, J.A.Jr., and Twerski, A.D., "Doctrinal Collapse in Product Liability:

- The Empty Shell of Failure To Warn," *New York University Law Review* 65:265-327, 1990.
73. Hensler, D., Vaiana, M., and Kakalik, J., *Trends in Tort Litigation: The Story Behind the Statistics* (Santa Monica, CA: RAND Institute for Civil Justice, 1987).
 74. Hensler, D., et al., *Compensation for Accidental Injuries in the U.S.* (Santa Monica, CA: RAND Institute for Civil Justice, 1991).
 75. Hilts, P.J., "Agency Faults a U.C.L.A. Study for Suffering of Mental Patients," *New York Times*, pp. A1, B10, Mar. 10, 1994.
 76. Hogan, N., "Shielded from Liability," *American Bar Association Journal* 56-59, May 1994.
 77. Hoke, F., "Optimistic Report Predicts Rebound for Biotechnology," *The Scientist* 8:1,11, Oct. 31, 1994.
 78. Holmes, O.W., *The Common Law* (Boston, MA: Little, Brown, 1881 [1963 edition]).
 79. Huber, P.W., "Safety and the Second Best: The Hazards of Public Risk Management in the Courts," *Columbia Law Review* 85:277-337, 1985.
 80. Huber, P.W., *Liability: The Legal Revolution and Its Consequences* (New York, NY: Basic Books, Inc., 1988).
 81. Huber, P.W., and Litan, R.E. (eds.), *The Liability Maze: The Impact of Liability Law on Safety and Innovation*, (Washington, DC: The Brookings Institution, 1991).
 82. Institute of Medicine, *Vaccine Supply and Innovation* (Washington, DC: National Academy Press, 1985).
 83. Institute of Medicine, *Medical Liability and the Delivery of Obstetrical Care* (Washington, DC: National Academy Press, 1989).
 84. Institute of Medicine, *Developing New Contraceptives: Obstacles and Opportunities*, Report of the Committee on Contraceptive Development (Washington, DC: National Academy Press, 1990).
 85. Institute of Medicine, *Adverse Effects of Pertussis and Rubella Vaccines* (Washington, DC: National Academy Press, 1991).
 86. Institute of Medicine, *Expanding Access to Investigational Therapies for HIV Infection and AIDS: Summary of a Conference* (Washington, DC: National Academy Press, 1991).
 87. Institute of Medicine, *DPT Vaccine and Chronic Nervous System Dysfunction: A New Analysis* (Washington, DC: National Academy Press, 1994).
 88. Jones, J.H., *Bad Blood: The Tuskegee Syphilis Experiment* (New York, NY: Free Press, 1981).
 89. Kahneman, D., Slovic, P., and Tversky, A. (eds.), *Judgments Under Uncertainty: Heuristics and Biases* (Cambridge, England: Cambridge University Press, 1982).
 90. Katz, J., *Experimentation with Human Beings* (New York, NY: Russell Sage, 1972).
 91. Katz, J., *The Silent World of Doctor and Patient* (New York, NY: The Free Press, 1984).
 92. Katz, J., "Human Experimentation and Human Rights," *St. Louis University Law Journal* 38:7-54, 1993.
 93. Keeton, W.P., "The Meaning of Defect in Products Liability Law—A Review of Basic Principles," *Missouri Law Review* 45:579-596, 1980.
 94. Keeton, W.P., et al. (eds.), *Prosser and Keeton on the Law of Torts*, 5th Ed. (St. Paul, MN: West Publishing Co., 1984).
 95. The Keystone Center, *Final Report of the Keystone AIDS Vaccine Liability Project* (Keystone, CO: The Keystone Center, 1990).
 96. The Keystone Center, "Final Report of the Keystone AIDS Vaccine Liability Project," *Vaccine* 9:703-709, 1991.
 97. Kitch, E.W., "The Vaccine Dilemma," *Issues in Science and Technology* II(2):108-121, 1986.
 98. Koff, W.C., and Hoth, D.F., "Development and Testing of AIDS Vaccines," *Science*, 241:426-42, 1988.
 99. Koff, W.C., and Six, H.R. (eds.), *Vaccine Research and Developments* (New York, NY: Marcel Dekker, Inc., 1992).

100. Koff, W.C., "The Next Steps Toward a Global AIDS Vaccine," *Science* 266:1335-1337, 1994.
101. Kong, D., "1,800 Tested in Radiation Experiments," *The Boston Globe*, pp.8, 22, Feb. 20, 1994.
102. Kramer, P., *Listening to Prozac* (New York, NY: Viking, 1992).
103. Ladimer, I., "Clinical Research Insurance," *Journal of Chronic Diseases* 16:1229, 1233, 1963.
104. Landes, W.M., and Posner, R.A., *The Economic Structure of Tort Law* (Cambridge, MA: Harvard University Press, 1987).
105. Lasagna, L., "The Chilling Effect of Product Liability on New Drug Development," *The Liability Maze: The Impact of Liability Law on Safety and Innovation*, Huber, P.W., and Litan, R.E. (eds.) (Washington, DC: The Brookings Institution, 1991).
106. Letvin, N.L., "Vaccines Against Human Immunodeficiency Virus—Progress and Prospects," *New England Journal of Medicine* 329:1400-1405, 1993.
107. Levine, C., "Women and HIV Research: The Barriers to Equity," *Evaluation Review* 14:447-463, 1990.
108. Levine, C., "Women as Research Subjects: New Priorities, New Questions," *Emerging Issues in Biomedical Policy: An Annual Review*, vol. 2., Blank, R.H., and Bonnicksen, A.L. (eds.) (New York, NY: Columbia University Press, 1993).
109. Localio, A.R., et al., "Relationship Between Malpractice Claims and Adverse Events Due to Negligence: Results of the Harvard Medical Practice Study III," *New England Journal of Medicine* 325:245-251, 1991.
110. Lurie, P., et al., "Ethical, Behavioral, and Social Aspects of HIV Vaccine Trials in Developing Countries," *Journal of the American Medical Association* 271:295, 1994.
111. Madge, N., et al., "The National Childhood Encephalopathy Study: A 10-Year Follow-up. A Report of the Medical, Social, Behavioral and Educational Outcomes After Serious, Acute, Neurologic Illness in Early Childhood," *Developmental Medicine & Child Neurology* 35 (suppl. no. 68):1-118, 1993.
112. Mariner, W.K., "Compensation Programs for Vaccine-Related Injury Abroad: A Comparative Analysis," *St. Louis University Law Journal* 31:599-654, 1987.
113. Mariner, W.K., "Informed Consent in the Post-Modern Era," *Law & Social Inquiry* 13:385-406, 1988.
114. Mariner, W.K., "The Ethical Conduct of Clinical Trials of HIV Vaccines," *Evaluation Review* 14:538-564, 1990.
115. Mariner, W.K., "The National Vaccine Injury Compensation Program," *Health Affairs* 11:255-265, 1992.
116. Mariner, W.K., "Compensation for Research Injuries," *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, vol. 2., Report of the Committee on the Ethical and Legal Issues Relating to the Inclusion of Women in Clinical Studies, Institute of Medicine, A.C. Mastroianni, et al., (eds.) (Washington, DC: National Academy Press, 1994).
117. Mariner, W.K., and Gallo, R.C., "Getting to Market: The Scientific and Legal Climate for Developing an AIDS Vaccine," *Law, Medicine & Health Care* 15:17-26, 1987.
118. Mastroianni, A.C., Faden, R., Federman, D. (eds.), *Women and Health Research: Ethical and Legal Issues of Including Women in Clinical Studies*, 2 vols., Report of the Committee on the Ethical and Legal Issues Relating to the Inclusion of Women in Clinical Studies, Institute of Medicine (Washington, D.C.: National Academy Press, 1994).
119. McKenna, R.M., "The Impact of Product Liability Law on the Development of a Vaccine Against the AIDS Virus," *University of Chicago Law Review* 55:943-64, 1988.
120. Miller, D.L., et al., "Pertussis Immunization and Serious Acute Neurological Illness in Children," *British Medical Journal* 307:1171-1176, 1993.

121. Mitchell, V.S., Philipose, N., and Sanford, J.P. (eds.), *The Children's Vaccine Initiative: Achieving the Vision, Report of the Committee on the Children's Vaccine Initiative, Institute of Medicine* (Washington, DC: National Academy Press, 1993).
122. National Institute of Allergy and Infectious Diseases, "AIDS Vaccines Contracts Pave Way for Large National and International Studies," *News from NIAID*, Oct. 10, 1993a.
123. National Institute of Allergy and Infectious Diseases Blue Ribbon Panel on Vaccine Research, *Summary* (Bethesda, MD: March 26, 1993b).
124. National Institute of Allergy and Infectious Diseases, "Chimpanzee Vaccine Model Protects Against HIV-1 Infection," *NIAID News*, Aug. 9, 1994a.
125. National Institute of Allergy and Infectious Diseases, "HIV Trials Continue But Without Expansion," *NIAID AIDS Agenda* 1,6, Summer 1994b.
126. National Institute of Allergy and Infectious Diseases, *Conference on Advances in AIDS Vaccine Development—Seventh Annual Meeting of the National Cooperative Vaccine Development Group for AIDS* (Bethesda, MD: 1994c).
127. National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, *The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (Washington, DC: U.S. Government Printing Office, 1978).
128. Naude, A., "Two Worlds: Sales of Adult and Pediatric Vaccines, Pharmaceuticals," *Chemical Marketing Reporter* 245:SR28, March 7, 1994.
129. Neustadt, R.E., and Fineberg, H.V., *The Swine Flu Affair: Decision-Making on a Slippery Disease* (Washington, DC: Dept. of Health, Education, and Welfare, 1978).
130. O'Connell, J., "Offers That Can't Be Refused: Foreclosure of Personal Injury Claims by Defendants' Prompt Tender of Claimants' Net Economic Losses," *Northwestern University Law Review* 77:589-632, 1982.
131. O'Connell, J., and Kelly, C.B., *The Blame Game: Injuries, Insurance, and Injustice* (New York, NY: Basic Books, 1988).
132. Page, J., "'Generic Product Risks': The Case Against Comment k and for Strict Product Liability," *New York University Law Review* 58:853-891, 1983.
133. Palca, J., "Testing Target Date Looms, But Will the Vaccines Be Ready?" *Science* 257:1472-1473, 1992.
134. Peterson, M., *Civil Juries in the 1980's: Trends in Jury Trials and Verdicts in California and Cook County, Illinois* (Santa Monica, CA: The RAND Corporation, 1987).
135. Peterson, M., Sarma, S., and Shanley, M., *Punitive Damages: Empirical Findings* (Santa Monica, CA: RAND Institute for Civil Justice, 1987).
136. Pharmaceutical Manufacturers Association, American Medical Association, *Brief of the Pharmaceutical Manufacturers Association and the American Medical Association, as Amici Curiae in Support of Petitioner, in Pacific Mutual Life Insurance Company v. Haslip*, Supreme Court of the United States, May 31, 1990.
137. Pharmaceutical Manufacturers Association, *Statistical Fact Book* (Washington, DC: Pharmaceutical Manufacturers Association, 1991).
138. Philipson, T.J., and Posner, R.A., *Private Choices and Public Health: The AIDS Epidemic in an Economic Perspective* (Cambridge, MA: Harvard University Press, 1993).
139. Physicians GenRx (Smithtown, NY: Data Pharmaceutica Inc., 1994).
140. Presidential Commission on the Human Immunodeficiency Virus Epidemic, *Report*, (Washington, D.C.: The White House, 1988).
141. President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, *Compensating for Research Injuries: The Ethical and Legal*

- Implications of Programs to Redress Injured Subjects*, vol. 1 (Washington, DC: U.S. Government Printing Office, 1982).
142. Prosser, W.L., and Keeton, P., *Prosser and Keeton On The Law of Torts* (St. Paul, MN: West Publication Co., 1984).
 143. Reuter, P., *The Economic Consequences of Expanded Corporate Liability* (RAND Institute for Civil Justice, 1988).
 144. Rheingold, P.D., "Products Liability - The Ethical Drug Manufacturer's Liability," *Rutgers Law Review* 18:947-1018, 1964.
 145. Rheingold, P.D., "The MER/29 Story-An Instance of Successful Mass Disaster Litigation," *California Law Review* 56:116-148, 1968.
 146. Rheingold, P.D., "The Expanding Liability of the Drug Manufacturer to the Consumer," *Food Drug & Cosmetic Law Journal* 40:135-44, 1985.
 147. Robbins, A., and Freeman, P., "Obstacles to Developing Vaccines for the Third World," *Scientific American*, pp. 126-133, Nov. 1988.
 148. Rosenberg, R., "Progress on AIDS Vaccine Boosted," *The Boston Globe* p. 47, Sept. 15, 1992.
 149. Rosenfeld, "The Strict Products Liability Crisis and Beyond: Is There Hope for an AIDS Vaccine," *Jurimetrics* 31:187, 1991
 150. Rosenthal, E., "Debate Fails to Explain Vaccine Costs," *New York Times* p. A8, Mar. 15, 1993.
 151. Russell, C., "AIDS Work Is Stern Test of Optimism," *Washington Post* p. A1, April 29, 1984.
 152. Rustad, M., *Demystifying Punitive Damages in Products Liability Cases: A Survey of a Quarter Century of Trial Verdicts* (Washington, DC: Rosco Pound Foundation, 1991).
 153. Saks, M., "Do We Really Know Anything About the Behavior of the Tort Litigation System—And Why Not?," *University of Pennsylvania Law Review* 140:1147-1292 (1992).
 154. Sanders, J., "The Bendectin Litigation: A Case Study in the Life Cycle of Mass Torts," *Hastings Law Journal* 43:301-418, 1992.
 155. Schwartz, G.T., "The Character of Early American Tort Law," *UCLA Law Review* 36:641-718, 1989.
 156. Schwartz, G.T., "The Beginning and the Possible End of the Rise of Modern American Tort Law," *Georgia Law Review* 26:601-702, 1992.
 157. Schwartz, T.M., "Products Liability Law and Pharmaceuticals: New Developments and Divergent Trends," *Food Drug & Cosmetic Journal* 43:33-53, 1988.
 158. Schwartz, V., "The Post-Sale Duty to Warn: Two Unfortunate Forks in the Road to a Reasonable Doctrine," *New York University Law Review* 58:892-904, 1983.
 159. Schwartz, V.E. "Unavoidably Unsafe Products: Clarifying the Meaning and Policy Behind Comment K," *Washington & Lee Law Review* 42:1139-1148, 1985.
 160. Scott, J., "Liability Protection Needed for Vaccines Studies, Experts Say," *Los Angeles Times*, p. A3, July 17, 1992.
 161. Shavell, S., *Economic Analysis of Accident Law* (Cambridge, MA: Harvard University Press, 1987).
 162. Shaw, Jr., D.C., Vice-President for Medical Affairs, Wyeth Laboratories, "Statement," *Vaccine Injury Compensation*, hearing before Subcommittee on Health and the Environment, Committee on Energy and Commerce, House of Representatives, U.S. Congress, December 19, 1984.
 163. Shuck, P.H. (ed.), *Tort Law and the Public Interest* (New York, NY: W.W. Norton, 1991).
 164. Shulman, S.R., "The Broader Message of Accutane," *American Journal of Public Health* 79:1565-68, 1989.
 165. Shulman, S.R., and Lasagna, L. (eds.), *Trends in Product Liability Law and No-Fault Compensation for Drug-Induced Inju-*

- ries (Boston: The Center for the Study of Drug Development, Tufts University, 1990).
166. Sloan, F.A., Mergenhagen, P.M., and Bovbjerg, R.R., "Effects of Tort Reform on the Value of Closed Medical Malpractice Claims: A Microanalysis," *Journal of Health Policy, Politics and Law* 14:663-89, 1989.
 167. Slovic, P., "Perception of Risk," *Science* 236:280-285, 1987.
 168. Smith, H. William, III, "Vaccinating AIDS Vaccine Manufacturers Against Product Liability," *Case Western Reserve Law Review* 42(1):207-254, 1992
 169. Spencer-Molloy, F., "Pregnant Women to be Vaccinated in Pediatric AIDS Trial in State," *The Hartford Courant* p. A1, December 19, 1992.
 170. Stark, F.H., "The National AIDS Vaccine Development and Compensation Act of 1992, H.R. 5893," Discussion Draft, August, 1992.
 171. Stein, R.E., "The Development of an HIV Vaccine: Legal and Policy Aspects," in Koff, W.C., Six, H.R. (eds.), *Vaccine Research and Developments*, vol. 1, 1992.
 172. Stein, R.E., "Insurance and Liability Issues in AIDS Vaccine Development," *AIDS Research and Human Retroviruses*, 9 (suppl. 1), 1993.
 173. Stein, R.E., "Selected Issues of AIDS Vaccine Liability," contractor report prepared for the Office of Technology Assessment, U.S. Congress, Washington, DC, 1994.
 174. Stratton, K.R., Howe, C.J., and Johnston, R.B., Jr. (eds.), *Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality* (Washington, DC: National Academy Press, 1994).
 175. Sturmer, U., Koepke, J.E., and Reischel, B., *New EEC Product Liability: The U.S. in Comparison* (Cologne: Gerling-Konsern Allgemeine Versicherungs-AG, 1988).
 176. Sugarman, S.D., *Doing Away with Personal Injury Law: New Compensation Mechanisms for Victims, Consumers, and Business* (New York, NY: Quorum Books, 1989).
 177. Sunstein, C.R., *The Partial Constitution* (Cambridge, MA: Harvard University Press, 1993).
 178. Swazey, J., "Prescription Drug Safety and Product Liability," *The Liability Maze: The Impact of Liability Law on Safety and Innovation*, Huber, P.W., and Litan, R.E. (eds.) (Washington, DC: The Brookings Institution, 1991).
 179. Swazey, J., and Glantz, L.H., "A Social Perspective on Compensation for Injured Research Subjects," *Compensating for Research Injuries: The Ethical and Legal Implications of Programs to Redress Injured Subjects*, President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research, vol. 2 (Washington, DC: U.S. Government Printing Office, 1982).
 180. Swine Flu Act (National Swine Flu Immunization Program), Pub. L. 94-380, 90 Stat. 113, 1976, codified at 42 U.S.C. 247b(j)-(l); repealed by Pub. L. 95-626, sec.202, 92 Stat. 3574, 1978.
 181. Tancredi, L.R., and Bovbjerg, R.R., "Rethinking Responsibility for Patient Injury: Accelerated-Compensation Events: A Malpractice and Quality Reform Ripe for a Test," *Law & Contemporary Problems* 54:147-78, 1991.
 182. Taragin, M.I., et al., "The Influence of Standard of Care and Severity of Injury on the Resolution of Malpractice Claims," *Annals of Internal Medicine* 117:780-84, 1992.
 183. Tuskegee Syphilis Study Ad Hoc Advisory Panel, *Final Report* (Washington, DC: U.S. Dept. of Health, Education and Welfare, 1973).
 184. U.S. Congress, General Accounting Office, *Medical Malpractice: 6 State Case Studies Show Claims and Costs Still Rise Despite Reforms*, GAO/HRD-87-21 (Washington, DC, December 1986).

185. U.S. Congress, General Accounting Office, *Product Liability: Extent of "Litigation Explosion" in Federal Courts Questioned* (Washington, DC, January 1988).
186. U.S. Congress General Accounting Office, *Product Liability: Verdicts and Case Resolution in Five States*, GAO/HRD-88-99 (Washington, DC, U.S. Government Printing Office, September 1989).
187. U.S. Congress, General Accounting Office, *Medical Malpractice: Maine's Use of Practice Guidelines to Reduce Costs*, GAO/HRD-94-8 (Washington, DC, October 1993).
188. U.S. Congress, General Accounting Office, *Human Experimentation: An Overview on Cold War Era Programs*, Testimony Before the Legislation and National Security Subcommittee, Committee on Government Operations, House of Representatives, U.S. Congress, Sept. 28, 1994, GAO/T-NSIAD-94-266 (Washington, DC: U.S. Government Printing Office, 1994).
189. U.S. Congress, House of Representatives, Committee on Energy and Commerce, Subcommittee on Health and the Environment, *Vaccine Injury Compensation*, hearing, Dec.19, 1984, Serial No. (Washington, DC: U.S. Government Printing Office, 1984).
190. U.S. Congress, House of Representatives, Committee on Energy and Commerce, Subcommittee on Energy Conservation and Power, *American Nuclear Guinea Pigs: Three Decades of Radiation Experiments on U.S. Citizens*, Report, (Washington, DC: U.S. Government Printing Office, 1986).
191. U.S. Congress, Office of Technology Assessment, *Compensation for Vaccine-Related Injuries—Technical Memorandum*, OTA-TM-H-6 (Washington, DC: U.S. Government Printing Office, November 1980).
192. U.S. Congress, Office of Technology Assessment, AIDS-Related Series: #5, "How Has Federal Research on AIDS/HIV Disease Contributed to Other Fields?" Staff Paper, NTIS#PB90-253774 (Washington, DC: U.S. Government Printing Office, 1990).
193. U.S. Congress, Office of Technology Assessment, *Impact of Legal Reforms on Medical Malpractice Costs*, OTA-BP-H-119 (Washington, DC: U.S. Government Printing Office, October 1993a).
194. U.S. Congress, Office of Technology Assessment, *Pharmaceutical R&D: Costs, Risks and Rewards*, OTA-H-522 (Washington DC: U.S. Government Printing Office, February 1993b).
195. U.S. Congress, Office of Technology Assessment, *Defensive Medicine and Medical Malpractice*, OTA-H-602 (Washington, DC: U.S. Government Printing Office, July 1994).
196. U.S. Congress, Senate, S. 1757, *Health Security Act*, (Washington, DC: U.S. Government Printing Office, 1993).
197. U.S. Congress, Senate, S.491, *American Health Security Act of 1993*, (Washington, DC: U.S. Government Printing Office, 1993).
198. U.S. Department of Health and Human Services, Office of Inspector General, *The National Vaccine Injury Compensation Program: A Program Review* (Washington, DC: DHHS, 1992).
199. U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, Division of Vaccine Injury Compensation, "National Vaccine Injury Compensation Program Monthly Status Report-September 7, 1994," (Washington, DC: DHHS, 1994).
200. U.S. Department of Health, Education, and Welfare, *HEW Secretary's Task Force on the Compensation of Injured Research Subjects, Report* (Washington, DC: DHEW, January 1977).
201. U.S. Department of Health, Education, and Welfare, *Liability Arising Out of Immunization Programs: Final Report to Congress* (Washington, DC: DHEW, May 1978).
202. U.S. Department of State, *Human Immunodeficiency Virus (HIV) Testing Requirements for Entry into Foreign Countries* (Washington, DC: November, 1993).

203. Viscusi, W.K., *Reforming Products Liability* (Cambridge, MA: Harvard University Press, 1991).
204. Wade, J.W., "An Evaluation of the 'Insurance Crisis' and Existing Tort Law," *Houston Law Review* 24:81-96, 1987.
205. Wade, J.W., "On the Effect in Product Liability of Knowledge Unavailable Prior to Marketing," *New York University Law Review* 58:734-764, 1983.
206. Wade, J.W., "On the Nature of Strict Liability for Products," *Mississippi Law Journal*, 44:825-851, 1973.
207. Walker, M.C., and Fast, P.E., "Clinical Trials of Candidate AIDS Vaccines," *AIDS* 8 (Supp.1): S213-S236, 1994.
208. Wiggins, S.N., "The Pharmaceutical Research and Development Decision Process," *Drugs and Health: Economic Issues & Policy Objectives*, Helms, Robert B. (ed.) (Washington, DC: American Enterprise Institute, 1981).
209. Williams, D., Vice-President & General Manager, Connaught Laboratories, Inc., "Statement," *Vaccine Injury Compensation*, hearing before Subcommittee on Health and the Environment, Committee on Energy and Commerce, House of Representatives, U.S. Congress, December 19, 1984.
210. Williams, G., "The Aims of the Law of Tort," *Current Legal Problems* 4:137-176, 1951.
211. Willig, "The Comment k Character: A Conceptual Barrier to Strict Liability," *Mercer Law Review* 29:545-581, 1978.
212. Zoon, K.C., and Beatrice, M.G., *New Directions for FDA's Center for Biologics Evaluation and Research (CBER). New Drug Approvals in 1992* (Washington, DC: Pharmaceutical Manufacturers Association, 1993).
213. Zuckerman, S., Bovbjerg, R.R., and Sloan, F., "Effects of Tort Reforms and Other Factors on Medical Malpractice Insurance Premiums," *Inquiry* 27:167-182, 1990.
- Court Cases**
214. *Abbott v. American Cyanamid Co.*, 844 F.2d 1108 (4th Cir.), cert. denied, 488 U.S. 908 (1988).
215. *Abbott v. Secretary*, V 1992 Cl. Ct. LEXIS 473 (1992), rev'd on other grounds, 27 Fed. Cl. 792 (1993).
216. *Adams v. G.D. Searle & Co.*, 576 So.2d 728 (Fla. Dist. Ct. App.), review denied, 589 So.2d 290 (Fla. 1991).
217. *Albala v. City of New York*, 445 N.Y.S. 2d 108 (1981).
218. *Allen v. G.D. Searle & Co.*, 708 F. Supp. 1142 (D. Or. 1989).
219. *Allison v. Merck & Company, Inc.*, 110 Nev. 762; 878 P.2d 948; 1994 Nev. LEXIS 112
220. *Anderson v. Owens-Corning Fiberglass Corp.*, 53 Cal.3d 987, 810 P.2d 549 (1991).
221. *Ayers v. Johnson & Johnson Baby Products Co.*, 117 Wash.2d 747, 818 P.2d 1337 (1991).
222. *Berkovitz v. United States*, 486 U.S. 531 (1988).
223. *Beshada v. Johns-Manville Products Corp.*, 90 N.J. 191, 447 A.2d 539 (1982).
224. *Brochu v. Ortho Pharmaceutical Corp.*, 642 F.2d 652 (1st Cir. 1981).
225. *Brown v. Superior Court*, 44 Cal.3d 1049, 245 Cal. Rptr. 412, 751 P.2d 470 (1988).
226. *Canterbury v. Spence*, 464 F.2d 772 (D.C. Cir. 1972).
227. *Carlenstope v. Merck*, 819 F.2d 33-37 (2nd Cir. 1987).
228. *Carmen v. Eli Lilly & Co.*, 32 N.E.2d 729 (Ind. App. 1941).
229. *Castrignano v. E.R. Squibb & Sons, Inc.*, 546 A.2d 755 (R.I. 1988); district court verdict aff'd, 900 F.2d 455 (1st Cir. 1990).
230. *Chan Tse Ming v. Cordis Corp.*, 704 Fed. Supp. 217-220 (S.D. Fl. 1989).
231. *Cobbs v. Grant*, 8 Cal. 3d 229, 104 Cal. Rptr. 505, 502 P.2d 1 (1972).
232. *Collins v. Eli Lilly Co.*, 116 Wis.2d 166, 342 N.W.2d 37, cert. denied, 469 U.S. 826 (1984).

233. *Corrigan v. Bjork Shiley Corp.*, 182 Calif. Appellate Reports 166-183 (1986).
234. *Daubert v. Merrell Dow Pharmaceuticals*, 113 S.Ct. 2786 (1993).
235. *Davis v. Wyeth Laboratories*, 399 F.2d 121 (9th Cir. 1968).
236. *DeMelo v. Lederle Laboratories*, 801 F.2d 1058 (8th Cir. 1986).
237. *Dowling v. Hyland Therapeutics*, 767 F. Supp 57 (S.D.N.Y. 1991)
238. *Dunn v. Lederle Laboratories*, 121 Mich. App. 73, 328 N.W.2d 576 (1983).
239. *Escola v. Coca Cola Bottling Co. of Fresno*, 24 Cal.2d 453, 150 P.2d 436 (1944) (Traynor, J., dissenting).
240. *Ezagui v. Dow Chemical Corp.*, 598 F.2d 727 (2d Cir. 1979).
241. *Falk v. Keene Corp.*, 113 Wash.2d 645, 782 P.2d 974 (1989).
242. *Feldman v. Lederle Laboratories*, 97 N.J. 429, 479 A.2d 374 (N.J. 1984) (Feldman I), rev'd after remand, 561 A.2d 288 (N.J. Super. Ct. App. Div. 1989), rev'd, 125 N.J. 117, 592 A.2d 1176 (N.J. 1991) (Feldman II), cert. denied, 112 S.Ct. 3027 (1992).
243. *Finn v. G.D. Searle & Co.*, 35 Cal. 3d 691; 677 P.2d 1147; 200 Cal. Rptr. 870 (1984).
244. *Flood v. Wyeth Laboratories*, 183 Cal. App. 3d 1272, 288 Cal. Rptr. 700 (1986).
245. *Fraley v. American Cyanamid*, 589 F. Supp. 826 (D. Col. 1984).
246. *Garside v. Osco Drug, Inc.*, 764 F.Supp. 208 (D. Mass. 1991).
247. *Gassman v. United States*, No. 79-314-ORL-CIV-06, Slip opinion (M.D. Fla. June 27, 1984).
248. *Gaston v. Hunter*, 588 P.2d 326 (Ariz. Ct. App. 1978).
249. *Givens v. Lederle*, 556 F.2d 1341 (5th Cir. 1977).
250. *Gottsdanker v. Cutter Laboratories*, 182 Cal. App. 2d 602, 6 Cal. Rptr. 320 (1960).
251. *Graham v. Wyeth Laboratories*, 906 F.2d 1399 (10th Cir. 1990), cert. denied, 498 U.S. 981 (1990).
252. *Grant v. Parke-Davis & Co.*, 544 F.2d 521 (7th Cir. 1976).
253. *Greenman v. Yuba Power Products, Inc.*, 59 Cal. 2d 67, 377 P.2d 897 (1963).
254. *Griffin v. United States*, 500 F.2d 1949 (3d Cir. 1974).
255. *Grundberg v. Upjohn Co.*, 813 P.2d 89 (Utah 1991).
256. *Haddad v. Richardson-Merrell, Inc.* 588 Fed. Supp. 1158-1164 (N.D. Ohio 1984).
257. *Hahn v. Richter*, 427 Pa. Super. 130, 628 A.2d 860 (1993).
258. *Hill v. Searle Laboratories*, 884 F.2d 1064 (8th Cir. 1989).
259. *Hillsborough County v. Automated Medical Laboratories*, 471 U.S. 707 (1985).
260. *Hockett v. United States*, 730 F.2d 709 (11th Cir. 1984).
261. *Hodson v. A.H. Robins Co., Inc.*, 528 Fed. Supp. 809-824 (E.D. Va. 1981).
262. *Hopkins v. Dow Corning Corporation*, 1994 U.S. App. LEXIS 23097 (9th Cir. 1994).
263. *Hunt v. Hoffman-LaRoche, Inc.*, 785 F. Supp. 547 (D. Md. 1992).
264. *Hurley v. Lederle Labs*, 863 F.2d 1173 (5th Cir. 1988).
265. *Hyman v. Jewish Chronic Disease Hospital*, 15 N.Y.2d 317, 206 N.E.2d 338 (1965).
266. *In re Sabin Oral Polio Vaccine Products Liability Litigation*, 743 F.Supp. 410 (D.Md. 1990).
267. *In re Tetracycline Cases*, 747 F. Supp. 543 (W.D. Mo. 1989).
268. *In re Union Carbide Corporation*, 634 F. Supp. 842-867 (S.D.N.Y. 1986), affirmed and modified, 809 F.2d 195-206 (2nd Cir. 1987), cert denied, 484 U.S. 871 (1987).
269. *Incollingo v. Ewing*, 444 Pa. 299, 282 A.2d 206 (1971).
270. *Johnson v. American Cyanamid*, 239 Kan. 279, 718 P.2d 1318 (1986).
271. *Jones v. Lederle Laboratories*, 785 F.Supp. 1123 (S.D.N.Y. 1992).
272. *Keane v. Lederle Laboratories*, 1994 U.S. Dist. LEXIS 4305 (1994).

273. *Kearl v. Lederle Laboratories*, 172 Cal. App. 3d 827, 218 Cal. Rptr. 453 (1985).
274. *King v. Collagen Corp.*, 983 F.2d 1130 (5th Cir. 1993), cert. denied, 114 S.Ct. 84 (1993).
275. *Larsen v. Pacesetter Systems, Inc.*, 837 P.2d 1273 (Haw. 1992).
276. *Mazur v. Merck & Co., Inc.*, 742 F. Supp. 239 (E.D. Pa. 1990) (Mazur I), 767 F. Supp. 697, aff'd, 964 F.2d 1348 (3d Cir. 1992) (Mazur II).
277. *McKee v. Moore*, 648 P.2d 21 (Okla. 1982).
278. *Mitchell v. Iolab Corp.*, 700 F. Supp. 877 (E.D. La. 1988).
279. *Moore v. Kimberly-Clark*, 867 F.2d 243 (5th Cir. 1989).
280. *Morris v. Parke-Davis & Co.*, 667 F.Supp. 1332 (C.D. Cal. 1987).
281. *Natanson v. Kline*, 186 Kan. 393, opinion on denial of motion for rehearing, 187 Kan. 186 (1960).
282. *Oresman v. Searle & Co.*, 321 F. Supp. 449 (R.I. 1971).
283. *Pacific Mutual Life Insurance Company v. Haslip*, 499 U.S. 1 (1991).
284. *Parke-Davis & Co. v. Stromsodt*, 411 F.2d 1390 (8th Cir. 1969).
285. *Pease v. American Cyanamid Co.*, 795 F. Supp. 755 (D. Md. 1992).
286. *Petty v. United States*, 740 F.2d 1428 (8th Cir. 1984).
287. *Piper Aircraft Co., v. Reyno*, 454 U.S. 235 (1981), rev'g 630 F.2d 149 (3rd Cir. 1980) rev'g 479 F. Supp. 727 (M.D. Pa. 1979).
288. *Plummer v. Lederle Laboratories*, 819 F.2d 349 (2d Cir.) cert. denied, 484 U.S. 898 (1987).
289. *Pollard v. Ashby*, 793 S.W.2d 394 (Mo. Ct. App. 1990).
290. *Reyes v. Wyeth Laboratories*, 498 F.2d 1264 (5th Cir.), cert. denied, 419 U.S. 1096 (1974).
291. *Roberts v. Patel*, 620 F. Supp. 323 (N.D. Ill. 1985).
292. *Rohrburgh v. Wyeth Laboratories, Inc.*, 719 F. Supp. 470 (N.D.W. Va. 1989), aff'd, 916 F.2d 970 (4th Cir. 1990).
293. *Salgo v. Leland Stanford Jr. University*, 317 P.2d 170 (Cal. Ct. App. 1957).
294. *Samuels v. American Cyanamid Co.*, 130 Misc.2d 175, 495 N.Y.S.2d 1006 (1985).
295. *Sandel v. State*, 126 S.C.1, 119 S.E. 776, appeal dismissed, 269 U.S. 532 (1922).
296. *Savina v. Sterling Drug, Inc.*, 247 Kan. 105, 795 P.2d 915 (1990).
297. *Schackil v. Lederle Laboratories*, 116 N.J. 155, 561, A.2d 511 (1989).
298. *Schafer v. American Cyanimid Co.*, 1994 U.S. App. LEXIS 5477 (1st Cir. 1994).
299. *Schindler v. Lederle Laboratories*, 725 F.2d 1036 (6th Cir. 1984).
300. *Senn v. Merrill-Dow Pharmaceuticals, Inc.* 850 F.2d 611 (9th Cir. 1988).
301. *Shanks v. Upjohn Co.*, 835 P.2d 1189 (Alaska 1992).
302. *Sheffield v. Eli Lilly & Co.*, No. A013100, Cal. Ct. App. 1st Dist. 1983 .
303. *Singer v. Sterling Drug, Inc.*, 461 F.2d 288 (7th Cir. 1972).
304. *Slater v. Optical Radiation Corp.*, 961 F.2d 1330 (7th Cir.), cert. denied, 113 S.Ct. 327 (1992).
305. *Spencer v. United States*, 569 F. Supp. 325 (W.D. Mo. 1983).
306. *Stamps v. Collagen Corp.*, 1993 U.S.App. LEXIS 2745 (1st Cir. 1993), cert. denied, 114 S.Ct. 86 (1993).
307. *Stanback v. Parke, Davis & Co.*, 657 F.2d 642 (4th Cir. 1981).
308. *Sulesky v. United States*, 545 F. Supp. 426 (S.D. W. Va. 1982).
309. *Taggart v. Richards Medical Company, Inc.*, 677 F. Supp. 1102 (Col. 1988).
310. *Thomas v. Hoffman La-Roche, Inc.*, 949 F.2d 806 (5th Cir. 1992).
311. *Tinnerholm v. Parke-Davis & Co.*, 411 F.2d 48 (2d Cir. 1969).
312. *Toner v. Lederle Laboratories*, 112 Idaho 328, 732 P.2d 297 (1987).
313. *Tracey v. Merrell Dow Pharmaceuticals, Inc.* 569 N.E.2d 875 (Ohio 1991).

314. *Tremaine v. H.K. Mulford Co.*, 317 Pa. 97, 176 A.2d 212 (1935).
315. *Unthank v. United States*, 732 F.2d 1517 (10th Cir. 1984).
316. *Vincent v. Thompson*, 79 Misc.2d 1029, 361 N.Y.S.2d 282 (1974), rev'd in part, 50 App. Div. 211, 377 N.Y.S.2d 118 (1975).
317. *Walker v. Merck & Co.*, 648 F. Supp. 931 (M.D.Ga. 1986), aff'd without opinion, 831 F.2d 1069 (11th Cir. 1987).
318. *West v. G.D. Searle & Co.*, 305 Ark. 33, 806 S.W.2d 608 (1991).
319. *White v. Wyeth Laboratories*, 40 Ohio St. 3d 390, 533 N.E.2d 748 (1988).
320. *Whitlock v. Duke University*, 637 F. Supp. 1463 (M.D.N.C. 1986), aff'd, 829 F.2d 1340 (4th Cir. 1987).
321. *Williams v. Lederle*, 591 F. Supp. 381 (S.D. Ohio 1984).
322. *Wyeth Labs, Inc. v. Fortenberry*, 530 So.2d 688 (Miss. 1988).